### Editorial Board

#### Global Journal of Medical Research

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Cancer Preventive Therapies Should be Reason-Based
By Manfred Doepp

Abstract- One should act on the level of the causes and not the effects. Cancer does not come by coincidence, it does not come out of nowhere. There is usually a chain of prerequisites or conditions that can be divided into somatic, mental, and psychological. If you limit yourself to only fighting the tumor, you do not change the fact that the organism produced it for a reason. Therefore, it is worth going to the level of possible causes and trying to treat and eliminate them. Such causes are, for example, toxins of chemical nature, but also mental and psychological poisons such as repressed conflicts. The purification of the body-mind-soul unity is the best cancer prevention therapy.

GJMR-F Classification: NLM: QZ

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Cancer Preventive Therapies Should be Reason-Based

Manfred Doepp

Abstract: One should act on the level of the causes and not the effects. Cancer does not come by coincidence, it does not come out of nowhere. There is usually a chain of prerequisites or conditions that can be divided into somatic, mental, and psychological. If you limit yourself to only fighting the tumor, you do not change the fact that the organism produced it for a reason. Therefore, it is worth going to the level of possible causes and trying to treat and eliminate them. Such causes are, for example, toxins of chemical nature, but also mental and psychological poisons such as repressed conflicts. The purification of the body-mind-soul unity is the best cancer prevention therapy.

I. Introduction

We do not get cancer, we make it. Cancer is by no means like a usual disease, it is not something that comes by chance. It is something that the body starts to produce meaningfully. What integrative oncologists have figured out is: The way that you naturally fight cancer, is to find out why the body is making it in the first place. So to just treat it with chemotherapy and radiation is no real solution. Better is to help the body stop producing or develop cancer. It must be noted that chemotherapies kill the sensitive cells but not the resistant cell clones. These are selected out and subsequently multiply, without restraint. Therefore, fewer cancer patients die from the primary tumor, but preferentially from the metastases, which are nothing more than chemotherapy-resistant cell clones. Individualization of cancer therapy using liquid biopsy could solve this problem.

This includes the understanding that the organism does nothing without a reason. The body-mind-soul entity is wise. The organism primarily uses other minor diseases to solve its problems. Only when it sees no other possibility than to trigger a cancer, it performs it. The cancer represents, so to speak, a multi-tasking method to bring several problems to a single solution.

The organism accumulates a lot of stresses in the course of life, not only physical but also psychological and mental. Minor illnesses, especially inflammations, serve to relieve at least part of the burdens. The motto of the body is: “what leaves me, no longer burdens me”. Not only the excretions via the kidneys, the liver and the intestines serve this purpose, but also many other excretory pathways, e.g. via the skin (the third kidney), hair, nails, saliva, tears, mucus, etc. Hardly anyone realizes that hair loss is nothing more than a detoxification of toxins such as metals.

When the organism’s compensatory capacity for stress, hyperacidity and poisoning is exceeded, it looks for a radical way that promises to solve multiple problems. It can be first a cyst, then a benign lump, later a malignant tumor. This cancer involves accumulation of cellular and environmental toxins. If the body gets rid of it without additional poisoning, it is a success. Therefore, interfering methods that disturb the tumor such as biopsies, applying pressure, pressing, squeezing etc. are contraindicated. On the other hand, it makes sense to carefully and gently peel out the tumor as a whole surgically without affecting it in any way. Hence, the amount of poisons and toxins in the body is reduced by surgery. On the other hand, the body now lacks a “waste depot” that it had become accustomed to using. It may therefore be that the body needs another (“recurrence”) or a metastatic tumor and consequently produces it.

II. An American Approach

American-European natural healer Dr. Dana F. Flavin (5,6) has done extensive research into the causes of cancer. It is worthwhile to look into her findings. She founded THE FOUNDATION FOR COLLABORATIVE MEDICINE AND RESEARCH (COLLMED). She says: “Cancer is nothing more than trapped emotion, surrounded by toxins and contaminations.” She emphasizes: “I’m like an engineer, taking a destroyed building and learning every nook and cranny, every nut and bolt, with the intention to rebuild. This is the pharmacology, nutrition, and medicine. First, I clean the building and rid it of all the garbage so that the building can be properly repaired. This is the detoxification process, to clean up the fungi, parasites, viruses, bacteria, heavy metals and more that weigh our systems down.

Then I rebuild the walls with healthy nutrition and exercise to stabilize the building. This provides a structure upon which to further strengthen the inside and outside. I clean the windows so that one can see both inside and out. This is the pure water and fluids needed for the body to work optimally. But that’s still not enough. I open the windows and let in oxygen, releasing the
poisonous gases like stress and fear and shifting the pH to a healthy one.

What’s missing? The light! Light is the spirit of hope we send to our minds and bodies. It’s what displays the building in all of its glory. The building could be the soundest one in the world but without the suffusion of light, it remains in the dark. There’s an old expression: “Darkness cannot disperse the light, but light can disperse the darkness.” My intention is not to simply provide a recipe for wellness but uncover the spirit underneath. It’s that spirit, that light that’s more magnificent, more powerful than any medicine or nutritional program I could create. It’s the force of life itself. » Dr. Dana Flavin starts with this: « There are nine key toxins that gather in your liver, pancreas, and other organs that disrupt your DNA and signal your body to grow cancer.»

Thus, we can conclude that it should be a threefold detoxification to prevent and treat cancer: mental, psychological and somatic.(7,8)

III. Mentally

In the mental realm of thoughts and words, there is a complex that is particularly capable of generating stressful negative energies: it is valuing, devaluing, judging, condemning. Here it would make sense to apply the law of mirrors and correspondence: « What disturbs or annoys me in the other person, I have in myself. » If this is the case, one should reflexively stop putting oneself above the other one. In this way, one can prevent the emergence of a mental causation for a disease.

IV. Psychologically

The psychological causes include above all repressed conflicts, and within them the so-called territorial conflicts. What does that mean? Every human being has - similar to animals - a territory in which only he wants to exercise dominance. When other people invade the territory by influencing, manipulating or aggression, a conflict arises. It can be resolved by a clear: "No, this far and no further". If one does not manage to do this, one can work through the conflict by forgiving. If this does not happen either, the content of the conflict is shifted/repressed into the subconscious. It is then apparently gone, but continues to smolder until a later resolution, e.g. in the context of hypnosis. As long as it is not resolved, it can trigger an illness. Several or many conflicts of the same theme increase the subconscious pressure, and cancer may result. The conflict issues can also be found by means of myogeloses (nodular hardenings) in the muscles and/or geloses in the fasciae. If one squeezes such a knot, images of the conflict may rise up into consciousness and - if one is open to it - a solution can be facilitated.

V. Somatically

At the somatic level, a largely unknown cause is the presence of one (or more) foci in the area of the gums and/or jaw bones. These may be infectious or non-infectious, e.g., NICO-type oily maxillary osteitis. They also have the energy to cause cancer. Next step is to cleanse the cancer-causing toxins.

For the purpose of somatic detoxification there is a therapy with intracellular enzymes. They are produced in Italy by the company Citozeatec.(9) They are used to clean first the intestine, then the blood, then the mesenchyme and finally intracellularly.

On the subject of toxins, the CDC lists more than 200 substances that are dangerous but in our environment.(10) A large part of them we ingest all the time. In addition, there is the production of endotoxins, especially in the intestine. Most of them are free radicals that steal electrons from the body’s own molecules. Therefore, it is advisable to take antioxidants daily. In addition, one should strengthen the detoxifying abilities of the organism on a daily basis.

Many foods have the ability to prevent cancer and assist in its treatment. However, these do not include: gluten, cow’s milk, pasta, fast food, junk food, sugar, preservatives, grilled meat, flavor enhancers, GMO, etc. When one examines what the diet of a large part of the population looks like, one begins to doubt... The new way of preventing and treating cancer is simple: We don’t fight cancer, we don’t try to poison the tumors... We just tell the body to stop producing or growing it.

The rise in toxins, chemicals, heavy and light metals, and the rise in cancer rates show an exact match. One can do all the chemo, radiation, and radical surgery one wants. But they won’t stop the body from "making" cancer.(11,12)

VI. Conclusion

It is promising to go to the root cause level in the prevention and sometimes also the treatment of cancer. It is always problematic to treat only the effects, as recurrences and metastases can then occur. Chemotherapy always has a positive effect on the cancer cells, which are sensitive and responsive. However, there are always cell clones that are resistant. These are not captured and eliminated, but survive and are virtually selected, so that they continue to spread and form so-called metastases. This crux of cancer treatment can be addressed by prevention. It includes somatic, mental and psychological detoxification methods described above.
REFERENCES RÉFÉRENCES REFERENCIAS

5. https://drdanaflavin.com/
6. https://collmed.org/
9. www.citozeatecsrl.ch
11. Doepp, Manfred: Topic: Mouth, Teeth, and Dentition; Journal of Advances in Bioengineering and Biomedical Science Research (ISSN: 2640-4133), 5(3): 186- 187. doi.org/10.33140/ABBSR.05.03.04
12. Doepp, Manfred MD, Could Dentistry Be a Major Factor in Human Poisonings? IOSR Journal of Dental and Medical Sciences, (IOSR-JDMS), 21(03), 2022, pp. 48-49. ISSN: 2279-0853, DOI: 10.9790/0853-2103104849
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Management of COVID-19-Positive Bangladeshi Patients at Home: A Telephone-Based Pilot Study

By Muntasir Faisel, Nusrat Jabin, Maksudul Islam Mazumder, Nuhad Raisa Seoty, Sayeda Shabnam Malik & Abu Jamil Faisel

Abstract- The recent COVID-19 pandemic highlighted the challenges in healthcare settings due to the scarcity of medical resources like hospital beds and healthcare professionals to manage critical cases. During this critical period, healthcare professionals emphasized on saving life-threatening cases, including moderate to severe COVID-19 cases, as they might need either ventilators or treatment in intensive care units. As a result, the national and international health policymakers, including WHO, suggested managing the suspected or confirmed COVID-19 patients without symptoms or having mild symptoms at home to reduce the burden on hospitals and trained healthcare professionals. Hence, we aimed to conduct a telephone-based pilot study to examine the feasibility before conducting a large-scale study on home-care treatment and management of the confirmed or suspected COVID-19 Bangladeshi patients, either asymptomatic or mild-symptomatic, during the home quarantine period.

Keywords: COVID-19-positive, Bangladeshi patients, treatment and management, home-care.

GJMR-F Classification: LCC: RC150-RC260

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Management of COVID-19-Positive Bangladeshi Patients at Home: A Telephone-Based Pilot Study

Home Management of COVID-19-Positive Bangladeshi Patients

Muntasir Faisel a, Nusrat Jabin b, Maksudul Islam Mazumder c, Nuhad Raisa Seoty d, Sayeda Shabnam Malik e, & Abu Jamil Faisel f

Abstract: The recent COVID-19 pandemic highlighted the challenges in healthcare settings due to the scarcity of medical resources like hospital beds and healthcare professionals to manage critical cases. During this critical period, healthcare professionals emphasized on saving life-threatening cases, including moderate to severe COVID-19 cases, as they might need either ventilators or treatment in intensive care units. As a result, the national and international health policymakers, including WHO, suggested managing the suspected or confirmed COVID-19 patients without symptoms or having mild symptoms at home to reduce the burden on hospitals and trained healthcare professionals. Hence, we aimed to conduct a telephone-based pilot study to examine the feasibility before conducting a large-scale study on home-care treatment and management of the confirmed or suspected COVID-19 Bangladeshi patients, either asymptomatic or mild-symptomatic, during the home quarantine period. We conducted a cross-sectional telephone-based study combining a mixed-methods approach. We collected quantitative data using a structured questionnaire from 101 adult COVID-19 patients, both male and female, who received treatment at home after being diagnosed as COVID-19-positive and were residing in four administrative divisions (Dhaka, Barisal, Mymensingh, and Sylhet). In addition, we conducted semi-structured in-depth interviews with healthcare providers who provided consultancy to these patients. Besides, we composed two case studies. Most of the study respondents were young adults, male, married, Muslim, and residing in the peripheral divisions of Bangladesh. Half of the COVID-19-infected participants reported having signs and symptoms between 7-15 days; on average, they received their COVID-19 test results within seven days. Fever (70%) was the most frequent symptom, followed by generalized weakness (50%), cough (46%), sore throat (44%), and malaise & body ache (35%). Slightly more than half (52%) of the respondents made face-to-face consultations with doctors, and 38% consulted with doctors over the telephone. Respondents also consumed different kinds of supplementary foods and took multiple precautionary measures. Almost all respondents (92.4%) did not want to tell their neighbors, friends, and family members that they were infected and took medicines at home to avoid the social stigma. Qualitative findings provided by healthcare professionals also supported the quantitative findings of COVID-19 patients. This pilot study provides necessary information on home management of COVID-19-positive Bangladeshi patients. These preliminary study findings also provided information on the feasibility of conducting a large-scale study, which needs to be conducted before making suggestions to revise the National COVID-19 Case Management guideline.

Keywords: COVID-19-positive, Bangladeshi patients, treatment and management, home-care.

I. Introduction

For more than a century, human history tackled several significant infectious diseases outbreaks, including the first worldwide flu pandemic (1729-1730), the “Spanish flu” as the first pandemic of the 20th century, and the “H1N1 pandemic of 2009” in the 21st century [1]. A recent addition was the Coronavirus Disease 2019 (COVID-19) outbreak acknowledged by the World Health Organization (WHO) on March 11, 2020, as a global pandemic due to its worldwide distressing levels of spread and severity related to morbidity and mortality [2]. Globally, more than 645 million confirmed cases of COVID-19, including more than six million deaths, were reported on December 11, 2022 [3].

Before the initiation of the recent COVID-19 pandemic in Wuhan, China, in December 2019, caused by the novel coronavirus “Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2)”, two more highly contagious coronaviruses (CoVs) belonged to the Coronaviridae family emerged in the 21st century to lead an outbreak. One was the Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) which appeared first in southern Foshan, China, before spreading to more than 30 countries from 2002 to 2003. After ten years, the Middle East Respiratory Syndrome Coronavirus (MERS-CoV) emerged in Saudi Arabia and affected two dozen countries from 2012 to 2016 [4]. Though these three highly pathogenic and deadly human coronaviruses were more or less similar [5] and are primarily spread through the respiratory droplet route, and direct contact [6], SARS-CoV2 is much more...
transmissible and communicable. Hence, this latest coronavirus is responsible for a global outbreak and health disaster [7].

Even though the world faced the SARS-CoV and MERS-CoV outbreaks early, these experiences did not contribute much to improving the healthcare system, particularly the public health practice, to mitigate the devastating impact of COVID-19. Instead, this pandemic identifies the health inequalities and challenges the healthcare system of both developed and developing countries [8, 9]. The COVID-19 pandemic not only severely affected the access and healthcare service utilization of non-COVID-19 health issues like maternal health [10], mental health [11], and non-communicable diseases [12] due to having a fear of being contaminated with COVID-19 infection while receiving treatment in healthcare facility settings; it also affected the treatment and management of asymptomatic and mild COVID-19 patients in the healthcare settings due to shortage of medical resources like hospital beds and healthcare professionals to manage the critical cases [13]. Due to inaccessible and timely healthcare services and difficulty in accessing treatment, asymptomatic or mild symptomatic COVID-positive patients had to depend on home-based treatment.

During this critical period, more emphasis was given to saving life-threatening cases, including moderate to severe COVID-19 cases, through reshaping the healthcare facilities [14] as these infected patients might need either ventilators or treatment in intensive care units. Besides, to prevent the spread of this deadly viral infectious disease, one of the effective preventive strategies was lockdown which restricted human mobility as it slowed down the spread of this infectious disease mainly by direct contact [15]. Throughout the COVID-19 pandemic period, more than 140 countries around the globe enforced this movement restriction to slow down the rapid spread of coronavirus [16], which also affected healthcare-seeking behaviours. Studies conducted in developed countries like New Zealand and Germany found that lockdowns negatively affected healthcare-seeking behaviour; respondents delayed seeking healthcare, leading to fewer consultations and hospital admissions [17, 18].

As the lack of sufficient medical resources and movement restrictions destructively and undesirably affected healthcare utilization in a formal setting, it initiated the continuity of healthcare at home. To reduce the burden on hospitals and trained healthcare professionals, the WHO suggested managing suspected or confirmed COVID-19 patients without symptoms or who have mild symptoms at home [19]. The Directorate General of Health Services (DGHS) under the Ministry of Health & Family Welfare, Bangladesh, also developed the national guideline to manage the clinical cases of COVID-19 where they suggested treating and managing the asymptomatic and mild COVID-19 patients at home [20]. Until November 27, 2022, there were 2,036,527 confirmed COVID-19 cases, including 29,431 deaths in Bangladesh, one of the most affected countries. Half of the reported cases were from Dhaka, the capital city and 62% were from the Dhaka division [21].

Bangladesh has an inadequate and inequitable medical workforce (only five physicians and two nurses serve on average every 10,000 population) [22]; besides, low-quality medical equipment like masks and personal protective equipment was provided to the Bangladeshi health front liners to manage the pandemic situation in healthcare facility settings [23]. Subsequently, many medical professionals suffered from COVID-19-related morbidity and mortality. Bangladesh has one of the highest medical professional mortality rates globally [24]. This workforce crisis and suffering also limited the healthcare-seeking behaviour of Bangladeshi COVID-19-positive patients. As a result, it was found that 79% of patients preferred to stay at home to get treatment [23].

It becomes essential to investigate the home-care management of confirmed COVID-19 Bangladeshi patients, especially what kinds of treatment regimen they used to receive to recover while staying at home, whether they consulted with any qualified doctors or not, which kinds of medicine they received, either allopathic (science-based modern medicine) or alternative or supplementary medicine, whether they took any precautionary measures to prevent the spread of infection in addition to the treatment regimen. Hence, we aimed to conduct a telephone-based pilot study to examine the feasibility before conducting a large-scale study to contribute to the development of healthcare policy to strengthen the institutional and community support systems to provide the best home-care treatment and management to the confirmed COVID-19 Bangladeshi patients during the home quarantine period. It also targets to develop an effective protocol for home-based treatment for asymptomatic and mild-symptomatic COVID-19 patients, who can stay at home during their illness & home quarantine period. It can reduce the burden on hospitals where healthcare professionals can dedicate their services to save the lives of moderate to severe symptomatic, even very critical patients.

II. MATERIALS AND METHODS

Study design & study population: We conducted a cross-sectional telephone-based pilot study combining a mixed-methods approach between June 10, 2020, and August 30, 2020, during the lockdown period. Our trained data collectors, who were junior doctors, obtained informed verbal consent before the initiation of each interview; they also informed the study respondents about their right to withdraw or stop the
We conducted a mini-pilot study with 10 adult COVID-19-positive patients before we finalized the questionnaire. We also developed a semi-structured guideline to conduct the in-depth interview with healthcare professionals, which was submitted as a Supplementary document.

### Statistical analysis:
We performed the descriptive analysis and presented the study findings in frequency and percentage. We analysed the data using version 4.0.3 of the R program, an open-source software. Qualitative data were analysed under themes and sub-themes.

