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Contents of the Issue

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Antimicrobial Photodynamic Therapy in the Treatment of Peri-Implantitis

By Fernanda dos Santos Lacerda & Fabiano Luiz Heggendorn

University of Grande Rio

Abstract- Peri-implantitis is a chronic inflammation that compromises osseointegration and the longevity of dental implants. This study reviewed the literature on the efficacy of antimicrobial photodynamic therapy (aPDT) in the treatment of peri-implantitis, analyzing its mechanisms, protocols, and clinical and microbiological outcomes. This exploratory literature review analyzed articles published between 2020 and 2025 in the SciELO, PubMed, LILACS, and Google Scholar databases, meeting previously defined inclusion and exclusion criteria. aPDT proved effective in reducing biofilm, inflammatory parameters, and probing depth, especially when combined with mechanical debridement. Despite the heterogeneity of protocols, the results suggest that aPDT is a safe and promising approach with no risk of bacterial resistance. Further studies are needed for standardization and clinical validation.

Keywords: *peri-implantitis, dental implants, low-level light therapy, osseointegration.*

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Antimicrobial Photodynamic Therapy in the Treatment of Peri-Implantitis

Terapia Fotodinámica Antimicrobiana en el Tratamiento de la Periimplantitis

Terapia Fotodinâmica Antimicrobiana no Tratamento da Peri-Implantite

Fernanda dos Santos Lacerda [α] & Fabiano Luiz Heggendorn [σ]

Abstract- Peri-implantitis is a chronic inflammation that compromises osseointegration and the longevity of dental implants. This study reviewed the literature on the efficacy of antimicrobial photodynamic therapy (aPDT) in the treatment of peri-implantitis, analyzing its mechanisms, protocols, and clinical and microbiological outcomes. This exploratory literature review analyzed articles published between 2020 and 2025 in the SciELO, PubMed, LILACS, and Google Scholar databases, meeting previously defined inclusion and exclusion criteria. aPDT proved effective in reducing biofilm, inflammatory parameters, and probing depth, especially when combined with mechanical debridement. Despite the heterogeneity of protocols, the results suggest that aPDT is a safe and promising approach with no risk of bacterial resistance. Further studies are needed for standardization and clinical validation.

Keywords: peri-implantitis, dental implants, low-level light therapy, osseointegration.

Resumen- La periimplantitis es una inflamación crónica que compromete la osteointegración y la longevidad de los implantes dentales. Este estudio revisó la literatura sobre la eficacia de la terapia fotodinámica antimicrobiana (TFDPA) en el tratamiento de la periimplantitis, analizando sus mecanismos, protocolos y resultados clínicos y microbiológicos. Esta revisión exploratoria de la literatura analizó artículos publicados entre 2020 y 2025 en las bases de datos SciELO, PubMed, LILACS y Google Scholar, que cumplían con los criterios de inclusión y exclusión previamente definidos. La TFDPA demostró ser eficaz en la reducción del biofilm, los parámetros inflamatorios y la profundidad de sondaje, especialmente al combinarse con el desbridamiento mecánico. A pesar de la heterogeneidad de los protocolos, los resultados sugieren que la TFDPA es un enfoque seguro y prometedor, sin riesgo de resistencia bacteriana. Se necesitan más estudios para su estandarización y validación clínica.

Palabras Clave: periimplantitis, implantes dentales, terapia por luz de baja intensidad, oseointegración.

Resumo- A peri-implantite é uma inflamação crônica que compromete a osseointegração e a longevidade dos implantes dentários. Esta revisão de literatura integrativa objetivou investigar, discutir e analisar a eficácia da aPDT no tratamento da peri-implantite, considerando seus mecanismos de ação, protocolos clínicos utilizados e os desfechos microbiológicos e clínicos observados. A pesquisa bibliográfica de caráter exploratório, incluiu a análise de artigos publicados entre 2020 e 2025 nas bases SciELO, PubMed, LILACS e Google Scholar, obedecendo aos critérios de inclusão e exclusão previamente definidos. A aPDT demonstrou-se eficaz na redução do biofilme, de parâmetros inflamatórios e da profundidade de sondagem, especialmente quando associada ao desbridamento mecânico. Apesar da heterogeneidade nos protocolos, os resultados sugerem que a aPDT é uma abordagem segura, promissora e sem risco de resistência bacteriana. Novos estudos são necessários para padronização e validação clínica.

Palavras-chave: peri-implantite, implantes dentários, terapia com luz de baixa intensidade, osseointegração.

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I. Introdução

Após a reabilitação com implantes dentários, espera-se que a osseointegração proporcione estabilidade funcional, longevidade do tratamento e resultados estéticos satisfatórios. Contudo, complicações biológicas como a peri-implantite, uma inflamação dos tecidos peri-implantares associada à perda óssea progressiva, têm se tornado uma das principais causas de falhas tardias em implantes osseointegrados (1) (2) (3) (4) (5) (6) (7). Clinicamente, a peri-implantite compartilha características com a periodontite, como sangramento à sondagem (BOP), supuração, aumento da profundidade de sondagem (PD) e reabsorção óssea em torno do implante (1) (2) (5) (6) (8) (7).

A etiologia dessa condição é multifatorial e inclui aspectos como higiene oral inadequada, tabagismo, histórico de periodontite, sobrecarga oclusal e presença de biofilme bacteriano nas superfícies implantossuportadas (1) (6) (7). Assim, o controle microbiano efetivo torna-se um fator essencial no tratamento da peri-implantite, visando a preservação da estrutura óssea e o prolongamento da vida útil do implante (1) (2) (4) (6) (9).

Nesse contexto, a terapia fotodinâmica antimicrobiana (aPDT) surge como uma alternativa minimamente invasiva e promissora (4) (6) (7) (10) (11) (12). Trata-se de uma técnica que combina a aplicação de um corante fotossensível com a irradiação por luz com comprimento de onda específico, resultando na

produção de espécies reativas de oxigênio capazes de destruir seletivamente microrganismos patogênicos (1) (3) (6). A aPDT vem sendo estudada como tratamento adjunto ou complementar em casos de peri-implantite, com resultados promissores na redução do biofilme e na inflamação tecidual (13) (12) (3) (9) (1) (4) (5) (8) (14).

A ativação fotodinâmica atua de forma localizada, sem causar efeitos adversos aos tecidos adjacentes, sendo eficaz contra bactérias resistentes e biofilmes maduros (9) (1) (4) (15) (7) (16), além de não induzir resistência microbiana como os antibióticos tradicionais (17) (10) (2) (3) (4) (18) (5) (19) (14). Por esse motivo, a aPDT tem despertado crescente interesse em pesquisas voltadas para a terapêutica peri-implantar (11) (10) (13) (20) (2) (3) (1) (4) (18) (6) (15) (19) (8) (7) (16) (21).

Dessa forma, o objetivo desta revisão de literatura integrativa foi investigar, discutir e analisar a eficácia da aPDT no tratamento da peri-implantite, considerando seus mecanismos de ação, protocolos clínicos utilizados e os desfechos microbiológicos e clínicos observados.

II. Metodologia

Esta pesquisa analisou de forma qualitativa a eficácia da aPDT no tratamento da peri-implantite. A busca foi realizada nas bases de dados PubMed (National Library of Medicine), SciELO (Scientific Eletronic Library Online), LILACS (Literatura Latino-Americana e do Caribe em Ciências da Saúde) e pelo endereço eletrônico scholar.google.com.br, entre os anos de 2020 a 2025, utilizando os seguintes descritores, em inglês e português, associados aos operadores booleanos, resultando nas duas estratégias de busca: (peri-implantite OR inflamação peri-implantar OR doença peri-implantar OR infecção peri-implantar) AND (terapia fotodinâmica antimicrobiana OR aPDT) AND (implante dental OR implantodontia OR implante) e (peri-implantitis OR peri-implant inflammation OR peri-implant disease OR peri-implant infection) AND (antimicrobial photodynamic therapy OR aPDT) AND (dental implant OR implant dentistry OR implant).

Os títulos e os resumos de todos os artigos encontrados nas buscas foram analisados com base nos critérios de inclusão, identificando os artigos que relatavam investigar os efeitos da aPDT sobre os tecidos peri-implantares, abordando seus mecanismo de ação, protocolos utilizados e os principais resultados microbiológicos e clínicos relevantes ao tratamento da peri-implantite. Foram incluídos artigos completos, publicados entre os anos de 2020 a 2025, que abordavam diretamente o uso da aPDT como intervenção terapêutica para peri-implantite. Foram excluídos artigos publicados fora do período delimitado, teses, monografias, dissertações, livros, artigos incompletos ou que não apresentassem relação direta com o objetivo da pesquisa.

III. Resultados e Discussão

Após a aplicação dos descritores nas bases de dados selecionadas, foram encontrados 24 artigos. Destes, foram incluídos na presente análise aqueles que abordavam o uso da aPDT como estratégias adjuvantes para o controle inflamatório e regeneração tecidual em casos de peri-implantite.

A análise dos estudos selecionados nesta revisão evidencia que a aPDT tem se destacado como uma abordagem promissora e complementar ao desbridamento mecânico (DM) no tratamento da peri-implantite. Diversos ensaios clínicos randomizados e revisões sistemáticas reforçam sua eficácia na melhora dos parâmetros clínicos, microbiológicos e imunológicos, especialmente em populações com fatores de risco como diabetes, tabagismo ou uso de narguilé (17) (10) (3) (8) (6).

A associação da aPDT com o DM demonstrou reduções significativas no BOP, PD e índice de placa (PI) em diferentes grupos populacionais, inclusive diabéticos tipo 2 (17) e usuários de produtos à base de nicotina (23) (19) (8). No estudo de Afrasiabi *et al*. (2023) observou-se redução significativa no BOP após 6 meses (SMD = -2.15; $p = 0.01$) e no PI aos 3 meses (SMD = -0.79; $p < 0.001$), embora a redução no PD não tenha alcançado significância estatística (SMD = -3.13; $p = 0.08$). De forma consistente, AlMubarak (2025) relatou que, em usuários habituais de nicotina, a aPDT promoveu reduções significativas no PD, PI e BOP em todos os estudos avaliados.

A metanálise conduzida por Fonseca *et al*. (2024), mostrou melhora clínica significativa com redução do PD quando a aPDT foi utilizada como adjuvante (3), resultado semelhante ao encontrado por Bahrami *et al*. (2024) (2) e Patil *et al*. (2023) (5), que também destacaram a diminuição dos níveis inflamatórios, como IL-6 e TNF-α.

No tocante aos desfechos microbiológicos, a aPDT mostrou-se eficaz na redução de patógenos como *Porphyromonas gingivalis*, *Aggregatibacter actinomycetemcomitans* e *Prevotella intermedia*, tanto em estudos clínicos quanto laboratoriais (9) (21) (24) (6). (15). Segundo Fraga *et al.* (2018), observou-se uma diminuição estatisticamente significativa na contagem de *Porphyromonas gingivalis* (OR = 4,08), *Aggregatibacter actinomycetemcomitans* (OR = 1,31) e *Prevotella intermedia* (OR = 1,66), reforçando o potencial da terapia como adjuvante no controle da infecção peri-implantar. Adicionalmente, estudos demonstraram redução da colonização subgengival por leveduras em pacientes com mucosite peri-implantar após uma única sessão de aPDT (16).

