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Highlights

Management of Pemphigus Vulgaris

Analytical Retrospective Comparative Study

Discovering Thoughts, Inventing Future

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Humanization: The Solution for Non-Physical Pain in the Hospital Environment

By Sabrina Carvalho Miname

Abstract- Getting sick, in general, is an unexpected and frustrating event in people's lives, providing feelings such as anxiety, fear and anguish. Cicely Saunders classifies the set of physical, emotional, environmental, and social sensations that such an event causes as "Total Pain", which includes both the patient and the companions. In this context, it is essential that the health professional is prepared to welcome the patient and company with a humanized approach, also seeking to solve non-physical pain in the hospital environment. Thus, humanization becomes an indispensable item at all levels of care.

Keywords: *humanization, total pain, hospital care.*

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HUMANIZATION THE SOLUTION FOR NONPHYSICAL PAIN IN THE HOSPITAL ENVIRONMENT

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Humanization: The Solution for Non-Physical Pain in the Hospital Environment

Humanização: A Solução Para Dores Não Físicas Do Ambiente Hospitalar

Sabrina Carvalho Miname

Resumo- Adoecer, de modo geral, é um evento inesperado e frustrante na vida das pessoas, proporcionando sentimentos como ansiedade, medo e angústia. Cicely Saunders classifica o conjunto de sensações físicas, emocionais, ambientais e social que tal evento provoca como “Dor Total”, que inclui tanto o paciente como os acompanhantes. Nesse contexto, é essencial que o profissional da saúde esteja preparado para acolher o paciente e companhia com uma abordagem humanizada, buscando solucionar também as dores não físicas no ambiente hospitalar. Assim, a humanização se torna um item indispensável em todos os níveis de cuidado.

Palavras-Chave: humanização, dor total, atendimento hospitalar.

Abstract- Getting sick, in general, is an unexpected and frustrating event in people's lives, providing feelings such as anxiety, fear and anguish. Cicely Saunders classifies the set of physical, emotional, environmental, and social sensations that such an event causes as “Total Pain”, which includes both the patient and the companions. In this context, it is essential that the health professional is prepared to welcome the patient and company with a humanized approach, also seeking to solve non-physical pain in the hospital environment. Thus, humanization becomes an indispensable item at all levels of care.

Keywords: humanization, total pain, hospital care.

I. INTRODUÇÃO

A classificação de um paciente terminal se dá quando esgotam-se as possibilidades de regate das condições de saúde, e a possibilidade de morte próxima parece inevitável e imprevisível. A esses pacientes existem práticas de assistência que promovem uma melhora na qualidade de vida: os cuidados paliativos. (Gutierrez, 2001)

Cicely Saunders foi a pioneira de tais práticas no século XX, com a inclusão de um novo modelo no ambiente hospitalar: compreender e atender as suas necessidades na medida possível. Ainda que esse seja o princípio dos cuidados paliativos, a médica e assistente social ainda criou uma tese sobre dor, que integra áreas não físicas aplicadas à condição terminal.

II. DOR TOTAL E TEORIA DO CONFORTO

Ao longo do desenvolvimento dos cuidados paliativos, Cicely Saunders deixa uma percepção sobre

os pacientes: a dor é multidimensional, sendo um conjunto de sintomas físicos, sofrimento mental, contexto social e dificuldades emocionais. A fim de agrupar essas dimensões, surgiu o conceito de “Dor Total”, de modo que a intervenção apenas nos sintomas físicos, por exemplo, não promove a resolução da dor.

Em continuação ao estudo de Saunders, Katharine Kolcaba, enfermeira do século XX, buscou entender as soluções para a dor integrada por meio do conforto, “uma experiência imediata de ser fortalecido por ter as necessidades de alívio, tranquilidade e transcendência atendidos em quatro contextos: físico, psicoespiritual, social e ambiental”. Nesse contexto, a Teoria do Conforto abrange práticas que abordam o conforto em várias dimensões, buscando resolver a dor de forma integrada. (Castro, Fuly, Santos, & Chagas, 2021).



Imagem 01: Dimensões da Teoria do ConfortoFonte: imagem autoral

Ainda que as reflexões de Kolcaba não incluam a dor existencial, a busca pelo “Conforto Total” gerou um direcionamento importante para gerações futuras de profissionais da saúde: investir em soluções para dores não físicas no ambiente hospitalar.

Coincidentemente, Kolcaba usufruiu da humanização ao por em prática suas teses, a exemplo dos “alimentos para a alma”: massagens, ambientação e imaginação guiada. Isso porque, humanizar é observar cada pessoa em sua individualidade, ampliando as possibilidades para que possa exercer sua autonomia. (Simões, Bittar, Mattos, & Sakai, 2007)

Adoecer, de modo geral, é um evento inesperado e frustrante na vida das pessoas, proporcionando sentimentos como ansiedade, medo e angústia. Nesse contexto, é essencial que o profissional da saúde esteja preparado para acolher o paciente com uma abordagem humanizada, e portanto, humanizar se torna o marco inicial para solucionar dores não físicas no ambiente hospitalar, se tornando um item indispensável em todos os níveis de cuidado. (Vinhando, Otani, Higa, Mielo, & Lemes, 2019)

Apesar do paciente ser prioridade, é importante ressaltar que a multidimensionalidade da dor também inclui os acompanhantes. A família, como exemplos principais de acompanhantes, é a principal fonte de apoio no adoecimento, e se tornam tão vulneráveis ao medo, angústia e impotência quanto o paciente. (Silva & Guedes, 2017)

Apesar da ausência de estudos específicos, na prática percebe-se que em cuidados paliativos, principalmente, os acompanhantes sentem uma dor total ainda mais intensa que o paciente, por exemplo quando o paciente está em coma. Desse modo, os acompanhantes se tornam uma figura importante no ambiente hospitalar, não apenas em compreender a informação, melhorar a comunicação e ser apoio.

Assim, a humanização se faz essencial em todas as pessoas associadas às enfermidades hospitalares.

III. OBJETIVOS

Tendo em vista os aspectos discutidos, o objetivo desse trabalho é ressaltar a humanização como forma de solução para dores não físicas no ambiente hospitalar.

IV. MÉTODOS

Trata-se de uma revisão bibliográfica que se deu por meio de consulta das seguintes fontes: Lilacs (Literatura Latino-Americana e do Caribe em Ciências da Saúde), SciELO (Scientific Electronic Library Online) e Pubmed, abrangendo o período das publicações entre 2001 e 2021. As buscas se deram em julho de 2022, utilizando-se dos seguintes descritores: “dor total”, “humanização hospitalar” e “atendimento humanizado”.

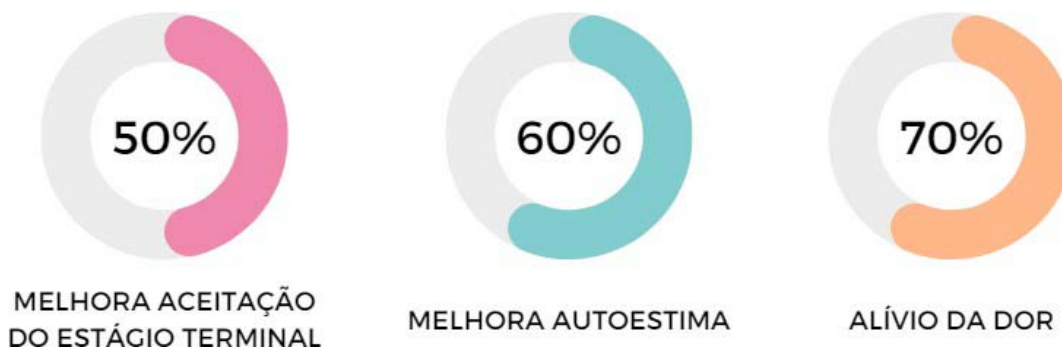
Dentre os artigos encontrados foram selecionados 10 deles que atendiam aos critérios: publicação entre 2001 e 2021, acesso livre aos artigos nas bases de dados pesquisadas. A seleção dos artigos foi realizada de acordo com relevância ao tema estudado, atendimento aos critérios e leitura na íntegra dos artigos remanescentes após etapas anteriores.

V. RESULTADOS E DISCUSSÃO

Ainda que o termo “humanização” seja algo novo para ambientes hospitalares, inclui práticas que estão sendo feitas há séculos em unidades alternativas de cuidado, na forma de “alimentos para a alma” como sugere o estudo de Kolcaba. Tais práticas, por integrarem diversas áreas da dor total, promovem resultados multidimensionais e portanto, são indispensáveis quando se encontra uma dor integrada.

Um estudo feito em Bioética e humanização na fase final da vida: visão de médicos, 2011 aponta os efeitos positivos de um atendimento humanizado, com ênfase em cuidados paliativos, de modo que os

resultados apontam características decisivas para um tratamento melhor. (Oliveira, Flávio, Marengo, & Silva, 2011).



Fonte: imagem autoral

Imagem 02: Resultados apresentados no artigo Bioética e humanização na fase final da vida: visão de médicos, 2011.

Os efeitos da humanização na saúde são comprovadamente eficazes, entretanto, ainda assim não é uma prática frequente dentro do ambiente hospitalar. Isso porque existem muitas detalhas a serem discutidas antes de torná-la efetiva, como o estímulo dentro das instituições de ensino voltadas à saúde. Como aponta (Izabel Cristina & Sirino, 2015), a formação médica tende a ser voltada para aspectos biomédicos, reduzindo propostas das práticas de saúde de ensino a ações de amenização de tensões cotidianas na área da saúde.

Assim, os estudos de Kolcaba ressaltam cada vez mais a necessidade de complementar a medicina tradicional, cujo ensino não reconhece as dores não físicas e portanto, não sugere soluções para o impasse. Martins (2001), citado no trabalho de Mota et.al, tenta explicar o motivo da ausência desse complemento: “a humanização é um processo amplo, demorado e complexo, pois envolvem mudanças de comportamento, que sempre despertam insegurança”.

É relevante ressaltar que o ato de humanizar é como qualquer qualidade humana, só se consolidará se for praticada. Isso se torna ainda mais complexo uma vez que a dor total é considerada algo imensurável, por ser um conjunto de vários fatores, tornando cada paciente único. Se os profissionais da saúde apresentam tamanha dificuldade em reconhecer a dor total, sendo treinados para reconhecer e direcionar parte dela, é indubitavelmente mais difícil para o acompanhante ser intermediário de comunicação e apoio.

Desse modo, se faz ainda mais essencial humanizar o ambiente como um todo, incluindo os acompanhantes. Um estudo feito em o Atendimento humanizado em unidade pediátrica: percepção do acompanhante da criança hospitalizada exemplifica, com palavras dos acompanhantes, os efeitos da humanização: “Tem um médico que atendeu ele muito

bem, me explicava o que tava acontecendo e até mostrava as fotos, e pedia se eu tinha mais alguma pergunta. Eu saía satisfeita, entendeu?”.