### III. Results

In this study, 101 respondents were interviewed; most of the respondents were young adults with mean and median ages of 32±10 years and 29 years [minimum 17 years to maximum 65 years], respectively. Slightly more than half (54%) were male, and almost two-thirds (71%) were married. Almost all respondents (93%) were Muslim, and more than half (63%) of the respondents completed their graduation. The majority (83%) of the respondents were residing in the peripheral divisions, considered semi-urban and rural residence places. Slightly more than one-third (37%) of the respondents were service holders working either in government or private sectors; 22% were healthcare professionals consisting of doctors, nurses, and health workers. Only 13% were housemakers, and 15% were students. More than half (58%) had a monthly income of 30K Bangladesh Taka (BDT) and above (286US$, at the rate of 105BDT/US$), though 7% did not want to share their income with researchers.

We also analysed the socio-demographic characteristics of study respondents by sex and place of residence. We did not find substantial variations between males and females regarding socio-demographic characteristics except for their occupations. There were more employed male participants (64%) than female participants (52%); the majority (38%) of them worked in the government sector, followed by the private sector (13%). Among the female respondents, almost one-third (28%) were homemakers. Besides, the most common profession of the employed female respondents was health professionals (33%), followed by government employees (15%).

Regarding the place of residence, we found variation between those who lived in rural areas and those who lived in urban areas; only 17% lived in urban areas. The detailed socio-demographic characteristics of the study respondents are presented in Table 1 under three categories: overall, by sex, and place of residence.
Table 1: Socio-demographic characteristics of study respondents

<table>
<thead>
<tr>
<th>Socio-demographic characteristics</th>
<th>Total (n=101)</th>
<th>Male (n=55)</th>
<th>Female (n=46)</th>
<th>Urban (n=17)</th>
<th>Rural (n=84)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number (%)</td>
<td>Number (%)</td>
<td>Number (%)</td>
<td>Number (%)</td>
<td>Number (%)</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (±SD)</td>
<td>32 (±10)</td>
<td>32 (±10)</td>
<td>31 (±11)</td>
<td>35 (±10)</td>
<td>31 (±10)</td>
</tr>
<tr>
<td>20 years and below</td>
<td>7 (7%)</td>
<td>2 (4%)</td>
<td>5 (11%)</td>
<td>0 (0%)</td>
<td>7 (8%)</td>
</tr>
<tr>
<td>21 to 40 years</td>
<td>78 (77%)</td>
<td>44 (80%)</td>
<td>34 (74%)</td>
<td>12 (71%)</td>
<td>66 (79%)</td>
</tr>
<tr>
<td>41 years and above</td>
<td>16 (16%)</td>
<td>9 (16%)</td>
<td>7 (15%)</td>
<td>5 (29%)</td>
<td>11 (13%)</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>55 (54%)</td>
<td>9 (53%)</td>
<td>46 (55%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>46 (46%)</td>
<td>8 (47%)</td>
<td>38 (45%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Marital status</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unmarried</td>
<td>25 (25%)</td>
<td>12 (22%)</td>
<td>13 (28%)</td>
<td>5 (29%)</td>
<td>20 (24%)</td>
</tr>
<tr>
<td>Married</td>
<td>72 (71%)</td>
<td>41 (75%)</td>
<td>31 (67%)</td>
<td>11 (65%)</td>
<td>61 (73%)</td>
</tr>
<tr>
<td>Widow/Widower/Divorce</td>
<td>3 (3.0%)</td>
<td>1 (2%)</td>
<td>2 (4%)</td>
<td>1 (6%)</td>
<td>3 (3.0%)</td>
</tr>
<tr>
<td>Missing</td>
<td>1 (1.0%)</td>
<td>1 (1.8%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>1 (1%)</td>
</tr>
<tr>
<td><strong>Religion</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Islam</td>
<td>94 (93%)</td>
<td>51 (93%)</td>
<td>43 (93%)</td>
<td>15 (88%)</td>
<td>79 (94%)</td>
</tr>
<tr>
<td>Hindu</td>
<td>5 (5%)</td>
<td>3 (5%)</td>
<td>2 (4%)</td>
<td>2 (12%)</td>
<td>3 (4%)</td>
</tr>
<tr>
<td>Catholic</td>
<td>2 (2%)</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>0 (0%)</td>
<td>2 (2%)</td>
</tr>
<tr>
<td><strong>Education</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SSC/O Level and below</td>
<td>15 (15%)</td>
<td>7 (13%)</td>
<td>8 (17%)</td>
<td>1 (6%)</td>
<td>14 (17%)</td>
</tr>
<tr>
<td>HSC/ A Level</td>
<td>21 (21%)</td>
<td>16 (29%)</td>
<td>5 (11%)</td>
<td>1 (6%)</td>
<td>20 (24%)</td>
</tr>
<tr>
<td>Graduate</td>
<td>51 (50%)</td>
<td>26 (47%)</td>
<td>25 (54%)</td>
<td>10 (59%)</td>
<td>41 (49%)</td>
</tr>
<tr>
<td>Post graduate</td>
<td>13 (13%)</td>
<td>5 (9%)</td>
<td>8 (17%)</td>
<td>5 (29%)</td>
<td>8 (10%)</td>
</tr>
<tr>
<td>Missing data</td>
<td>1 (1%)</td>
<td>1 (2%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>1 (1%)</td>
</tr>
<tr>
<td><strong>Place of residence</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urban/Central division</td>
<td>17 (17%)</td>
<td>9 (16%)</td>
<td>8 (17%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rural/Periphery division</td>
<td>84 (83%)</td>
<td>46 (84%)</td>
<td>38 (83%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Division of residence</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dhaka [urban, central division]</td>
<td>17 (17%)</td>
<td>9 (16%)</td>
<td>8 (17%)</td>
<td>17 (100%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Chattogram [rural, periphery division]</td>
<td>2 (2%)</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>0 (0%)</td>
<td>2 (2%)</td>
</tr>
<tr>
<td>Mymensingh [rural, periphery division]</td>
<td>11 (11%)</td>
<td>5 (9%)</td>
<td>6 (13%)</td>
<td>0 (0%)</td>
<td>11 (13%)</td>
</tr>
<tr>
<td>Rangpur [rural, periphery division]</td>
<td>65 (64%)</td>
<td>36 (65%)</td>
<td>29 (63%)</td>
<td>0 (0%)</td>
<td>65 (77%)</td>
</tr>
<tr>
<td>Sylhet [rural, periphery division]</td>
<td>6 (6%)</td>
<td>4 (7%)</td>
<td>2 (4%)</td>
<td>0 (0%)</td>
<td>6 (7%)</td>
</tr>
<tr>
<td><strong>Occupation</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Government service</td>
<td>28 (28%)</td>
<td>21 (38%)</td>
<td>7 (15%)</td>
<td>4 (24%)</td>
<td>24 (29%)</td>
</tr>
<tr>
<td>Private sector service</td>
<td>9 (9%)</td>
<td>7 (13%)</td>
<td>2 (4%)</td>
<td>0 (0%)</td>
<td>9 (11%)</td>
</tr>
<tr>
<td>Health professional</td>
<td>22 (22%)</td>
<td>7 (13%)</td>
<td>15 (33%)</td>
<td>7 (41%)</td>
<td>15 (18%)</td>
</tr>
<tr>
<td>Health professional (doctors, nurses, health workers)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Student</td>
<td>15 (15%)</td>
<td>8 (15%)</td>
<td>7 (15%)</td>
<td>1 (6%)</td>
<td>14 (17%)</td>
</tr>
<tr>
<td>Homemakers/housewives</td>
<td>13 (13%)</td>
<td>0 (0%)</td>
<td>13 (28%)</td>
<td>3 (18%)</td>
<td>10 (12%)</td>
</tr>
<tr>
<td>Others</td>
<td>14 (14%)</td>
<td>12 (22%)</td>
<td>2 (4%)</td>
<td>2 (12%)</td>
<td>12 (14%)</td>
</tr>
<tr>
<td><strong>Income</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than 30K BDT</td>
<td>36 (36%)</td>
<td>22 (40%)</td>
<td>14 (30%)</td>
<td>3 (18%)</td>
<td>33 (39%)</td>
</tr>
<tr>
<td>30K-60K BDT</td>
<td>39 (39%)</td>
<td>20 (36%)</td>
<td>19 (41%)</td>
<td>3 (18%)</td>
<td>36 (43%)</td>
</tr>
<tr>
<td>61K-100K BDT</td>
<td>9 (9%)</td>
<td>3 (5%)</td>
<td>6 (13%)</td>
<td>2 (12%)</td>
<td>7 (8%)</td>
</tr>
<tr>
<td>More than 100K BDT</td>
<td>10 (10%)</td>
<td>4 (7%)</td>
<td>6 (13%)</td>
<td>9 (53%)</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>Did not want to share</td>
<td>7 (7%)</td>
<td>6 (11%)</td>
<td>1 (2%)</td>
<td>0 (0%)</td>
<td>7 (8%)</td>
</tr>
</tbody>
</table>

In this study, half (50%) of the COVID-19-infected participants reported having signs and symptoms within 7-15 days; this finding is more or less the same between male and female respondents and among those who lived in urban and rural areas. Of the total participants, 44% had symptoms within seven days or less, i.e., they became asymptomatic within a week. We found that more females (48%) and those who lived in rural areas (46%) became asymptomatic within seven days or less. Only 7% had prolonged symptoms as they...
remained symptomatic for more than 15 days, mainly those who were male (9%) and lived in urban areas (18%) (Table 2).

On average, study respondents received their COVID-19 test results within seven days, except those residing in urban areas; they received their results within 4-5 days. The study also found a wide range of durations to receive the confirmed test results, ranging from one day to 19 days. Additionally, 8% of the respondents, mainly females (13%) residing in rural areas (8%), could not recall when they received the test results.

Table 2: Duration of signs and symptoms of COVID-19-positive persons and duration of COVID-19 test confirmation

<table>
<thead>
<tr>
<th>Duration of Symptoms (%)</th>
<th>Total (n=101)</th>
<th>Male (n=55)</th>
<th>Female (n=46)</th>
<th>Urban (n=17)</th>
<th>Rural (n=84)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;7 days</td>
<td>Number (%)</td>
<td>Number (%)</td>
<td>Number (%)</td>
<td>Number (%)</td>
<td>Number (%)</td>
</tr>
<tr>
<td>44 (44%)</td>
<td>22 (40%)</td>
<td>22 (48%)</td>
<td>5 (29%)</td>
<td>39 (46%)</td>
<td></td>
</tr>
<tr>
<td>7-15 days</td>
<td>50 (50%)</td>
<td>28 (51%)</td>
<td>22 (48%)</td>
<td>9 (53%)</td>
<td>41 (49%)</td>
</tr>
<tr>
<td>&gt;15 days</td>
<td>7 (7%)</td>
<td>5 (9%)</td>
<td>2 (4%)</td>
<td>3 (18%)</td>
<td>4 (5%)</td>
</tr>
<tr>
<td>Duration of COVID-19 Test confirmation</td>
<td>Mean (±SD), days</td>
<td>Median [Min, Max], days</td>
<td>Could not remember</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total (n=101)</td>
<td>Male (n=55)</td>
<td>Female (n=46)</td>
<td>Urban (n=17)</td>
<td>Rural (n=84)</td>
<td></td>
</tr>
<tr>
<td>Mean (±SD), days</td>
<td>7.1 (3.7)</td>
<td>7.0 (3.5)</td>
<td>7.1 (4.1)</td>
<td>4.7 (3.0)</td>
<td>7.6 (3.7)</td>
</tr>
<tr>
<td>Median [Min, Max], days</td>
<td>7.0 [1.0, 19]</td>
<td>6.0 [2.0, 16]</td>
<td>7.0 [1.0, 19]</td>
<td>4.5 [1.0, 13]</td>
<td>7.0 [2.0, 19]</td>
</tr>
<tr>
<td>Could not remember</td>
<td>8 (8%)</td>
<td>2 (4%)</td>
<td>6 (13%)</td>
<td>1 (6%)</td>
<td>7 (8%)</td>
</tr>
</tbody>
</table>

Fig. 1: Signs and symptoms of the respondents during COVID-19 infection

Fever was the most frequent symptom reported by respondents; less than two-thirds (70%) had a fever during their illnesses. The second most common symptom was generalized weakness (50%), followed by cough (46%), sore throat (44%), and malaise & body ache (35%). One-fourth of the respondents complained about anorexia, and less than one-fourth (23%) lost their taste. In our study, less than one-fourth (21%) had severe symptoms like breathlessness (14%) and chest tightness (7%), yet, they continued to stay at home even after knowing that their health conditions could be critical at any point in time due to these symptoms (Fig 1).

Though the respondents continued treatment at home, slightly more than half (52%) of the respondents made face-to-face consultations with doctors before starting the home-based treatment, and 38% consulted with doctors over the telephone. Only 6%, who were doctors, started taking the treatment by themselves. Most of the respondents (90%) depended on allopathy medicine (science-based modern medicine). On average, respondents took six medicines for the COVID-19 treatment. However, there was no variation between males and females, and was found that urban respondents took more medicines (seven medicines) than rural respondents. On average, respondents spent
22,000 BDT (USD 209, at the rate of 105BDT/US$) to buy medicines during their illnesses (Table 3); we found that male respondents spent more than female respondents, though there was no variation between urban and rural respondents.

**Table 3: COVID-19 treatment and its cost related information**

<table>
<thead>
<tr>
<th>Source of treatment information (%)</th>
<th>Total</th>
<th>Male</th>
<th>Female</th>
<th>Urban</th>
<th>Rural</th>
</tr>
</thead>
<tbody>
<tr>
<td>In-person consultation with Doctor</td>
<td>53 (52%)</td>
<td>30 (55%)</td>
<td>23 (50%)</td>
<td>5 (29%)</td>
<td>48 (57%)</td>
</tr>
<tr>
<td>Telephonic consultation with Doctor</td>
<td>38 (38%)</td>
<td>20 (36%)</td>
<td>18 (39%)</td>
<td>10 (59%)</td>
<td>28 (33%)</td>
</tr>
<tr>
<td>Self</td>
<td>6 (6%)</td>
<td>4 (7%)</td>
<td>2 (4%)</td>
<td>2 (12%)</td>
<td>4 (5%)</td>
</tr>
<tr>
<td>ShaysthoBatayon</td>
<td>1 (1%)</td>
<td>0 (0%)</td>
<td>1 (2%)</td>
<td>0 (0%)</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>Advice from Doctor at any social media</td>
<td>1 (1%)</td>
<td>1 (2%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>Missing</td>
<td>2 (2%)</td>
<td>0 (0%)</td>
<td>2 (4%)</td>
<td>0 (0%)</td>
<td>2 (2%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Types of treatment</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Allopathy</td>
<td>91 (90%)</td>
<td>46 (84%)</td>
<td>45 (98%)</td>
<td>16 (94%)</td>
<td>75 (89%)</td>
</tr>
<tr>
<td>Ayurveda</td>
<td>2 (2%)</td>
<td>2 (4%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>2 (2%)</td>
</tr>
<tr>
<td>Homeopathy</td>
<td>6 (6%)</td>
<td>5 (9%)</td>
<td>1 (2%)</td>
<td>1 (6%)</td>
<td>5 (6%)</td>
</tr>
<tr>
<td>Missing</td>
<td>2 (2%)</td>
<td>2 (4%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>2 (2%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Number of Medicine consumed</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>(Mean ±SD)</td>
<td>5.6 (2.2)</td>
<td>5.7 (2.4)</td>
<td>5.5 (2.1)</td>
<td>7.2 (2.6)</td>
<td>5.3 (2.0)</td>
</tr>
<tr>
<td>Median [Min, Max]</td>
<td>5.0 [1.0, 12]</td>
<td>5.0 [1.0, 12]</td>
<td>5.0 [1.0, 11]</td>
<td>6.0 [4.0, 12]</td>
<td>5.0 [1.0, 11]</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Treatment cost</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>(Mean ±SD) in Taka</td>
<td>22000 (30000)</td>
<td>26000 (38000)</td>
<td>16000 (13000)</td>
<td>21000 (16000)</td>
<td>22000 (32000)</td>
</tr>
</tbody>
</table>

Among allopathy medicine, paracetamol was the commonest; 80% of respondents took it. Most participants also reported taking vitamin C (77%) and Zinc (72%). More than half of the participants (65%) consumed the Azithromycin antibiotic, while a smaller proportion (only 17%) used Ivermectin.
Respondents also consumed different kinds of supplementary foods as recommended by local physicians, relatives, and friends; 92% took extra lemon to get rid of this disease, 89% consumed a high protein diet as they believed that it would be beneficial for them, and 83% had taken ginger to counteract the deadly disease. More than half of the respondents also added other supplement food items in their diets, such as spice tea (70%), fruits (62%), nigella seeds (55%), cardamom (54%), cloves (54%), cinnamon (52%), and lemon tea (51%). While comparing between males and females, we found that male respondents took slightly more additional supplements than female respondents. (Table 4).

Table 4: Frequency of different supplements taken by overall, male and female participants

<table>
<thead>
<tr>
<th></th>
<th>Overall</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=101</td>
<td>N=55</td>
<td>N=46</td>
</tr>
<tr>
<td>Lemon</td>
<td>93(92%)</td>
<td>48(48%)</td>
<td>45(46%)</td>
</tr>
<tr>
<td>High protein diet(Egg/Meat/Fish)</td>
<td>90(89%)</td>
<td>50(50%)</td>
<td>40(40%)</td>
</tr>
<tr>
<td>Ginger</td>
<td>84(83%)</td>
<td>46(46%)</td>
<td>38(38%)</td>
</tr>
<tr>
<td>Spice tea</td>
<td>71(70%)</td>
<td>39(39%)</td>
<td>32(32%)</td>
</tr>
<tr>
<td>Fruits</td>
<td>63(62%)</td>
<td>35(35%)</td>
<td>28(28%)</td>
</tr>
<tr>
<td>Nigella seeds</td>
<td>56(55%)</td>
<td>31(31%)</td>
<td>25(25%)</td>
</tr>
<tr>
<td>Cardamom</td>
<td>55(54%)</td>
<td>30(30%)</td>
<td>25(25%)</td>
</tr>
<tr>
<td>Clove</td>
<td>55(54%)</td>
<td>26(26%)</td>
<td>29(29%)</td>
</tr>
<tr>
<td>Cinnamons</td>
<td>53(52%)</td>
<td>27(27%)</td>
<td>26(26%)</td>
</tr>
<tr>
<td>Lemon tea</td>
<td>52(51%)</td>
<td>29(29%)</td>
<td>23(23%)</td>
</tr>
<tr>
<td>Honey</td>
<td>45(45%)</td>
<td>22(22%)</td>
<td>23(23%)</td>
</tr>
<tr>
<td>Bay leaves</td>
<td>34(34%)</td>
<td>14(14%)</td>
<td>20(20%)</td>
</tr>
<tr>
<td>Garlic</td>
<td>34(34%)</td>
<td>20(20%)</td>
<td>14(14%)</td>
</tr>
<tr>
<td>Black pepper</td>
<td>26(26%)</td>
<td>13(13%)</td>
<td>13(13%)</td>
</tr>
</tbody>
</table>
In addition to medicine and supplementary foods, respondents also provided information on multiple precautionary measures they practiced during their sickness period (Fig 3). Among them, hot water gurgling (84%), steam inhalation (79%), and drinking hot water (76%) were the three most frequently reported precautionary measures. Over half (66%) of the respondents stayed in a separate room and used a separate toilet during isolation. Respondents also engaged in different kinds of exercise as a precautionary measure; breathing exercise (35%) was the most common, as it is very effective in maintaining proper oxygen concentration at the tissue level. This precautionary measure was mainly practiced by female participants (46%) compared to male participants (25%).