Apesar dos resultados positivos, algumas limitações devem ser consideradas. A heterogeneidade metodológica, principalmente no número de sessões, entre uma e quatro aplicações, nos fotossensibilizadores utilizados, como azul de metileno e toluidina azul, e nos comprimentos de onda variando entre 635 e 810 nm, torna difícil a padronização de um protocolo terapêutico ideal (4) (24) (14) (20). Enquanto Lähteenmäki *et al*. (2022) utilizaram duas sessões com intervalo semanal, Ali *et al*. (2024) optaram por quatro sessões semanais consecutivas, evidenciando a falta de consenso quanto à frequência ideal de aplicação da aPDT. Ainda assim, as evidências sugerem que sessões únicas ou repetidas podem reduzir de forma significativa a inflamação e a carga microbiana sem efeitos colaterais relevantes (18) (1) (12) (13) (11).

Estudos anteriores que analisaram os efeitos do laser na osseointegração também sugeriram benefícios significativos na modulação inflamatória, estimulação celular e deposição de matriz mineralizada (25), reforçando o potencial terapêutico complementar da aPDT na regeneração tecidual peri-implantar.

Zhao et al. (2022) realizaram uma metanálise com fumantes, observando redução estatisticamente significativa em PD (MD = -1,26 mm) e PI (MD = -10,6%) com o uso da aPDT combinada ao DM, confirmando sua superioridade ao tratamento convencional isolado(19). De forma similar, Al-Hamoudi (2023) relatou melhora clínica e redução dos níveis de RANK-L em usuários de narguilé, sugerindo benefício adicional da aPDT também sobre biomarcadores de reabsorção óssea(8).

Alguns estudos avaliaram a aplicação domiciliar da aPDT com uso de dispositivos de luz dupla, observando melhorias no controle do biofilme e marcadores inflamatórios (24), o que abre perspectivas para sua incorporação como ferramenta auxiliar na manutenção da saúde peri-implantar.

Adicionalmente, a aPDT demonstrou benefícios comparáveis ou superiores aos antibióticos locais, com a vantagem de não induzir resistência bacteriana (14). Este achado reforça seu potencial como alternativa segura em um cenário de crescente preocupação com resistência antimicrobiana.

Embora mais estudos clínicos bem delineados e de longo prazo sejam necessários para consolidar protocolos e ampliar a aplicabilidade da técnica, os achados da presente revisão sustentam o uso da aPDT como terapia adjuvante eficaz, segura e promissora no manejo da peri-implantite.

IV. Conclusão

O estudo demonstrou que a utilização da aPDT apresenta um impacto positivo no controle inflamatório e microbiológico da peri-implantite, além de contribuir para a preservação dos tecidos peri-implantares e o sucesso clínico dos implantes dentários. No entanto, deve ser considerado um viés devido ao número limitado de estudos clínicos e à ausência de um protocolo terapêutico padronizado. Mais pesquisas devem ser realizadas para confirmar a eficácia da aPDT em termos de estabilidade dos tecidos peri-implantares e manutenção longitudinal da osseointegração, consolidando sua aplicação segura e reprodutível na implantodontia.

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Diagnosis and Orthodontic Treatment of Obstructive Sleep Apnea Syndrome Children

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Abstract- Obstructive sleep apnea syndrome (OSAS) is a respiratory illness that is associated with recurrent episodes of either partial or full obstruction of the upper airways, or apnea, among other sleep disorders. This study aims to analyze, through a literature review, whether orthodontic treatment can be a good treatment strategy for this type of disorder. We performed a database search on Scopus, Web of Science, and Pubmed with the keywords OSA(S) and orthodontics to select the papers under evaluation. The criteria for inclusion were articles related to OSA(S) children undergoing an orthodontic treatment and clinical studies or case series, excluding systematic reviews, narrative reviews, meta-analyses, adult studies, animal models, and in vitro studies.

Keywords: *OSA(S); orthodontics; orthodontic treatment; sleep apnea; OSAS disease.*

GJMR-J Classification: *NLM: WU 440*

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Abstract- **Obstructive sleep apnea syndrome (OSAS) is a respiratory illness that is associated with recurrent episodes of either partial or full obstruction of the upper airways, or apnea, among other sleep disorders. This study aims to analyze, through a literature review, whether orthodontic treatment can be a good treatment strategy for this type of disorder. We performed a database search on Scopus, Web of Science, and Pubmed with the keywords OSA(S) and orthodontics to select the papers under evaluation. The criteria for inclusion were articles related to OSA(S) children undergoing an orthodontic treatment and clinical studies or case series, excluding systematic reviews, narrative reviews, meta-analyses, adult studies, animal models, and in vitro studies. The screening phase ended with the selection of 16 publications for this work. RME, or rapid maxillary expansion, turned out to be the preferred orthodontic treatment in cases of pediatric OSAS. The goal of this orthodontic procedure is to increase the hard palate's transverse diameter by reopening the midpalatal suture. Children with maxillary contraction and dental malocclusion typically undergo such a procedure and have excellent results. However, OSAS is a multifactorial disorder; it does not seem related to the morphology of the oral cavity, and therefore, it is not always possible to cope with this problem exclusively through orthodontic treatment.**

Keywords: OSA(S); orthodontics; orthodontic treatment; sleep apnea; OSAS disease.

I. Introduction

Sleep is a periodic, natural, biological occurrence that includes the loss of awareness, a reduction in or partial cessation of nerve center functioning, and a slowdown in the performance of certain bodily activities like breathing, circulation, and metabolism [1].

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It turns out that sleep is essential to human existence; just consider that each person sleeps for roughly one-third of their lifetime [2,3]. Because it is intimately linked to the preservation of brain metabolism, the health of the rest of the cardiovascular system, and the equilibrium of glucose metabolism, it plays a significant role in preserving psychophysical balance [4–12]. Therefore, it is easy to see how sleep abnormalities could impact a person's psychological and mental health [13–15]. Speaking of a child makes the situation considerably more significant [16–18]. Consider that a newborn's first few months of life are spent sleeping for 70–80% of the day [19]. The first week of life is estimated to require 16–17 h of sleep, followed by 15 h at around 6 months, 14 h at roughly 1 year, 13 h at around 2 years, and 12 h at around 3 years [20]. After the age of six, children typically sleep for nine hours, ten hours, and eight hours during puberty [21–32]. The young sleep more because sleep serves multiple purposes, including boosting immune system strength, allowing the brain to "cleanse" waste toxins produced during wakefulness, consolidating memory and learning, promoting the release of growth hormones, and promoting brain development (especially REM sleep) [19,33,34]. Because of this, it is important to try to catch sleep disturbances in children early, on as they have a significant impact on their health. Obstructive sleep apnea syndrome (OSAS) is a respiratory illness that is associated with recurrent episodes of either the partial or full obstruction of the upper airways, or apnea, among other sleep disorders [35–37]. They can be of two types: peripheral, caused by a mechanical obstruction of the airways, or central, caused by a disruption in the neurological system's capacity to stimulate the breathing muscles [38,39]. Just consider how common this is: depending on the case studies and polysomnographic criteria employed, the frequency of obstructive sleep apnea syndrome (OSAS) in children ranges from 0.69% to 5.7% [40,41].

a) Risk Factors

The main risk factors for the development of OSAS in children are adenotonsillar hypertrophy, obesity, craniofacial abnormalities, neuromuscular disorders, and hypercapnia [42] (Table 1).

Table 1: Some Pathologies in Which OSAS May be Present [4]

Diseases with a Craniofacial Component	Associations with Soft Tissues	Neuromuscular Associations	Inflammatory Associations
Apert's syndrome	Obesity	Cerebral palsy	Asthma
Crouzon's syndrome	Cystic hygroma	Hypothyroidism	Metabolic syndrome
Pfeiffer's syndrome	Papillomatosis (oroparingea)	Achondroplasia	Sickle cell disease
Pierre–Robin syndrome	Prader–Willi syndrome	Patients with cleft palate after repair	
Treacher Collins syndrome	Mucopolysaccharidosis	Down syndrome	
Goldenhar syndrome (hemifacial microsomy)	Beckwith–Wiedernann's syndrome		
Atresia/coanal stenosis	Down syndrome		
Hallermann–Streiff's syndrome	Syndromes with cleft		
Klippel–Feil syndrome			
Osteopetrosis			
Sickle cell anemia (sickle cell disease)			
Syndromes with cleft			

i. *Hypertrophy of Adenotozsillary*

The most typical risk factor for the onset of OSAS is adenotonsillary hypertrophy. Adenotonsillary hypertrophy in children peaks in occurrence between the ages of 2 and 6 [43–45]. Within the same age range, the transverse section and volume of the upper airways are smaller, and the adenotonsillary volume-to-airway ratio is favorable to the former [46–48]. After six years, the ratio reverses, and the airway's transverse volume/section increases, but this is typically not accompanied by an increase in tonsillar or adenoid volume (the latter often tends to decline until normalization is achieved) [11,49–51]. Significant obstruction of the upper respiratory tract can occur when the tonsils and adenoids increase their encumbrance in the coan space and the hypopharynx, respectively [52–54]. However, significant adenotonsillary hypertrophy must still be linked to an upper airway-relative hypotonia for OSAS to manifest [55,56]. There is no obvious correlation between the adenoids and tonsils' sizes and the severity of OSAS, and not all children with notable adenotonsillary hypertrophy have OSAS [57–59].

The condition of mono- or bilateral cleft lip and palate also affects the volume of the airway and nasopharyngeal space. A study by Kiaee showed a significant reduction in oropharyngeal and total volume in 30 patients aged 9 to 12 years with unilateral cleft lip and palate compared with 30 age- and sex-matched controls ($p < 0.05$) [60].

ii. *Obesity*

Owing to the substantial quantities of adipose tissue that are accumulated at the level of the ribs, upper airways, and abdomen, obesity results in a reduction in minute ventilation, as well as static and dynamic lung volumes and capacities [61,62]. The close relationship between respiratory disorders in sleep and obesity and, specifically, between OSAS and obesity can be explained by the combination of changes in respiratory function brought on by obesity and those physiologically determined by sleep [61]. OSAS is far more common in obese subjects than in the general population [63–66]. Prevalence values range from 14% to 78% [67]. These differences result from how obesity and OSAS are defined by different authors [68–73]. Studies have shown that the degree of obesity and the severity of OSAS are correlated and that adenotonsillary hypertrophy is more common as a risk factor in obese subjects than in the non-obese population with OSAS [18,74,75].

iii. *Craniofacial Syndromes*

The obstruction and appearance of OSAS are linked to primitive skeletal anatomical modifications of the upper airways, which are connected to syndromes of the craniofacial region [76,77]. Anatomical abnormalities in the upper airways associated with hypotonia and, in some cases, obesity may account for the unique prevalence of OSAS in this population [78–81]. A typical example of this would be the clinical picture of Down syndrome.

iv. *Neuromuscular Diseases*

OSAS is more common in children with neuromuscular diseases because of muscle hypotonia, which is frequently brought on by scoliosis, restrictive dysventilatoria syndrome, and muscle pump deficiency. These children exhibit dysventilatorial or atelectasic areas more frequently because of their lack of cough and relative incapacity to clear respiratory secretions. These variables favor the appearance of changes in gas exchanges by changing the ventilation/perfusion ratio.

v. *Hypercapnia*

An elevated blood carbon dioxide level is among the signs and symptoms associated with hypercapnia.