Vale ressaltar que nesse estudo os pacientes não tinham ideia do que é humanização, mas foram incluídos em sua prática. Informar o paciente e o acompanhante sobre o tratamento é o exemplo mais claro de como aplicar a humanização, mas não é o único. Durante o desenvolvimento desta qualidade, surgem cada dia mais oportunidades de humanizar adequados a cada situação, de modo que não existe um passo a passo assim como todas as condições são ensinadas na medicina.

VI. CONCLUSÃO

A partir dos estudos apresentados, humanizar o atendimento à saúde é o marco inicial para solucionar dores não físicas no ambiente hospitalar, se tornando um item indispensável em todos os níveis de cuidado.

Cicely Saunders definiu o conceito de dor total aplicado à condições terminais, no entanto, a dor integrada vale para quaisquer situações hospitalares. Em sequência ao ilustre pensamento da médica, Kolcaba sugere soluções com “alimentos pra a alma”, que existem há séculos. Imprevistamente, Kolcaba deixa o principal desafio para as novas gerações de profissionais da saúde: integrar tais “alimentos” com o ensino médico tradicional, a fim de melhorar a relação médico-paciente e médico-acompanhante.

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Advances in the Management of Pemphigus Vulgaris: A Review Article

By Reshale Johar & Rahaf Alhabbab

King Saud Bin Abdul-Aziz University

Abstract- Pemphigus Vulgaris (PV) is a debilitating autoimmune disease with a genetic predilection. In most cases, PV affects the oral mucosa, but can also occur in conjunction with skin lesions affecting different areas of the body. Lesions affecting the oral mucosa are characterized by the presence of erosions whereas, skin lesions appear mainly as flaccid bulla in their early stages or as erosions later in the disease course. Pemphigus Vulgaris characterized by the formation of highly fragile bulla that frequently ruptures, forming denuded, painful, easily bleeding erosions that often become crusted.

Proper diagnosis is considered a significant component of early and efficient management, resulting in less morbidity. The use of corticosteroids in conjunction with immunosuppressant drugs such as azathioprine and mycophenolate in the management of acute attacks has been applied throughout the years (1).

Keywords: flaccid bulla, desmosomes, nikolsky sign, asboe-hansen sign, immunofluorescence, corticosteroids, immunosuppressant, anti-cd20 monoclonal antibodies.

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ADVANCES IN THE MANAGEMENT OF PEMPHIGUS VULGARIS: A REVIEW ARTICLE

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Reshale Johar^α & Rahaf Alhabbab^α

Abstract- Pemphigus Vulgaris (PV) is a debilitating autoimmune disease with a genetic predilection. In most cases, PV affects the oral mucosa, but can also occur in conjunction with skin lesions affecting different areas of the body. Lesions affecting the oral mucosa are characterized by the presence of erosions whereas, skin lesions appear mainly as flaccid bulla in their early stages or as erosions later in the disease course. Pemphigus Vulgaris is characterized by the formation of highly fragile bulla that frequently ruptures, forming denuded, painful, easily bleeding erosions that often become crusted.

Proper diagnosis is considered a significant component of early and efficient management, resulting in less morbidity. The use of corticosteroids in conjunction with immunosuppressant drugs such as azathioprine and mycophenolate in the management of acute attacks has been applied throughout the years (1). This practice has exposed patients to the consequential systemic complications associated with prolonged use of these drugs. However, safer and more cost-effective treatments have been introduced. In this review article, we present the clinical, pathophysiologic, diagnostic, and therapeutic aspects of Pemphigus Vulgaris.

Keywords: flaccid bulla, desmosomes, nikolsky sign, asboe-hansen sign, immunofluorescence, corticosteroids, immunosuppressant, anti-cd20 monoclonal antibodies.

I. PURPOSE

To review Pemphigus Vulgaris in regards to clinical manifestations, diagnosis, and management, presenting the latest therapeutic measures in treating patients with safer and less long-term complications.

II. METHODS

In this article, we present the prevalence of Pemphigus Vulgaris and the ethnic considerations taken in the development of the disease. We also discuss different methods of diagnosing Pemphigus Vulgaris and managing patients to yield the best prognostic results. The article publishes data obtained from the Medline/PubMed online database, using the following search terms and key words: "Pemphigus Vulgaris,

Corticosteroids, Immunosuppressant and Anti-CD20 monoclonal antibodies".

III. RESULTS

The article identifies clinical and laboratory findings that must be considered in the evaluation of patients with Pemphigus Vulgaris (PV). Early diagnosis and management using Anti-CD20 monoclonal antibodies in PV patients reveal longer-lasting results with less corticosteroids use when compared to immunosuppressant therapy associated with better short and long-term outcomes.

IV. CONCLUSION

All patients with chronic mucous membranes ulcers with or without skin bulla must undergo a thorough history and physical evaluation, including intra and extra oral examinations. Correctly diagnosing patients with Pemphigus Vulgaris using histopathology and immunofluorescence facilitates early management utilizing optimal therapeutic options with the least possible side effects.

V. INTRODUCTION/DISCUSSION

Pemphigus Vulgaris (PV) is the most common type of autoimmune bullous disease known as Pemphigus, characterized by chronic relapse that usually occurs within two years following diagnosis (2). Pemphigus Vulgaris is rare, affecting both the skin and mucous membranes. Oral mucosa can be the only site affected in many cases and usually precedes skin involvement (3,4). It occurs most commonly in adults between the ages of 40 and 60 (5), with rare occurrences in children. Pemphigus Vulgaris has a higher propensity for people with Jewish inheritance and those from the Middle East and India (6), with most studies indicating female predisposition (7). It presents clinically as painful blisters or erosions that can result in patient debilitation. Skin epidermal integrity is maintained by the desmosomes present between keratinocytes (8). In Pemphigus Vulgaris, IgG antibodies attack cell surface receptors, particularly desmoglein Dsg3 and Dsg1 of the cadherin family (9), destroying the junction between cells resulting in loss of integrity manifested clinically by blisters (10). Developed blisters are highly fragile. They can rupture easily and coalesce together, resulting in large painful ulcers at a high risk of

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infection. Approximately 50% of patients only develop intraoral blisters, with palatal and buccal mucosa being the two most commonly affected sites. Other vulnerable locations include the nose, larynx, pharynx, esophagus, conjunctiva, and genitalia (11,12).

Pemphigus Vulgaris should always be suspected in patients presenting with chronic mucosal ulcers, especially when they are associated with skin bullae. They must also be differentiated from other bullous dermatoses.

Clinical examination of suspected cases is used to detect loss of epidermal cell adhesion. Positive Nikolsky and Asboe-Hansen signs are indicative of PV. Nikolsky sign is considered positive if normal epidermal skin layer adjacent to formed bulla moves laterally upon pressure application (13). Asboe-Hansen sign is tested by applying gentle pressure on intact unruptured bulla resulting in subdermal fluid spreading away from the site of pressure (14). Enzyme-linked immunosorbent assays (ELISA) is used to identify and quantify the autoantibodies, it is also used to titrate the circulating autoantibodies to guide the treating physician in the management decision at the remission phase (15). A correlation between autoantibodies (anti-Dsg1/anti-Dsg3) titer has been associated with the disease activity, showing earlier relapse during remission in patients with high anti-Dsg3 titers (> 20 U/mL) (16). Where lower Dsg-1 titers are found to be associated with longer relapse time (17). However, a biopsy of the lesion with the surrounding skin is indicated to confirm diagnosis. Histopathological examination of the affected tissue will reveal intracellular acantholysis with an intact, unseparated basement membrane (18). This feature differentiates it from bullous pemphigoid, which is considered a less severe entity. Direct immunofluorescence (DIF) testing will reveal IgG and C3 immune deposits bound to cellular desmogleins (DSG), creating a "net-like" pattern that indicates intercellular separation. Indirect immunofluorescence (IIF) of the serum antibodies is a tool to monitor the progression of the diseases and the outcome of the treatment (19).

Different scoring systems have been used in assessing the disease severity and its response to treatment, such as the Autoimmune Bullous Skin Disorder Intensity Score (ABSIS) and the Pemphigus Disease Area Index (PDAI). The former scoring system measures the changes in pemphigus disease severity, providing both qualitative and quantitative information, and both objective and subjective information for oral involvement, making it superior to other scoring systems (20). The later scoring system (PDAI) consists of three components, including skin, scalp, and mucous membranes, measuring both disease activity and damage level. It has a total possible score ranging from zero to 263, with 250 points representing disease activity, divided as 120 points for skin activity, 10 points for scalp activity and 120 points for mucosal activity, and

13 from damage scores (21). Other less common scoring systems have been applied, including; Pemphigus area and activity score (PAAS), Ikeda index, and Mahajan et al. severity scoring) (22).

The main goal in treating patients with PV is to lower the production of pathogenic autoantibodies. Managing patients in the acute phase of Pemphigus Vulgaris has traditionally been conducted by administering the smallest possible dose of systemic glucocorticoids such as prednisolone (23) to avoid the possible major systemic complications associated with using higher doses. At this stage, patients are also prescribed immunosuppressant drugs such as azathioprine and mycophenolatemofetil (MMF) (24). Tapering the corticosteroids can only be done after the patient has achieved remission; frequent negative Nikolsky's sign is indicative of remission. After the cessation of corticosteroids, other immunosuppressant drugs can also be tapered while maintaining remission based on the patient's renal and liver function (25,26). Both Azathioprine and MMF are purine synthesis inhibitors (purine analog) that require close monitoring to reduce their known possible side effects. The most common side effect associated with Azathioprine use is nausea, but other complications, such as bone marrow suppression resulting in pancytopenia, thrombocytopenia, and leukopenia, are also documented (27). MMF is also associated with possible side effects such as nausea, vomiting and gastrointestinal disturbances, and discomfort.

Long-term use of systemic corticosteroids in patients can result in many serious complications, including osteoporosis, causing fractures in up to 50% of patients and osteonecrosis in up to 40% (28). Other complications include hyperglycemia, hypertension, arrhythmias, edema, weight gain, skin thinning and atrophy, cataracts, GI bleeding, impaired wound healing, and neuropsychiatric adverse effects (29).

Anti-CD20 monoclonal antibodies, such as rituximab and ofatumumab, have been introduced to the management of PV, revealing a significant clinical improvement in patients along with reducing the use of concomitant immunosuppressive medication. These medications function by inhibiting B lymphocytes maturation into autoantibody-producing plasma cells by targeting CD20 antigen on pre-B, immature, and mature B, resulting in antibody-dependent cytotoxicity followed by apoptosis (30), without affecting immunoglobulin synthesis since CD20 is not expressed on stem cells and plasma cells, resulting in the best possible outcome with reduced or complete elimination of corticosteroids use with long lasting results with a single treatment course (31). A randomized, controlled trial comparing the use of rituximab and mycophenolatemofetil in managing PV patients reported superior outcomes with Rituximab therapy producing sustained complete remission at 52 weeks with a higher reduction in

glucocorticoid use (32). Another predictive study of relapse concluded that positively identifying either anti-Dsg1 or anti-Dsg3 antibodies detected with ELISA test following rituximab treatment showed to be associated with disease relapse (33,34). Maho-Vaillant et al. demonstrated that long-lasting Rituximab therapy efficacy is associated with long duration of serum anti-DSG-1 and anti-DSG-3 IgGp Abs disappearance following the absence of DSG-specific B cells (35).