<table>
<thead>
<tr>
<th></th>
<th>Total (%)</th>
<th>Male (%)</th>
<th>Female (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tulsi leaves</td>
<td>7(7%)</td>
<td>3(3%)</td>
<td>4(4%)</td>
</tr>
<tr>
<td>Mustard oil</td>
<td>5(5%)</td>
<td>3(3%)</td>
<td>2(2%)</td>
</tr>
<tr>
<td>Turmeric</td>
<td>3(3%)</td>
<td>0(0%)</td>
<td>3(3%)</td>
</tr>
<tr>
<td>Green tea</td>
<td>2(2%)</td>
<td>0(0%)</td>
<td>2(2%)</td>
</tr>
<tr>
<td>Others</td>
<td>18(18%)</td>
<td>9(9%)</td>
<td>9(9%)</td>
</tr>
</tbody>
</table>

Qualitative study findings on social issues, including stigma: Almost all respondents (92.4%) did not want to disclose to their neighbors, friends, and even family members that they were infected and taking medicines at home. All of their household members, who learned that the study respondents were infected, were scared that they might become infected at any time. To avoid spreading the infection and reduce fear and anxiety, the infected persons stayed inside their rooms and used a separate toilet during isolation. The respondents, who did not have the opportunity to stay in a separate room, used separate beds and tried not to go close to the other family members. During this time, respondents wore face-mask even if they were staying inside the room to curb the transmission of the virus.

In the case of 12 positive patients, Government officials hung a small red flag on the front wall of their houses. This government act raised local level fear, and the community people started making further negative comments about the infected persons. This situation was not at all appreciated by the COVID-19-patients and their relatives. Besides, by seeing the red flag in front of the house, the community people came to know about the infected person who did not go out during their illness periods. It also initiated rumours. One of the common negative comments made by the community was that the COVID-19 infection was the outcome of some sins made by the infected person. Community people were aware that this disease was highly contagious, and as such, they deliberately stay away...
from the sick person, which turned out to be a good practice, particularly in maintaining social distancing.

**Study findings of in-depth interview**

According to the study protocol, we interviewed three doctors in-depth. Two doctors were working in Government Hospitals and one in a private Medical College Hospital; they were assigned to manage the COVID-19 patients by their respective hospital authorities. They knew that many COVID-19 patients had to stay at home, where they recovered without facing any problems. Very few patients wanted to visit hospitals for admission and treatment during June-August 2020 as they were scared of exposure to COVID-19 infection. This situation was different in April – June 2020; at that time, many patients visited hospitals during the pandemic’s earlier phase as they were unaware of the highly contagious nature of COVID-19 infection.

During the in-depth interview, we collected data that covered the following three themes: a) signs, symptoms, and complaints of the COVID-19 patients who visited hospitals; b) what kind of medicines were taken by the COVID-19 patients before admission; c) co-morbidities of the COVID-19 patients who visited hospitals. The study findings of the in-depth interview are presented below:

a) **Signs, symptoms, and complaints of the COVID-19 patients who visited hospitals:** Most COVID-19 patients gave a history of fever a couple of days before visiting hospitals, and some visited with a fever. Most of them had a dry cough, irritation in the throat, and sore throat. Many were asymptomatic but visited hospitals as they had positive COVID-19 test results. Almost all of them had tension, anxiety, and fear that their health situation might turn serious quickly within a short time. Most of them complained of generalized weakness and a lethargic feeling. A small percentage complained of loss of taste and anosmia. Very few persons (5% to 10%) complained of tightness in the chest, shortness of breath, difficulty breathing, and a smaller percentage had hypoxia. Many COVID-19 patients presented their CT scan chest reports with findings of having pneumonia. Most patients visited of their own interest, while very few were referred by private practitioners or some smaller hospitals/clinics.

b) **Types of medicines taken by the COVID-19 patients before admission:** Almost all COVID-19 patients took Azithromycin, Doxycycline, and other broad-spectrum antibiotics, and in some cases, they took two antibiotics together. In the pandemic’s earlier phase, COVID-19 patients had taken Hydroxychloroquine; in the recent phase, COVID-19 patients have taken Ivermectin. Almost all patients had started taking an antihistamine in tablet form and cough syrup. Very few patients started Favimipramid, prednisolone, and blood thinner/low-dose heparin. Many patients, along with allopathic medicines, opted to use herbal medicines such as Tulsi, Nigel seeds, lemon, and honey. They regularly drank warm water and gargled with warm water several times during the day; this was the common practice among many patients.

c) **Co-morbidities of the COVID-19 patients who visited hospitals:** Diabetes was the most common co-morbidity among the COVID-19 patients who visited hospitals. Followed by the common co-morbidities were hypertension, heart disease, asthma, kidney disease, arthritis, and cancer of different organs. Very few patients (2% - 3%) became critically ill and had to be transferred to ICU.

**Case Study-1: Tension, anxiety, and fear almost killed Shafi (not the real name):**

Shafi works in a trading agency. One day, while returning home, he felt his head was heavy and feverish. Immediately, he thought about the dreaded virus, Corona, as it was spreading around. He decided to isolate himself from the other family members. He noticed the worry on his wife’s face; children were asking whether their father would be recovered, and his old father was worried about his son. Anxiety and fear started to mount gradually. After two days, he went to give his sample for the RT-PCR test. While waiting for the results, he developed weakness and body aches; simultaneously, he noticed a loss of taste for all his favourite foods. Waiting for the result was the most challenging time to pass. A few days later, he received his COVID-19 positive result. Then, he started to take the treatment; he took lots of tablets and a capsule after consulting a doctor over the phone. He also received suggestions and advice from friends and well-wishers but decided to stick to the doctor’s prescription.

He started drinking “masala” tea three times daily, which soon became tedious. He also maintained a physical distance from everyone and stayed isolated in his room. At the same time, he was taken a few preventive measures, such as washing his hands, gargling with hot water, and wearing a mask. He felt all these measured as a burden; he was not enjoying while continuing it. He started to have sleepless nights. The thought of providing how to support his family was constantly bothering him. Will there be a layoff? Will he be able to go back to his job? He continuously counted the days; meanwhile, only 14 days passed, which he felt as 14 months. Finally, his stressful period gradually came to an end. He started to feel better, and his symptoms started to go away. He thanked Allah for not developing any complications, which he had heard of so much from others. The actual relief came in his and his family’s life when he tested COVID-19 negative on the 20th day.
Case Study-2: Tender loving care and mental support are the winning points: Sheer simplicity and small happenings leave us spellbound and mesmerized. Such is the story of a young couple Parul and Ahmed (not their real names), living in a village about 2 kilometers away from the Upazilla Head Quarters with two children. Parul’s husband, a shopkeeper, tested positive for COVID-19. They could not find the source from where he became infected with the virus. He sent his two children with their grandfather and grandmother to their uncle’s house. His wife, Parul, did not want to leave her husband. Neighbors and community people warned that she would be infected too, but she stayed there with her husband and kept her vows. When we wanted to know the reasons, she replied with a smile, “where would I go, he’s my everything”. Soon her husband developed diarrhea and became very weak. Parul not only nursed her husband but also cooked food and did everything that she could do. By the Grace of Almighty Allah, Parul never became sick and tested COVID-19 negative when she did her test with her husband, who went to repeat his test on day 18, at the end of his illness period. Ahmed said this was all possible by the Almighty’s blessings on Parul, who was just an angel to him.

IV. Discussion

The COVID-19 pandemic provides an invaluable lesson to international and national health policymakers by highlighting the weakness of public healthcare and healthcare systems around the world in managing the different spectrum of COVID-19 patients, starting from asymptomatic suspected or confirmed to critical cases due to limited capacity, lack of medical forces and resources in the healthcare system in addition to the absence of effective antiviral therapeutics or vaccine [25]. During the early stage of the pandemic, when intense virus circulation was leading to high morbidity and mortality rates, many developed countries even faced difficulty in managing the high patient load in hospitals as patients were admitted with critical clinical features and often required ventilation support [26-29]. This sudden and unexpected increase in COVID-19 hospitalized patients played a critical role in enhancing anxiety, depression, burnout, and stress among healthcare professionals and affected the quality of care [30-35].

The COVID-19 pandemic not only burdens the healthcare system due to a lack of resources and shortage of healthcare professionals; it emphasizes the necessity for more extensive reinforcement of healthcare services. As it was not possible to increase the hospital bed capacity and the number of healthcare professionals with appropriate expertise and skill during the crisis period instantly to cope with the pandemic demand, international and national health policymakers gave emphasis on the management of asymptomatic or mild symptomatic COVID-19 patients at home, and accordingly they developed the clinical management guideline [36]. A similar situation was observed in Bangladesh, where 79% of the COVID-19 patients underwent home-based treatment according to the national clinical management guideline [23].

Our study found that fever was the most common symptom, followed by generalized weakness, cough, sore-throat, malaise & body ache, anorexia, and loss of taste. This study finding is supported by a systematic review investigating the clinical manifestations of 41,409 COVID-19-confirmed patients in 23 countries [37]. We also found that less than one-fourth (21%) of our study respondents could not visit COVID-19-designated hospitals to seek treatment even after developing severe symptoms like breathlessness and chest tightness due to a shortage of hospital beds. This kind of situation not only happened in low-resource countries like Bangladesh but also in Korea, where overcrowded patients and limited hospital resources forced the confirmed patients to stay at home [38].

COVID-19 is caused by a virus and there were antiviral medicines (Nirmatrelvir with Ritonavir (Paxlovid) and Remdesivir (Veklury) which can halt this virus to grow inside the body, and can diminish the risk of hospitalization and death [39, 40]. But in our study, we did not find any respondents who had taken these antiviral medicines; instead, they have taken antibiotics that are needed to manage bacterial infection, such as 66% had taken Azithromycin, followed by Ivermectin (17%), Doxycycline (10%) and Chloroquine (9%). Very few patients had taken other antibiotics such as Amoxicillin, Levofloxacin, and Amoxicillin plus Clavulanic acid. A similar situation has been noticed in the African region, where 10 countries used antibiotics unreasonably to treat a viral disease [41]. Though, a five-day course of Ivermectin, an antiparasitic drug, was found harmless and effective in treating mild COVID-19 patients in Bangladesh [42]. On average, respondents had to spend 22,000 BDT (USD 209, at the rate of 105BDT/US$) to buy medicines during their illnesses and faced financial burdens as the pharmacists took unjustifiable benefit of the situation to make a considerable turnover. A similar situation was found in Ghana, where COVID-19 patients had to pay high for home-based treatment [43].

Our study respondents also consumed different kinds of supplementary foods, including herbal products and home-based remedies to counteract the deadly viral disease. We also discussed this issue with Bangladeshi herbal medicine specialists; they recommended these supplementary foods, such as Nigella seeds. Different studies also found that these
supplementary products had an inhibitory effect on preventing human coronavirus [44-46]. Studies found that these home-based certain supplementary foods have protective effects, mainly to boost the immune system, against the COVID-19 infection [47-49].

In addition to food, our respondents also had taken multiple precautionary measures, which they practiced at home during their sickness period. Among them, hot water gurgling, steam inhalation, and drinking hot water were the three most frequently reported precautionary measures. Another Bangladeshi study also reported similar findings regarding these precautionary measures, though they did not find any impact of these measures on COVID-19 recovery phases [50]. There is insufficient evidence to support these precautionary measures to treat and prevent COVID-19 [51]; hence further studies are needed. Our study respondents also stayed in a separate room and used a separate toilet during isolation, and this measure is also suggested by the Centres for Disease Control and Prevention (CDC), the national public health agency of the United States [52]. Social distancing is also proven to be highly effective in alleviating the COVID-19 spread [53].

They also did breathe exercises, which effectively maintained proper oxygen concentration at the tissue level. Evidence supports our study finding that breathing exercises serve as pulmonary rehabilitation and aid in the recovery of COVID-19-positive patients.

We also found how our study respondents’ home-based treatment is affected by social stigma, and this is not uncommon in other low and middle-income countries, including India, Pakistan, Nepal, and Indonesia [56-59]. The government needs to develop culturally sensitive strategies to improve knowledge of the community and reduce the mental stress of COVID-19 patients.

Based on the study findings, we would like to propose a few suggestions. Though this is a pilot study, in the large-scale study, the authors would like to collect substantial information on the use of medicines to contribute to revising the National COVID-19 Case Management guideline. More emphasis should be given to identifying a few safe medicines which can be prescribed for home-based treatment. Patients had to purchase medicine at a high cost as the pharmacists took undue advantage of the situation and made a considerable profit. The government should emphasize this aspect and strengthen supervision and monitoring so that patients do not suffer.

Regarding dietary supplements, we found that respondents consumed lots of lemon and citrus fruits; in this case, they should only take a few of the vitamins, particularly Vit. C and certain food, such as Nigella seeds. We also recommend making the use of breathing or respiratory exercise mandatory. Besides, all COVID-19-positive patients should receive psychological and mental support through counselling over the telephone to overcome the social stigma.

V. Limitations

This study is not free from limitations. Although all four data collectors were doctors, they faced minor and major challenges as they collected data when the COVID-19 pandemic was at its highest transmission level. The major challenge was to collect the complete addresses and telephone numbers of COVID-19-positive cases as the authors used the snowball technique to collect this information. This difficulty may happen as interviewing anybody over the telephone when both ends people are not known to each other, it leads to a big challenge. Though the Public Health Expert Advisors provided support to collect the details of the patients, the study interviewers had to call the respondents 3–4 times to elicit information.

After putting in a substantial amount of effort, only 101 respondents joined the study. These respondents hesitated to give an interview over the telephone, even though the data collectors explained the background, purpose, and use of the information that would be collected for the study. We could not collect the information of the treating physicians as none of the respondents wanted to tell the name of the doctors who had given a prescription to the respondents. In the case of some female respondents, the male members of their families brought the medicines, and as such, they did not even know the name of their doctors. In addition, many respondents consulted more than one doctor, so they could not tell the name of a particular doctor. While collecting data, the data collectors felt that the respondents were taking more medicines than they mentioned, and it was not possible to collect the correct information. The data collectors faced challenges in collecting data from healthcare professionals during the in-depth interviews, as they did not have time to provide information while managing COVID-19 patients. As a result, we were only able to collect data from three doctors.

VI. Conclusion

To our knowledge, this is the first study conducted in Bangladesh. This pilot study was conducted when the COVID-19 pandemic just started, and most of the science of the infection was not known clearly to the scientists. Many people were dying, and the element of fear was increasing day by day. Despite all odds, the respondents stayed at home, which is evidence of their helpless situation. Almost all respondents did not want to tell their neighbors, friends, and family members that they were infected and took medicines at home to avoid the social stigma, which was supported by the qualitative findings of healthcare professionals.
This pilot study provides necessary information on home management of COVID-19-positive Bangladeshi patients, which includes taking many food supplements. These findings also provided information on the feasibility of conducting a large-scale study, which needs to be conducted before making suggestions to revise the National COVID-19 Case Management Guideline about taking proper medicines, effective supplementary foods, and precautionary measures to counteract the deadly viral disease and to reduce morbidity and mortality.

The World Health Organization recently announced that COVID-19 is no longer a global public health emergency. However, the risk remains as new variants may emerge, which may cause new surges in morbidity and mortality. Before facing any new pandemic, Bangladeshi health policymakers need to develop an effective protocol for home-based treatment for asymptomatic and mild-symptomatic COVID-19 patients, who can stay at home during their illness & home quarantine period, and this paper will significantly contribute to this purpose.

List of Abbreviation
BDT: Bangladesh Taka
BHW: Bangladesh Health Watch
CDC: Centres for Disease Control and Prevention
COVID-19: Coronavirus Disease 2019
DGHS: Directorate General of Health Services
MERS-CoV: Middle East Respiratory Syndrome Coronavirus
MOHFW: Ministry of Health and Family Welfare
SARS-CoV: Severe Acute Respiratory Syndrome Coronavirus
SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus-2
WHO: World Health Organization

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Competing/Conflicts of interest: The authors declare that they have no conflict of interest to announce. They did not receive any financial or non-financial benefits or will receive from any party directly or indirectly related to the subject of this article; hence, they have no relevant financial or non-financial interests to disclose.

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Data availability: All the data that were collected during this study are presented in the paper.

Authors’ Contributions: All authors contributed to the conceptualization of the study and research design. NJ was involved in the statistical analysis. MF & AJF completed the original draft writing. All authors reviewed and edited the writing for approving the final version of the manuscript.

References Références Referencias
52. TTEESSTT IY. Isolation and Precautions for People with COVID-19.


Indications for the use of Dobutamine in the Cardiology Ward and Emergency Room of a Public Hospital in the Federal District

By Lázara Camyla Lopes Cabral

Abstract- Dobutamine is an inotropic drug used in the treatment of decompensated heart failure and septic and cardiogenic shock. It is a sympathomimetic amine that stimulates beta-1 and beta-2 adrenoceptors, leading to the inotropic effect. Acting on stroke volume and cardiac output in a directly proportional manner, it slightly increases blood pressure and heart rate and reduces peripheral vascular resistance. The main clinical indication of Dobutamine occurs through the findings of tissue hypoperfusion on physical examination, presented by slow capillary refill, cold skin, thin pulse and/or tachycardia. To evaluate the main indications for the use of dobutamine in patients in a cardiology ward and emergency room of a public hospital in the Federal District. a retrospective study was carried out based on the analysis of 80 medical records of patients (using the TRAK CARE ® version 2015 system, SES/DF data system) admitted to the cardiology ward and emergency room (cardiology units) of the Regional Hospital of Taguatinga, between December 2020 and July 2021.

Keywords: dobutamine. heart failure. cardiology.