Abnormalities in the heart or lungs, such as respiratory acidosis or altered acid-base balance, are often the cause of this phenomenon. The inadequate ventilation of the alveoli is another common cause. Children are generally more likely than adults to suffer from hypercapnia when they sleep.

vi. *Pediatric OSAS Symptoms and Signs*

The most common symptoms of OSAS include chronic and persistent snoring (HS), often with breathing pauses, paradoxical or otherwise difficult night breathing, sleeping disorders with frequent night awakenings, excessive night sweating, and occasionally secondary enuresis (in a child who has acquired urinary continence for at least 6 months). Additional indications and symptoms at night include nightmares, agitation, adopting specific sleeping positions (such as saluting Mohammed), and a posture that causes the neck to extend excessively. Children with OSAS may exhibit signs and symptoms during the day, including excessive daytime sleepiness, headaches upon waking, irritability, and poor academic performance. There are occasionally opposing expressions in the two more traditional phenotypes. The adenotonsillar phenotype is often characterized by thinness and inadequate growth in addition to facies adenoidea. The issue in the obese phenotype is the opposite and is typified by overgrowth (Table 2).

Table 2: Symptoms and Signs of Pediatric OSAS [3]

Night Symptoms	Daytime Speaker	Signs
Snoring	Difficulty awakening	Tonsil hypertrophy
Gasping	Lack of rest upon waking	High/wide lingual position
Noisy breathing (typically inspiratory)	Drowsiness	Growth disorders (obesity, insufficient growth)
Respiration paradox	Hyperactivity	Pulmonary hypertension
Indentations (jugular or rib)	Aggression, bad mood	Systemic hypertension
Apnee testifies	Oral respiration	Craniofacial abnormalities
Restless sleep	Meager appetite	Laryngeal
Hyperextension of the neck	Dysphagia	Obstruction of the nasal airways
Oral respiration	School difficulties	Hypotonia
Night sweating	Daytime speaker	Gastroesophageal reflux

b) Complications

There are three methods by which OSAS complications are assessed:

Arousals, or micro-awakenings, at the conclusion of hypnotic episodes; sporadic hypoxias with fast re-oxygenation (following the outlet at the end of apneic episodes), linked or unrelated to hypercapnia; and changes in intrathoracic pressure during obstructive events caused by respiratory effort.

These three processes function by initiating an intricate web of oxidative stress, free radical and pro-inflammatory cytokine release, elevated phlogosis indexes, epithelial dysfunction, and sympathetic nervous system activation. The result is decreased vagal tone; catecholamine release; and elevated heart rate and variability. Neurocognitive and behavioral issues, growth retardation, systemic arterial hypertension, pulmonary hypertension, and disorders of the cardiovascular and metabolic systems are all encouraged by this intricate network (Table 3).

Table 3: Complications of OSAS [2]

Metabolic	Neurocognitive	Cardiovascular
Increased C-reactive protein	Decreased quality of life	Autonomic dysfunction
Insulin resistance	Aggressive behavior	Systemic hypertension
Hypercholesterolemia	Poor school performance	Absence of drop in blood pressure in sleep
Increased transaminases	Depression	Left ventricular dysfunction
Reduced insulin-like growth factor	Attention deficit	Pulmonary hypertension
Reduced/altered growth hormone secretion	Hyperactivity	Variability of heart rate altered
	Moodiness	Increased vascular endothelial growth factor

c) *Management*

i. *Adenotonsillectomy (AT)*

With an estimated 70–100% case efficacy, adenotonsillary hypertrophy is still the most frequent cause of OSAS in children, and the suggested course of treatment is still AT. A polysomnographic check will be scheduled following AT to determine whether any OSAS is still present.

ii. *CPAP*

Nasal continuous positive airway pressure, or CPAP, is a successful treatment for OSAS even in younger children. However, a major barrier to the efficient use of CPAP can be treatment adherence. Because of this, when AT is a more sensible option, it is not recommended to use CPAP as the first line of treatment for OSAS. However, CPAP is recommended for children who do not react well to surgery, children for whom surgery is not recommended, and children whose families refuse to give their consent for surgery.

iii. *Medical Therapy*

Numerous investigations have evaluated the effectiveness of leukotriene antagonists, such as montelukast, and topical nasal corticosteroids, such as fluticasone and budesonide, in the treatment of pediatric OSAS. Topical nasal corticosteroids are helpful for mild OSAS, but they should not be the only treatment for moderate or severe OSAS.

iv. *Bariatric Surgery*

In 2012, guidelines were released regarding the use of bariatric surgery to treat severe obesity in carefully selected adolescents. Numerous studies have demonstrated how well gastric bandages, gastric bypasses, and gastrectomy sleeves work to lower apnea indices (AHIs) and body mass indices (BMIs).

v. *Orthodontic Treatment*

RME, or rapid maxillary expansion, has been used as a treatment for pediatric OSAS. The goal of this orthodontic procedure is to increase the hard palate's transverse diameter by reopening the mid-palatal suture. This is accomplished by using a stationary apparatus with an expansion screw for approximately three to four months. Children with maxillary contraction and dental malocclusion typically undergo such a procedure.

II. Materials and Methods

a) *Protocol and Registration*

This systematic review was conducted following Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA), and it was submitted to PROSPERO with number ID 490431.

b) *Search Processing*

We performed a search of databases such as Scopus, Web of Science (WoS), and PubMed using the keywords "OSA(S)" and "orthodontics" to select papers suitable for this topic, and the search was related to the last ten years (December 2013–December 2023).

c) *Eligibility Criteria*

The reviewers, in a double-blind manner, included papers that satisfied the following criteria for inclusion: (1) articles related to OSA(S) children undergoing an orthodontic treatment; (2) clinical studies or case series.

Exclusion criteria were represented by reviews (systematic and/or narrative) with/without meta-analyses, studies regarding adult populations, animal models, and
in vitro studies.

d) *Data Processing*

The screening procedure, carried out by reading the article titles and abstracts chosen in the earlier identification step, allowed for the exclusion of any publications that varied from the themes looked at, and the full texts of publications previously included were then read. The reviewers discussed the selected articles, and in cases of disagreement, a third reviewer (FI) was consulted.

e) *Quality Assessment*

The quality of the included papers was assessed by two reviewers, R.F. and E.I., using ROBINS, a tool developed to assess the risk of bias in the results of non-randomized studies that compare the health effects of two or more interventions. Seven points were evaluated, and each was assigned a degree of bias. A third reviewer (F.I.) was consulted in the event of a disagreement until an agreement was reached.

III. Results

Keyword searches of the Web of Science (40), Scopus (11), and PubMed (705) databases yielded a total of 756 articles.

The subsequent elimination of duplicates (42) resulted in the inclusion of 714 articles.

Of these 714 studies, 665 were excluded because they deviated from the previously defined inclusion criteria (383 off-topic, 2 vitro/animal studies, 122 reviews, 135 adult studies, 23 no free full-text).

The screening phase ended with the selection of 16 publications for this work.

The PRISMA flowchart of this review is summarized in Figure 1, and the data from each selected study (author(s), type of study, aim of the study, materials, and results) are reported in Table 4.

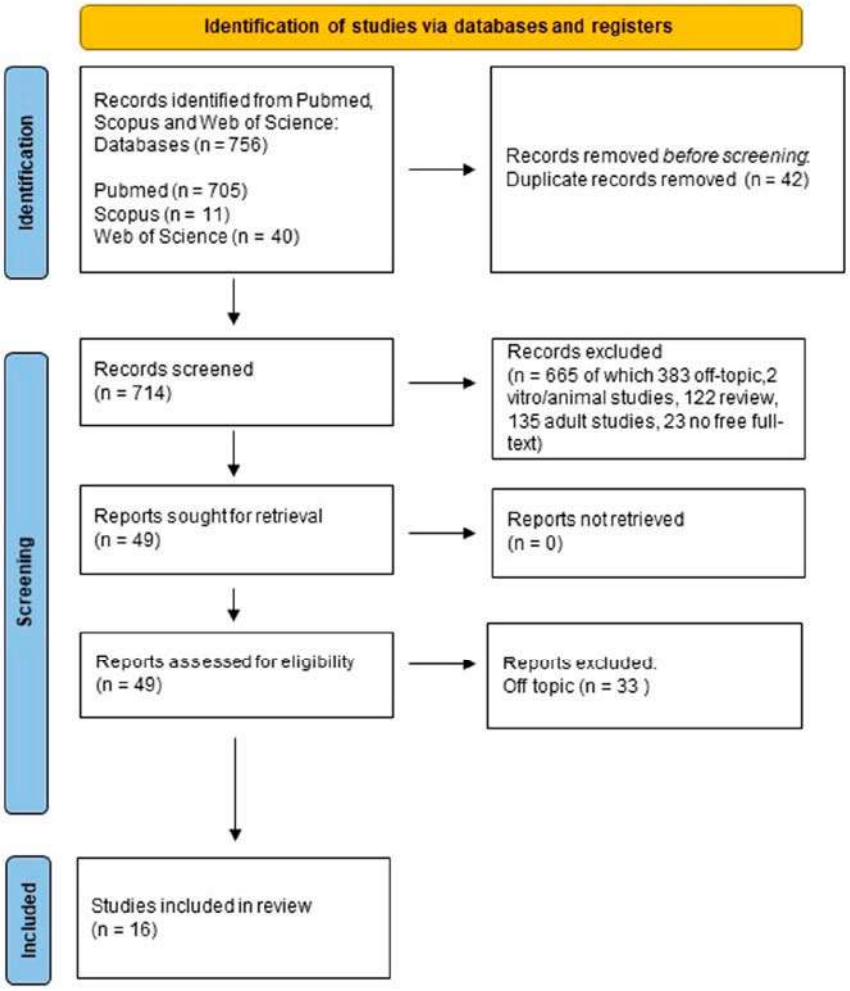


Figure 1: PRISMA Flowchart used in this Review Paper

Quality Assessment and Risk of Bias

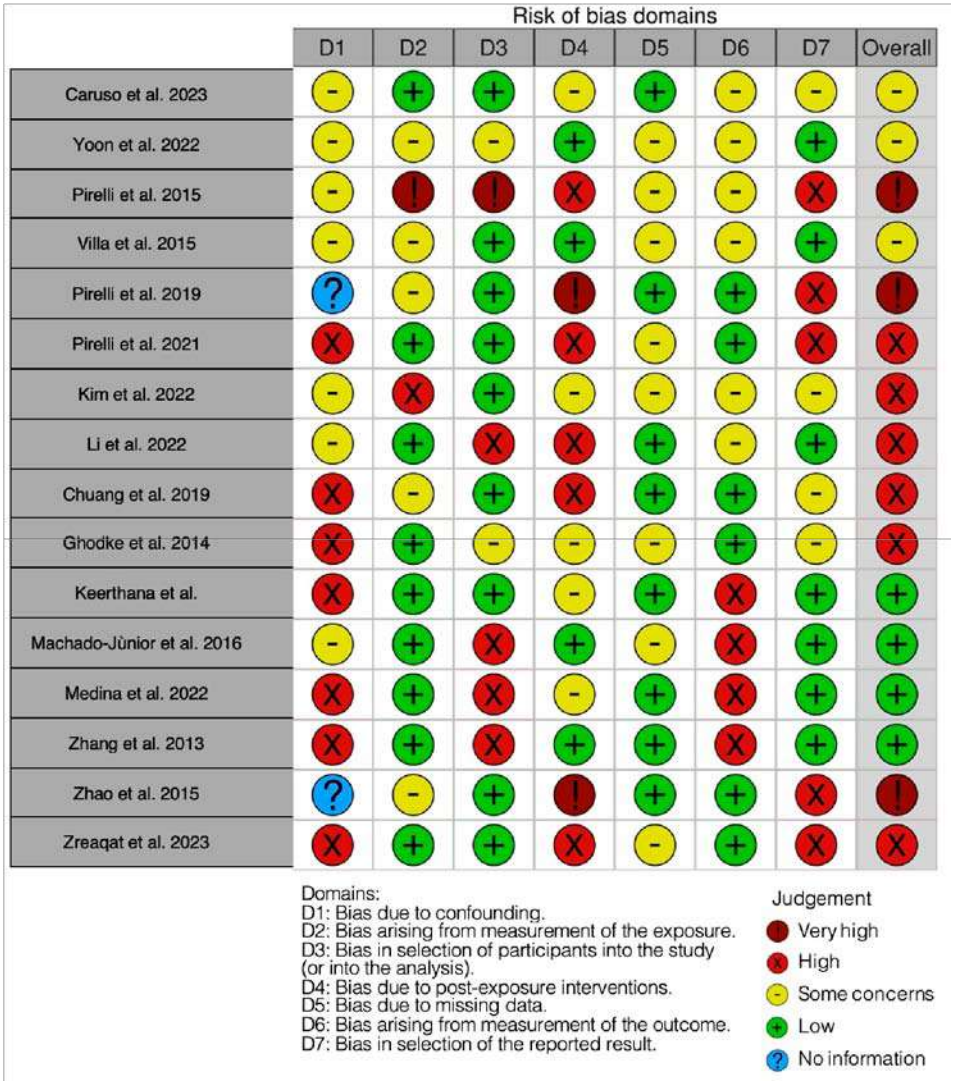
The risk of bias in the included studies is reported in Scheme 1. Regarding bias due to confounding, most studies have a high risk. The bias arising from measurement is a parameter with a low risk of bias. The majority of studies have a low risk of bias because of bias in the selection of participants. Bias due to post-exposure cannot be calculated because of high heterogeneity. Bias due to missing data is low in the majority of studies. Bias arising from the measurement of the outcome is low. Bias in the selection of the reported results is high in the majority of studies. The final results show that four studies have a low risk of bias, six studies have a high risk of bias, three have a very high risk of bias, and the remainder have a questionable risk of bias.