Rituximab therapy is associated with multiple side effects, including nausea, vomiting, fever, and headaches, reported to occur mainly during the first infusion. However, other complications have been reported, such as pneumonia and septic arthritis (36). Another rare but serious complication that can result secondary to Rituximab use is the development of viral infection of the brain white matter known as progressive multifocal leukoencephalopathy (PML) (37).

VI. CONCLUSION

Pemphigus Vulgaris is an autoimmune disease, mainly managed with corticosteroids and immunosuppressants, subjecting patients to multiple serious complications. The introduction of Anti-CD20 monoclonal antibodies treatment revealed significant long-term clinical improvement with single course infusion and a noticeable reduction of the concurrent corticosteroid use in patients with PV. However, future antigen-specific targeted treatments need to be further studied to improve therapeutic outcomes and decrease disease relapse.

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Effect of Long-Term use of N95 Masks on Respiratory Gases, Volumes and Capacities of Medical and Paramedical Personnel: A Pilot Study

By Saloni Rani Kumar, Dr. Anuj Kumar, Dr. Ankush Jindal,
Dr. Hargunbir Singh, Adhish Beri & Gurmehar Singh Hundal

Abstract- Background: The spread of coronavirus can be greatly reduced by the usage of face coverings, as coronavirus is mainly spread through droplets when people talk, cough or sneeze, and through airborne transmission. N95 respirator mask is a protective device which is used to filter out the airborne particles with a very high efficiency, which is approximately up to 95%. The use of N95 mask in India has increased by a very high proportion due to the on-going coronavirus pandemic.

Objectives: The constant use of N95 respirators by the personnel on duty for about six hours or more may influence the respiratory gases, volumes and capacities.

Keywords: statistical knowledge, respiratory volumes and capacities, respiratory gases, medical curriculum, evidence-based medicine, critical appraisal, medical and paramedical personnel, oxygen saturation, pCO_2 , FEV_1 , FVC.

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Effect of Long-Term use of N95 Masks on Respiratory Gases, Volumes and Capacities of Medical and Paramedical Personnel: A Pilot Study

Saloni Rani Kumar ^α, Dr. Anuj Kumar ^σ, Dr. Ankush Jindal ^ρ, Dr. Hargunbir Singh ^ω, Adhish Beri [¥], & Gurmehar Singh Hundal [§]

Abstract- Background: The spread of coronavirus can be greatly reduced by the usage of face coverings, as coronavirus is mainly spread through droplets when people talk, cough or sneeze, and through airborne transmission. N95 respirator mask is a protective device which is used to filter out the airborne particles with a very high efficiency, which is approximately up to 95%. The use of N95 mask in India has increased by a very high proportion due to the on-going coronavirus pandemic.

Objectives: The constant use of N95 respirators by the personnel on duty for about six hours or more may influence the respiratory gases, volumes and capacities. Since the usage of masks has increased manifold, it is very important to know the effects of using the mask for longer duration of time. Thus, the research is focused on finding its effect on the respiratory gases, volumes and capacities.

Methods: A one-time assessment for every subject was performed, wherein the subject underwent a proposed work of venous blood gas analysis (accompanied by saturation from pulse oximeter) and spirometry. A total of 50 medical and paramedical personnel participated in the study, and their FEV₁, FVC and FEV₁/FVC values were determined from the spirometer, while the physiological and biochemical parameters of pCO₂ and oxygen saturation were determined from the blood gas analysis and pulse oximeter. Statistical analysis compared the fore-mentioned parameters in wearing a N95 respirator with those wearing only a three-ply surgical mask.

Results: There was no significant impact on the FEV₁, FVC and FEV₁/FVC ratio of the individuals wearing both N95 respirator and surgical mask. No significant difference was observed in the normal values for the individuals, according to their physiological and physical condition, and the results obtained on spirometry. The percentage saturation of oxygen and carbon dioxide was within the normal ranges for both three-ply surgical mask and N95 respirator users.

Conclusions: Six hours of continuous N95 respirator use did not cause any significant increase in carbon dioxide levels

compared to the usage of a three-ply surgical mask for the same duration of time. The N95 respirators are safe to use for long work- hours without causing any detrimental effects on the metabolic and pulmonary physiology of the wearer.

Keywords: statistical knowledge, respiratory volumes and capacities, respiratory gases, medical curriculum, evidence-based medicine, critical appraisal, medical and paramedical personnel, oxygen saturation, pCO₂, FEV₁, FVC.

I. INTRODUCTION

With the start of the year 2020, the SARS-CoV-2 gripped the world and became one of the deadliest pandemics the world had ever seen. The severe acute respiratory syndrome novel coronavirus 2 (SARS-nCoV-2), according to the studies by Lai C et al.¹, is transmitted from one human to the other through a direct contact, or through droplets, with an average incubation period standing at 6.4 days.

The aerosol transmission has been not focused on, but there are various essential reasons to doubt that it might play a role in the high transmission rate of the virus. Booth et al.² performed air sampling, which was used to establish that a patient, who had been hospitalized due to an infection of SARS during the 2003 pandemic, released the virus into the air in an aerosolised form. It is important to mention that SARS-CoV-1 is the next of kin to the current pandemic of SARS-nCoV-2.

Currently, with evidence to support this, many infected individuals have been transmitting the virus without showing any symptoms. Such asymptomatic individuals, in general, do not cough or sneeze, which leaves direct/ indirect contact modes and aerosol transmission as the leading likely modes of transmission.³ Chan et al.⁴, Zou et al.⁵, Hu et al.⁶, in China, have reported the positive test results of various individuals despite of them showing no symptoms at all. The transmission of the virus from these asymptomatic carriers was confirmed by Rothe et al.⁷. Studies led by Li et al.⁸ also calculated that 86% of the infections in China, before the travel restrictions were implemented, were

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through individuals who have not been documented and showed no or mild symptoms and thus, had not been tested.

The wearing of masks by the community can possibly help in preventing the spread of COVID-19 by decreasing the emission of infected saliva and the respiratory droplets (described above as probable modes of transmission) from individuals with a subclinical or a mild case of the disease.⁹ The use of facemasks by the medical and paramedical workers has decreased the rate of transmission of droplets while working on patient with respiratory infections.¹⁰ Studies by Jefferson et al¹¹ calculated the reduction in the spread of infection by 80% if the health care workers wore masks while caring for patients.

With the increase in the usage of the masks came the question of the effect of the long- term use of the masks on the respiratory physiology of the user, and the effects seen on the respiratory gases, volumes and capacities as well.

20 young and healthy healthcare workers were subjected to exercise on a treadmill, at a low- moderate work rate, while wearing four different models of N95 fitting facepiece respirators, for one hour each. Two of the respirators were equipped with exhalation valves. Kim et al¹² concluded that the pulmonary and heart rate responses were relatively small and they should be, on a general basis, tolerated by healthy persons.

To face the short supply and to extend the life of a N95 respirator during the pandemic influenza outbreak, the Institute of Medicine had advocated the use of surgical mask over N95 filtering face piece respirator. 30 National Institute for Occupational Safety and Health (NIOSH) – approved N95 models were taken, accompanied or unaccompanied by a surgical mask, and they were evaluated using automated breathing and metabolic simulator through six incremental work rates. As a result, the concentrations of average inhaled carbon dioxide and the average inhaled oxygen were increased with increasing oxygen consumption for both the subject groups. For a majority of the work rates, the peak inhalation and exhalation pressures were found to be statistically higher in N95 mask with a surgical mask as compared to the N95 mask only. In conclusion by Edward et al¹³, the difference in the concentration of inhaled gases, in both the subject groups, was notable, particularly at lower levels of energy expenditure.

A study was also conducted to find the relation between the use of N95 respirator with the nasal physiology. A total of 77 volunteers (healthcare workers) were a part of the study by Zhu et al.¹⁴ After resting at room temperature for thirty minutes, the initial measurement of the nasal geometry was done using acoustic rhinometry. After the initial assessment, the subjects were exhorted to wear the above two respirators for three hours.

This was immediately followed by rhinomanometry and acoustic rhinometry measurements. Repeated measurements were also done at 30- minute intervals for a continuous period of 1.5 hours. The results of the study showed that the N95 respirator was found to cause a higher post- wearing nasal resistance.

Hua et al¹⁵ concluded that the N95 respirator trapped the respired air within the respirator which increased the volume of fraction of respired air during inspiration, which could feasibly be one of the vital promoters for an increased level of carbon dioxide. During expiration, the volume of fraction (VOF) of respired air was above 95%. The study was done by using a “three-dimensional model of normal human nasal cavity to simulate the volume of fraction of both fresh air and respired air within the nasal cavity”.

Studies conducted by Davis et al¹⁶ showed that at 2 metabolic equivalents (example, walking slowly during rounds), N95 mask use conspicuously increased inhaled carbon dioxide, reduced inspired oxygen, and increased the work of breathing. The resulting inhaled carbon dioxide of 2 to 3% (normal 0.04%) produced transient acidosis and compensatory increases in minute ventilation, work of breathing and cardiac output. Maintaining 4 metabolic equivalents of activity for 10 to 30 minutes, 3 to 5 days per week for four weeks improves respiratory muscle endurance. Such conditioning of respiratory muscle strength and respiratory muscle endurance improves ventilation efficiency (example, ventilation perfusion and alveolar ability exchange), oxygen delivery/lactate removal at locomotor muscle, and overall exercise performance.

With the increase in constant use of N95 respirators and three-ply surgical masks by the personnel on duty for about six hours or more, it has become important to determine the long-term effect that these respirators may have on the respiratory gases, volumes and capacities of the individual.

II. METHOD

a) Subject population

In this case-control trial, the long-term effect of using a N95 mask alone versus using only a three-ply surgical mask was assessed on the biochemical and pulmonary parameters of the healthcare workers. The junior resident doctors of Government Medical College and Hospital, Chandigarh were taken as the subjects.