GJMR-F Classification: NLM: WG 210

Strictly as per the compliance and regulations of:
Indications for the use of Dobutamine in the Cardiology Ward and Emergency Room of a Public Hospital in the Federal District

Indicações Do uso De Dobutamina Na Enfermaria E Pronto-Socorro De Cardiologia De Um Hospital Público Do Distrito Federal

Lázara Camyla Lopes Cabral

Resumo - A dobutamina é um fármaco inotrópico utilizado no tratamento da insuficiência cardíaca descompensada e nos choques sépticos e cardiogênico. É uma amina simpaticomimética que estimula adrenoceptores beta-1 e beta-2, levando ao efeito inotrópico. Atuando no volume sistólico e no débito cardíaco e de maneira diretamente proporcional, eleva discretamente a pressão arterial e a frequência cardíaca e reduz a resistência vascular periférica. A principal indicação clínica da dobutamina ocorre através dos achados de hipoperfusão tecidual ao exame físico, apresentados pelo enchimento capilar lento, pele fria, pulso fino e/ou taquicardia. Este trabalho irá avaliar as principais indicações do uso de dobutamina em 80 pacientes internados na enfermaria e pronto-socorro de Cardiologia de um hospital público do Distrito Federal. Realizou-se por meio de um estudo retrospectivo observacional, analítico e transversal baseado na análise dos prontuários desses pacientes, entre dezembro de 2020 e julho de 2021. Avaliou-se o uso da dobutamina de acordo com sua prescrição, perfil clínico hemodinâmico, tempo de internação, intercorrências e desfechos clínicos dos pacientes, além das seguintes variáveis: idade, sexo, classificação de risco, agravo. Do total dos 80 pacientes, apenas 10% (8/80) usaram dobutamina. Destes, 60% dos pacientes que usaram o fármaco receberam alta hospitalar, 20% foram encaminhados à UTI e 20% foram a óbito. Ainda do total de indivíduos que usaram a medicação, apenas 20% otimizaram o tratamento pelo uso de saturação venosa central. Embora o fármaco tenha sido utilizado apenas em oito pacientes, pode-se inferir o benefício do uso da medicação, visto que, dentre aqueles que a usaram, a maioria evoluiu com alta hospitalar. Não obstante o tamanho da amostra, propõe-se que a dobutamina possa ser utilizada em quadros de insuficiência cardíaca congestiva perfil C, em choque cardiogênico associado ou não à choque séptico, principalmente se bem otimizada.

Palavras-chave: dobutamina. insuficiência cardíaca. cardiologia.

Abstract - Dobutamine is an inotropic drug used in the treatment of decompensated heart failure and septic and cardiogenic shock. It is a sympathomimetic amine that stimulates beta-1 and beta-2 adrenoceptors, leading to the inotropic effect. Acting on stroke volume and cardiac output in a directly proportional manner, it slightly increases blood pressure and heart rate and reduces peripheral vascular resistance. The main clinical indication of Dobutamine occurs through the findings of tissue hypoperfusion on physical examination, presented by slow capillary refill, cold skin, thin pulse and/or tachycardia. To evaluate the main indications for the use of dobutamine in patients in a cardiology ward and emergency room of a public hospital in the Federal District, a retrospective study was carried out based on the analysis of 80 medical records of patients (using the TRAK CARE ® version 2015 system, SES/DF data system) admitted to the cardiology ward and emergency room (cardiology units) of the Regional Hospital of Taguatinga, between December 2020 and July 2021. The use of dobutamine was evaluated according to its prescription, clinical hemodynamic profile, length of stay, complications and clinical outcomes of the patients, in addition to the following variables: age, sex, classification of risk, aggravation. Of the total 80 patients, only 10% (8/80) used dobutamine. Of these eight patients who used the drug, 60% were discharged from the hospital, 20% were referred to the ICU and 20% died. Of the total number of individuals who used the medication, only 20% optimized the treatment by using central venous saturation. Although the drug was used in only 8 patients, the benefit of using the medication can be inferred, since among those who used it, most evolved with hospital discharge. Despite the sample size, it is proposed that dobutamine can be used in cases of profile C congestive heart failure, in cardiogenic shock associated or not with septic shock, especially if well optimized.

Keywords: dobutamine. heart failure. cardiology.

1. INTRODUÇÃO

A dobutamina é um fármaco inotrópico utilizado no tratamento da insuficiência cardíaca descompensada e nos choques sépticos e cardiogênico. É uma amina simpaticomimética que estimula receptores beta-1 adrenérgico e, em doses mais altas, receptores alfa-1 e beta-2, levando ao seu efeito inotrópico e ao aumento da atividade cardíaca. Atua no volume sistólico, eleva o débito cardíaco, a
pressão arterial e a frequência cardíaca, além de reduzir a resistência vascular periférica (DUBIN; LATTANZIO; GATTI, 2017).

As principais indicações da dobutamina são choque cardiogênico, choque séptico e insuficiência cardíaca descompensada (GONÇALVES; SUZUKI, 1972).

O choque se caracteriza por uma síndrome hemodinâmica, na qual há baixa perfusão tissular, baixo débito cardíaco e resistência periférica aumentada (TUTTLE; MILLS, 1975). Na sepse, um foco primário infeccioso leva a uma disfunção orgânica e 20% dos casos podem se complicar e levar ao choque hemodinâmico (GONÇALVES; SUZUKI, 1972).

A fisiopatologia da sepse envolve diversos mecanismos a partir da exposição do organismo a algum patógeno ou suas toxinas, desencadeando uma resposta imune mediadas por citocinas, ativando neutrófilos, plaquetas e monócitos que geram a inflamação e danos aos tecidos do organismo. Essa resposta descontrolada leva o endotélio vascular reduzindo a perfusão devido a vasoconstrição, o que contribui para uma maior ativação das vias inflamatórias, tornando os mecanismos da sepse um ciclo vicioso (GONÇALVES; SUZUKI, 1972).

A dobutamina, associada à noradrenalina, é o inotrópico mais usado em pacientes com choque séptico em cardiopatias, pois aumenta o débito cardíaco e atua no transporte de oxigênio, melhorando a acidose e a hiperlactatemia (SALLES et al., 2006).


O choque cardiogênico é uma condição clínica de inadequada perfusão tecidual devido à disfunção cardíaca. A etiologia mais comum é o infarto agudo do miocárdio que provoca insuficiência ventricular esquerda (FEITOSA FILHO et al., 2013).

Os inotrópicos endovenosos (dobutamina, dopamina, milrinona e adrenalina) podem ser utilizados no choque cardiogênico para tratar colapso hemodinâmicos ou como ponte de sustentação de vida até a terapia definitiva (BRAUNWALD, 2006). São comumente usados no choque cardiogênico ao paciente com Insuficiência Cardíaca (IC), uma doença que se caracteriza pela incapacidade do coração em suprir as demandas do organismo. Sua principal etiologia se caracteriza por alterações estruturais e funcionais. Segundo ainda Braunwald (2006), a descompensação, seja por causa infecciosa ou congesta, é uma das principais causas de internação hospitalar.

A IC pode ser classificada em quatro estágios iniciais, a qual se associa a diferentes mecanismos etiológicos. Em busca de facilitar o manejo clínico dos pacientes com IC, foram criadas várias classificações, dentre elas a por perfis hemodinâmicos, que se faz por avaliação da volemia e da perfusão periférica (A – quente e seco, B – quente e úmido, C – frio e úmido e L – frio e seco). (BRAUNWALD, 2006).

Utiliza-se a dobutamina, principalmente no perfil C, nas doses de 2 – 20 mcg/kg/min, em infusão contínua, e deve ser reduzida por etapas. Pode ser associada a vasodilatadores, uso de diuréticos ou ser utilizada como primeira escolha para compensação clínica do paciente. A titulação da dose depende da avaliação clínica e, se associada a saturação venosa central, há maior segurança para que o tratamento seja eficaz. Indica-se a dobutamina quando a saturação venosa central estiver menor que 70% e hematocrito baixo (NASSAR JUNIOR, 2010).

O uso de dobutamina está associado a reações adversas como hipotensão, arritmias ventriculares ou atriais, estreitamento de vasos e aumento da mortalidade a longo prazo, em especial, em paciente com doença arterial coronariana, no qual a redução da pressão arterial reduz a perfusão da cânula, com possível isquemia e lesão do miocárdio (BRAUNWALD, 2006).

II. Objetivos

Avaliar as principais indicações do uso de dobutamina na enfermaria e pronto-socorro de Cardiologia de um hospital público do Distrito Federal (DF), identificando o perfil dos pacientes que necessitaram da prescrição de dobutamina, o tempo do uso de dobutamina e efeitos adversos associados, e analisar trabalhos recentes sobre indicações e benefícios da dobutamina.

III. Métodos

a) Tipo de estudo

Foi realizado um estudo observacional, analítico e transversal, através da coleta de dados registrados em prontuário.

b) Local e período

O presente trabalho avaliou homens e mulheres acima de 18 anos, com base em registros realizados no pronto-socorro e enfermaria da Unidade de Cardiologia do um Hospital Regional de Taguatinga (HRT), no DF, entre dezembro de 2020 e julho de 2021.
c) **Amostra**
   Fizeram parte da amostra total, prontuários de 80 pacientes, submetidos ou não ao uso de dobutamina, que estiveram internados na Cardiologia.
   
   i. **Critérios de inclusão**
   Pacientes acima de 18 anos que estavam na enfermaria ou pronto-socorro de Cardiologia.
   
   ii. **Critérios de exclusão**
   Indivíduos que não estavam internados na Cardiologia e os que tinham prontuários incompletos.
   
   d) **Coleta dos dados**
   Os dados foram reunidos no período entre dezembro de 2020 e julho de 2021, a partir de registros de prontuários dos pacientes internados na Unidade de Cardiologia do HRT. Foi investigado o uso da dobutamina nos pacientes de acordo com sua prescrição, analisando seu perfil, tempo de internação, intercorrências e desfechos clínicos e as seguintes variáveis: idade, sexo, classificação de risco, agravo, e tempo de permanência do uso de dobutamina durante internação na enfermaria ou pronto-socorro de Cardiologia. Foi avaliado se houve a otimização da dose usando saturação venosa central. Essa coleta foi realizada após a aprovação pelo Comitê de Ética em Pesquisa (CEP). Os dados foram coletados do sistema TRAK CARE ®versão 2015 (sistema de dados da SES/DF), após as internações e agrupados em uma única planilha formato Excel.
   
   e) **Abordagem e esclarecimentos**
   O projeto, sob número de registro 5.239.257, foi aprovado pelo CEP da Fundação de Ensino e Pesquisa em Ciências da Saúde (FEPECS) da Secretaria de Estado de Saúde (SES) do DF. A pesquisa ocorreu de acordo com as diretrizes éticas da Resolução CNS/MS nº 466/2012. Durante toda a pesquisa, os pacientes incluídos no projeto não foram identificados e os pesquisadores envolvidos não tiveram contato direto com quaisquer pacientes envolvidos para a realização da coleta das informações. Esses dados não foram, em absoluto, associados aos pacientes-fonte, mas organizados em modelos estatísticos, em forma de tabelas, planilhas, gráficos, portanto, foi dispensado o uso de Termo de Consentimento Livre e Esclarecido (TCLE).
   
   f) **Aspectos éticos e legais**
   O projeto foi submetido ao CEP da FEPECS/SES/DF para aprovação e a pesquisa conduzida de acordo com as diretrizes éticas estabelecidas pela Resolução CNS/MS nº 466/2012.
   
   g) **Riscos e Benefícios**
   Os riscos éticos são sigilo, confidencialidade e autonomia. A identificação dos participantes da pesquisa foi codificada pela equipe de pesquisa, preservando o sigilo e confidencialidade dos dados coletados, minimizando o risco ético de forma a se manter a privacidade e não provocar danos de exposição. Apenas os pesquisadores tiveram acesso aos documentos-fonte do participante da pesquisa. O prontuário médico foi consultado pelo pesquisador, sendo assegurado o compromisso profissional com o sigilo absoluto das informações. Como benefícios, espera-se avaliar a real efetividade do uso da dobutamina em uma enfermaria e pronto-socorro de Cardiologia.
   
   h) **Análise dos Dados**
   Para apresentação dos dados coletados e dos dados descritivos, foram avaliadas as médias, os desvios-padrão, as frequências e gráficos através do programa Microsoft Excel 2015 Office, onde foram consideradas as seguintes variáveis: idade, sexo, antecedente, indicação, classificação de risco, agravo, otimização e tempo de permanência do uso de dobutamina durante internação na enfermaria ou pronto-socorro de Cardiologia do HRT.
   
   IV. **Resultados**
   Os resultados estão apresentados conforme os objetivos deste estudo. Primeiramente, são descritos os dados da amostra (Gráfico 1), a qual representa a porcentagem de pacientes que usaram ou não a dobutamina. Fizeram parte da amostra total, prontuários de 80 pacientes com média de idade de 62,98 anos (38 a 96 anos), sendo a maioria do sexo masculino.
No Gráfico 2, observam-se as principais indicações do uso de dobutamina: a indicação por Insuficiência Cardíaca Perfil C corresponde a 50%; as demais indicações foram Choque Séptico (10%), Choque Séptico e Cardiogênico (10%), Insuficiência Cardíaca Perfil B (20%) e Insuficiência Cardíaca Perfil L (10%).

Gráfico 2: Principais indicações de uso da dobutamina no setor de Cardiologia
No Gráfico 3, foi analisado que, dos 80 pacientes, apenas 20% foram avaliados pela Saturação Venosa Central, otimizando a dose da dobutamina. Os outros 80% foram otimizados da dose por critérios clínicos.

Gráfico 3: Uso de saturação venosa central para otimização do tratamento da dobutamina

No Gráfico 4, foram analisados os desfechos clínicos de cada paciente, após o uso da dobutamina: 60% usaram dobutamina no setor de Cardiologia e foram de Alta Hospitalar com a Doença de Base controlada; dos outros 40%, 20% foram transferidos para Unidade de Terapia Intensiva e os outros 20% foram a óbito.

Gráfico 4: Desfechos clínicos de pacientes que usaram dobutamina no setor de Cardiologia

V. Discussão

A pesquisa englobou um total de 80 pacientes, no qual 10% (8 pacientes) usaram dobutamina e 90% (72 pacientes) não usaram a referida medicação durante a Internação Hospitalar no setor de Cardiologia do HRT, como demonstrado na primeira figura. O número de pacientes analisados foi abaixo do esperado, devido a má organização de prontuários médicos.

Em relação aos indivíduos expostos à dobutamina e à etiologia de base, foi possível calcular a prevalência, conforme apresentado nos resultados e na segunda figura. Foram os pacientes cardiopatas que
Indications for the use of Dobutamine in the Cardiology Ward and Emergency Room of a Public Hospital in the Federal District

As principales indicações da dobutamina, como observado nesta pesquisa, foram choque séptico, choque cardiogênico e insuficiência cardíaca descompensada. O estudo contou com um número pequeno de prontuários, inclusive abaixo do esperado pelos pesquisadores. O hospital é referência regional em cardiolgia e apresenta número considerável de pacientes com IC. Portém, observaram-se prontuários desorganizados, com falta de informações importantes, fatos que prejudicaram a pesquisa.

Concluí-se, por meio deste estudo de prevalência, que pacientes cardiopatas se beneficiam com o uso da dobutamina. Este inotrópico melhora a perfusão sistêmica, o débito cardíaco e, consequentemente, o débito urinário. Como avaliado na Figura 4, houve melhor desfecho para os pacientes que fizeram o uso da referida medicação.

Foi possível analisar que poucos pacientes usaram a dose recomendada de dobutamina, baseando-se o uso do inotrópico, apenas em parâmetros clínicos. Os estudos reiteram a importância do uso adequado da dose da medicação com base na avaliação da saturação venosa central para otimização clínica. Portanto, se realizado o tratamento indicado, apresentaria melhores resultados.

Espera-se que, com este estudo regional, possa ser possível elaborar estratégias para um uso mais adequado, pautado na literatura e na realidade da população adstrita.

VI. Conclusão

References Références Referencias

5. FEITOSA FILHO, Francisco Hedilberto et al. Evolução hospitalar de pacientes com choque cardiogênico por infarto agudo do miocárdio com

mais se beneficiaram do uso da medicação e, principalmente, o com ICC perfil C, devido ao aumento do débito cardíaco, da diminuição da pós-carga, assim aumentando a perfusão periférica e a sobrevida desses pacientes.

A II Diretriz Brasileira de Insuficiência Cardíaca reforça a importância do uso de dobutamina, quando bem indicada, principalmente em pacientes com Insuficiência Cardíaca com perfil de baixo débito e perfusão lentificada (MONTERA et al., 2009).

No choque séptico, o uso da dobutamina aumentou a sobrevida desses pacientes, devido a seu efeito no transporte de oxigênio, que desencadeia melhora da acidose e da hiperlactatemia, inclusive, abaixo da dose recomendada em literatura (DUBIN; LATTANZIO; GATTI, 2017). Este fato pode estar relacionado com o maior tempo para compensação clínica de internação. Foi observado neste estudo que os pacientes se beneficiaram do uso da dobutamina associada a noradrenalina, pois o efeito inotrópico da referida medicação analisada se estabelece somente com uma pressão arterial sistólica maior que 80 mmHg.

O choque cardiogênico se beneficia do uso da dobutamina pela diminuição da pré-carga, da resistência vascular periférica, elevando o débito cardíaco, a frequência cardíaca, o volume sistólico e a contratilidade cardíaca. Os inotrópicos endovenosos podem ser utilizados no choque cardiogênico para prevenir colapso hemodinâmicos como ponto de sustentação de vida até a terapia definitiva, que pode ser suporte circulatório mecânico, dispositivo de sustentação de vida até a terapia definitiva, que pode ser suporte circulatório mecânico, dispositivo de assistência ventricular ou transplante cardíaco (BRAUNWALD, 2006).

A Gasometria Venosa é um exame de fácil manejo, que utiliza a saturação venosa central para otimizar a dose da dobutamina e, dessa forma, melhorar os desfechos clínicos desses pacientes, usando a Saturação Venosa Central entre 70% e 80% (NASSAR JUNIOR, 2010). Observou-se na pesquisa a pressão arterial sistólica maior que 80 mmHg.

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Appropriate Management of Splenic Trauma


Abstract- Introduction: Inappropriate management of splenic trauma is related to high rates of morbidity and mortality, and an effective understanding of its mechanisms is vital. Closed abdominal or thoracoabdominal trauma, such as localized contusions from various incidents, is typically the cause of splenic injuries. Splenic trauma must be promptly evaluated in the context of urgency, and a surgical approach must be performed according to the degree of injury.

Methods: This is a retrospective, quantitative, and cross-sectional analysis of the medical records of operated-on patients.

Keywords: splenectomy; advanced trauma life support care; traffic trauma care.

GJMR-F Classification: NLM: WO 650
Appropriate Management of Splenic Trauma


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Methods: This is a retrospective, quantitative, and cross-sectional analysis of the medical records of operated-on patients.

Results: The medical records of 50 patients were analyzed, scored, and selected based on the following variables: mechanism of trauma, clinical signs of splenic injury, splenectomy as an emergency approach, degree of injury, postoperative period, complications, sequelae, and length of stay after surgery, as well as the need for intensive care unit admission and mortality. Data from 50 medical records of patients undergoing urgent splenectomy allowed researchers to draw the conclusion that 48% of patients had experienced splenic trauma as a result of auto accidents, and 38% of patients had Kehr's sign. Additionally, it was determined that grade III–V injuries were the most common in 70% of the cases submitted for urgent splenectomy after an anatomopathological investigation. Further, localized abscesses, the most common type of complications, were present in 50% of the patients. The average length of stay was 8 days, and 38% of the patients needed an intensive care unit. Finally, it was possible to conclude that 10% died. In terms of care, a profile has been established in which a direct and effective approach is required because, when compared with current literature, the number of patients with complications is very low when compared to patients approached conservatively, who present a degree of sequelae of 70% depending on the degree of injury.

Conclusion: As a result, the demand for more effective policies that aim to reduce morbidity and mortality is reinforced. This is critical given the high frequency of instances.

Keywords: splenectomy; advanced trauma life support care; traffic trauma care.