Table 4: Examined Articles

Authors (Year)	Type of Study	Aim of the Study	Materials	Results
Caruso et al., 2023 [82]	Clinical study	To evaluate the cephalometric variations in upper airway dimensions and OSA-related clinical conditions after orthodontic treatment with an RME and the Delaire mask in patients affected by class III malocclusion.	In total, 14 children, ages 6 to 10, with mixed dentition were treated with a Delaire mask and an RME.	The study reports an increase in nasopharyngeal and oropharyngeal spaces. Improvements in OSAS-related clinical conditions and airway patency result from this increase.
Yoon et al., 2022 [83]	Retrospective cohort study	To assess the alterations in palatine and adenoid tonsil sizes subsequent to RPE through 3D volumetric analysis of cone beam computed tomography (CBCT) images.	In total, 60 pediatric patients with tonsillar hypertrophy were divided into 2 groups: one treated with RPE and a control group without any treatment.	RPE enormously decreased the size of the palatine and adenoid tonsils.
Pirelli et al., 2015 [84]	Clinical prospective study	To assess the long-term effectiveness of rapid maxillary expansion (RME) in a group of children with obstructive sleep apnea (OSA); RPE was found to significantly reduce the size of both the palatine and adenoid tonsils.	The study Ided 31 children with an OSA diagnosis. At baseline, these children had isolated maxillary narrowing and no enlarged adenotonsils. The subjects experienced repeated polysomnography (PSG) in their late teens or early 20s, as well as ongoing clinical evaluation.	Following RME treatment for a history of OSA, a subgroup of OSA children with isolated maxillary narrowing (initially followed up into adulthood) showed stable, long-term results.
Villa et al., 2015 [85]	Clinical retrospective study	To validate the effectiveness of RPE in children with mild to moderate adenotonsillar hypertrophy.	Pediatric patients with narrow palate, tonsillar hypertrophy, and OSA undergoing RPE therapy and reassessed over time.	RPE therapy was confirmed to be effective in resolving malocclusions associated with OSA.
Pirelli et al., 2019 [86]	Clinical prospective study	To evaluate the skeletal effects of RPE via low-dose computed tomography (CT).	In total, 14 pediatric patients with contracted palate and OSA underwent RPE therapy.	Opening of the mid-palatal suture was demonstrated in all cases.
Pirelli et al., 2021 [87]	Clinical study	To evaluate skeletal changes and changes in dimensions and volume of the upper airways before and after rapid RPE in children with OSA via CBCT. To evaluate if RPE therapy can improve both the patency of the nasal airways and the obstructive sleep apnea syndrome (OSAS).	In total, 19 pediatric patients with contracted palate and OSA underwent RPE therapy.	In all cases, the opening of the mid-palatal suture was demonstrated. Significant increases were observed in nasal osseous width, nasal cavity volume, total upper airway volume, and the nasopharynx and oropharynx.
Kim et al., 2022 [88]	Clinical study	To assess changes in respiratory function related to increased upper airway volume in patients with OSA treated with RPE.	In total, 26 patients (mean age, 13.6 years) were treated with RPE. Pre- and post-treatment CBCT assessment of airway and pre- and post-treatment assessment of mean apnea-hypopnea index (AHI).	In all cases, there was an increase in the size of the nasomaxillary complex, with improvement in parameters related to OSA.
Li et al., 2022 [89]	Clinical study	To evaluate the efficacy of nasomaxillary expansion via trans-palatal distraction (TPD) with skeletal anchorage in the resolution of OSA.	In total, 25 children without maxillary contraction with OSA were treated with TPD.	In children treated with RPE previously but without transverse maxillary deficiency, nasomaxillary expansion via skeletally anchored TPD improved OSA.
Chuang et al., 2019 [90]	Comparative cohort study	To compare the quality of life and the morphology of the airways, and cranium both before and after a year of passive myofunctional treatment (MFT) in children with OSA.	For a year, forty OSA youngsters who wore an oral device every night (the treatment group) and seventeen who did not (the control group) were monitored.	One year of passive MFT enhanced nasal breathing during sleep, as well as mandibular development and upper airway morphology in the oropharyngeal area.
Ghodke et al., 2014 [91]	Clinical study	To assess how class II malocclusion participants with retrognathic mandibles respond to a twin block device in terms of pharyngeal airway passage dimensions and posterior pharyngeal wall thickness.	Thirty-eight class II malocclusion individuals with mandibular retrusion, ages 8 to 14	The twin block device enhanced PAP dimensions while maintaining posterior pharyngeal wall thickness prior to treatment.
Keerthana et al., 2022 [92]	Case series	To summarize the results of using the AdvanSync2 Class II corrector in the treatment of three orthodontic patients who complained of breathing issues and a retrognathic mandible that interfered with their ability to sleep.	Three people who require treatment for class II malocclusion were linked to sleep apnea.	By increasing airway dimensions, the AdvanSync2 Class II corrector, when used in conjunction with fixed orthodontic equipment, improved the quality of life for class II patients.
Machado-Júnior et al., 2016 [93]	Pilot study	To assess mandibular advancement appliance in children who have OSA.	Adolescents diagnosed as apneic were those with an apnea–hypopnea index of one or more events per hour.	One year following the implementation of mandibular advancement devices, there was a reduction in the apnea–hypopnea index as compared with the non-user group.

Table 4: Cont.

Authors (Year)	Type of Study	Aim of the Study	Materials	Results
Medina et al., 2022 [94]	Clinical study	To ascertain if using this equipment causes healthy children's upper airways to enlarge and their sleep-breathing habits to improve.	In total, 39 healthy children: 20 for the activator group; 19 for the control group.	By opening the upper airway, the activator helps to enhance the quality of breathing during sleep.
Zhang et al., 2013 [95]	Clinical study	To look at how twin block (TB) appliances affect children who have mandibular retrognathia and OSA.	In total, 46 children (aged 9.7 ± 1.5 years, BMI: 18.1 ± 1.04 kg/m^2) with mandibular retrognathia and OSA.	The patients' facial profiles improved following therapy with the TB appliance.
Zhao et al., 2015 [96]	Pilot Study	To find out if class II hyperdivergent individuals undergoing complete orthodontic treatment are affected differently by the existence of OSA.	Patients who underwent orthodontic treatment and were between the ages of 12 and 14.	The results of these children's orthodontic treatments may be impacted by the early detection and treatment of pediatric OSA.
Zreaqat et al., 2023 [97]	CBCT study	To assess rapid maxillary expansion (RME)'s long-term effectiveness in treating a group of children with obstructive sleep apnea (OSA).	In this study, 31 children with OSA diagnoses were included. At baseline, these children did not have enlarged adenotonsils and only had isolated maxillary constriction. The subjects experienced repeat polysomnography (PSG) in their late teens or early 20s, as well as ongoing clinical reevaluation.	Following RME therapy for juvenile OSA, a subgroup of children with isolated maxillary constriction who were first followed up into adulthood showed consistent, long-term improvements.



Scheme 1: Bias Assestment [82–97]

IV. Discussion

a) OSAS Treatment with Rapid Palatal Expander

i. *Effectiveness of RPE in Modifying the Upper Airway*

A 2023 clinical study by Caruso et al. evaluated cephalometric changes recorded in 14 young patients affected by class III malocclusion and OSAS treated with RPE and Delaire's mask. In the cephalometric analysis, carried out on pre- and post-treatment laterolateral radiographs, in addition to the classic values for verticality and sagittality, millimeter measurements of upper airway space dimensions were examined. At the end of therapy, there was a statistically significant increase in linear upper airway measurements and oropharyngeal and nasopharyngeal dimensions in all patients, creating an improvement in airway patency and OSAS-related clinical conditions [82].

A 2016 retrospective study by Yoon et al. evaluated the effectiveness of REP in decreasing palatine tonsil and adenoid volume in pediatric patients with OSA. Sixty children with an average age of 8 years were split into a study group treated with REP and a control group that received no treatment. At the end of therapy, patients treated with REP showed a statistically significant reduction in the volume of tonsils and adenoids in contrast to patients in the control group, in whom there was no improvement. This work is very interesting because it represents the first clinical study to quantify changes in tonsil volume following palatal expansion [83].

Kim et al., in a 2022 clinical study, assessed changes in respiratory function related to increased upper airway volume in patients with OSA treated with RPE. In all 26 cases treated, there was an increase in the size of the nasomaxillary complex, with improvement in parameters related to OSA: there was a reduction in AHI and oxygen saturation values, and snoring had markedly improved [88] (Figure 2).