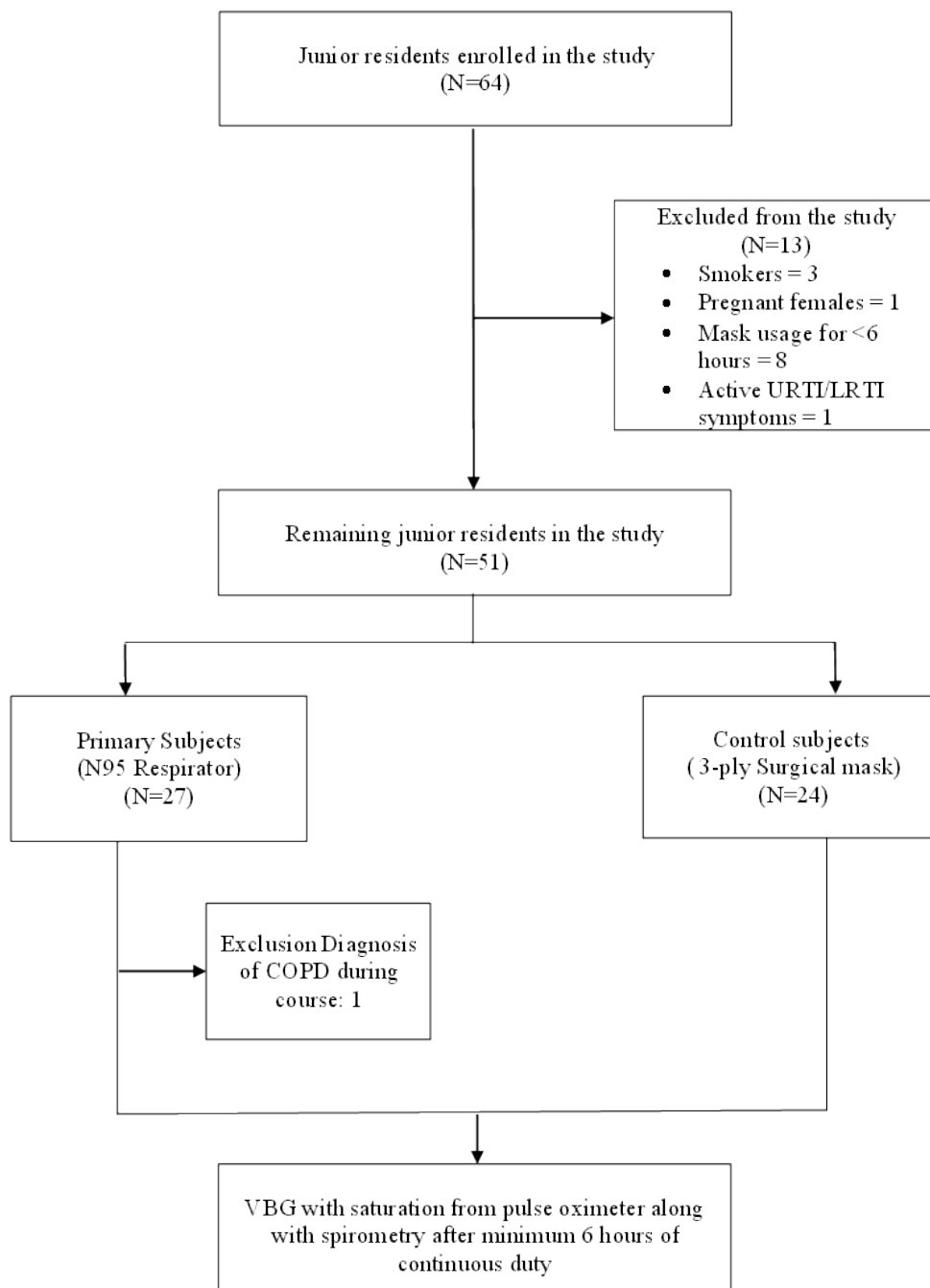
The resident doctors, aged between 20-35 years, working in ICU, Emergency or OPD, able to pass the quantitative fit test, non-smokers (defined as someone who has either never smoked, or not smoked in the last year) with minimum six hours of duty a day and active mask-usage of either N95 or surgical mask for the past minimum six months were considered in the inclusion criteria. The junior residents were excluded on

the conditions which could conceivably cause any risk due to the prolonged wearing of either N95 mask or the surgical mask. These conditions included the usage of mask for less than six hours, a pregnant and/or lactating woman, arrhythmia and/or hypertension, history of any recent major surgery (within the past three months), history of any active medications (allergy medicines, etc.), febrile condition during the course of the research, history of diagnosis of any restrictive/obstructive pulmonary disease, history of smoking and symptoms of any active upper respiratory tract infection (URTI) or lower respiratory tract infection (LRTI) and positive covid test in the past 6 months.

Sixty-four junior residents showed interest in participating in the study. A total of fifty- one subjects were considered as participants, out of which one subject was diagnosed with obstructive lung disease during the course of the research.

b) Respirator and Surgical Mask Selection

Only the subjects that passed the eligibility assessment were taken as participants and divided, randomly, into two groups- one group comprising of residents wearing only a N95 mask and the second group of residents wearing only a three-ply surgical mask.



Flowchart 1

c) *Test Procedures*

Both the control and the N95 studies were randomly allotted the days and times of the procedures after they had completed minimum six months of wearing either a three-ply surgical or a N95 facemask. The timing of procedure was fixed after the completion of minimum six hours of active duty on that particular day. The measurement of the respiratory volumes and capacities was recorded using a spirometer and a venous blood gas sample was taken for the biochemical analysis.

d) *Experimental Design*

Before every procedure, the mouth piece of the spirometer was changed and assessed for adequacy to avoid contamination and to prevent the spread of infection amongst the subjects. A leak test was performed to avoid any discrepancy in the data collection. The procedure of the test was explained in detail to the subject and the subject was allowed to undertake three runs of the test. The subject was then asked to perform the test on another day owing to the difficulty in maintaining a continuous expiratory flow of gases. The blood sample was taken and submitted in the laboratory for the estimation of the values of parameters mentioned below.

e) *Variable Measurements*

The forced expiratory volume in the first second of expiration (FEV_1), forced vital capacity (FVC) and the ratio of FEV_1 to FVC (FEV_1/FVC) were the three chosen criteria for the comparison and compilation of data for the assessment of changes in respiratory volumes and capacities. The values of the same were compared to the standard data set by National Institute of Health, USA.

The venous blood sample of the subject was assessed for the partial pressure of carbon dioxide (pCO_2) and pulse oximeter was used to assess the percentage saturation of oxygen (SpO_2). The values of each parameter were then compared with the standard values released by National Institute of Health, USA.

f) *Statistical Analysis*

We have compared the Forced Expiratory Volume in the first second (FEV_1) and the Forced Vital Capacity (FVC) of every individual involved in the study.

The ratio between these two values has also been compared and plotted as box-plot graph. Percentage saturation of oxygen has been compared for both the masks. To demonstrate statistical significance, a two-sided P value of 0.05 or lower has been considered. The dependent variables were first summarised as means (standard deviations). All the analyses were run to compare the outcome of the variables to see the difference between wearing an N95 mask and wearing a surgical mask on the respiratory volumes and capacities. The analysis was performed using a statistical software package (SPSS v28.0.0.0 (190); IBM, Somerset, NY).

III. RESULTS

A total of sixty-four junior residents were enrolled in the study, out of which thirteen were excluded from the study (smoker-3, pregnant female-1, mask usage for less than six hours-8 and active URTI/LRTI-1) and one participant was excluded during the course of the study due to a diagnosis of COPD. A total of twenty-six subjects wore an N95 mask and twenty-four subjects wore three-ply surgical mask during the study [Flowchart 1]. FEV_1 , FVC, FEV_1/FVC ratio, percentage saturation of oxygen and partial pressure of carbon dioxide were chosen as the parameters. The average FEV_1 for N95 mask users was 3.45L and for three-ply surgical mask users was 3.49L [Table 1]. The average FVC for N95 masks was 3.91L and for three-ply surgical mask users was 3.97L [Table 2]. However, the average FEV_1/FVC ratio for N95 mask users was 88.3% and for three-ply surgical mask users was 87.7% [Table 3].

The percentage saturation of oxygen, calculated by using a spirometer, in N95 respirator and three-ply surgical mask wearers averaged out to be 97.50% and 97.66% respectively [Table 4]. The mean of partial pressure of carbon dioxide was found to be 43.23 mm of Hg with N95 respirator use and at 44.58 mm of Hg with three-ply surgical mask usage [Table 5].

Two-sided p-value for FEV_1 , FVC, FEV_1/FVC ratio, percentage saturation of oxygen and partial pressure of carbon dioxide came out to be 0.736, 0.586, 0.711, 0.426, 0.440 respectively [Table 1-5].

Table 1: Results for Forced Expiratory Volume (FEV_1)

Mask Type	Number of Individuals	Mean	Standard Deviation	Two-sided p Value
N95 mask	26	3.45	.21	0.736
Three-plySurgical Mask	24	3.49	.49	

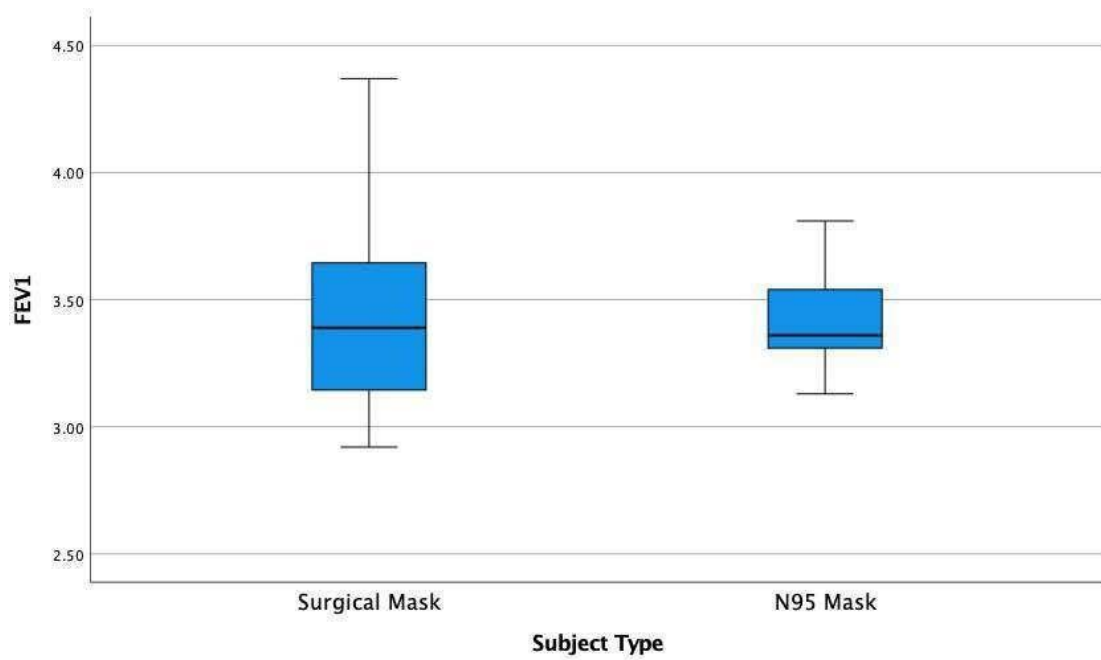


Figure 1: Box-plot graph has been plotted for forced expiratory volume in the first second (FEV_1) with the mask type on the x-axis and the mean value obtained for the individuals on the y-axis.