I. Introduction

High rates of morbidity and mortality are associated with inadequate therapy for splenic trauma, requiring an in-depth comprehension of its mechanisms. The most common cause of splenic injuries is confined abdominal or thoracoabdominal trauma, such as contusions resulting from a variety of accidents.

Splenic trauma must be promptly evaluated in the context of urgency, and a surgical approach must be performed according to the degree of injury. The comprehension of splenic trauma demands the comprehension of crucial aspects, such as the function and cause of the spleen's increased involvement, as well as the management necessary to prevent complications and sequelae.

In addition, there is a correlation between high rates of morbidity and mortality and the frequency of abdominal trauma, with the spleen being the most commonly damaged organ. The most common cause is trauma caused by accidents or being run over. A patient with a splenic injury must be evaluated and, if necessary, a surgical procedure performed. The surgical operation is urgent to prevent and permit a decrease in morbidity and death since the majority of patients underwent surgery after a parenchymal laceration measuring more than 3 cm confirmed the lesion.
II. METHODS

This is a retrospective, quantitative, and cross-sectional analysis of the medical records of the operating patients. The objective of this study is to examine the epidemiology and clinical condition of patients undergoing urgent splenectomy, as well as the most common complications associated with the procedure. The trial design and baseline patient information were not published since they were kept confidential. Before being approved for production, the study was conceived at the hospital and supervised by the regional Ethics and Research committee. There are no sponsors for the study. The authenticity of the trial as well as the quality and comprehensiveness of the data and analyses are all guaranteed by the authors.

III. RESULTS

During the time period analyzed, a preponderance of males was observed among patients assisted with urgent splenectomy. The "Trakcare" system, which is used in patient care services at secondary hospitals in the Federal District, was the foundation for the collection of secondary data used in this study.

The medical records of 50 patients were analyzed, scored, and selected according to the following variables: mechanism of trauma, clinical signs of spleen injury, splenectomy as an emergency approach, degree of injury, postoperative period, complications, sequelae, and length of stay after surgery, as well as the need for an intensive care unit and death.
Data from 50 medical records of patients undergoing urgent splenectomy allowed researchers to draw the conclusion that 48% of patients had experienced splenic trauma as a result of auto accidents, and 38% of patients had Kehr's sign in the positive range.

Additionally, it has been found that grade III to V injuries were the most common in 70% of the cases submitted requiring urgent splenectomy after an anatomopathological investigation.

Among the complications, 50% of the patients had localized abscesses, the most frequent form.

The average duration of stay was eight days, and 38% of patients required intensive care.

Lastly, 10% of the population passed away.

Concerning care, a profile was perceived in which a direct and effective approach is required, because the number of patients with complications is very low when compared to patients approached conservatively, presenting a degree of sequelae of 70% depending on the degree of injury, when compared to patients approached conservatively, presenting a degree of sequelae of 70% depending on the degree of injury.

IV. Conclusion

In order to prevent sequelae and improve these patients' chances of survival, it is inferred that there is a strong demand for appropriate surgical therapy. This highlights the need for more effective measures that aim to reduce morbidity and mortality, which is crucial given the high frequency of occurrences.

REFERENCES


3. RAMIRES, Bárbara Dulor et al. Conduita expectante (não cirúrgica) em pacientes pediátricos vítimas de trauma abdominal contuso com lesão de baço e/ou fígado/Observational.


6. KLEINSORGE, Gustavo Henrique Dumont. Impacto da introdução da angioembolização para o tratamento não operatório do trauma esplênico contuso grau III e IV no Hospital João XXIII, Belo Horizonte/Brasil.

7. BLANCO, Rafael Ribeiro. Frequência de esplenectomias em pacientes vítimas de traumas abdominais por acidentes automobilísticos no mundo. 2019.


9. KALWITZ, INTERNA EILEEN MAC-ADOO; FERNANDEZ, DR HUMBERTO FLISFISCH; SUR, DEPTO DE CIRURGIA. TRATAMENTO DO TRAUMA ESPLÊNICO, OPCIONES ACTUALES DE MANEJO.

Early Inflammatory Response Mediated by Angiotensin II in Cardiac Arteries of Normotensive Mice

By Thais Cristina de Souza Oliveira, Katia Aparecida da Silva Viegas, Rariane Silva de Lima, Nara Baptistela Rabechi, Camila de Jesus Piva, Tatiana C. Alba-Loureiro, Leando Ezequiel de Souza, Cintia Taniguti Lima, Luciene Cristina Gastalho Campos, Valerio Garrone Barauna, Rui Curi, Maria Claudia Irigoyen & Silvia Lacchini

Universidade de Sao Paulo

Abstract- To verify if a low dose of angiotensin II (Ang II) can induce an inflammatory response in cardiac arteries, even though blood pressure remains at normal values. Were used C57Bl/6J male mice treated with a low dose of Ang II (30ng/kg IP) and AT1R blockers. Blood pressure was recorded after 10, 30, 60min, 2 and 6hours after Saline or Ang II injection. Time curve (30 and 60min, 2, 6, 12, 24, and 48hours after treatment) for expression of inflammatory markers was evaluated in cardiac arteries (TGF-β, IL-1β, IL-6, TNF-α and ICAM-1) by immunohistochemistry and western blot. Serum TNF-α and IL-6 were analyzed by ELISA. Although Ang II did not alter blood pressure, local TGF-β and IL-6 presented an early increase in cardiac arteries.

Keywords: angiotensin II, AT1 receptor, AT2 receptor, inflammatory markers, cardiac arteries, normal blood pressure.

GJMR-F Classification: LCC Code: RC666.6
Early Inflammatory Response Mediated by Angiotensin II in Cardiac Arteries of Normotensive Mice

Vascular Inflammation Mediated by Angiotensin II

Thais Cristina de Souza Oliveira, Katia Aparecida da Silva Viegas, Rariane Silva de Lima, Nara Baptista Rabeche, Camila de Jesus Piva, Tatiana C. Alba-Loureiro, Leandro Ezequiel de Souza, Cintia Taniguti Lima, Luciene Cristina Gastalho Campos, Valerio Garrone Barauna, Rui Curi, Maria Claudia Irigoyen, Silvia Lacchini

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Keywords: angiotensin II, AT1 receptor, AT2 receptor, inflammatory markers, cardiac arteries, normal blood pressure.

1. Introduction

The Renin-angiotensin system (RAS) plays an important role in both physiological mechanisms of vascular control and pathological conditions. The activation of RAS after vascular injury or endothelial dysfunction has been related to vascular remodeling and atherosclerosis [Rakugi et al, 1993]. Studies have shown an association between the increased expression of Angiotensin I converting enzyme (ACE) and the formation of atherosclerotic plaques [Ohishi et al, 1997]. ACE is involved in major functions of the vasculature controlling the contractility, growth, and migration of vascular smooth muscle cells (VSMC), contributing to the development of hyperplasia in the tunica intima and hypertrophy in the tunica media [Dzau et al, 1995]. A previous study has demonstrated that an increase of ACE gene copies is closely related to the augment of ACE vascular activity and vascular injury in genetically modified mice [Lacchini et al, 2009]. Others have shown that the levels of ACE and Angiotensin II (Ang II) are increased in the atheromatous plaque of aortic atherosclerosis and restenosis after angioplasty or stent implantation. Moreover, AT1 receptor antagonism reduces endothelial dysfunction and intimal thickening in atherosclerotic vessels [Ohishi et al, 1997; Ribichini et al, 2000]. It is well described that Ang II is produced in the vasculature and its production is capable of generating intimal hyperplasia independently of hemodynamic or neurohumoral effects [Dzau et al., 1995; Li et al., 2016, Naftilan, 1994; Ross, 1999]. Considering that Ang II is associated with the proliferation and migration of VSMCs, collagen deposition, inflammation, and oxidative stress, this peptide can be described as one of the main mediators of vascular adaptation and remodeling [Schiffrin & Touyz, 2004; Paradis & Schiffrin, 2009].

Indeed, several studies have linked the action of Ang II-AT1 receptors to the development of vascular diseases, whereas Ang II-AT2 receptors have been shown opposing effects [Navar et al., 2000]. Also, it has been demonstrated that hypertensive patients exhibit increased serum adhesion molecules and inflammatory cells, which may be directly associated with the inflammatory actions of Ang II [Ruiz-Ortega et al., 2001]. Besides being a hormone that plays a central role in cardiovascular homeostasis by regulating...
vasoconstriction and blood pressure, Ang II is considered a multifunctional cytokine with non-hemodynamic properties, modulating other cytokines as well as coagulation and growth factors [Taubman, 2003; Wolff et al., 2003]. Recently, it was shown that a low dose of Ang II (which does not alter the blood pressure) induces the expression of inflammatory markers and migration of CD45 positive cells into the aorta of normotensive mice [de Lima et al., 2019]. Thus, the precise role and the direct activity of inflammatory cytokines in vascular diseases are still unknown.

As shown in the literature, Ang II is strongly associated with hypertension in clinical and experimental studies. However, such an association may represent a confusing factor if considering that hypertension per se is capable of inducing inflammatory mechanisms [Harwani, 2018; Jafri & Ormiston, 2017]. Therefore, the possibility of evaluating Ang II-directly mediated signaling from blood pressure is important to understand each moment in the remodeling process and to analyze the transition from the healthy to a pathological condition.

The correlation between the inflammatory process and the physiological action of Ang II, as well as molecular mechanisms involved, and how they modify the cell behavior highlights the importance of this study, which could contribute to a better understanding of how Ang II may be involved in inflammatory processes of cardiovascular diseases or during vascular remodeling, even in normotensive condition.

This study hypothesizes that a non-hypertensive dose of Ang II, acting on AT1 and AT2 receptors, can trigger an early inflammatory process in small arteries, such as cardiac arteries. This process may participate in the mechanisms involved in the vascular injury or even increase any already existing damage. To test this hypothesis, the aims of this study were (1) to evaluate the expression of inflammatory markers of cardiac arteries in response to Ang II and (2) to determine by which receptor (AT1 or AT2) Ang II leads to the expression of these inflammatory markers, independently of blood pressure changes.

II. Material and Methods

a) Animals

The present study used adult male C57BL/6 mice provided from the animal care unit of the Department of Anatomy of the Institute of Biomedical Sciences at the University of Sao Paulo. The mice were kept in a temperature-controlled room (22°C) with a 12-h dark-light cycle and received standard laboratory chow and water ad libitum. This study was performed following the Guidelines for Ethical Care of Experimental Animals from the International Animal Care and Use Committee. Also, it was approved and conducted according to the ethical principles established by the Ethics Committee on the Use of Animals by the Department of Anatomy of the Institute of Biomedical Sciences at the University of Sao Paulo.

To meet the study goals, three experiments were proposed: 1) to confirm that Ang II dose does not induce BP changes, 2) to evaluate a time-frame for the inflammatory response to Ang II, and 3) to study the participation of Ang II receptors in this inflammatory response.

b) Confirmation of non-hypertensive dose of Ang II

Treatment with angiotensin II (Sigma®) (30ng/kg, Ang II group) and saline solution (NaCl 0.9%, control group) was performed by intraperitoneal injection with a volume of 300µL for both groups [de Lima et al., 2019]. Saline solution (NaCl 0.9%) was used as a vehicle for Ang II injection. Direct blood pressure (BP) and heart rate (HR) were evaluated in different experimental times after Ang II or saline injections. For carotid catheter implantation (PE-10, with an internal diameter of 0.1mm, connected to a PE-50 catheter, with an internal diameter of 0.5mm), the animals were anesthetized with isoflurane. The thinner catheter (PE-10) was introduced in the carotid artery; the thicker catheter (PE-50) was passed subcutaneously, being externalized on the back, in the cervical region. The catheters were fixed with cotton thread. Following the surgery, the animals were monitored until full recovery, and received analgesic (tramadol 40 mg/kg, every 12 hours for 2 days) and antibiotic (Benzathine Penicillin, 50 U/kg, single dose) by intramuscular injections. Forty-eight hours after complete recovery, the carotid catheter was connected to a transducer (Kent Instruments, USA) and preamplifier (Hewlet-Packard 8805C, Puerto Rico, USA). Pulse pressure was recorded on a computer by using an acquisition system (Windak 4KHz, DATAQ Instruments, Akron, OH, USA), allowing beat-to-beat analysis with 8 kHz of sampling rate per channel. Were obtained values of diastolic BP (DBP), systolic BP (SBP), mean BP (MBP), and HR for each animal.

After connecting the carotid catheter to the monitoring system, the animals were allowed to adapt to the new environmental conditions (at least 20 minutes, observing when the animals were visually calm). Basal BP and HR were measured for 20 minutes (before the injections, time 0), and after injection of saline solution (n=5) or Ang II (n=5) at the following times: 10 minutes, 30 minutes, 60 minutes, 2 hours and 6 hours.

c) Time-frame for the inflammatory response to Ang II

To avoid inflammatory response inherent to surgical procedures, this experiment evaluated mice submitted only to Saline or Ang II injections (non submitted to surgeries). Heart and blood samples were collected 30 and 60 minutes and 2, 6, 12, 24, and 48 hours after Ang II injection. The control groups were evaluated after 30 minutes and 48 hours. Were analyzed 5 mice for each treatment and experimental time for
histological (immunohistochemistry) and biochemical (western blotting and ELISA) analysis. Ex vivo analysis involved the study of local inflammatory markers by immunohistochemistry and western blotting in cardiac arteries and systemic inflammatory markers in serum by ELISA.

d) Evaluation of AT1 and AT2 receptors in the inflammatory response to angiotensin II

Based on the inflammatory response to Ang II experiment, the times of 30 minutes and 12 hours were identified as moments of expression of local inflammatory markers; such times were used to study the effect of Ang II receptor blockers. To study the participation of AT1 or AT2 receptors, six groups (n=5 for each group and time) were formed as follows: 1- control (saline solution), 2- Ang II, 3- Losartan (AT1R blocker), 4- Los+Ang II, 5- PD123319 (AT2R blocker, ToCris®) and 6- PD+Ang II.

Ang II receptor blockers were given 30 minutes before Ang II or saline injections to allow receptor blockade before Ang II treatment. All treatments were also administered by intraperitoneal injection. The AT1 receptor blockade was done by using losartan (20mg/kg) and the AT2 receptor blockade was done by using PD123319 (15mg/kg), even in doses that do not alter blood pressure [Chen et al., 2005]. For this evaluation, Ang II was also administered at a dose of 30ng/kg.

At the end of experimental times, the hearts were used for the analysis of local inflammatory markers by immunohistochemistry.

e) Tissue collection and histological preparation for immunohistochemistry

At the end of each experimental time, the animals were euthanized by using an intraperitoneal overdose of ketamine (180mg/kg) supplemented with xylazine (20mg/kg). The vascular system was subsequently perfused with saline solution (0.9% NaCl) at constant pressure (80–90 mmHg) through the left ventricle followed by a buffered 4% formalin solution.

Hearts were collected and maintained in 4% buffered formalin for 24 to 48 hours allowing the complete fixation. After this period, the tissues were processed and embedded in paraplast for histological evaluation. Immunohistochemistry (IHC) was performed in four-micrometer tissue section to assess local inflammatory markers: interleukin IL-1β (abcam®9722) and IL-6 (abcam®6672), tumor necrosis factor-alpha TNF-α (abcam®6671), transforming growth factor-beta TGF-β (abcam®64715) and intercellular adhesion molecule 1-ICAM1 (abcam®25375). Briefly, ABC (streptavidin-biotin-peroxidase) method was performed using antigen retrieval by citrate buffer pH 6.0 for TGF-β, TNF-α, and ICAM-1. Slices were deparaffinized and rehydrated, following the blockade of endogenous peroxidase activity with 3% H2O2 solution for 30 minutes. After that, tissues were rinsed with phosphate-buffered saline (PBS). The primary antibodies were diluted in blocking solution (Bovine Serum Albumin 3% in PBS) and incubated in the sections for 16 hours at 4°C. The slides were washed and the biotinylated secondary antibody (Zymed Laboratories, South San Francisco, CA) was incubated for one hour at room temperature. Subsequently, the streptavidin-peroxidase complex (1: 500) was incubated for 60 minutes at room temperature. Then, 3,3'-diaminobenzidine solution (DAB, Vector Labs.) was used as a chromogen. The counterstaining was performed with hematoxylin and the slides were mounted. The negative control reactions were obtained by omitting the primary antibody in one tissue section on each slide assessed. The analyses were done blinded to the identity of experimental groups. The evaluation of immunohistochemistry was performed as previously described [Lacchini et al., 2009; Lima et al., 2015].

Briefly, the semiquantitative analysis used a score of 0 to 4, where 0 represents no staining, 1=weak staining, 2= weak to moderate staining, 3= moderate staining, and 4=intense staining. Three to five sections per heart were evaluated, examining at least five cardiac arteries per animal (each heart was represented by the mean from all analyzed arteries).

f) Tissue and blood collection to study inflammatory markers by Western Blot and ELISA

At the end of experimental times, mice were euthanized as described previously. All time-frame groups (n=5 for treatment and time) were assessed to determine whether Ang II was able to change cardiac protein expression (western blot) and if it was also capable of inducing systemic effects on inflammatory markers (ELISA). For these evaluations, blood samples were collected directly from the chest cavity after the right atrium had been cut. Following, the heart was collected and immediately frozen in liquid nitrogen for further western blot analysis.

g) Protein quantification in the heart

Western blot analysis was performed by lysing hearts in RIPA buffer (1mMEDTA, 1mMEGTA, 2mM MgCl2, 5mM KCl, 25mM Hepes, pH 7.5, 2mM DTT, 1mM PMSF, 0.1% Triton X-100, and 1:100 cocktail of protease inhibitors) and stirring for 30 minutes at 4°C. Homogenates were centrifuged (10000 ×g for 10min, 4°C), and the supernatant collected. Tissue lysate (50µg) was heated up in a sample buffer (200mM Tris-HCl, pH 6.8, 40% glycerol, 8% sodium dodecyl sulphate, 0.1% DDT, and 0.4% bromophenol blue) at 100°C for 5 minutes. The samples were run in a sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE), transferred to a nitrocellulose membrane Hybond-C Extra (GE Healthcare) in transfer medium (0.025MTris, 0.192Mglycine, 0.1% SDS, and 20% methanol). Membranes were washed (3 times in 1X TBS-T, 5 minutes), blocked (5% BSA, 3 hours), washed in TBS-T and 3,3' -diaminobenzidine solution (DAB, Vector Labs.) was used as a chromogen. The counterstaining was performed with hematoxylin and the slides were mounted. The negative control reactions were obtained by omitting the primary antibody in one tissue section on each slide assessed. The analyses were done blinded to the identity of experimental groups. The evaluation of immunohistochemistry was performed as previously described [Lacchini et al., 2009; Lima et al., 2015]. Briefly, the semiquantitative analysis used a score of 0 to 4, where 0 represents no staining, 1=weak staining, 2= weak to moderate staining, 3= moderate staining, and 4=intense staining. Three to five sections per heart were evaluated, examining at least five cardiac arteries per animal (each heart was represented by the mean from all analyzed arteries).
(3 times), and incubated overnight with antibody anti-TGF-β (1:500, sc-146, Santa Cruz Biotechnology) or anti-IL-6 (1:500, ab6672, Abcam). Membranes were exposed in ECL WB Detection Reagents (GE Healthcare) and revealed in Image Quant LAS 4000 mini (GE Healthcare) equipment. Protein bands were quantified by optical densitometry using ImageJ software (version 1.32), NIH. GAPDH expression (1:1000, Santa Cruz) was used to normalize the results.

h) Protein quantification in the serum

Systemic evaluation of inflammatory markers (IL-6 and TNFα) was made by enzyme-linked immunosorbent assay (ELISA) in serum. ELISA evaluation used Mouse TNF-alpha/TNFSF1A DuoSet and Mouse IL-6 DuoSet according to the manufacturer’s specifications. Results were obtained by using the ELISA reader Spectramax PLUS v3 ROM with a wavelength of 450nm. The reader is coupled to a microcomputer and data were analyzed by software SoftMax Pro 5.2 for the calculations.

i) Statistical Analysis

Values are expressed as mean±standard deviation. The hemodynamic and western blot data were statistically evaluated by one-way variance analysis (ANOVA) complemented using Bonferroni’s test. As immunohistochemistry evaluation for time curve and AT1R blockers was made by using score analysis, the results were treated by the Kruskal-Wallis test complemented by the test of Dunns. For all analyses, the significance level of p≤0.05 was adopted.