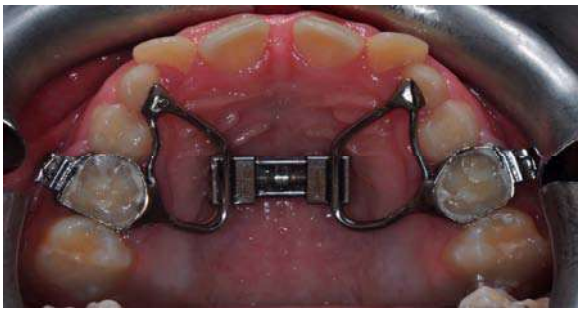


Figure 2: RPE Device

ii. *Radiographic Evaluation of the Effects of RPE*

Pirelli et al., in a 2019 clinical study, evaluated the skeletal effects of RPE therapy in children with OSA through low-dose computed tomography (CT) measurements of the first molar angulation, maxillary base width, nasal cavity width, and the mid-palatal suture opening. The examinations performed demonstrated effective mid-palatal suture opening in all treated cases and improvements in the other parameters considered [86]. The same group of authors, in a 2021 study, demonstrated that RPE treatment is effective in children who have OSA and persistent snoring, causing an increase in the volume of the nasal cavity and nasopharynx. An increase in maxillary size results in an increase in upper airway volume, improving nasal breathing. The findings demonstrate that RPE therapy can eliminate obstructive sleep-breathing disorders and restore and enhance normal nasal airflow. The 19 children included in the study underwent CBCT before and after RPE treatment, and orthodontic and otolaryngological examination to confirm the above results [87].

iii. *Alternative Treatments in Cases of RPE Failure*

A 2022 clinical study by Li et al. investigated the effects of skeletally fixed transpalatal distraction (TPD) on nasomaxillary expansion in patients with OSA previously treated with RPE. These patients, although they had resolved their malocclusions, still had residual OSA. As a result of this additional treatment, apnea episodes were significantly reduced: a nearly parallel anteroposterior opening of the mid-palatal suture enables the enlargement of the entire nasal passage with improved airflow characteristics in the nasal and pharyngeal airways. Improved airflow characteristics significantly correlated with enhanced polysomnographic results, indicating that nasomaxillary expansion is a feasible therapeutic option for patients who have previously undergone expansion [89].

iv. *Long-Term Effectiveness*

A 2015 clinical study by Pirelli et al. followed a group of 31 pediatric patients diagnosed with OSA treated with RPE over time. The patients, at the start of treatment, presented maxillary contraction in the absence of tonsillar and adenoid hypertrophy. At the end of treatment, annual follow-up was performed for the next 12 years. A total of 23 individuals completed follow-up and underwent final PSG. All patients showed stable orthodontic outcomes and resolution of OSA. RPE treatment, therefore, was also shown to be effective in the long term [84].

The same conclusions were reached in a 2015 retrospective clinical study by Villa et al., in which the benefits of RPE therapy in the resolution of malocclusions characterized by a high and narrow palate in patients with OSA and moderate tonsillar hypertrophy were evaluated. At the 10-year follow-up, most patients had resolved their OSA issues, and the best results were seen in those who underwent an orthodontic treatment earlier [85].

b) OSAS Treatment with Mandibular Advancement Devices

The condition known as obstructive sleep apnea (OSA) is characterized by the abnormal, intermittent total or partial blockage of breathing during sleep that interferes with regular ventilation. On the spectrum of obstructive breathing sleep disorders, it is the most severe kind [A]. Children with this kind of illness typically display symptoms throughout the day, such as irregularities in their behavior, development, cognitive abilities, and hearts [34].

Although the few data available now may imply that mandibular advancement appliances (MAAs) increase AHI scores, it is not possible to draw the conclusion that MAAs are useful in treating pediatric OSA. In 2016, in order to prove that evidence, Machado-Junior Almiro-Josè et al. conducted a randomized controlled pilot study.

They came to the conclusion that individuals who are hyperdivergent and undergoing thorough orthodontic treatment do not fare as well if they have OSA. Planning regular therapy for sleep-breathing problems and airway blockage should include an examination. The results of these children's orthodontic therapy may be influenced by early detection and the treatment of pediatric OSA [93].

One type of oral functional appliance used for the early treatment of children with mandibular retrognathia is called a twin block (TB) (Figure 3). Because of the mandible's forward location, TB could be an appropriate oral appliance for treating children with OSA [98].

In a preliminary study conducted in 2013, Chen Z. et al. aimed to determine the initial effectiveness and tolerability of TB treatment for children patients with mandibular retrognathia and OSAS [9,99–101]. Taking into account certain limitations in the study's design, such as the lack of a control group to compare with and the need to rule out other variables like growth that could have an impact on the findings, the authors came to the conclusion that TB appliances might help the selected patients with their facial profiles and OSA symptoms [95].

Ghodke S. et al., in a study conducted in 2014, analyzed the impact of TB appliance on the anatomy of pharyngeal airway passage (PAP) in a group of class II malocclusion patients in an age range of 8 to 14 years. They stated that, for class II malocclusion subjects, the TB appliance to treat mandibular retrusion enhanced PAP dimensions while maintaining the same pre-treatment posterior pharyngeal wall thickness. Consequentially, by removing predisposing factors and adaptive alterations in the upper airway during infancy, class II correction using a TB device may help lower the likelihood of developing OSA as an adult [91].

Figure 3: Twin Block Device

In a pilot study in 2018, Zhao T. et al. aimed to find out if OSA affects the orthodontic treatment outcome for class II hyperdivergent patients undergoing complete orthodontic therapy.

They highlighted how, in the young OSA patients selected for the study, the pattern of bone growth became more vertical, in contrast with the non-OSA group, where the pattern of bone growth became more horizontal. Along with that, both groups' treatment outcomes in terms of occlusion and sagittal bone growth were comparable [96].

Keerthana P. et al., in 2022, presented a case series to highlight the effectiveness of an AdvanSync2 Class II corrector in the treatment of three orthodontic patients with OSA conditions. The modifications to airway size after the use of AdvanSync2 were evaluated

by comparing lateral cephalograms taken before and after therapy. In all three cases, a notable improvement in airway dimensions was seen [92].

In a 2019 comparative cohort research, Chuang Li-Chuan et al. assessed the quality of life and craniofacial and airway morphology in children with OSA before and after a year of passive myofunctional therapy (PMFT). The PMFT device tested consistently in a custom-designed oral appliance with a built-in tongue bead. For the duration of the study (1 year) every night while they slept, study participants were to wear their appliances and roll the bead with their tongues.

They came to the conclusion that PMFT can enhance nasal breathing during sleep, as well as mandibular growth and upper airway morphology in the oropharyngeal region. The OSA-18 survey indicated a significant improvement in the quality of life of treated patients, particularly in relation to emotional distress [90].

In a 2023 study, Zreaqat M. et al. used cone beam computed tomography (CBCT) in conjunction with three-dimensional analysis to evaluate the effects of TB appliance therapy on upper airway parameters and dimensions, as well as the apnea–hypopnea indexes (AHIs), in children with OSA who had class II malocclusions and mandibular retrognathia before and after completing myofunctional TB therapy.

It has been demonstrated that CBCT imaging is a reliable and accurate diagnostic method for examining craniofacial tissues and upper airways [97].

The authors segmented the upper airway into three regions (nasopharynx, oropharynx, hypopharynx), and for each region, they measured the airway volume and the minimum cross-sectional area (MCA) in the axial view.

They concluded that the TB therapy performed to treat class II mandibular retrognathic skeletal malocclusion led to a significant decrease in AHI but no change in nasopharynx parameters. Upper airway volume; the MCA; the anteroposterior and lateral distances of the MCA at the level of the oropharynx; the MCA at the level of the hypopharynx; and upper airway length were significantly increased as a result of the findings [97].

Since, as we have shown, different studies agree that the mandible forward advancement with an orthodontic activator can improve the AHI in pediatric patients who have both abnormal maxilla–mandible relationships and OSA, Medina C.C. et al., in 2022, were interested in verifying the theory that, in addition to its intended function of inducing mandibular development, activators may enhance the dimensions of skeletal class II children's upper airways to promote healthy sleep-breathing patterns even in the absence of sleep disturbances.

Many assessments, such as radiographic examinations of the upper airway, sleepbreathing monitoring, and questionnaires sent to parents and examined children, were used to test this theory.

They came to the conclusion that the activator not only allows for harmonic occlusion and healthy mandibular development but also widens the upper airway and lowers the frequency of disordered breathing events in children receiving this therapy, which enhances the quality of sleep and breathing [94].

v. Conclusions

Respiratory sleep disorders are a rather common condition in the pediatric population, OSAS being the most common among them. As in other fields of science, intervention as early as possible can change the natural course of the disorder. In this regard, an early orthodontic intervention, such as REP or mandibular advancement with functional appliances, may be effective in the management of pediatric OSAS, suggesting that the correction of craniofacial structure imbalances during growth can reduce snoring and OSAS in children and young adolescents. Specifically, there is limited evidence to support mandibular advancement appliances (MAAs) in improving pediatric OSA, so further investigation is needed to establish their efficacy conclusively, while studies that have evaluated RPE in pediatric patients with obstructive sleep apnea syndrome (OSAS) have shown promising results, with significant cephalometric changes finding an increase in linear upper airway measurements and the subsequent expansion of nasal airflow. The goal of this early interceptive treatment is clearly to restore the balance of the maxillary bone bases so that oral cavity functions (phonation, swallowing, breathing, and chewing) can be performed properly.

Further studies with a large number of patients are needed, especially on mandibular advancement devices used during the pediatric age, to evaluate their possible benefits in terms of OSAS-related symptoms and to develop structural modifications to improve airway morphology.

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Abbreviations

AT	Adenotonsillectomy
AHI	Apnea hypopnea index
BMIs	Body mass indices
CBCT	Cone beam computational tomography
CPAP	Continuous positive airway pressure
CT	Computed tomography
MAA	Mandibular advancement appliance
MCA	Minimum cross- sectional area
OSA	Obstructive sleep apnea
OSAS	Obstructive Sleep Apnea Syndrome
PAP	Pharyngeal airway passage
PMFT	Passive myofunctional therapy
PSG	Polysomnography
RME	Rapid maxillary expansion
RPE	Rapid palatal expansion/Rapid palatal expander
TB	Twin Block
TPD	Nasomaxillary expansion using skeletally anchored trans-palatal distraction

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The Silent Sufferers: Congenital Insensitivity to Pain with Anhidrosis (CIPA): A Case Report

By Dr. Kalpna Chaudhry, Dr. Diganta Rava, Dr. Deepshikha Singh & Dr. Pooja Panwar

Abstract- Congenital Insensitivity to Pain with Anhidrosis (CIPA) is a rare hereditary condition that affects the nervous system, leading to an absence of pain sensation and impaired thermal regulation. This case report highlights the diagnostic process of a 9-year-old patient suspected to be suffering with CIPA in a dental setting where early recognition of the condition plays a critical role in preventing complications. The report discusses the implications of CIPA for pediatric dental care, emphasising the need for increased awareness and modified management approaches.

Keywords: *anhidrosis, congenital, insensitivity, pain, pediatric dentistry.*

GJMR-J Classification: *NLMC Code: WL140, WU480*

Strictly as per the compliance and regulations of:

The Silent Sufferers: Congenital Insensitivity to Pain with Anhidrosis (CIPA): A Case Report

Dr. Kalpna Chaudhry [α], Dr. Diganta Rava [σ], Dr. Deepshikha Singh [ρ] & Dr. Pooja Panwar [Ω]

Abstract- **Congenital Insensitivity to Pain with Anhidrosis (CIPA) is a rare hereditary condition that affects the nervous system, leading to an absence of pain sensation and impaired thermal regulation. This case report highlights the diagnostic process of a 9-year-old patient suspected to be suffering with CIPA in a dental setting where early recognition of the condition plays a critical role in preventing complications. The report discusses the implications of CIPA for pediatric dental care, emphasising the need for increased awareness and modified management approaches.**

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I. Introduction

Congenital Insensitivity to Pain with Anhidrosis (CIPA) is classified under Hereditary Sensory and Autonomic Neuropathies (HSAN Type IV). Due to a mutation in the NTRK1 gene, affected individuals are unable to feel pain or temperature, leading to frequent self-injuries, delayed wound healing and other complications.

While CIPA has been widely studied in medical literature, its impact in pediatric dentistry is not well documented. In dentistry, the absence of pain can mask serious oral conditions, posing a significant challenge for diagnosis and management. CIPA is an exceedingly rare disorder, with a reported incidence of one in 125 million[1]. The disease shows geographic variability, which may be attributed to founder mutations and consanguineous marriages[2]. The condition exhibits an autosomal recessive inheritance pattern, necessitating the presence of two mutated alleles for phenotypic expression[3]. The majority of affected individuals originate from consanguineous unions, emphasizing the importance of genetic counseling in at-risk populations. There is no reported study about the gender predilection of this disease particularly.