Table 2: Results for Forced Vital Capacity (FVC)

Mask Type	Number of Individuals	Mean	Standard Deviation	Two-sided p Value
N95 mask	26	3.91	.25	0.586
Three-ply Surgical Mask	24	3.97	.47	

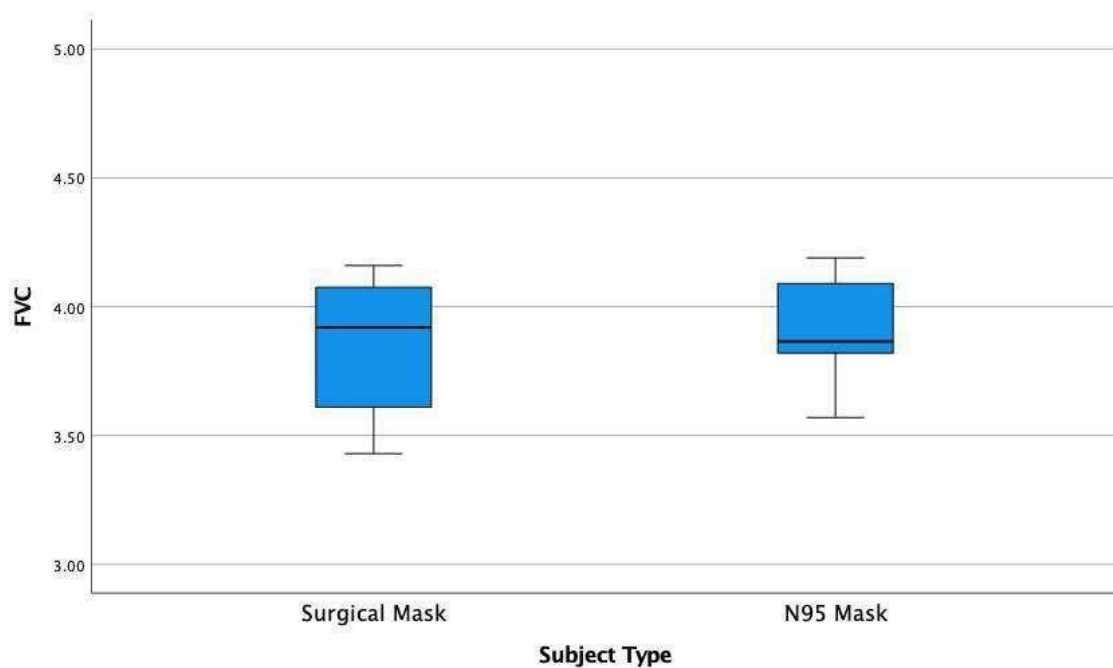


Figure 2: Box-plot graph has been plotted for forced vital capacity (FVC) with the mask type on the x-axis and the mean value obtained for the individuals on the y-axis.

Table 3: Results for FEV₁/FVC ratio,

Mask Type	Number of Individuals	Mean	Standard Deviation	Two- sided p-Value
N95 mask	26	88.3	5.62	0.711
Three-ply Surgical Mask	24	87.7	5.38	

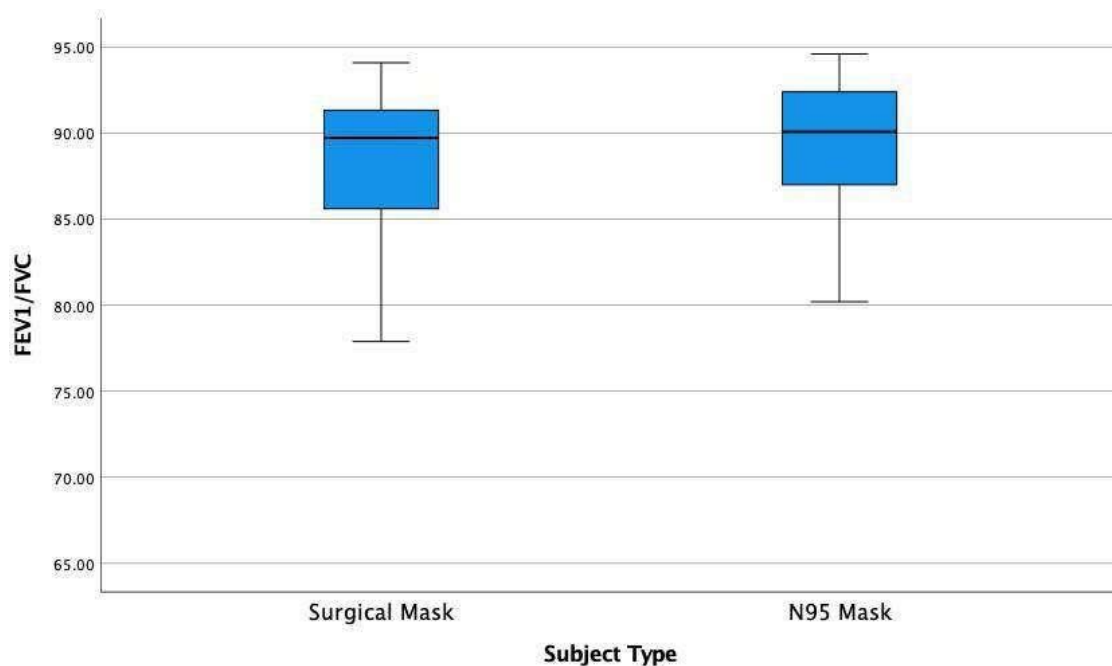


Figure 3: Box-plot graph has been plotted for the ratio between forced expiratory volume in the first second (FEV₁) and forced vital capacity with the mask type on the x-axis and the mean value obtained for the individuals on the y-axis.

Table 4: Results for percentage saturation of oxygen (SpO₂),

Mask Type	Number of Individuals	Mean	Standard Deviation	Two-sided p-Value
N95 mask	26	97.50	0.761	0.426
Three-ply Surgical Mask	24	97.66	0.702	

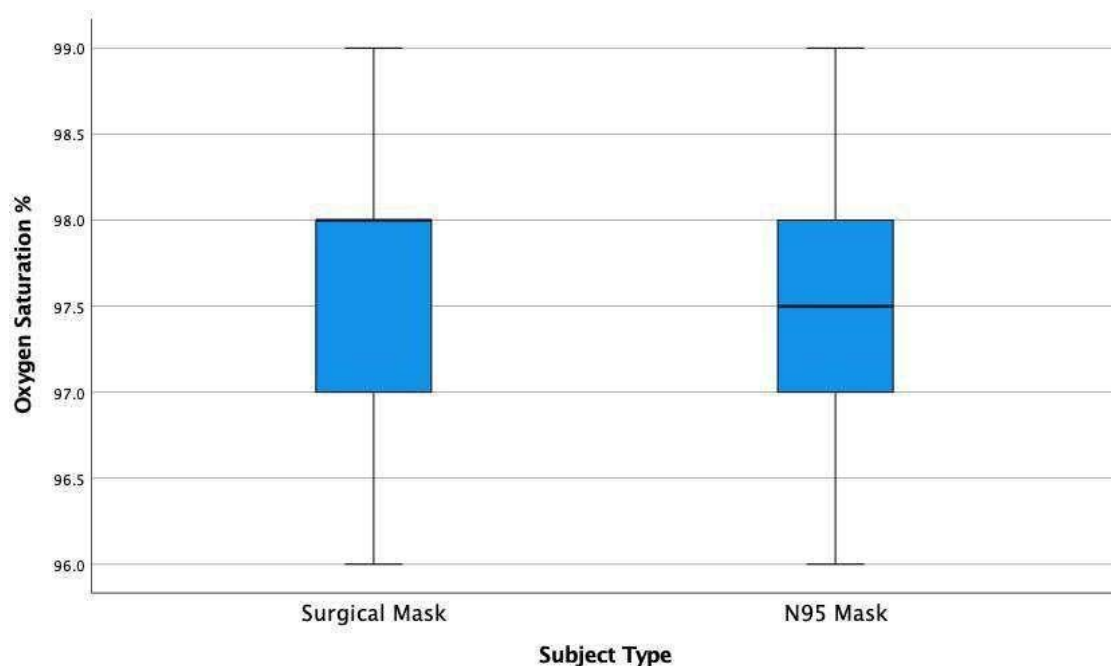


Figure 4: SpO₂ has been compared using a box-plot graph with the mask type on the x- axis and the mean value obtained for the individuals on the y- axis.

Table 5: Results for partial pressure of carbon dioxide (pCO₂)

Mask Type	Number of Individuals	Mean	Standard Deviation	Two-sided p Value
N95 mask	26	43.23	6.30	0.440
Three-ply Surgical Mask	24	44.58	5.96	

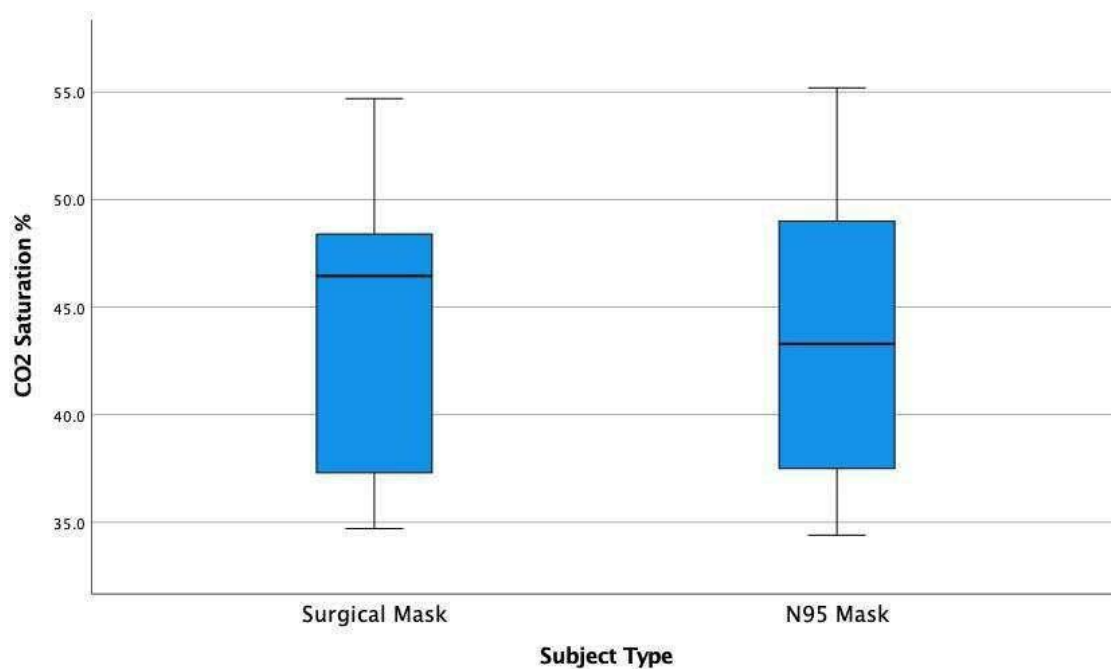


Figure 5: pCO₂ has been compared using a box-plot graph with the mask type on the x- axis and the mean value obtained for the individuals on the y- axis

IV. DISCUSSION

The pandemic of the coronavirus took the world by storm, causing the entire world to come at a standstill in 2020. To prevent the spread of the disease, the use of three-ply surgical masks and N95 respirator was recommended by various health agencies across the world. Cheng et al^[9], in his study, suggested the use of masks to decrease the spread of the virus.