III. RESULTS

a) Confirming of a non-hypertensive dose of Ang II

Direct blood pressure assessment was performed to confirm the absence of hypertensive effect mediated by injected dose of Ang II. Thus, variations in inflammatory markers would not be related to blood pressure changes, but rather to a direct effect of Ang II. Table 1 shows diastolic blood pressure (DBP), systolic blood pressure (SBP), mean blood pressure (MBP) and heart rate (HR). As it is demonstrated, the treatments did not affect blood pressure or heart rate even after 10 or 30 minutes until 6 hours after injection, corroborating with previous studies [Lacchini et al., 2009; Lima et al., 2019].

b) Time-frame of the inflammatory response to Ang II

i. Analysis of local inflammatory markers

The local inflammatory markers evaluated were: TGF-β, TNF-α, IL-1β, IL-6 and ICAM-1. This analysis in sequential times after treatment allowed us to have a temporal idea of the phenomenon and to understand how the artery responds to the stimulus. Briefly, it was possible to identify two types of inflammatory response: one earlier (30-120 minutes) and one later (6 to 48 hours).

Figure 1 shows the analysis by score obtained in inflammatory markers with an earlier response. It is possible to observe a fast response of the cardiac arteries, showing an increase in TGF-β staining from 30 to 120 minutes after the injection with Ang II (Figure 1A). After 120 minutes, the positive staining resembles that seen in the Saline groups. A similar response was observed when evaluating the positive label for IL-6 (Figure 1B), showing an increase in this protein from 20 to 60 minutes. Both TGF-β and IL-6 showed early increases, which can be attributed to a direct action of Ang II.

On the other hand, IL-1β and ICAM-1 show later increase. IL-1β increased in cardiac arteries from 2 to 24 hours after the injection of Ang II (Figure 2A), ICAM-1 was more produced only 6 to 12 hours after the stimulus (Figure 2B). TNF-α did not show any significant changes at all studied times (Figure 2C).

ii. Analysis of cardiac inflammatory markers

As the inflammatory markers that showed an early change in the cardiac arteries were TGF-β and IL-6, it was considered important to verify whether this response would be only vascular or would involve the entire cardiac tissue. Therefore, the protein expression of such markers was measured by Western blot. Interestingly, an early cardiac response to Ang II was found for both markers. Figure 3 shows the percentual (Ea/Gapdh ratio) increase in protein expression of TGF-β after 120 minutes and IL-6 after 60 minutes. This result suggests that the inflammatory response mediated by a small dose of Ang II may induce a fast tissue response, including vessels and the entire tissue.

iii. Evaluation of systemic inflammatory markers by ELISA

Systemic inflammatory markers were quantified in serum by ELISA. Table 2 shows the time curve obtained for TNF-α and IL-6. Although it was possible to observe an increase in the serum concentration of TNF-α, this was not statistically significant, corroborating the local inflammatory analysis. The concentration of IL-6, on the other hand, increased significantly 60 minutes after the injection of Ang II, coinciding with the results observed in cardiac arteries and heart, as previously described.

c) Role of AT1 and AT2 receptors in the local inflammatory response to angiotensin II

The analysis of the possible role of Ang II receptors on the local expression of inflammatory markers was based on the time curve, where we verified that TGF-β and IL-6 present early changes (the time of 30 minutes after Ang II injection was chosen), while IL-1β and ICAM-1 show later changes (the time of 12 hours after injection was chosen).

The early analysis (30 minutes) after treatment reinforced the previous result that Ang II increases TGF-β and IL-6 expression in cardiac arteries. As can be
seen in Figure 4, Losartan was able to inhibit the increase of TGF-β (Figure 4A) and IL-6 (Figure 4B), suggesting that AT1 receptor is mediating such an increase of both cytokines. On the other hand, the concomitant treatment of Ang II with the AT2R blocker PD123.319 shows the same inhibition of the TGF-β expression in cardiac arteries, indicating a possible role of both AT receptors in this response.

The late evaluation supports the previous results, showing that Ang II increases IL-1β and ICAM-1 immunostaining in cardiac vessels (Figure 5). On the other hand, we observed inhibition in the expression of these cytokines in the losartan-combined treatment suggesting that Ang II effect is also related to the AT1 receptor. PD123.319 was not efficient in reducing IL-1β, which indicates that the AT2 receptor possibly does not participate in the modulation of this cytokine performed by Ang II. Interestingly, PD123.319 alone or combined with Ang II increased ICAM-1 levels in the cardiac arteries. Although these results are not statistically significant, it is debatable a possible action of AT2 antagonizing the effects of AT1 in these vessels.

IV. DISCUSSION

This study aimed to determine if Ang II is capable of inducing an inflammatory response in cardiac arteries even under normal values of blood pressure. It is well known that BP elevation per se can stimulate tissues to produce inflammatory cytokines as a repair mechanism [Guzik & Touyz, 2017]. The concept of angiotensin II with non-hemodynamic functions arose from studies conducted mainly in the late 1990s [Das, 2005]. Specifically, the proinflammatory effect of Ang II started correlating the action of Ang II with the production of reactive oxygen species leading to the production of inflammatory cytokines, and the expression of adhesion molecules [Baeuerle & Baltimore, 1996; Ushio-Fukai et al., 1999]. This idea was supported by the demonstration that AT1 receptor blockers can reduce inflammation, leading to atherosclerotic plaque stabilization [Cipollone et al., 2004].

Besides the proinflammatory action, it is important to consider that studies evaluating the effect of angiotensin II are usually made in animal models of hypertension. Thus, this hypertensive state can lead to a cardiovascular inflammatory condition, creating a confounding complementary factor. For example, hypertensive patients have an increase in adhesion molecules in serum and inflammatory cells [Ruiz-Ortega et al., 2001] but this fact can be directly associated with the inflammatory actions of Ang II. Therefore, this study addressed the inflammatory effect of angiotensin II, seeking to isolate the hemodynamic aspect using a dose that is not capable of altering BP. Trying to respond to this important question, the present study intended to isolate the Ang II stimulus from BP variations. Here, we demonstrate that a low dose of Ang II (30ng/kg) is unable to induce BP changes and leads to an early local and systemic inflammatory response.

Regarding the effect of Ang II, we believe that it presents a fast response and the entire result comes from the action of Ang II itself. We presume that Ang II, even being metabolized very quickly, is responsible for creating a chain-reaction mediating an inflammatory response. Apart from this, if we consider the fast metabolization of Ang II, which could not be time effective in promoting a systemic response, even the chronic treatment with osmotic mini-pumps, would also not be effective once to reach the circulatory system, the Ang II needs to be absorbed by the capillaries formed around the osmotic pumps, thus the effect of the Ang II would be reduced by the use of the osmotic mini-pumps. However, it has been shown that the administration of a low or high dose of Ang II by a osmotic mini-pumps is very effective [Daugherty et al., 2000; Guan et al., 2017; Guzik et al., 2007]. For this reason, we believe that the intraperitoneal administration of a single dose of Ang II reaches the circulatory system when in contact with a well-developed venous network that absorbs this Ang II very quickly, transporting it via the hepatic portal system to the heart. Therefore, a cardiac effect is expected, as was observed in this study. To better understanding whether the injection itself would have a stress-based effect, we also administered a saline solution to a control group. It should be noted that for ethical reasons, and also to reduce the number of animals, we did not perform the entire time-frame for the control group. We decided to analyze this effect in the times 30 minutes and 48 hours. Furthermore, as we did not observe a significant difference in the levels of IL6 and TNF-α by immunostaining, we did not consider relevant analyzing these inflammatory markers in the saline group by ELISA.

In this study, we observed no significant changes in blood pressure and heart rate comparing periods of 10 minutes to 6 hours after Ang II injection with a basal period, which agree with a previous study (de Lima et al, 2019). This study also confirmed the non-hypotensive dose of Losartan (AT1 receptor blocker) and the combination of Losartan and Ang II, as previously demonstrated [Lacchini et al., 2009]. The fact that no significant change was observed in blood pressure or heart rate suggests that the Ang II-induced responses are independent of hemodynamic alterations.

a) Study of the time-frame in response to angiotensin II

The time curve allowed us to identify moments when the inflammatory response is activated, both locally and systemically. This effect occurred both locally (cardiac arteries and cardiac tissue) and systemically (serum), reflecting the importance of a small Ang II
increase in cardiovascular regulation. The evaluation of inflammatory markers allowed to identify early and late inflammatory responses to Ang II.

TGF-β and IL-6 markers already had an increase in vascular and tissue expression from 30 to 120 minutes after the Ang II stimulus. Moreover, we verified a significant increase of IL-6 in serum 60 minutes after the injection of Ang II. Some studies show the fast expression of IL-6 in response to different types of stress such as infection or exercise. In chronic inflammation, the expression of TNF-α precedes IL-6; however, the stimulus without inflammation expresses IL-6 without being preceded by TNF-α [Pedersen & Febbraio, 2008], corroborating with the results obtained in the present study.

IL-6 is produced by a large number of cell types, and its release includes the presence of other pro-inflammatory cytokines, oxidation of lipoproteins, and the activation of extracellular matrix metalloproteinases [Schuett et al., 2009]. It is known that Angiotensin II is capable of inducing the vascular production of pro-inflammatory cytokines such as IL-6 and TNF-α [Schieffe et al., 2000]. In this case, Angiotensin II would lead to an increase in the production of reactive oxygen species, inducing an increase in IL-6 production (WASSMANN et al., 2004), and creating a chain-reaction in response to Angiotensin II, promoting an increase in IL-6, oxidative stress and vascular injury.

It has been shown that TGF-β is a multifunctional protein, participating in the regulation of cell division, differentiation, migration, cell adhesion, extracellular matrix production, and is involved in several diseases including cardiovascular disease [Ruiz-Ortega et al., 2007]. It should be noted that TGF-β protein is synthesized as inactive, but has within its structure the latency-associated peptide (LAP). This protein interacts with protein binding of latent TGF-β (LTBP) which is anchored to the extracellular matrix. This TGF-β is activated by proteolytic cleavage by plasmin, microenvironment acid, and matrix metalloproteinases (MMP-2 and 9) [Annes et al., 2003]. In vitro studies show that Ang II stimulates the gene expression and activation of TGF-β in vascular smooth muscle cells [Weigert et al., 2001]. However, the fast response observed in TGF-β evaluation suggests that it is probably anchored to proteins in the extracellular matrix and is released under-stimulation. In this study, Ang II was able to promote a rapid release of TGF-β in cardiac arteries. This idea corroborates a previous study, showing a similar pattern of TGF-β release in the aorta of normotensive mice (de Lima et al., 2019). Moreover, by participating in the balance between inflammation and extracellular matrix deposition, the local imbalance in TGF-β can lead to the development of early vascular lesions and atherosclerosis [Ruiz-Ortega et al., 2007].

The results for both IL-1β, TNF-α, and ICAM-1 are consistent with the observation of an early increase in IL-6 both locally and in serum. In response to a harmful stimulus, the body triggers an innate nonspecific reaction activating an acute protein reaction (APR), as IL-1β, IL-6, and TNF-α, involved in local inflammation [Schuett et al., 2009]. IL-6 is the main mediator of such mechanism [Heinrich et al., 1998] acting on the expression of other cytokines and inflammatory mediators. It has been demonstrated that IL-6 has an inhibitory effect on the production of TNF-α [Mizuhara et al., 1994] which corroborates the results found in this study because, unlike a situation of infection, the injection of Ang II led to increased IL-6 without being preceded by an increase in TNF-α. In contrast, IL-6 stimulates the release of IL-1β maintaining the inflammatory response as observed. This response was maintained between 2 and 24 hours and possibly declined at 48 hours due to a lack of stimulus (in this case, the injection of Ang II). The maintenance of an inflammatory stimulus leads to the facilitation of adhesion and cell migration in the target tissue. In this context, the observation of increased staining of ICAM-1 suggests also a proinflammatory action, and this is corroborated by the fact that both IL-6 and IL-1β are stimulating factors as ICAM-1 [Zhang et al., 2009].

b) Study of the effect of Ang II receptors on inflammatory response

Although this study showed that Ang II, independent of hemodynamic changes, can trigger a local inflammatory response in cardiac arteries, it is questionable whether this action is mediated by the direct action of its receptors or if it can be an indirect mechanism that acts on this response. Thus, the study of the receptor blockade of Ang II allowed us to observe the possible participation of each AT receptor on the inflammatory process triggered by Ang II.

As can seeing in results, the injection of Ang II leads to a fast increase in TGF-β and IL-6 in cardiac arteries. Also, it can increase IL-1β and ICAM-1 after 12 hours in such vessels. It has been well described that this Ang II effect is related to its action on AT receptors [Ferrario & Strawn, 2006; Sadoshima, 2000; Sakuta et al., 2010; Sata & Fukuda, 2010] but is always associated with different pathologies. The present study shows that this effect is either non-associated to pathologies or hemodynamic changes.

The proinflammatory effect of Ang II-mediated by the AT1 receptor is confirmed by blockade with Losartan. As Losartan abolished the effect of Ang II, we may consider that AT1 acts directly to increase vascular TGF-β and IL-6 after 30 minutes. However, the experimental design of this study does not allow us to assert that the effects on IL-1β and ICAM-1 12 hours after Ang II injection are directly determined by AT1 activation. This expression may be given indirectly after...
the activation of AT1. In this context, it opens a new possibility for study, analyzing the mechanisms by which activation of AT1 leads to increased expression of late inflammatory mediators, such as IL-1β and ICAM-1. The effects of the AT2 receptor are recognized and widely studied as AT1 antagonists. Thus, AT2 has classically exerted antiproliferative and antiinflammatory actions, among others [Ferrario & Strawn, 2006; Horiuchi et al., 1999]. Furthermore, we found that AT2 does not always participate in Ang II-related effects, restricting the actions of Ang II to those mediated by AT1. In this sense, we found that the AT2 receptor seems to have an AT1 antagonism action, especially related to IL-1β.

c) Study limitations

In this study, the observed effects of Ang II on inflammatory markers in cardiac arteries were associated with AT1 receptors. Although the protein expression has been analyzed, the results obtained represent a set mostly composed of cardiomyocytes, diluting the specific analysis of the cardiac arteries. However, this evaluation allowed us to verify that the cardiac tissue itself responded to the treatment, producing an inflammatory response.

Another limitation that we consider for this work is the difficulty of working with small groups of animals, since many experimental groups are evaluated, and the reduction strategies of the ethics committee provide for the use of a minimum number of animals. Studies using immunohistochemistry can show a lot of variation within an experiment and attention should be maximum, especially with small groups.

Furthermore, the results related to the AT2 receptor can be confused with results from the other groups. The idea of the interaction between the two Ang II receptors has existed for over 10 years but the topic is controversial. It is believed that the clinical effects of AT1 receptor antagonists may be due to the blockade of AT1 and AT2 stimulation whereas Ang II would act on the AT2 receptor preferentially when AT1 is blocked [Horiuchi et al., 1999]. The real contribution of the AT2 receptor antagonizing the effects of AT1 can be better understood in studies with dual blockade of the receptors. This opens new perspectives in understanding the role of both AT1 and AT2 in the physiological responses to Ang II.

V. Conclusion

It is noteworthy that the effect of Ang II on the early or late expression of inflammatory markers in the arteries of healthy individuals may not represent risks; however, we do not know whether the time and/or the repetition of these insults can participate in the development of the cardiovascular disease. Considering the importance of understanding the adaptive processes in the transition between normotensive to hypertension, the understanding of how certain changes occur in the absence of established hypertension can be fundamental to determine how and when certain changes can be reversed. In conclusion, this study showed for the first time that angiotensin II might trigger an inflammatory process mediated by the AT1 receptor on cardiac arteries, in dose small enough to keep unchanged the blood pressure. AT2 receptor seems to be involved in the counterbalance of AT1R during modulation of IL-1β production in cardiac arteries.

ACKNOWLEDGMENT

Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) and Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP, process nº 2007/57416-3 adn 2009/15693-6) for financial support.

Table 1: Blood pressure (BP) and heart rate measurements: diastolic BP (DBP), mean BP (MBP), systolic BP (SBP) and heart rate (HR) were measured in Saline and Ang II treated mice. The same animal was recorded at basal time (baseline) and 10, 30, 60 120 minutes and 6 hours after injections.

<table>
<thead>
<tr>
<th></th>
<th>DBP (mmHg)</th>
<th>SBP (mmHg)</th>
<th>MBP (mmHg)</th>
<th>HR (bpm)</th>
<th>DBP (mmHg)</th>
<th>SBP (mmHg)</th>
<th>MBP (mmHg)</th>
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<tbody>
<tr>
<td>Baseline</td>
<td>103.7±4.8</td>
<td>135.2±1.2</td>
<td>120.3±3.4</td>
<td>563±144</td>
<td>89.9±8.4</td>
<td>127.4±4.8</td>
<td>108.8±6.7</td>
<td>528±57</td>
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<tr>
<td>10 min</td>
<td>105.8±0.7</td>
<td>135.1±2.3</td>
<td>121.5±0.8</td>
<td>626±186</td>
<td>91.8±10.2</td>
<td>131.4±13.4</td>
<td>111.9±11.4</td>
<td>538±59</td>
</tr>
<tr>
<td>30 min</td>
<td>100.3±1.2</td>
<td>128.6±3.0</td>
<td>115.8±0.6</td>
<td>587±108</td>
<td>86.9±6.2</td>
<td>120.9±4.7</td>
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<tr>
<td>60 min</td>
<td>100.2±4.2</td>
<td>126.1±3.1</td>
<td>114.7±3.5</td>
<td>655±81</td>
<td>84.8±4.7</td>
<td>118.7±6.7</td>
<td>102.4±3.9</td>
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<tr>
<td>120 min</td>
<td>90.7±2.0</td>
<td>122.3±8.8</td>
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<td>583±123</td>
<td>86.9±14.3</td>
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<td>6 hours</td>
<td>79.9±2.7</td>
<td>115.7±7.1</td>
<td>99.2±3.7</td>
<td>537±153</td>
<td>80.9±11.6</td>
<td>114.4±7.2</td>
<td>98.4±9.5</td>
<td>510±61</td>
</tr>
</tbody>
</table>

Statistical analysis did not show differences between treatments for all parameters. n=5 per treatment and time.