CIPA is characterized mainly by 3 symptoms: pain, anhidrosis and temperature. Notably, lacrimation, salivation, and touch perception are unaffected. Due to their lack of pain perception, affected persons are more vulnerable to infections and self-inflicted injuries, such as intraoral injuries. The inability to sweat is a contributing factor to anhidrosis, which raises the risk of hyperthermia. A nerve biopsy, genetic testing, and clinical assessment all contribute to the diagnosis. To detect the precise mutation and validate the diagnosis, NTRK1 gene genetic analysis is required.[4] This case report focuses on the identification of CIPA in a 9-year-old patient and its implications for pediatric dental practice.

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II. Case Report

a) Patient Information

A 9-year-old male was brought to the Department of Pediatric and Preventive Dentistry in Seema Dental college & Hospital, Rishikesh, for a routine dental check-up. The patient's medical history revealed no significant dental complaints, but the parents reported frequent self-injuries and an inability to perceive pain since birth. According to his mother the patient would inflict self-injuries using hot iron rods or would sit on top of the fire and get burns but won't feel any pain. Based on clinical history, the patient was suspected to be suffering from a very rare condition known as congenital insensitivity to pain with anhidrosis (Table 1). The patient belonged to low socio economic background therefore his parents never bothered to undergo any kind of investigation for his medical condition.

b) Clinical Presentation

Upon extraoral examination, the patient displayed several healed scars on the extremities and head, likely resulting from repeated self-inflicted injuries as shown in Figure 1(a). Despite the presence of noticeable injuries, the patient exhibited no signs of discomfort.

Intraoral examination revealed generalized attrition of teeth, early carious lesions in the posterior teeth with no complaints of sensitivity or pain, multiple areas of soft tissue scarring on the inner lips and buccal mucosa, no other visible pathologies or acute dental issues were noted as shown in Figure 2.

The patient did not respond to any pain stimuli during the examination, confirming the clinical signs of CIPA. Radiographic imaging was performed, which showed deep carious lesions with periapical radiolucency as shown in Figure 3. The diagnosis made was deep carious lesion with periapical abscess w.r.t 46.

c) Diagnostic Process

The diagnostic process is based on clinical evaluation, genetic testing, and a nerve biopsy. Genetic analysis of the NTRK1 gene is essential for confirming

the diagnosis and identifying the specific mutation.[5] The mother used to work at AIIMS Rishikesh as a cleaning staff and she mentioned that she had consulted a neurologist about the condition once and she was told that it might be due to neurological problems. No further investigation of any kind was done. Given the patient's unique presentation and the reported medical history and comparing it with other similar neuropathies, CIPA was suspected as the underlying condition. While the patient did not present with any immediate dental concerns, the absence of pain posed challenges in evaluating the true extent of oral damage. Routine dental tests, such as percussion or sensitivity testing, were not applicable, necessitating a more cautious approach in future monitoring.

d) Management

No immediate treatment was provided during this visit. The focus remained on educating the parents regarding the long-term implications of CIPA on oral health. Preventive dental care, regular check-ups, and close monitoring were strongly recommended. Customized preventive strategies, including the use of mouthguards and improved oral hygiene practices, were discussed to minimize the risk of self-inflicted injuries in the future. Since the mother was a labor moving from place to place in search for work, the patient didn't turn up for further treatment.

III. Discussion

CIPA presents a unique diagnostic challenge in pediatric dentistry due to the patient's inability to experience pain. In a typical dental scenario, pain acts as a key indicator for diagnosing conditions such as caries, pulpitis, or infections.[6] However, in patients with CIPA, dental practitioners must rely on visual and radiographic cues rather than patient-reported symptoms, potentially delaying the diagnosis of critical conditions. Although this syndrome can be diagnosed by clinical and paraclinical tests together, but a confirmatory genetic test is better to fully understand the disease. [3] In this case the child was first suspected to be victim of child abuse and neglect asit can be easily confused for child abuse as described by Yagev et al.[8] After thorough conversation with the child and his mother as well his sister individually it was found out that the child has masochistic habits. Upon further conversation it was found out that the child doesn't feel any pain.

Pediatric dentists should be aware of the increased risk of oral trauma, caries progression, and periodontal disease in these patients, as they often go unnoticed without the protective mechanism of pain. In a case presented by Kouvelas N et al. parents gave a history of self-extraction of the teeth as the child did not feel any pain.[1]. Additionally, these patients may develop severe infections or complications if oral conditions are left untreated. Caregivers should be informed about maintaining meticulous oral hygiene, frequent dental visits, and injury prevention techniques.

The case also highlights the need for a multidisciplinary approach, involving pediatricians, neurologists, and dentists, to ensure comprehensive care. We suggest psychological interventions for CIPA primarily focusing on patient education, coping mechanisms development and emotional support to help individuals understand their condition, learn strategies to prevent injuries and manage psychological impact of not experiencing pain, including anxiety related to potential harm and social challenges arising from their unique situation. In a similar case presented by Neves BG et al, they reported that it is important to include a dentist in the multidisciplinary team to reduce the frequency and severity of the self-inflicted lesions in these patients.[9] Early diagnosis of CIPA in a dental setting can prevent severe complications, contributing to better long-term outcomes for the patient. At an early age and with parent's cooperation, the use of a night-guard, grinding sharp edges of the teeth, or the addition of a composite are helpful; rather than the performance of a full mouth extraction which is an extremely radical treatment that causes bone loss.[10]

The management of these individuals is quite challenging, and there is little information in dentistry literature about this problem. Unrecognizing of the clinical pictures of CIPA and minimal literature references in the past, misleads to late diagnosis and management.[11]

a) Significance in Pediatric Dentistry

CIPA significantly alters the approach to pediatric dental care. Key considerations include:

- *Preventive Focus:* Regular dental visits should be scheduled to monitor oral health since patients will not report symptoms of pain.
- *Education:* Educating caregivers about injury prevention and the importance of maintaining oral health is crucial in preventing self-inflicted damage and infections.
- *Modified Treatment:* Treatment approaches must be adjusted, focusing on visual diagnostics rather than patient-reported symptoms. Pain management strategies should be carefully considered due to the patient's lack of pain perception.

A rubber dam should always be used to avoid any serious iatrogenic injuries since the patient is unable to feel any pain and wouldnot be able to report about the same.

- *Team Approach:* A collaborative approach between dental and medical professionals is essential to ensure the patient's overall well-being.

IV. Conclusion

CIPA is a rare condition with profound implications for pediatric dental care. Although no immediate dental treatment was required for the 9-year-old patient in this case, the diagnosis emphasizes the need for a specialized approach to oral care. Pediatric dentists must be vigilant and proactive in identifying and managing such cases to prevent complications and maintain oral health in the absence of pain as a diagnostic tool.

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Table 1: Characteristics in Similar Sensory Neuropathies[4]

	Hereditary sensory Neuropathy type I	Hereditary sensory Neuropathy type II	Congenital Insensitivity to pain	Familial Dysautonomia or HSN III	Congenital Insensitivity to pain with anhidrosis
Onset	Childhood-Adulthood	Birth	Birth	Birth	Birth
Hereditary	Dominant	Recessive	Recessive	Recessive	Recessive
Intelligence	Normal	Normal	Dull	Retarded	Retarded
Sweating	Normal	Normal	Normal	Increased	Absent
Unknown fever	?	?	?	Present	Present
Pain	Absent	Absent	Absent	Absent	Absent

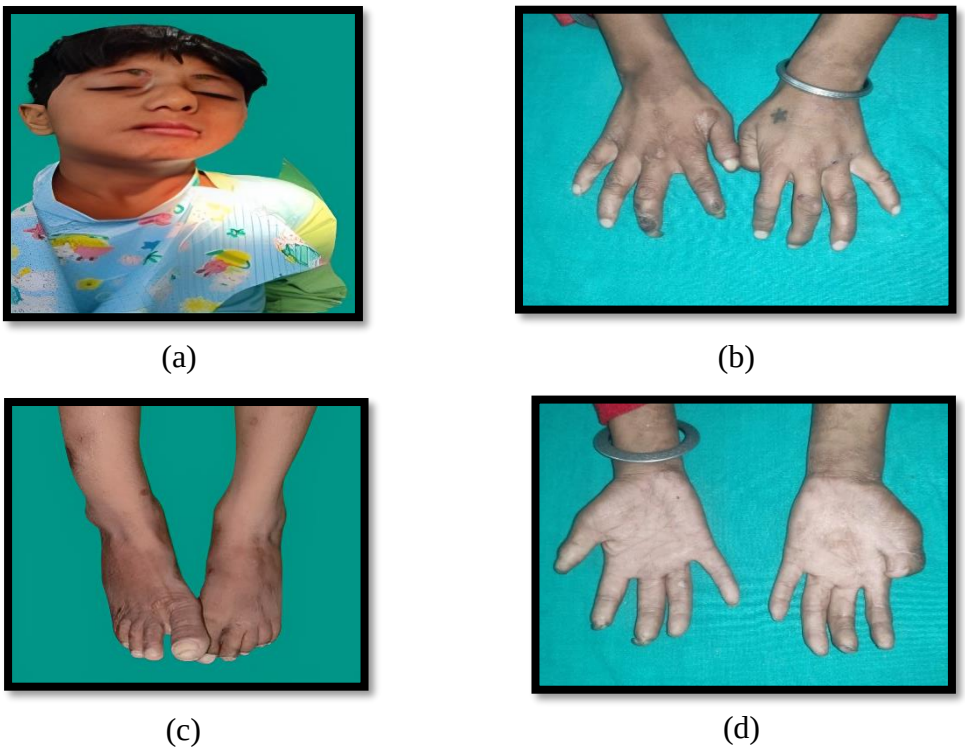

Figure 1: (a) Healing scars on face, (b&c) Foreshortening of distal phalanges of hand (d) Multiple burn scars on leg

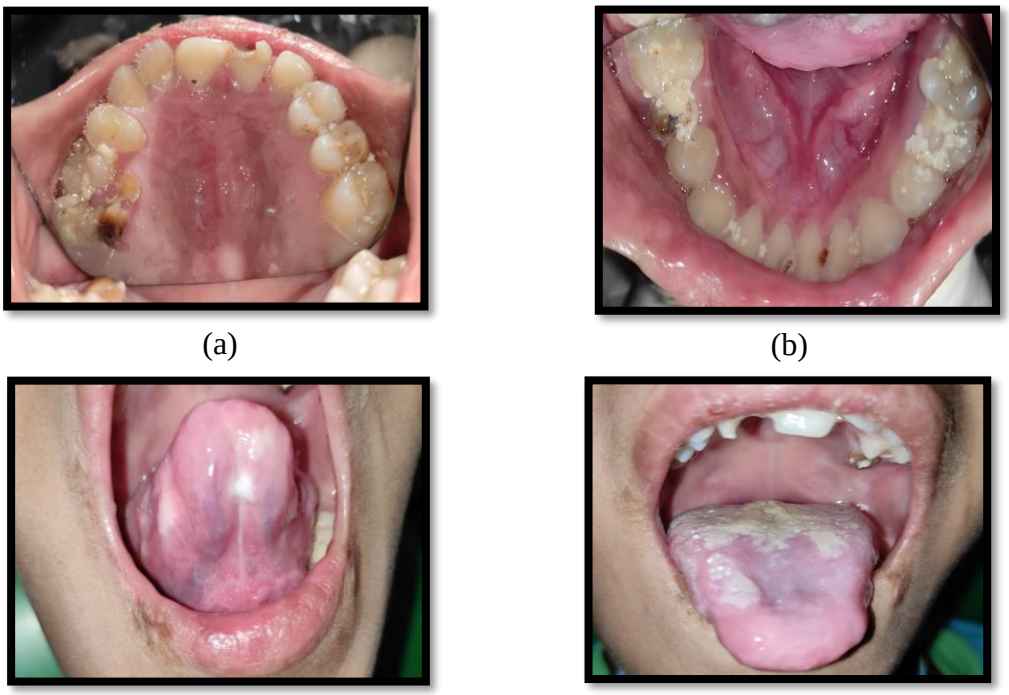

Figure 2: Intraoral examination (a&b) Multiple carious teeth, poor oral hygiene, (c&d) Diffused whitish mucosal lesions seen on the dorsal and ventral aspect of tongue, Labial soft tissue deformity of the patient due to biting