To assess the effect of wearing both these masks on the respiratory volumes and capacities, the box-plot graphs have been mentioned in the results above. Since the two-sided p value of these parameters, that is, forced expiratory volume in the first second, the forced vital capacity and the ratio between the two, has been greater than 0.05, the values are non-significant. Therefore, there is no long-term deleterious effect of wearing either N95 respirator and three-ply surgical mask on the respiratory volume and capacities of the wearer. To compare between the two, a modest effect has been observed due to N95 respirator than by three-ply surgical mask which does not cause any additional physiological burden on the lungs.

The percentage saturation of oxygen, calculated by using a spirometer, in N95 respirator and three-ply surgical mask averaged out to be 97.50% and 97.66% respectively, which is within the normal physiological range. Therefore, there has been no significant effect observed by wearing these masks on the percentage saturation of oxygen of the wearer.

The mean of partial pressure of carbon dioxide was found to be 43.23 mm of Hg with N95 respirator use and at 44.58 mm of Hg with a three-ply surgical mask usage. These values are within the normal range of 35-45 mm of Hg. Hence, there was no significant change in partial pressure of carbon dioxide in the mask users.

Since the p-values observed for the aforementioned parameters were greater than 0.05 for all, the results of the study are non-significant.

The conclusions of the study by Raymond et al^[17] included that in a healthy healthcare worker, a one-hour use of filtering facepiece respirator did not inflict any significant burden on the physiology, but the levels of carbon dioxide were above and the levels of oxygen were below the surrounding workplace standards in the filtering facepiece respirator's dead-space. There was also a likelihood of the increase in PaCO₂. The respirator's comfort issues need to be addressed further to maximise healthcare workers adherence to its use.

To battle the short supply of N95 mask during the large-scale infectious outbreaks, and to extend their life, it was suggested to use a surgical mask over the N95 respirator as an outer barrier. 10 healthcare workers wore a N95 respirator with a surgical mask over it, for one hour each, of two work rates. The respiratory rate, the tidal volume, the minute volume, the heart rate,

oxygen saturation, transcutaneous carbon dioxide levels and the respiratory dead space gases were monitored by Roberge et al.^[18] These were juxtaposed with the controls, which were subjects with N95 filtering facepiece without a surgical mask. It was concluded that the utilisation of a surgical mask, as an outer barrier, did not notably influence the physiological burden of comfort and exhaustion by the wearer in comparison to the one wearing just a N95 respirator.

Ten nurses were considered as subjects, with a twelve-hour work shift for a two-day assessment. Blood pressure, heart rate, the levels of carbon dioxide and oxygen were the variable physiological components considered by Rebmann et al.^[19] Carbon dioxide and oxygen were measured using SenTec CO₂ and O₂ saturation sensors. The persistent use of N95 respirators, either accompanied or unaccompanied by a surgical mask as an external barrier, did not significantly lead to a physiological burden for the personnel, over the course of two work-shifts of twelve hours each.

It is, therefore, highly recommended to wear either mask types to prevent the spread of the coronavirus. These masks do not impose any physiological burden on the respiratory volumes and capacities, as well as the percentage saturation of oxygen and partial pressure of carbon dioxide of the wearer even in cases of extended use.

V. CONCLUSION

Long term continued usage of N95 respirator or a three-ply surgical mask does not impose any significant physiological burden on the healthy medical personnel. Findings from this study have indicated that there is no significant effect on percentage saturation of oxygen and partial pressure of carbon dioxide by wearing these masks in the healthcare workers. Long-term usage has also not reported any effect on the respiratory volumes and capacities. Additional studies have also backed up these results. It is therefore, highly recommended to wear the mask to prevent the spread of the disease in the community.

Ethical Considerations

The study was conducted after due approval from the Research and Ethical Committee, Government Medical College and Hospital, Chandigarh.

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Conflict Declaration

The authors declare that none of the authors has any conflict of interest in this manuscript.

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Management of Retinopathy of Prematurity in an African Population- An Analytical Retrospective Comparative Study

By Francis Kwasi Obeng, Vipan Kumar Vig, Emmanuel Parbie Abbeyquaye,
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Aim: To assess outcome and complication profile of large series of children who underwent different treatment modalities after being diagnosed with ROP.

Materials and Methods: Records of patients who had been managed for ROP were reviewed retrospectively for safety, complication, and visual outcome. Patients' demographic data, indications of treatment and length of follow up were collected and analyzed using Chi-square and paired t-tests.

Keywords: retinal neovascularization, prematurity, childhood blindness, low birth weight, neonatal oxygen therapy.

GJMR-F Classification: DDC Code: 617.735 LCC Code: RE661.D5



MANAGEMENT OF RETINOPATHY OF PREMATUREITY IN AN AFRICAN POPULATION AN ANALYTICAL RETROSPECTIVE COMPARATIVE STUDY

Strictly as per the compliance and regulations of:



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Management of Retinopathy of Prematurity in an African Population- An Analytical Retrospective Comparative Study

Francis Kwasi Obeng ^α, Vipan Kumar Vig ^ο, Emmanuel Parbie Abbeyquaye ^ρ, Preetam Singh ^ω,
Rajbir Singh [¥] & Yin Baba Dennis [§]

Abstract- Introduction: Retinopathy of prematurity (ROP) is a common cause of blindness if not properly diagnosed and promptly managed. Treatment modalities used are indirect laserophthalmoscopy(ILO), intravitreal anti-vascular endothelial growth factors injection monotherapy (IAVEGFIM), and Retinal Detachment Surgery (RDS).

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Materials and Methods: Records of patients who had been managed for ROP were reviewed retrospectively for safety, complication, and visual outcome. Patients' demographic data, indications of treatment and length of follow up were collected and analyzed using Chi-square and paired t-tests.

Results: A total of 100 eyes of 50 children (26 females and 24 males) were identified. The mean postmenstrual age at diagnosis was 36.4 + 5 weeks (range 31-41 weeks) with a minimum follow- up period of 5 years (5 – 8). Ten eyes (10%) had ILO with complications, the most common of which were peripheral visual field loss (PVFL), 3 eyes (3%) and nyctalopia three eyes (3%). Treatment with IAVEGFIM in 85 eyes (85%) resulted in normal retinal vascularization without any sequelae. Three eyes (3%) had RDS with proliferative vitreoretinopathy (PVR) as the outcome in 2 cases and cataract in one. Two eyes (2%) had gone blind on reporting.

Conclusion: IAVEGFIM is the best among all the available monotherapies in management of ROP.

Keywords: retinal neovascularization, prematurity, childhood blindness, low birth weight, neonatal oxygen therapy.

1. INTRODUCTION

ROP is one of the leading aetiologies of avoidable blindness in children globally [1]. One out of every five children born prematurely in the world is prone to having ROP [2]. The erroneous thought that ROP was not usually found in the black African child led to many eye care programs neglecting the quest for the disease and its management on the continent [3]. The fact is that ROP is as old as the existence of humanity in all geographical regions of the world, independent of race. Enhancement in retina care coupled with increased survival rates of preterm babies in Africa has deceitfully created impression that the disease is now

on the ascendancy on the continent. Although some experts think that the disease is less severe in black than white babies [4,5], this assertion has not been proved scientifically and, therefore can be relegated to the background.

ROP is a vascular disease of the retina which affects premature babies of low birth weight who have received oxygen. Other exacerbating factors include but are not limited to hypercarbia, postnatal hyperglycemia, reduced postnatal weight gain, hypoxemia and neonatal infections [6,7,8]. A baby is said to be *premature* when born at less than 37 weeks, *very premature* at less than 32 weeks and *extremely premature* at or before 28 weeks of gestation [9]. Similarly, birth weight can be low (< 2500g), very low (<1500g) and extremely low (1000g) [9]. Oxygen therapy, essential for the maturation of lungs and survival of a premature baby, may be toxic to the retina leading to ROP [10]. If not diagnosed in time and adequately managed, ROP naturally leads to visual impairment, blindness, social deprivation, psychomotor and cognitive developmental retardation [11].

The purpose of management is to curb detrimental effects from retinal ischemia, neovascularization, tractional bands formation and detachment. Cryotherapy, used for treatment several decades ago, is no more accepted because of the plethora of complications associated with it. Among them are cicatricial disease, ectopic maculae, disc dragging and retinal detachment [12]. The CRYOROP trial also reported on ocular and systemic side effects. Eye-related ones were conjunctival hematoma and laceration, retinal, pre-retinal and vitreous hemorrhage. Systemically, there were bradycardia, arrhythmias and significant apnoea.

Although ILO has currently replaced cryotherapy, the former is equally fraught with complications such as tunnel vision, nyctalopia, high myopia and optic disc atrophy [13,14]. Undoubtedly, ILO destroys the retina leaving behind several scars as aftermath. The underlying principal factor which triggers ROP is the release of vascular endothelial growth factors (VEGF) from the avascular retina [15,16]. A modern paradigm shift in ROP management is the use of

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IAVEGFIM which, apart from helping in appropriate vascularisation of the retina [17], stops the retinopathy, lacks complications and does not need use of general anesthesia [18].

To date, a few published case series have shown favorable results when IAVEGFIM is utilized in managing undetached ROP[17,18]. To the best of our knowledge, this is the first time such a new treatment is assessed in Africans in a large cohort of patients.

The purpose of the study was to analyze the outcome and complication profile of patients in Sub-Saharan Africa who underwent IAVEGFIM and other modalities of treatment after being diagnosed with ROP.

II. MATERIAL AND METHODS

This article is an analytical retrospective comparative study carried out from January 2022 to review medical records of 50 children(100 eyes) who underwent IAVEGFIM and other treatment modalities from September 2013 to September 2021 after being diagnosed with ROP in the study hospital.

The children in question were followed up for at least five years. One consultant retina surgeon with the help of theatre assistants, performed all the procedures. Institutional ethical approval was acquired for this research. In a broader measure, tenets of the Declaration of Helsinki were used to preserve the human rights of participants whose consents were given by respective parents.

Inclusion criteria- Patients in the study were those who were examined and diagnosed at the retina clinic of 37 Military Hospital in Accra, Ghana. The criterium for IAVEGFIM was clients who had type 1 ROP. Ten eyes went on ILO because the clients could not afford IAVEGFIM. The criteria for surgeries were stage 4 or worse.

Exclusion criteria for IAVEGFIM and ILO were retinal tractional bands, RD, painful red eye, conjunctivitis and blind eye. Out of 68 children whose medical records were reviewed, 18 were excluded from the study because they were either followed up for less than five years, lost to follow up, or did not meet the criteria for IAVEGFIM and other modalities of treatment. Some of the patients had been referred from other Sub-Saharan African countries. In addition to general demographic data, information on procedure indications, post-procedure complications, and latest Best Corrected Visual Acuity (BCVA) were collected and analyzed.