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Table 2: Systemic (serum) TNFα and IL-6 measured by ELISA. Each group was designed for a treatment (saline or Ang II) and the blood was collected after the time specified

<table>
<thead>
<tr>
<th>Treatment</th>
<th>TNF-α (pg/mL)</th>
<th>IL-6 (pg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saline 30’</td>
<td>0 ± 0</td>
<td>0 ± 0</td>
</tr>
<tr>
<td>Ang II 30’</td>
<td>3.27 ± 7.32</td>
<td>1.60 ± 3.59</td>
</tr>
<tr>
<td>Ang II 60’</td>
<td>6.28 ± 14.04</td>
<td>29.21 ± 11.86 *</td>
</tr>
<tr>
<td>Ang II 120’</td>
<td>0 ± 0</td>
<td>1.65 ± 3.70</td>
</tr>
<tr>
<td>Ang II 6hs</td>
<td>0 ± 0</td>
<td>0 ± 0</td>
</tr>
<tr>
<td>Ang II 12hs</td>
<td>0 ± 0</td>
<td>0 ± 0</td>
</tr>
<tr>
<td>Ang II 24hs</td>
<td>0 ± 0</td>
<td>0.56 ± 1.26</td>
</tr>
<tr>
<td>Ang II 48hs</td>
<td>0 ± 0</td>
<td>1.17 ± 2.63</td>
</tr>
<tr>
<td>Saline 48hs</td>
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*p≤0.05 compared to Saline groups and other times of Ang II; n=5 per treatment and time

Figure 1: Time curve in response to Saline or Ang II injection, showing score staining for TGF-β (A) and IL-6 (B) on left; on right side are presented representative images comparing basal condition (Saline) and higher response (30’ after Ang II injection). *p≤0.05 compared to Saline 30’ (a), Ang II 12h (b), Ang II 48h (c) and Saline 48h (d). Scale bar=0.4 µm.
Figure 2: Time curve in response to Saline or Ang II injection, showing score staining for IL-1β (A), ICAM-1 (B) and TNF-α (C) on left; on right side are presented representative images comparing basal condition (Saline) and higher response (6 or 48 hours after Ang II injection). *p ≤ 0.05 compared to Saline 30' (a), Ang II 30' (b), Ang II 48h (c) and Saline 48h (d). Scale bar=0.4 µm.
Figure 3: Cardiac expression of TGF-β and IL-6. The results are presented as percentage of protein/GAPDH ration in all times after Saline or Ang II injection. *p ≤ 0.05 compared to Saline and other Ang II groups.
Figure 4: Study of the participation of AT receptors on local expression of TGF-β (A) and IL-6 (B) in early inflammatory response (30 minutes after treatments). On left is presented the score of staining in each group, and on right is presented a panel with representative images of the results obtained after treatments and ATR blockings. *p≤0.05 compared to Saline (a), losartan (b), los+Ang (c) and PD+Ang (d). Magnification: 1000x
Figure 5: Study of the participation of AT receptors on local expression of IL-1β (A) and ICAM-1 (B) in late inflammatory response (12 hours after treatments). *p≤0.05 compared to losartan (a) and los+Ang (b). Magnification: 1000x

REFERENCES RÉFÉRENCES REFERENCIAS

5. Committee for the Update of the Guide for the Care and Use of Laboratory Animals. *Guide for the Care and Use of Laboratory Animals*. Institute for...


34. Schiffrin EL and R. M. Touyz, “From bedside to bench to bedside: role of renin-angiotensin-aldosterone system in remodeling of resistance arteries in hypertension,” American Journal of...


Myocardial Revascularization in Women, An Epidemiological Analysis


Abstract- Introduction: Due to its high mortality rate, it is necessary to discuss and understand the aspects surrounding atherosclerotic diseases, including the current role of revascularization in a large number of cases. Additionally, it is necessary to discuss the aging process in women and the effects of hormonal changes.

Methodology: This is a literature review with a search in databases, using 60 scientific articles as a basis and being filtered based on scientific impact and approach.

Keywords: revascularization of the myocardium; risks; atherosclerotic conditions.

GJMR-F Classification: NLM: WG 169.5
Myocardial Revascularization in Women, An Epidemiological Analysis

Vitória Patrícia Rodrigues Cunha a, Marina Mota De Oliveira Madruga a, Bruna Daher Fonseca a, Clarice Senna Goepfert a, Victor De Oliveira Bessa a, Victor Farias Coelho a, Raphael Vinicius Mendes Abreu a, Alexandre Eustáquio De Almeida Rezende Filho a, Dayane Carolini Rodrigues a, Edson Brunetti Da Silva a, Bruno Renan De Carvalho Lopes a, Milena Freire Guinazi a, Maria Luisa Giguino Carvalho a, Gabriela Salomão Espirito Santo Mendonça a, Guilherme Silva Miranda a, Giovana Jenifer Santana De Oliveira a & Dra. Aline de Amorim Duarte d

Abstract: Introduction: Due to its high mortality rate, it is necessary to discuss and understand the aspects surrounding atherosclerotic diseases, including the current role of revascularization in a large number of cases. Additionally, it is necessary to discuss the aging process in women and the effects of hormonal changes.

Methodology: This is a literature review with a search in databases, using 60 scientific articles as a basis and being filtered based on scientific impact and approach.

Results: Complex atherosclerotic diseases are more common in female patients, and these conditions often coexist with other conditions like diabetes and hypertension, as well as obesity and sedentary lifestyles. As the most common chronic non-communicable disease in the nation, hospitalizations have a significant influence on public health, which must be understood and discussed. As the most common chronic non-communicable disease in the nation, hospitalizations have a significant influence on public health, which must be understood and discussed.

Final considerations: Since patients who required myocardial revascularization were men, it is crucial to comprehend this shift in the landscape because there are numerous risk factors, primarily related to aging's physiological changes. In order to maintain a higher quality of life and lower death rates associated with atherosclerotic diseases and myocardial revascularization, it is crucial to monitor women's health starting at an adult age and provide counseling for healthy living practices.

Keywords: revascularization of the myocardium; risks; atherosclerotic conditions.

1. Introduction

Atherosclerotic disease and myocardial revascularization as treatments come into play when studying chronic non-communicable diseases; these topics are frequently brought up in clinical and academic discussions because they are among the illnesses that account for the majority of fatalities in the nation. (GUTIERRE, CARDORE). In addition, it is important to note that the major changes in human life have a significant impact on the development of this pathology, as evidenced by bad eating habits and a sedentary lifestyle (LINS, 2017). Acute myocardial infarction (AMI) and stroke are the main causes of death in Brazil for women over 50, according to the Ministry of Health (MS). Among these discussions, it is important to note that eating habits have a direct impact on this, as the increase in the consumption of industrialized products and the constant occupation of a routine have led people to choose to eat Fast Food, with foods high in fats being a series of negative actions that, as one ages, one begins to feel the negative effects of these lifelong practices. In addition, neglect of health and ignorance have a significant impact on the increase in serious cases, and ignorance has a significant impact on neglect and lack of care. The factors of habits already mentioned are corroborated by this picture, yet without the necessary follow-up for a search for disease prevention, the numbers of hospitalizations and deaths have increased (GWENDOLIN, 2017). By realizing that estrogen functions as a preventive factor and that age, particularly the reproductive age of women, has a direct impact on the processes of atherosclerotic disease development. However, in the postmenopausal period, this factor does not happen due to the hormonal low, which, combined with other risk factors such as advanced age, hypertension, diabetes, obesity, and lifestyle, leads to a worsening in the morbidity and mortality of patients. In order to develop projects and preventive measures, as well as to adjust the current framework given its significance in epidemiological terms, it is therefore interesting to link these parameters with the epidemiological characteristics. Since there are many patients undergoing coronary artery bypass graft surgery, it is important to comprehend and embrace the patient as a whole before analyzing the factors surrounding the procedure, such as risk factors and aging processes. (TAVARES, 2020)

Myocardial revascularization surgery plays a crucial role in resolving coronary artery disease, in which fat accumulates in the coronary arteries. As it is an
extensive surgery and requires good postoperative support, the preoperative study is extensive and covers all risk, morbidity, and mortality factors.

II. METHODS

This is a literature review whose sources were taken from the SciELO and PubMed data platforms. The research period was July 2023, meeting the inclusion criteria of articles from the years 2000 to 2023, in Portuguese and English, online texts, and full texts. As strategies for better evaluation of the texts, the following health descriptors (DeCS) were used: "Myocardial revascularization", "Women" and "Risks". In addition, the public database DATASUS was used on an epidemiological basis.

III. RESULTS AND DISCUSSION

By understanding the importance and impact of risk factors for the need for myocardial revascularization, it is understood that the risk factor that most surrounds the main studies is the gender factor, as seen in the study (CADORE, 2007) at Hospital San Lucas da PUC-RS in 2007. This study identified 11 predictors for death in coronary artery bypass graft surgery, which formed the score: age $\geq 60$ years, surgery in women. In the present study, mortality was higher in women (11.9% versus 9% in men), which is an independent risk factor for hospital death.

In another aspect, in females, obesity is twice as evident in patients with atherosclerotic disease (BRUNORI EHFR et al., 2014). An interesting factor relates to the eating and living habits of a large part of the population. By addressing the bias of a sedentary lifestyle, the risks become more evident, as do the main impacts on the patients’ lifestyle habits.

It is understood as a risk factor for the need for myocardial revascularization: Risk factors for the development of coronary artery disease (CAD) are systemic arterial hypertension (SAH), smoking, dyslipidemias, obesity, diabetes mellitus (DM), family history, and a sedentary lifestyle; however, in women, some of these factors have a more pronounced effect. In addition, women are subject to specific causes, such as hypertension in the pregnancy cycle, gestational diabetes, and premature birth, which are related to increased cardiovascular risk in the long term.

Figure 1: Epidemiological table of hospital morbidity by place region

Figure 1 illustrates the impact of atherosclerotic disease by showing that there were 11,349 deaths in 5 months. In addition, it is worth mentioning and emphasizing the focus on the Southeast Region, given the routine and life dynamics of most residents, as well as their lifestyle habits, which provide more risk factors for the development of atherosclerotic disease.
Figure 2: Epidemiological table of hospital morbidity by place of hospitalization for females

Given that this is the chronic, non-communicable disease that kills the most people in the nation, it is crucial to comprehend and debate the effect that hospitalization rates have on public health. Figure 2 indicates that female patients account for a significant proportion of hospitalizations, and it should be understood that this is reflected in the images of myocardial revascularization.

According to the study, “Clinical profile of women undergoing revascularization surgery,” patients undergoing coronary artery bypass grafting and valve replacement were predominantly female (33.8%) and elderly (60.89 years), which is a rare finding in the literature given that studies show that males and the elderly make up the majority of patients undergoing coronary artery bypass grafting surgeries (GUTIERRES, 2020).

On the other hand, according to (Choles FE, et al. 2015), diabetic women have more coronary lesions compared to non-diabetic women. There is evidence that women with diabetes mellitus have worse outcomes than men. In addition, diabetic women with atherosclerotic disease undergoing revascularization have a higher risk of restenosis due to pathophysiological changes at the vascular level, a decrease in the protective effect of estrogens after menopause, and the fact that the caliber of their arteries is smaller than that of non-diabetic women and smaller than that of men. In them, revascularization of the anterior descending artery with coronary artery bypass grafting surgeries is associated with a higher incidence of adverse outcomes in the short and medium term (MOTA, 2015).

IV. Final Considerations

Thus, it is essential to understand this change in perspective since patients who needed myocardial revascularization were men, and this profile is constantly changing since there are several risk factors, mainly due to the physiological changes of aging. Finally, monitoring women's health since adulthood, with guidance for healthy lifestyle habits and specialized monitoring in the climacteric period, is essential to maintaining a better quality of life and reducing mortality rates related to atherosclerotic diseases and myocardial revascularization.

References

7. RISSARDI, Bruna; SOARES, Roberta Alessandra; AYALA, Ariene Laurenti Monterrosa. Fatores de risco da doença coronariana entre os pacientes submetidos à revascularização miocárdica (RM) em...


A Rare Case of Methionine Adenosyltransferase Deficiency in an 8-Month-Old Infant Presenting with Jaundice and Bleeding Episodes

By Mohammad Yunus Choudhary

Abstract - Methionine adenosyltransferase (MAT) deficiency is a rare inherited disorder of methionine metabolism that can lead to a wide range of symptoms, including jaundice, bleeding episodes, and neurological impairment. We report the case of an 8-month-old female infant, who presented with yellowish discoloration of skin, distended abdomen, and bleeding episodes. On further evaluation, she was found to have high levels of methionine in her blood. A diagnosis of MAT deficiency was made, and was started on appropriate treatment with a methionine-restricted diet and supplements.

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Abstract- Methionine adenosyltransferase (MAT) deficiency is a rare inherited disorder of methionine metabolism that can lead to a wide range of symptoms, including jaundice, bleeding episodes, and neurological impairment. We report the case of an 8-month-old female infant, who presented with yellowish discoloration of skin, distended abdomen, and bleeding episodes. On further evaluation, she was found to have high levels of methionine in her blood. A diagnosis of MAT deficiency was made, and was started on appropriate treatment with a methionine-restricted diet and supplements.

I. Introduction

Methionine adenosyltransferase (MAT) deficiency is a rare autosomal recessive disorder caused by mutations in the MAT1A gene that encodes the alpha subunit of the enzyme MAT. MAT is responsible for the synthesis of S-adenosylmethionine (SAMe), a critical methyl donor involved in many essential biochemical pathways. MAT deficiency leads to an accumulation of methionine and its toxic metabolites in the body, which can cause a wide range of symptoms.

II. Case Presentation

A 8-month-old female infant, presented with yellowish discoloration of skin and a distended abdomen. She had no history of hematemesis, rashes, blood in stools, melena, or discolored urine. She had also experienced episodes of unconsciousness and bleeding episodes in the past. On examination, she was alert and conscious with a distended abdomen. Her respiratory and cardiovascular systems were normal, and her central nervous system was intact.

Further evaluation revealed high levels of methionine in her blood, leading to a diagnosis of MAT deficiency. She was started on a methionine-restricted diet and supplements to reduce the levels of methionine in her body. Her symptoms gradually improved, and she was discharged from the hospital with regular follow-up visits.

III. Discussion

MAT deficiency is a rare disorder with a wide range of clinical manifestations. Jaundice, bleeding episodes, and neurological impairment are the most common symptoms. The diagnosis is usually made by measuring the levels of methionine and SAMe in the blood, and genetic testing can confirm the diagnosis. Treatment for MAT deficiency involves a methionine-restricted diet and supplements to improve the levels of SAMe in the body. Early diagnosis and treatment can prevent or reduce the severity of symptoms and improve the quality of life of affected individuals.

IV. Conclusion

MAT deficiency is a rare inherited disorder of methionine metabolism that can lead to a wide range of symptoms, including jaundice, bleeding episodes, and neurological impairment. Early diagnosis and treatment are essential to prevent or reduce the severity of symptoms and improve the quality of life of affected individuals. This case highlights the importance of considering rare metabolic disorders in the differential diagnosis of infants presenting with jaundice and bleeding episodes.
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- Two columns with equal column width of 3.38 and spacing of 0.2.
- First character must be three lines drop-capped.
- The paragraph before spacing of 1 pt and after of 0 pt.
- Line spacing of 1 pt.
- Large images must be in one column.
- The names of first main headings (Heading 1) must be in Roman font, capital letters, and font size of 10.
- The names of second main headings (Heading 2) must not include numbers and must be in italics with a font size of 10.

Structure and Format of Manuscript

The recommended size of an original research paper is under 15,000 words and review papers under 7,000 words. Research articles should be less than 10,000 words. Research papers are usually longer than review papers. Review papers are reports of significant research (typically less than 7,000 words, including tables, figures, and references)

A research paper must include:

a) A title which should be relevant to the theme of the paper.
b) A summary, known as an abstract (less than 150 words), containing the major results and conclusions.
c) Up to 10 keywords that precisely identify the paper’s subject, purpose, and focus.
d) An introduction, giving fundamental background objectives.
e) Resources and techniques with sufficient complete experimental details (wherever possible by reference) to permit repetition, sources of information must be given, and numerical methods must be specified by reference.
f) Results which should be presented concisely by well-designed tables and figures.
g) Suitable statistical data should also be given.
h) All data must have been gathered with attention to numerical detail in the planning stage.

Design has been recognized to be essential to experiments for a considerable time, and the editor has decided that any paper that appears not to have adequate numerical treatments of the data will be returned unrefereed.
i) Discussion should cover implications and consequences and not just recapitulate the results; conclusions should also be summarized.
j) There should be brief acknowledgments.
k) There ought to be references in the conventional format. Global Journals recommends APA format.

Authors should carefully consider the preparation of papers to ensure that they communicate effectively. Papers are much more likely to be accepted if they are carefully designed and laid out, contain few or no errors, are summarizing, and follow instructions. They will also be published with much fewer delays than those that require much technical and editorial correction.

The Editorial Board reserves the right to make literary corrections and suggestions to improve brevity.
Format Structure

It is necessary that authors take care in submitting a manuscript that is written in simple language and adheres to published guidelines.

All manuscripts submitted to Global Journals should include:

Title
The title page must carry an informative title that reflects the content, a running title (less than 45 characters together with spaces), names of the authors and co-authors, and the place(s) where the work was carried out.

Author details
The full postal address of any related author(s) must be specified.

Abstract
The abstract is the foundation of the research paper. It should be clear and concise and must contain the objective of the paper and inferences drawn. It is advised to not include big mathematical equations or complicated jargon.

Many researchers searching for information online will use search engines such as Google, Yahoo or others. By optimizing your paper for search engines, you will amplify the chance of someone finding it. In turn, this will make it more likely to be viewed and cited in further works. Global Journals has compiled these guidelines to facilitate you to maximize the web-friendliness of the most public part of your paper.

Keywords
A major lynchpin of research work for the writing of research papers is the keyword search, which one will employ to find both library and internet resources. Up to eleven keywords or very brief phrases have to be given to help data retrieval, mining, and indexing.

One must be persistent and creative in using keywords. An effective keyword search requires a strategy: planning of a list of possible keywords and phrases to try.

Choice of the main keywords is the first tool of writing a research paper. Research paper writing is an art. Keyword search should be as strategic as possible.

One should start brainstorming lists of potential keywords before even beginning searching. Think about the most important concepts related to research work. Ask, “What words would a source have to include to be truly valuable in a research paper?” Then consider synonyms for the important words.

It may take the discovery of only one important paper to steer in the right keyword direction because, in most databases, the keywords under which a research paper is abstracted are listed with the paper.

Numerical Methods
Numerical methods used should be transparent and, where appropriate, supported by references.

Abbreviations
Authors must list all the abbreviations used in the paper at the end of the paper or in a separate table before using them.

Formulas and equations
Authors are advised to submit any mathematical equation using either MathJax, KaTeX, or LaTeX, or in a very high-quality image.