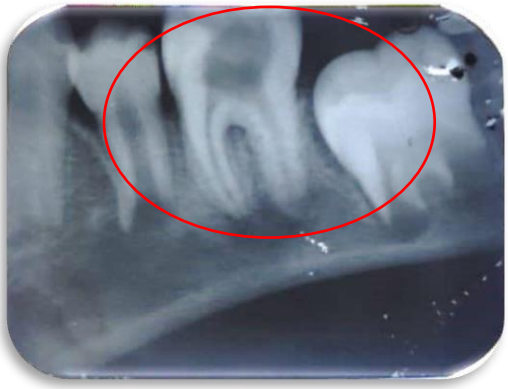

Figure 3: Radiolucency involving enamel, dentin and pulp, loss of lamina dura in mesial and distal root, diffused periapical radiolucency with mesial and distal root i.r.t 46

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Evaluation of the Incidence and Risk Factors of Nausea and Postoperative Vomiting in Oral and Maxillofacial Surgeries

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Abstract- The persistence of postoperative nausea and vomiting (PONV) episodes can cause further complications to the patient, such as: dehiscence of the surgical wound, dehydration, esophageal rupture, hematoma, hemorrhage, and may even lead to death. Considering its high incidence in surgical procedures of the face and oral cavity, the present study aimed to evaluate the incidence of PONV episodes in oral and maxillofacial surgeries under general anesthesia as well as to identify the main risk factors associated with these episodes. This analytical, observational, retrospective study was based on the documentary analysis of 200 medical records of patients who underwent oral and maxillofacial surgery at the Walter Cantídio University Hospital of the Federal University of Ceará.

Keywords: *anesthesia, nausea, vomiting.*

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Evaluation of the Incidence and Risk Factors of Nausea and Postoperative Vomiting in Oral and Maxillofacial Surgeries

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Abstract- The persistence of postoperative nausea and vomiting (PONV) episodes can cause further complications to the patient, such as: dehiscence of the surgical wound, dehydration, esophageal rupture, hematoma, hemorrhage, and may even lead to death. Considering its high incidence in surgical procedures of the face and oral cavity, the present study aimed to evaluate the incidence of PONV episodes in oral and maxillofacial surgeries under general anesthesia as well as to identify the main risk factors associated with these episodes. This analytical, observational, retrospective study was based on the documentary analysis of 200 medical records of patients who underwent oral and maxillofacial surgery at the Walter Cantídio University Hospital of the Federal University of Ceará. Data on patient profile and surgical procedures were collected. PONV episodes were reported in 9% of cases, with 100% occurring in the first 12 postoperative hours. Non-smoking patients, who underwent surgery via intraoral access lasting 3 hours or longer and with greater blood loss were more likely to experience PONV episodes. The identification of patients at greater risk as well as the understanding of the impact that certain surgical procedures have on the occurrence of PONV are fundamental to plan and establish strategies to control PONV episodes.

Keywords: *anesthesia, nausea, vomiting.*

I. Introduction

Elective surgery under general anesthesia is a very safe procedure, especially nowadays with the advent of new technologies aimed at patient comfort. Nevertheless, surgeries may still cause postoperative complications regardless of the procedure, such as bleeding, infections, wound dehiscence, nausea, vomiting, etc.Among these complications, post-operative nausea and vomiting (PONV) is often neglected, given that there is still no well-defined prevention protocol.

Nausea is an unpleasant sensation associated with epigastric discomfort and the urge to vomit (1) whereas vomiting is the rapid and forced expulsion of gastric contents through the mouth (2). PONV is defined as the development of any emetic episode (nausea and/or vomiting) resulting from surgical procedures (McCracken, 2008).

The persistence of postoperative emetic episodes could lead to further complications such as dehiscence of the surgical wound, dehydration, esophageal rupture, hematoma, hemorrhage, aspiration of gastric contents, increased intracranial and intraocular pressure, and may even result in death (4). Numerous factors have been associated with a higher incidence of these complications, including those related to the patient (age, sex, smoking, previous history of PONV and gastrointestinal tract problems), anesthesia (duration, type, use of inhalation agents, use of opioids, hydration, etc.), and the surgical procedure (duration and type; laparoscopic, abdominal surgery, etc.) (5).

Treatment of PONV has been carried out with classic antiemetics or drugs of different classes with secondary antiemetic effects, as is the case of antihistamines, propofol (6-8), and dexamethasone (9). The latter is frequently cited in the literature for its antiemetic and membrane-stabilizing effect; however, its mechanism of action and its application have not been widely studied (9). The medication used to control PONV generally presents inconvenient side effects, such as extrapyramidal reactions, and also generates financial burden for the patient and the hospital, as postoperative complications increase the length of hospital stay of the patient (10).

In oral surgery, emetic phenomena can extend beyond a simple discomfort and inconvenience. Vomiting episodes can potentially lead to open sutures, contamination of the surgical site in intraoral surgeries and aspiration of gastric content in patients with intermaxillary fixation (10).

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Considering the relative frequency of PONV episodes in surgical procedures involving the face and oral cavity, the need for a safe and comfortable postoperative recovery for patients and the need to recognize patient groups at higher risk of PONV, the purpose of this study is to identify the incidence of this postoperative complication as well as the main associated risk factors.

II. Materials and Methods

This analytical, observational, retrospective study carried out a documentary analysis of medical records of patients who underwent oral and maxillofacial surgery in a hospital environment and under general anesthesia, from September 2012 to September 2017, at the Oral and Maxillofacial Surgery and Traumatology Service of the Walter Cantídio University Hospital of the Federal University of Ceará (UFC). This project was approved by the UFC Research Ethics Committee, section of the Walter Cantídio University Hospital, under registration number 2,804,771.

Medical records of patients with no systemic comorbidities, classified as ASA I according to the ASA Physical Status Classification System of the American Society of Anesthesiologists (ASA), of both sexes and with no ages age restriction were included after patients signed a consent form agreeing to participate in the study. Poorly filled out and/or illegible records were excluded from the sample.

The sample was calculated based on the PONV frequency in previous studies which reported a frequency of approximately 20%. We also considered the average of the total patient population operated at the Oral and Maxillofacial Surgery and Traumatology Service of the Walter Cantídio University Hospital in the study period of 5 years, totaling approximately 800 patients. Using a 95% reliability criterion, we reached the minimum number of 189 patients for the sample to be representative.

A standardized form collected the following data: a) patient biometrics (age, sex, weight and height), b) previous medical history (surgeries, systemic disease, episodes of nausea and vomiting), c) social history (smoking, alcohol and drugs); d) medications used in the preoperative period; e) anesthetic evaluation (drugs used in general anesthesia and anesthesia time); f) surgical evaluation (type of surgery, type of access, surgery duration and volume of blood loss); g) assessment of episodes of nausea (presence or not, which period of the postoperative recovery, if rescue medication was used, which medication, dose); and h) evaluation of vomiting episodes (presence or not, which period of the postoperative recovery, if rescue medication was used, which medication, dose).

The obtained data were submitted to statistical analysis with the Statistical Package for the Social Sciences (SPSS -version 17.0 for Windows® 2018). Descriptive statistics (mean, median and standard deviation) and frequency were calculated. Kolmogorov-Smirnov test was used to assess the normality of data distribution. Chi-square test was applied to analyze the association of the study variables (parametric data). The comparison of non-parametric data was performed with the Mann-Whitney and Krukal Wallis tests. Additionally, logistic regression models were used to assess which variables influenced postoperative nausea and / or vomiting. The level of statistical significance adopted for all tests was 5% ($p < 0.05$).

III. Results

The sample of this study consisted of 200 patients with a mean age of 33 years (± 13.23), 66% of whom were male. Episodes of PONV were recorded in 9% of cases, with 100% of them occurring in the first 12 postoperative hours.

The most frequent reason for surgery was trauma, with 100 cases (50% of the total sample), followed by orthognathic surgery with 40 cases (20%), maxillary pathologies in 26 cases (13%) and surgically assisted rapid maxillary expansion (SARME) (9%).

Patient age did not appear to interfere in PONV occurrence (Table 6). We also found statistical significance regarding smoking in which non-smoking patients corresponded to 66.66% of the patients with PONV episodes. In the non-smoking group 12 patients had PONV, whereas 6 patients in the smoker group reported PONV.

Considering the intubation method, 122 patients were under nasotracheal intubation and 78 under orotracheal intubation. All patients who presented PONV were in the group under nasotracheal intubation.

Regarding surgical access, all patients who reported PONV (18 cases) were submitted to intra oral access. Blood loss at surgery was higher in patients with PONV, with an average of 114 ml, whereas patients who did not present emetic events lost an average of 78 ml of blood during operation.

A significant difference was detected for PONV when comparing intubation method (table 1), type of surgical access (table 2), duration of the surgical procedure (table 3), and blood loss during surgery (table 4).

Table 1: Average Weight of Patients Who Experienced or Did Not Experience PONV (Postoperative Nausea and Vomiting)

	PONV within 24h	
	Total	No
Weight	65±0.08	70±0.08

**p<0.05, aChi-square or Fisher's exact test (n, %); bANOVA/Tukey Test (mean±SD).*

Table 2: Number of Patients who Experienced PONV in Relation to the Type of Intubation

	PONV within 24h	
	Total	No
Intubation Type		
Nasotracheal	196	178
Orotracheal	4	4

Table 3: Number of Patients who Experienced PONV in Relation to the Type of Surgery

	PONV within 24h	
	Total	No
Surgery Type		
Orthognathic Surgery	40	32
Impacted Teeth	16	14
Trauma	100	98
ERMAC	18	12
Pathology	26	26

Table 4: Number of Patients who Experienced PONV in Relation to the Type of Surgical Approach

	PONV within 24h	
	Total	No
Surgical Approach		
Intraoral	122	78
Extraoral	78	104

IV. Discussion

The literature shows that the emetic events of PONV, although often neglected, are postoperative complications that can cause great harm to the patient. The incidence of these events is between 20 and 30% of all patients undergoing surgical procedures (11). In the present study, we observed a 9% incidence of PONV, with higher incidence in patients undergoing orthognathic surgery. This finding corroborates the study of Pleuvry (12) who demonstrated an association between orthognathic surgery and PONV events.

As observed in the present study and according to investigations published in the literature, PONV is not among the most recurrent complications in orthognathic surgery; however, it is described by patients as a being worse than postoperative pain. Moreover, emetic events could lead to discharge delay thereby increasing patient length of stay at the hospital (13).