One consultant vitreoretinal surgeon (FKO) performed the IAVEGFIM procedures on all the children in an operation theatre under aseptic and sterile conditions. The skin around the eyelids was cleaned with gauze and 10% povidone-iodine. After the instillation of topical anesthetic drops, 5% povidone-iodine was applied onto the ocular surface, a pediatric

speculum was used to open the eyelids, a 30-gauge needle was inserted through pars plana 1.5mm away from the limbus and bevacizumab (Avastin, 1.25 mg in 0.025 mL) injected into the vitreous. Shortage of bevacizumab on certain occasions made us use aflibercept and ranibizumab.

A 15-second pressure was applied with a cotton-tipped applicator at the site of injection immediately after needle withdrawal. The eye was then covered with gauze and plaster after the instillation of one drop of 5% povidone-iodine onto the ocular surface. Patches were taken away 2 hours after the procedure, and patients were reviewed 24 hours and one week after injection. A treat and extend approach was implemented in all patients with the total number of injections in an eye ranging from 3 to 6 depending on the severity of the disease(fig 1 and 2) on the first examination.

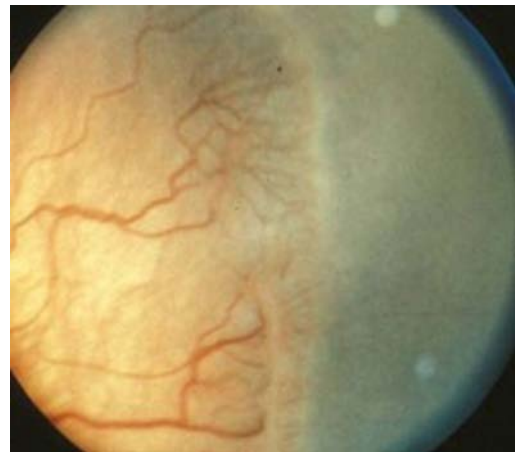


Fig. 1: Shows stage 3+ ROP



<https://imagebank.asrs.org/file/1662/retinopathy-of-prematurity>

Fig. 2: Shows stage 3+ ROP

Indication for ILO under local anesthesia was the inability of the parents to afford IAVEGFIM. A wire Vectis was used to indent the anterior retina, rotate and stabilize the globe. ILO was applied starting with 250 milliwatts for 150 milliseconds with repeat mode set at 300 milliseconds to achieve confluent grayish whitish burns at the avascular retina posterior to the ridge in 3600 fashion up to ora Serrata. Three thousand to 4000 spots were delivered in each eye. The baby was reviewed 1, 7 and 28 days after the procedure.

Eyes with tractional RD had lens sparing three port pars plana vitrectomy (1.5mm from limbus), membrane segmentation, membrane delamination, fluid-air exchange and endolaser under general anesthesia, sterile and aseptic conditions. If there was difficulty in membrane dissection between the retina and posterior capsule of the lens, then lensectomy was done. Sclerotomies were closed up with 8-vicryl.

Snellen BCVA was converted into logarithm of minimum angle of resolution (logMAR) units to get a better statistical analysis. Patients whose visual acuities were light perception were assigned an equivalence of 2.70 logMAR units.

Table-1 shows visual outcomes of various procedures or approaches used in the management of ROP. In all, 85% of eyes maintained their excellent visual

acuities while the rest had worsened final post-treatment visual acuities compared to pre-treatment measurement.

III. STATISTICAL ANALYSIS

The statistical analysis was done using paired t-test for normally distributed variables. Accordingly, all tests were considered statistically significant if the p-value was 0.05 or less. Chi-square test and paired t-test with SPSS and Graph Pad software were used, respectively.

IV. RESULTS

A total of 100 eyes of 50 children (26 females and 24 males) were identified. The mean postmenstrual age at diagnosis was 36.4 ± 5 weeks (range 31-41 weeks) with a minimum follow-up of 5 years (5 – 8).

Children screened, diagnosed and treated early with IAVEGFIM had the best of BCVA. On the other hand, those with complications on presentation had gone blind in the affected eye at the last follow-up visit. Mean pre-treatment visual acuity was 2.70 logMAR units as physiologically, these babies had not started seeing. The mean difference between final post- and pre-treatment visual acuity was 0.00 ± 0.20 log MAR units which was statistically significant ($p < 0.004$).

Table 1: Shows BCVA after procedures

BCVA quality	Procedure/ Approach	Number of eyes (%)
Maintenance	IAVEGFIM	85 (85%)
Worsening	ILO	10 (10%)
Worsening	RDS	3 (3%)
Worsening	Laisser Faire	2 (2%)

BCVA - Best Corrected Visual Acuity, IAVEGFIM – Intravitreal AntiVascular Endothelial Growth Factors Injection Monotherapy, ILO – Indirect Laser Ophthalmoscopy, RDS – Retinal Detachment Surgery

Table 2 shows statistically significant vast difference in the means of pre- and post-treatment visual acuities; thus, an improvement in the IAVEGFIMBCVA.

Table 2

T-TEST PAIRS=PRETREATMENT WITH POSTTREATMENT (PAIRED)
/CRITERIA=CI (.9500)
/MISSING=ANALYSIS.

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	PRE-TREATMENT VISUAL ACUITY	.0010000	100	.00000000	.00000000
	POST-TREATMENT VISUAL ACUITY	.900080	100	.2559516	.0255952

Paired Samples Correlations

		N	Correlation	Sig.
Pair 1	PRE-TREATMENT VISUAL ACUITY & POST-TREATMENT VISUAL ACUITY	100	.	.

Paired Samples Test

		Paired Differences			
		Mean	Std. Deviation	Std. Error Mean	95% Confidence ...
Pair 1	PRE-TREATMENT VISUAL ACUITY - POST-TREATMENT VISUAL ACUITY	-.89908000	.25595165	.02559516	Lower

Paired Samples Test

		Paired ...			
		95% Confidence Interval of the ...			
		Upper	t	df	Sig. (2-tailed)
Pair 1	PRE-TREATMENT VISUAL ACUITY - POST-TREATMENT VISUAL ACUITY	-.84829364	-35.127	99	.000

The major indication for the use of IAVEGFIM was type 1 ROP (n=85 eyes; 85%). Ten eyes (10%), which had ILO because of the inability to afford IAVEGFIM ended up with peripheral visual field loss (n=3;3%), nyctalopia (n=3;3%), tunnel vision (n=2;2%) and optic nerve atrophy (n=2;2%) in their last follow-up visit. Three eyes (3%) had RDS with poor outcomes. Two eyes from 2 different babies had gone blind on reporting to the study center for the first time.

Eighty-five out of 100 eyes received IAVEGFIM, which did not give rise to any complications (table 3). The most common complications were peripheral visual field loss and nyctalopia which resulted from ILO. In 2 eyes, recurrent retinal new vessels following ILO were managed with IAVEGFIM. Surgical intervention in clients who had retinal detachment did not yield a good outcome. Two eyes of 2 patients had gone phthisical on the first examination at the study center.

Table 3: Complications of Different Modalities of Treatment of ROP and their Management

SRL	Intervention	Number of Eyes Out of 100	Complication	Complication N (%) for Each Procedure	Management
1	IAVEGFIM	85	None	0 (0%)	Observation
2	ILO	3	PVFL	3 (100%)	Observation
3	ILO	3	Nyctalopia	3 (100%)	Observation
4	ILO	2	Optic Disc Atrophy	2 (100%)	Observation
5	ILO	2	RRNV	2 (100%)	IAVEGFIM
6	Laisser Faire	2	Phthisis	2 (100%)	Observation
7	RDS	2	PVR	2 (100%)	Observation
8	RDS	1	Cataract	1 (100%)	Cataract Surgery

IAVEGFIM Intravitreal AntiVascular Endothelial Growth Factors Injection Monotherapy; ILO Indirect Laser Ophthalmoscopy; RDS Retinal Detachment Surgery; PVFL Peripheral Visual Field Loss, RRNV Recurrent Retinal New Vessels; PVR Proliferative Vitreoretinopathy

V. DISCUSSION

ROP is better understood when its pathogenesis is well outlined [15,16]. Vasculogenesis and angiogenesis are physiological processes through which new blood vessels are formed. Whereas the former helps in the formation of the primitive vascular network, the latter aids in remodeling and growing of new capillaries which lack fully developed tunica media. Under ischaemic conditions, new vessels are formed through pathological angiogenesis [19].

Development of retinal blood vessels in humans starts at 16 weeks of gestation in a centrifugal fashion at a rate of 0.1 mm/day [20], with the nasal retina being vascularized at 36 and temporal 40 weeks post menstrual age (PMA). The retina is nourished by choriocapillaris before 16 weeks of PMA.

The pathogenesis and progression of ROP are categorized into phases 1 and 2 [21]. In the first phase, oxygen given to newly born premature babies causes cessation of vascular growth and eventually vaso-obliteration on the retina. In phase 2, withdrawal of oxygen and hypoxia lead to ischemia, which triggers the release of various substances, including Vascular Endothelial Growth Factors (VEGF), resulting in pathological angiogenesis and irreversible blindness through retinal detachment if left unattended to [19,21,22,23]. In the study hospital, it has been realized that earlier examinations of premature babies' retinæ before age 14 days are not helpful in the detection of

ROP because its clinical signs would not have developed yet. This means that effects of VEGF are manifested on the retina from day 14 and above after birth.

Certain published studies have established that lower oxygen concentration (85 to 89%) given to premature babies results in less probability in the occurrence of ROP while it leads to increased mortality [24]. Similarly, researchers in another study also discovered that lower concentrations (85-89%) brought about high mortalities and less ROP, while higher concentrations (91-95%) were associated with severe forms of ROP and less mortality [25, 26,27]. Canadian oxygenation trial, however, did not detect any difference in mortality between the higher and lower SpO₂ groups[28]. Although in the study hospital, SpO₂ of 98-100% is used with the aim of keeping babies alive, there has not been an increase in severity of ROP.