Tables, Figures, and Figure Legends
Tables: Tables should be cautiously designed, uncrowned, and include only essential data. Each must have an Arabic number, e.g., Table 4, a self-explanatory caption, and be on a separate sheet. Authors must submit tables in an editable format and not as images. References to these tables (if any) must be mentioned accurately.
Figures

Figures are supposed to be submitted as separate files. Always include a citation in the text for each figure using Arabic numbers, e.g., Fig. 4. Artwork must be submitted online in vector electronic form or by emailing it.

Preparation of Electronic Figures for Publication

Although low-quality images are sufficient for review purposes, print publication requires high-quality images to prevent the final product being blurred or fuzzy. Submit (possibly by e-mail) EPS (line art) or TIFF (halftone/photographs) files only. MS PowerPoint and Word Graphics are unsuitable for printed pictures. Avoid using pixel-oriented software. Scans (TIFF only) should have a resolution of at least 350 dpi (halftone) or 700 to 1100 dpi (line drawings). Please give the data for figures in black and white or submit a Color Work Agreement form. EPS files must be saved with fonts embedded (and with a TIFF preview, if possible).

For scanned images, the scanning resolution at final image size ought to be as follows to ensure good reproduction: line art: >650 dpi; halftones (including gel photographs): >350 dpi; figures containing both halftone and line images: >650 dpi.

Color charges: Authors are advised to pay the full cost for the reproduction of their color artwork. Hence, please note that if there is color artwork in your manuscript when it is accepted for publication, we would require you to complete and return a Color Work Agreement form before your paper can be published. Also, you can email your editor to remove the color fee after acceptance of the paper.

Tips for Writing a Good Quality Medical Research Paper

1. Choosing the topic: In most cases, the topic is selected by the interests of the author, but it can also be suggested by the guides. You can have several topics, and then judge which you are most comfortable with. This may be done by asking several questions of yourself, like "Will I be able to carry out a search in this area? Will I find all necessary resources to accomplish the search? Will I be able to find all information in this field area?" If the answer to this type of question is "yes," then you ought to choose that topic. In most cases, you may have to conduct surveys and visit several places. Also, you might have to do a lot of work to find all the rises and falls of the various data on that subject. Sometimes, detailed information plays a vital role, instead of short information. Evaluators are human: The first thing to remember is that evaluators are also human beings. They are not only meant for rejecting a paper. They are here to evaluate your paper. So present your best aspect.

2. Think like evaluators: If you are in confusion or getting demotivated because your paper may not be accepted by the evaluators, then think, and try to evaluate your paper like an evaluator. Try to understand what an evaluator wants in your research paper, and you will automatically have your answer. Make blueprints of paper: The outline is the plan or framework that will help you to arrange your thoughts. It will make your paper logical. But remember that all points of your outline must be related to the topic you have chosen.

3. Ask your guides: If you are having any difficulty with your research, then do not hesitate to share your difficulty with your guide (if you have one). They will surely help you out and resolve your doubts. If you can't clarify what exactly you require for your work, then ask your supervisor to help you with an alternative. He or she might also provide you with a list of essential readings.

4. Use of computer is recommended: As you are doing research in the field of medical research then this point is quite obvious. Use right software: Always use good quality software packages. If you are not capable of judging good software, then you can lose the quality of your paper unknowingly. There are various programs available to help you which you can get through the internet.

5. Use the internet for help: An excellent start for your paper is using Google. It is a wondrous search engine, where you can have your doubts resolved. You may also read some answers for the frequent question of how to write your research paper or find a model research paper. You can download books from the internet. If you have all the required books, place importance on reading, selecting, and analyzing the specified information. Then sketch out your research paper. Use big pictures: You may use encyclopedias like Wikipedia to get pictures with the best resolution. At Global Journals, you should strictly follow here.
6. **Bookmarks are useful**: When you read any book or magazine, you generally use bookmarks, right? It is a good habit which helps to not lose your continuity. You should always use bookmarks while searching on the internet also, which will make your search easier.

7. **Revise what you wrote**: When you write anything, always read it, summarize it, and then finalize it.

8. **Make every effort**: Make every effort to mention what you are going to write in your paper. That means always have a good start. Try to mention everything in the introduction—what is the need for a particular research paper. Polish your work with good writing skills and always give an evaluator what he wants. Make backups: When you are going to do any important thing like making a research paper, you should always have backup copies of it either on your computer or on paper. This protects you from losing any portion of your important data.

9. **Produce good diagrams of your own**: Always try to include good charts or diagrams in your paper to improve quality. Using several unnecessary diagrams will degrade the quality of your paper by creating a hodgepodge. So always try to include diagrams which were made by you to improve the readability of your paper. Use of direct quotes: When you do research relevant to literature, history, or current affairs, then use of quotes becomes essential, but if the study is relevant to science, use of quotes is not preferable.

10. **Use proper verb tense**: Use proper verb tenses in your paper. Use past tense to present those events that have happened. Use present tense to indicate events that are going on. Use future tense to indicate events that will happen in the future. Use of wrong tenses will confuse the evaluator. Avoid sentences that are incomplete.

11. **Pick a good study spot**: Always try to pick a spot for your research which is quiet. Not every spot is good for studying.

12. **Know what you know**: Always try to know what you know by making objectives, otherwise you will be confused and unable to achieve your target.

13. **Use good grammar**: Always use good grammar and words that will have a positive impact on the evaluator; use of good vocabulary does not mean using tough words which the evaluator has to find in a dictionary. Do not fragment sentences. Eliminate one-word sentences. Do not ever use a big word when a smaller one would suffice. Verbs have to be in agreement with their subjects. In a research paper, do not start sentences with conjunctions or finish them with prepositions. When writing formally, it is advisable to never split an infinitive because someone will (wrongly) complain. Avoid clichés like a disease. Always shun irritating alliteration. Use language which is simple and straightforward. Put together a neat summary.

14. **Arrangement of information**: Each section of the main body should start with an opening sentence, and there should be a changeover at the end of the section. Give only valid and powerful arguments for your topic. You may also maintain your arguments with records.

15. **Never start at the last minute**: Always allow enough time for research work. Leaving everything to the last minute will degrade your paper and spoil your work.

16. **Multitasking in research is not good**: Doing several things at the same time is a bad habit in the case of research activity. Research is an area where everything has a particular time slot. Divide your research work into parts, and do a particular part in a particular time slot.

17. **Never copy others’ work**: Never copy others’ work and give it your name because if the evaluator has seen it anywhere, you will be in trouble. Take proper rest and food: No matter how many hours you spend on your research activity, if you are not taking care of your health, then all your efforts will have been in vain. For quality research, take proper rest and food.

18. **Go to seminars**: Attend seminars if the topic is relevant to your research area. Utilize all your resources.

19. **Refresh your mind after intervals**: Try to give your mind a rest by listening to soft music or sleeping in intervals. This will also improve your memory. Acquire colleagues: Always try to acquire colleagues. No matter how sharp you are, if you acquire colleagues, they can give you ideas which will be helpful to your research.
20. **Think technically:** Always think technically. If anything happens, search for its reasons, benefits, and demerits. Think and then print: When you go to print your paper, check that tables are not split, headings are not detached from their descriptions, and page sequence is maintained.

21. **Adding unnecessary information:** Do not add unnecessary information like "I have used MS Excel to draw graphs." Irrelevant and inappropriate material is superfluous. Foreign terminology and phrases are not apropos. One should never take a broad view. Analogy is like feathers on a snake. Use words properly, regardless of how others use them. Remove quotations. Puns are for kids, not grunt readers. Never oversimplify: When adding material to your research paper, never go for oversimplification; this will definitely irritate the evaluator. Be specific. Never use rhythmic redundancies. Contractions shouldn't be used in a research paper. Comparisons are as terrible as clichés. Give up ampersands, abbreviations, and so on. Remove commas that are not necessary. Parenthetical words should be between brackets or commas. Understatement is always the best way to put forward earth-shaking thoughts. Give a detailed literary review.

22. **Report concluded results:** Use concluded results. From raw data, filter the results, and then conclude your studies based on measurements and observations taken. An appropriate number of decimal places should be used. Parenthetical remarks are prohibited here. Proofread carefully at the final stage. At the end, give an outline to your arguments. Spot perspectives of further study of the subject. Justify your conclusion at the bottom sufficiently, which will probably include examples.

23. **Upon conclusion:** Once you have concluded your research, the next most important step is to present your findings. Presentation is extremely important as it is the definite medium though which your research is going to be in print for the rest of the crowd. Care should be taken to categorize your thoughts well and present them in a logical and neat manner. A good quality research paper format is essential because it serves to highlight your research paper and bring to light all necessary aspects of your research.

**Informal Guidelines of Research Paper Writing**

**Key points to remember:**

- Submit all work in its final form.
- Write your paper in the form which is presented in the guidelines using the template.
- Please note the criteria peer reviewers will use for grading the final paper.

**Final points:**

One purpose of organizing a research paper is to let people interpret your efforts selectively. The journal requires the following sections, submitted in the order listed, with each section starting on a new page:

*The introduction:* This will be compiled from reference matter and reflect the design processes or outline of basis that directed you to make a study. As you carry out the process of study, the method and process section will be constructed like that. The results segment will show related statistics in nearly sequential order and direct reviewers to similar intellectual paths throughout the data that you gathered to carry out your study.

*The discussion section:*

This will provide understanding of the data and projections as to the implications of the results. The use of good quality references throughout the paper will give the effort trustworthiness by representing an alertness to prior workings.

Writing a research paper is not an easy job, no matter how trouble-free the actual research or concept. Practice, excellent preparation, and controlled record-keeping are the only means to make straightforward progression.

**General style:**

Specific editorial column necessities for compliance of a manuscript will always take over from directions in these general guidelines.

**To make a paper clear:** Adhere to recommended page limits.
Mistakes to avoid:

- Insertion of a title at the foot of a page with subsequent text on the next page.
- Separating a table, chart, or figure—confine each to a single page.
- Submitting a manuscript with pages out of sequence.
- In every section of your document, use standard writing style, including articles ("a" and "the").
- Keep paying attention to the topic of the paper.
- Use paragraphs to split each significant point (excluding the abstract).
- Align the primary line of each section.
- Present your points in sound order.
- Use present tense to report well-accepted matters.
- Use past tense to describe specific results.
- Do not use familiar wording; don't address the reviewer directly. Don't use slang or superlatives.
- Avoid use of extra pictures—include only those figures essential to presenting results.

Title page:
Choose a revealing title. It should be short and include the name(s) and address(es) of all authors. It should not have acronyms or abbreviations or exceed two printed lines.

Abstract: This summary should be two hundred words or less. It should clearly and briefly explain the key findings reported in the manuscript and must have precise statistics. It should not have acronyms or abbreviations. It should be logical in itself. Do not cite references at this point.

An abstract is a brief, distinct paragraph summary of finished work or work in development. In a minute or less, a reviewer can be taught the foundation behind the study, common approaches to the problem, relevant results, and significant conclusions or new questions.

Write your summary when your paper is completed because how can you write the summary of anything which is not yet written? Wealth of terminology is very essential in abstract. Use comprehensive sentences, and do not sacrifice readability for brevity; you can maintain it succinctly by phrasing sentences so that they provide more than a lone rationale. The author can at this moment go straight to shortening the outcome. Sum up the study with the subsequent elements in any summary. Try to limit the initial two items to no more than one line each.

Reason for writing the article—theory, overall issue, purpose.

- Fundamental goal.
- To-the-point depiction of the research.
- Consequences, including definite statistics—if the consequences are quantitative in nature, account for this; results of any numerical analysis should be reported. Significant conclusions or questions that emerge from the research.

Approach:

- Single section and succinct.
- An outline of the job done is always written in past tense.
- Concentrate on shortening results—limit background information to a verdict or two.
- Exact spelling, clarity of sentences and phrases, and appropriate reporting of quantities (proper units, important statistics) are just as significant in an abstract as they are anywhere else.

Introduction:
The introduction should "introduce" the manuscript. The reviewer should be presented with sufficient background information to be capable of comprehending and calculating the purpose of your study without having to refer to other works. The basis for the study should be offered. Give the most important references, but avoid making a comprehensive appraisal of the topic. Describe the problem visibly. If the problem is not acknowledged in a logical, reasonable way, the reviewer will give no attention to your results. Speak in common terms about techniques used to explain the problem, if needed, but do not present any particulars about the protocols here.
The following approach can create a valuable beginning:

- Explain the value (significance) of the study.
- Defend the model—why did you employ this particular system or method? What is its compensation? Remark upon its appropriateness from an abstract point of view as well as pointing out sensible reasons for using it.
- Present a justification. State your particular theory(-ies) or aim(s), and describe the logic that led you to choose them.
- Briefly explain the study's tentative purpose and how it meets the declared objectives.

**Approach:**

Use past tense except for when referring to recognized facts. After all, the manuscript will be submitted after the entire job is done. Sort out your thoughts; manufacture one key point for every section. If you make the four points listed above, you will need at least four paragraphs. Present surrounding information only when it is necessary to support a situation. The reviewer does not desire to read everything you know about a topic. Shape the theory specifically—do not take a broad view.

As always, give awareness to spelling, simplicity, and correctness of sentences and phrases.

**Procedures (methods and materials):**

This part is supposed to be the easiest to carve if you have good skills. A soundly written procedures segment allows a capable scientist to replicate your results. Present precise information about your supplies. The suppliers and clarity of reagents can be helpful bits of information. Present methods in sequential order, but linked methodologies can be grouped as a segment. Be concise when relating the protocols. Attempt to give the least amount of information that would permit another capable scientist to replicate your outcome, but be cautious that vital information is integrated. The use of subheadings is suggested and ought to be synchronized with the results section.

When a technique is used that has been well-described in another section, mention the specific item describing the way, but draw the basic principle while stating the situation. The purpose is to show all particular resources and broad procedures so that another person may use some or all of the methods in one more study or referee the scientific value of your work. It is not to be a step-by-step report of the whole thing you did, nor is a methods section a set of orders.

**Materials:**

*Materials may be reported in part of a section or else they may be recognized along with your measures.*

**Methods:**

- Report the method and not the particulars of each process that engaged the same methodology.
- Describe the method entirely.
- To be succinct, present methods under headings dedicated to specific dealings or groups of measures.
- Simplify—detail how procedures were completed, not how they were performed on a particular day.
- If well-known procedures were used, account for the procedure by name, possibly with a reference, and that's all.

**Approach:**

It is embarrassing to use vigorous voice when documenting methods without using first person, which would focus the reviewer's interest on the researcher rather than the job. As a result, when writing up the methods, most authors use third person passive voice.

Use standard style in this and every other part of the paper—avoid familiar lists, and use full sentences.

**What to keep away from:**

- Resources and methods are not a set of information.
- Skip all descriptive information and surroundings—save it for the argument.
- Leave out information that is immaterial to a third party.
Results:
The principle of a results segment is to present and demonstrate your conclusion. Create this part as entirely objective details of the outcome, and save all understanding for the discussion.

The page length of this segment is set by the sum and types of data to be reported. Use statistics and tables, if suitable, to present consequences most efficiently.

You must clearly differentiate material which would usually be incorporated in a study editorial from any unprocessed data or additional appendix matter that would not be available. In fact, such matters should not be submitted at all except if requested by the instructor.

Content:
- Sum up your conclusions in text and demonstrate them, if suitable, with figures and tables.
- In the manuscript, explain each of your consequences, and point the reader to remarks that are most appropriate.
- Present a background, such as by describing the question that was addressed by creation of an exacting study.
- Explain results of control experiments and give remarks that are not accessible in a prescribed figure or table, if appropriate.
- Examine your data, then prepare the analyzed (transformed) data in the form of a figure (graph), table, or manuscript.

What to stay away from:
- Do not discuss or infer your outcome, report surrounding information, or try to explain anything.
- Do not include raw data or intermediate calculations in a research manuscript.
- Do not present similar data more than once.
- A manuscript should complement any figures or tables, not duplicate information.
- Never confuse figures with tables—there is a difference.

Approach:
As always, use past tense when you submit your results, and put the whole thing in a reasonable order.

Put figures and tables, appropriately numbered, in order at the end of the report.

If you desire, you may place your figures and tables properly within the text of your results section.

Figures and tables:
If you put figures and tables at the end of some details, make certain that they are visibly distinguished from any attached appendix materials, such as raw facts. Whatever the position, each table must be titled, numbered one after the other, and include a heading. All figures and tables must be divided from the text.

Discussion:
The discussion is expected to be the trickiest segment to write. A lot of papers submitted to the journal are discarded based on problems with the discussion. There is no rule for how long an argument should be.

Position your understanding of the outcome visibly to lead the reviewer through your conclusions, and then finish the paper with a summing up of the implications of the study. The purpose here is to offer an understanding of your results and support all of your conclusions, using facts from your research and generally accepted information, if suitable. The implication of results should be fully described.

Infer your data in the conversation in suitable depth. This means that when you clarify an observable fact, you must explain mechanisms that may account for the observation. If your results vary from your prospect, make clear why that may have happened. If your results agree, then explain the theory that the proof supported. It is never suitable to just state that the data approved the prospect, and let it drop at that. Make a decision as to whether each premise is supported or discarded or if you cannot make a conclusion with assurance. Do not just dismiss a study or part of a study as "uncertain."
Research papers are not acknowledged if the work is imperfect. Draw what conclusions you can based upon the results that you have, and take care of the study as a finished work.

- You may propose future guidelines, such as how an experiment might be personalized to accomplish a new idea.
- Give details of all of your remarks as much as possible, focusing on mechanisms.
- Make a decision as to whether the tentative design sufficiently addressed the theory and whether or not it was correctly restricted. Try to present substitute explanations if they are sensible alternatives.
- One piece of research will not counter an overall question, so maintain the large picture in mind. Where do you go next? The best studies unlock new avenues of study. What questions remain?
- Recommendations for detailed papers will offer supplementary suggestions.

Approach:

When you refer to information, differentiate data generated by your own studies from other available information. Present work done by specific persons (including you) in past tense.

Describe generally acknowledged facts and main beliefs in present tense.

The Administration Rules

Administration Rules to Be Strictly Followed before Submitting Your Research Paper to Global Journals Inc.

*Please read the following rules and regulations carefully before submitting your research paper to Global Journals Inc. to avoid rejection.*

*Segment draft and final research paper:* You have to strictly follow the template of a research paper, failing which your paper may get rejected. You are expected to write each part of the paper wholly on your own. The peer reviewers need to identify your own perspective of the concepts in your own terms. Please do not extract straight from any other source, and do not rephrase someone else's analysis. Do not allow anyone else to proofread your manuscript.

*Written material:* You may discuss this with your guides and key sources. Do not copy anyone else's paper, even if this is only imitation, otherwise it will be rejected on the grounds of plagiarism, which is illegal. Various methods to avoid plagiarism are strictly applied by us to every paper, and, if found guilty, you may be blacklisted, which could affect your career adversely. To guard yourself and others from possible illegal use, please do not permit anyone to use or even read your paper and file.
Please note that following table is only a Grading "Paper Compilation" and not on "Performed/Stated Research" whose grading solely depends on Individual Assigned Peer Reviewer and Editorial Board Member. These can be available only on request and after decision of Paper. This report will be the property of Global Journals.

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