Emetic events are quite recurrent in the literature, being especially associated with gynecological, abdominal and otological procedures (14). However, the lack of investigations concerning PONV in patients undergoing oral and maxillofacial surgery hinders the establishment of a standard prevention protocol for PONV. In the present study, we observed that the highest percentage of PONV events was found in patients undergoing orthognathic surgery (8 cases), followed by SARME (6 cases), removal of impacted teeth (2 cases) and trauma (2 cases). Bhakta et al. found similar results to our findings with a higher prevalence of PONV in orthognathic surgeries (47%), followed by oral surgeries (41.7%) and oral pathologies (24.4%).

Other factors which can influence an increase emetic events are the patient's age and weight. In the present study, we observed that patients who exhibited PONV were, on average, 35 years old, whereas those who did not have PONV were, on average, 30 years old, which was statistically insignificant. This finding diverges from the reports by Lerman (15) who suggested age above 18 years as a protective factor against postoperative nausea and vomiting (15). The average weight was 70 kg for patients with PONV and 65 kg for those without. Kovac (16) found a higher incidence of nausea and vomiting in overweight patients in relation to their height. Conversely, some authors report that adipose tissue may serve as storage for some drugs because of their chemical characteristics. These drugs could eventually recirculate in the bloodstream and prevent episodes of late PONV from occurring.

The general health condition of the patient associated with harmful habits such as smoking is also described in the literature. However, some harmful habits such as chronic smoking or previous direct contact with smokers (passive smokers) could have a protective effect against PONV, as indicated by Apfel (9).

When assessing the intubation method, all patients with PONV episodes in our study were under nasotracheal intubation. Although the literature is not very clear on how the intubation method influences the occurrence of PONV, it is believed that orotracheal intubation stimulates the vagus nerve through the passage of the intubation tube close to the nerve bundle, which generates greater vagal stimulation and greater risk of nausea and vomiting (17). This was contrary to the findings of our study, in which we found a higher incidence of PONV in patients whose intubation method was nasotracheal.

Another factor observed in our study, which may be related to the increase in the amount of blood in the oral cavity during surgery, is the intraoral access. In our study, all patients with PONV underwent surgical procedures through intraoral access. A common factor in all surgeries performed in the oral cavity is the presence of blood, which can be swallowed by the patient and act as an irritant to the gastric mucosa. Therefore, nausea and vomiting events become more frequent, as there is emesis stimulation via the vagus nerve (18). This is in accordance with what we found in our study, where patients with the highest PONV rates

lost about 114 ml of blood on average, well above the average of 78 ml in those without episodes of PONV.

Studies have attempted to predict and anticipate risk factors of PONV, and the most used prediction model is the one proposed by Apfel (9). This model is based on 4 risk factors: female sex, non-smoking status, history of motion sickness or PONV, and the application of postoperative opioids. PONV incidence should be at 10%, 21%, 61% and 79%, respectively, if 1, 2, 3 or 4 risk factors are present. The prediction scores by Apfel and collaborators are easy to apply, presenting reasonable predictability of PONV. Many authors, however, criticize this model, which prevents it from being used as a gold standard in the identification of patients possibly prone to this complication. In the present investigation, we observed that the Apfel's model was accurate in only one aspect: gender (10 of the 18 patients with PONV were female). The other factors did not meet the prediction of the model proposed by Apfel and collaborators. (2005).

V. Conclusion

Non-smoking patients who underwent surgery via intraoral access lasting 3 hours or longer and with greater blood loss showed greater propensity for PONV episodes. It is of fundamental importance to be aware of the patient's profile and the characteristics of the selected surgical procedure to plan strategies to prevent PONV episodes. The establishment of an accurate and reliable PONV prediction and prevention protocol requires further investigations focused on the field of oral and maxillofacial surgery.

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- Printed material
- Graphic representations
- Computer programs
- Electronic material
- Any other original work

Authorship Policies

Global Journals follows the definition of authorship set up by the Open Association of Research Society, USA. According to its guidelines, authorship criteria must be based on:

1. Substantial contributions to the conception and acquisition of data, analysis, and interpretation of findings.
2. Drafting the paper and revising it critically regarding important academic content.
3. Final approval of the version of the paper to be published.

Changes in Authorship

The corresponding author should mention the name and complete details of all co-authors during submission and in manuscript. We support addition, rearrangement, manipulation, and deletions in authors list till the early view publication of the journal. We expect that corresponding author will notify all co-authors of submission. We follow COPE guidelines for changes in authorship.

Copyright

During submission of the manuscript, the author is confirming an exclusive license agreement with Global Journals which gives Global Journals the authority to reproduce, reuse, and republish authors' research. We also believe in flexible copyright terms where copyright may remain with authors/employers/institutions as well. Contact your editor after acceptance to choose your copyright policy. You may follow this form for copyright transfers.

Appealing Decisions

Unless specified in the notification, the Editorial Board's decision on publication of the paper is final and cannot be appealed before making the major change in the manuscript.

Acknowledgments

Contributors to the research other than authors credited should be mentioned in Acknowledgments. The source of funding for the research can be included. Suppliers of resources may be mentioned along with their addresses.

Declaration of funding sources

Global Journals is in partnership with various universities, laboratories, and other institutions worldwide in the research domain. Authors are requested to disclose their source of funding during every stage of their research, such as making analysis, performing laboratory operations, computing data, and using institutional resources, from writing an article to its submission. This will also help authors to get reimbursements by requesting an open access publication letter from Global Journals and submitting to the respective funding source.

Preparing your Manuscript

Authors can submit papers and articles in an acceptable file format: MS Word (doc, docx), LaTeX (.tex, .zip or .rar including all of your files), Adobe PDF (.pdf), rich text format (.rtf), simple text document (.txt), Open Document Text (.odt), and Apple Pages (.pages). Our professional layout editors will format the entire paper according to our official guidelines. This is one of the highlights of publishing with Global Journals—authors should not be concerned about the formatting of their paper. Global Journals accepts articles and manuscripts in every major language, be it Spanish, Chinese, Japanese, Portuguese, Russian, French, German, Dutch, Italian, Greek, or any other national language, but the title, subtitle, and abstract should be in English. This will facilitate indexing and the pre-peer review process.

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.
- The paragraph before spacing of 1 pt and after of 0 pt.
- Line spacing of 1 pt.
- Large images must be in one column.
- The names of first main headings (Heading 1) must be in Roman font, capital letters, and font size of 10.
- The names of second main headings (Heading 2) must not include numbers and must be in italics with a font size of 10.

Structure and Format of Manuscript

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

A research paper must include:

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

Design has been recognized to be essential to experiments for a considerable time, and the editor has decided that any paper that appears not to have adequate numerical treatments of the data will be returned unrefereed.

i) Discussion should cover implications and consequences and not just recapitulate the results; conclusions should also be summarized.
j) There should be brief acknowledgments.
k) There ought to be references in the conventional format. Global Journals recommends APA format.

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

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

Format Structure

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

All manuscripts submitted to Global Journals should include:

Title

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

Author details

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

Abstract

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

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

Keywords

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

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

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

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

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

Numerical Methods

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

Abbreviations

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

Formulas and equations

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

Tables, Figures, and Figure Legends

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

Figures

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

Preparation of Eletronic Figures for Publication

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

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

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

Tips for writing a good quality Medical Research Paper

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

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

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

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

5. Use the internet for help: An excellent start for your paper is using Google. It is a wondrous search engine, where you can have your doubts resolved. You may also read some answers for the frequent question of how to write your research paper or find a model research paper. You can download books from the internet. If you have all the required books, place importance on reading, selecting, and analyzing the specified information. Then sketch out your research paper. Use big pictures: You may use encyclopedias like Wikipedia to get pictures with the best resolution. At Global Journals, you should strictly follow here.

6. Bookmarks are useful: When you read any book or magazine, you generally use bookmarks, right? It is a good habit which helps to not lose your continuity. You should always use bookmarks while searching on the internet also, which will make your search easier.

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

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

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

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

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

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

13. Use good grammar: Always use good grammar and words that will have a positive impact on the evaluator; use of good vocabulary does not mean using tough words which the evaluator has to find in a dictionary. Do not fragment sentences. Eliminate one-word sentences. Do not ever use a big word when a smaller one would suffice.

Verbs have to be in agreement with their subjects. In a research paper, do not start sentences with conjunctions or finish them with prepositions. When writing formally, it is advisable to never split an infinitive because someone will (wrongly) complain. Avoid clichés like a disease. Always shun irritating alliteration. Use language which is simple and straightforward. Put together a neat summary.

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

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

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

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

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

19. Refresh your mind after intervals: Try to give your mind a rest by listening to soft music or sleeping in intervals. This will also improve your memory. Acquire colleagues: Always try to acquire colleagues. No matter how sharp you are, if you acquire colleagues, they can give you ideas which will be helpful to your research.

20. Think technically: Always think technically. If anything happens, search for its reasons, benefits, and demerits. Think and then print: When you go to print your paper, check that tables are not split, headings are not detached from their descriptions, and page sequence is maintained.

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

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

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

Informal Guidelines of Research Paper Writing

Key points to remember:

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

Final points:

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

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

The discussion section:

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

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

General style:

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

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

Mistakes to avoid:

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

Title page:

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

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

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

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

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

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

Approach:

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

Introduction:

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

The following approach can create a valuable beginning:

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

Approach:

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

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

Procedures (methods and materials):

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

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

Materials:

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

Methods:

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

Approach:

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

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

What to keep away from:

- Resources and methods are not a set of information.
- Skip all descriptive information and surroundings—save it for the argument.
- Leave out information that is immaterial to a third party.

Results:

The principle of a results segment is to present and demonstrate your conclusion. Create this part as entirely objective details of the outcome, and save all understanding for the discussion.

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

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

Content:

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

What to stay away from:

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

Approach:

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

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

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

Figures and tables:

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

Discussion:

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

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

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

Research papers are not acknowledged if the work is imperfect. Draw what conclusions you can based upon the results that you have, and take care of the study as a finished work.

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

Approach:

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

Describe generally acknowledged facts and main beliefs in present tense.

The Administration Rules

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

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

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

Written material: You may discuss this with your guides and key sources. Do not copy anyone else's paper, even if this is only imitation, otherwise it will be rejected on the grounds of plagiarism, which is illegal. Various methods to avoid plagiarism are strictly applied by us to every paper, and, if found guilty, you may be blacklisted, which could affect your career adversely. To guard yourself and others from possible illegal use, please do not permit anyone to use or even read your paper and file.

Criterion for Grading a Research Paper (Compilation) by Global Journals

Please note that following table is only a Grading of "Paper Compilation" and not on "Performed/Stated Research" whose grading solely depends on Individual Assigned Peer Reviewer and Editorial Board Member. These can be available only on request and after decision of Paper. This report will be the property of Global Journals.

Topics	Grades		
	A-B	**C-D**	**E-F**
Abstract	Clear and concise with appropriate content, Correct format. 200 words or below	Unclear summary and no specific data, Incorrect form Above 200 words	No specific data with ambiguous information Above 250 words
Introduction	Containing all background details with clear goal and appropriate details, flow specification, no grammar and spelling mistake, well organized sentence and paragraph, reference cited	Unclear and confusing data, appropriate format, grammar and spelling errors with unorganized matter	Out of place depth and content, hazy format
Methods and Procedures	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
Result	Well organized, Clear and specific, Correct units with precision, correct data, well structuring of paragraph, no grammar and spelling mistake	Complete and embarrassed text, difficult to comprehend	Irregular format with wrong facts and figures
Discussion	Well organized, meaningful specification, sound conclusion, logical and concise explanation, highly structured paragraph reference cited	Wordy, unclear conclusion, spurious	Conclusion is not cited, unorganized, difficult to comprehend
References	Complete and correct format, well organized	Beside the point, Incomplete	Wrong format and structuring

INDEX

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