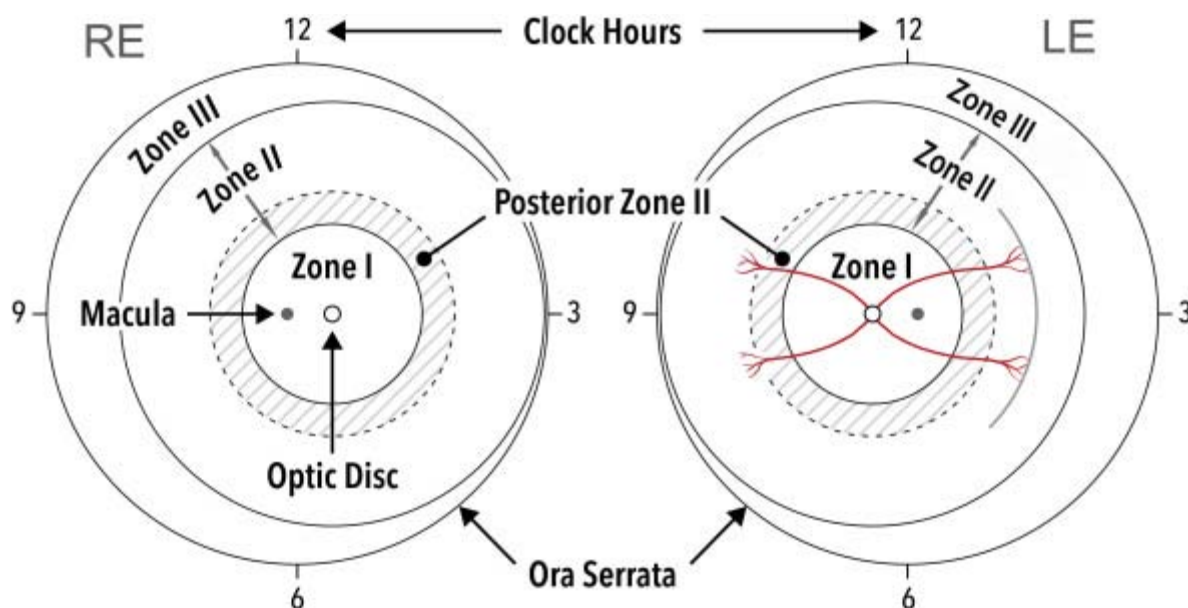


Fig 1

The location of the most posterior retinal vascularization determines the zone of ROP (fig1). The center of the circles is the optic disc. Zone I is the most posterior region and is determined by a circle whose radius is twice the distance between the optic disc center and the center of the fovea. Zone II extends nasally from the outer limit of zone I to the nasal or a Serrata with the same distance temporal, superior, and inferiorly. Posterior zone II is two disc diameters peripheral to zone I border, an area which when perturbed by ROP, usually goes through a guarded prognosis. Zone III is the remaining crescent of the peripheral retina, which extends beyond zone II [29]. In the study hospital, 65%(65), 20%(20) and 15%(15) of eyes were in zones III, II and I, respectively. The extent of the disease is as displayed in clock hours in fig 1.

Stages depict the severity of the disease. In 1, a demarcation line is found between the normally vascularized and peripheral avascular retina. In 2, the demarcation line becomes a ridge. Isolated superficial tufts of neovascular tissue on the retina, commonly called popcorn, can be seen posterior to the ridge but do not constitute stage 3 [30]. Stage 3 is characterized by extraretinal neovascularization with the capacity to progress to 4 and 5, in which there is partial and total retinal detachment, respectively [31]. In 4a, the fovea is spared but involved in 4b. In 5a, b and c, the optic disc is visible, not visible due to retrolental fibroplasia and worsened with anterior segment abnormalities, respectively.

In severe ROP, there is dilation and tortuosity of posterior pole vessels, termed plus disease [32]. In pre-plus, the vascular state is similar to plus disease but insufficient to be called as such [31]. When the condition becomes severe and rapidly progressive within zone I or posterior zone II with the plus disease, it

is known as aggressive-posterior ROP or rush disease [33].

In the CRYO-ROP study, threshold disease was defined as stage 3 disease or presence of plus in 5 contiguous clock hours or eight non-contiguous clock hours in zone I or II. It is recommended that babies with threshold disease be treated within 72 hours. Current indications for ILO are based on Early Treatment of Retinopathy of Prematurity (ETROP) study results which state that there are two groups of pre-threshold disease [34]. The first is high-risk or type 1 ROP, defined as any of the following: (1) zone 1 ROP, any stage, with plus disease; (2) zone 1 ROP, stage 3, without plus disease; or (3) zone II, stage 2 or 3, with plus disease. The second is low-risk or type 2 ROP defined as: (1) stage 1 or 2, not accompanied by plus disease in zone I; or (2) stage 3, without plus disease in zone II. ETROP study outlined that early treatment brings about major decline in complications associated with the high-risk pre-threshold disease. In 37 Military hospital, 85% (85) of eyes managed successfully with IAVEGFIM had type 1 ROP.

VEGF plays a crucial role in the angiogenesis of immature retina and the pathogenesis of ROP, as has been elucidated above [35]. Considering the detrimental effects of VEGF in the pathogenesis of the disease [19, 21, 22, 23], it is only scientifically prudent to halt them at the appropriate time by using anti-VEGF in the form of IAVEGFIM. It is on the basis of this theory that the RAINBOW trial was established with the aim of using anti-VEGF to manage severe ROP [36]. IAVEGFIM does not only stop the growth of pathological retinal vessels but also promotes the growth of normal retinal vessels leaving a healthy and intact retina, which ILO would have destroyed [37]. Henaine-Berra A et al published a study in which 47 eyes with ROP had regression of

neovascularization and normal retinal vascularization after being treated with IAVEGFIM [38]. Similarly, Wu et al reported a 90% regression rate after having used IAVEGFIM in 41 eyes with stage 3 ROP [39]. In the BEAT ROP study, 286 eyes with zone I-posterior II, stage 3+ disease were randomized to IAVEGFIM with bevacizumab, versus conventional laser. The former showed a significant decline in recurrence rate compared to the latter (6% vs 26%) [37]. Another group of researchers detected that 18 eyes with severe ROP refractory to ILO were managed successfully with IAVEGFIM. [40]. In another study in which 165 eyes with zone I-II, stage 3 disease were managed with IAVEGFIM, there was a regression in 89%, need for additional ILO in 9% and progression to stage 4 disease in 2% [41]. Harder BC and his colleagues used IAVEGFIM in 91% of 57 eyes with type 1 ROP and there was regression of the disease in all the eyes except 2 [42]. Yetik H et al also elucidated that in 122 clients with type 1 ROP managed with IAVEGFIM, there was a 95.4 % regression rate [43]. This result was corroborated by Huang Q et al who applied the same treatment to 283 eyes and had a 94% regression rate [44]. Wallace DK also used the same method of treatment in 58 babies with type I ROP and acquired a 95% rate of regression [45]. In all the evidence-based treatments above, the agent used was bevacizumab. In an attempt to know the efficacy of other anti-VEGFs in the management of the same disease, Chen SN and his colleagues treated 72 eyes that had zone I-II, stage 3+ ROP with IAVEGFIM using bevacizumab or ranibizumab. They had 99% regression of the disease without any significant difference in both arms of therapy [46]. In the study hospital, all 85 eyes had had 100% regression of ROP at the last follow-up visit, five years after treatment with IAVEGFIM. The choice of bevacizumab, ranibizumab or aflibercept did not make any difference in the outcome.

Although good in managing ROP, IAVEGFIM may be associated with eye and systemic complications. Endophthalmitis, vitreous hemorrhage, retinal detachment, cataract, choroidal ischemia and rupture, as well as delayed recurrence of ROP have been mentioned by some authors who refused to expound on the level of expertise of those surgeons [47,48,49,50]. Zhou Y et al published a study in which anti-VEGF was found in serum after its use in the eye resulting in a reduction in systemic VEGF [51]. The same study established that while the plasma half-life of ranibizumab was 1, that of bevacizumab was seven days. Since VEGF is vital in the growth of all organs and systems of children, the most significant scientific worry is the rate at which IAVEGFIM may cause systemic growth retardation in children who have received it. Although rare, some children have had complications such as nephropathy [52], upper respiratory tract infections[53], hepatic dysfunction[54], inappropriate

lung maturation [55] and respiratory failure [56] from the use of IAVEGFIM on account of ROP. These systemic complications are prevalent in premature children even without ROP, an assertion that scientifically goes against all the systemic side effects published by some authors with the use of IAVEGFIM in babies. In the study hospital, the patients did not get any of the above-mentioned complications, a fact which must be corroborated by another study looking into the protective role melanin plays in adverse effects from IAVEGFIM.

Some ocular diseases are associated with prematurity itself and not ROP treatment. Immaturity of the central nervous system in premature babies may lead to visual, motor and cognitive functional impairment [57,58]. Others are myopia [59], strabismus [60], amblyopia [61] and reduction in contrast sensitivity [62].

Although anatomical success may be achieved in lens sparing vitrectomy for stages 4 and 5 [63,64,65], there are usually permanent visual acuity problems challenging to solve. The patients who had surgery on account of stages 4 and 5 at the center of the study did not get good outcomes when reviewed during the last follow-up visit.

VI. LIMITATION

Limitations of this research include its retrospective nature, one-center focus, different follow-up periods and one retina specialist performing all procedures.

VII. CONCLUSION

The increased survival rate of preterm babies coupled with the relatively increasing number of retina consultants on the continent has revealed that ROP is as common in Africa as it is in other parts of the world. This fact which has been hidden for decades. Our study has proved that there is not a specific oxygen concentration needed for premature babies. Since every premature baby is different, just enough oxygen concentration for survival is safe for the retinae. All preterm babies must be screened at the end of the second week of life for ROP since earlier examinations will not give any clue about the disease because clinical signs would not have developed. Once diagnosed, its management must start within 72 hours with IAVEGFIM when it is type 1 to prevent it from worsening to stages 4 and 5, which require surgery. This study has elucidated that surgical outcomes, even if anatomically good initially, will usually deteriorate into severe visual impairment and eventually blindness after several years. The lesson from this study is that when IAVEGFIM is used applying the treat and extend method, it surpasses the supremacy of all other available treatment armamentaria. We achieved success because we kept changing from one anti-VEGF to

another in an eye. ILO or combination therapy ends up destroying the retina.

We noted that without IAVEGFIM, prematurity itself has its own systemic and defective ocular signs, which continue developing as the baby grows. Our study has proved that if properly administered, IAVEGFIM is very safe in the management of ROP. Therefore any ocular or systemic defects found after IAVEGFIM is ascribable to prematurity itself and not IAVEGFIM.

Contribution

FKO initiated the project, implemented and completed the data collection, YBD contributed to statistical analysis. EPA, VKV, PS and RS contributed to revision of the paper.

Financial or Other Competing Interests

None

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Acknowledgments

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The following is the official style and template developed for publication of a research paper. Authors are not required to follow this style during the submission of the paper. It is just for reference purposes.



Manuscript Style Instruction (Optional)

- Microsoft Word Document Setting Instructions.
- Font type of all text should be Swis721 Lt BT.
- Page size: 8.27" x 11", left margin: 0.65, right margin: 0.65, bottom margin: 0.75.
- Paper title should be in one column of font size 24.
- Author name in font size of 11 in one column.
- Abstract: font size 9 with the word "Abstract" in bold italics.
- Main text: font size 10 with two justified columns.
- Two columns with equal column width of 3.38 and spacing of 0.2.
- First character must be three lines drop-capped.
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- 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.
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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.
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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.

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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.

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

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

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

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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.



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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.

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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.

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

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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.

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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.



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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 through 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.

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- Submitting a manuscript with pages out of sequence.
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- 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.
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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.

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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.

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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.
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- 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.

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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.

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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.

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<i>Methods and Procedures</i>	Clear and to the point with well arranged paragraph, precision and accuracy of facts and figures, well organized subheads	Difficult to comprehend with embarrassed text, too much explanation but completed	Incorrect and unorganized structure with hazy meaning
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<i>References</i>	Complete and correct format, well organized	Beside the point, Incomplete	Wrong format and structuring



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