SANKALCHAND PATEL UNIVERSITY
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Contents

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Inaugural Message

It is with immense pride and heartfelt joy that I write this inaugural message for the *Journal of Integrative Health Research (JIHR)*, a flagship initiative of Sankalchand Patel University. This journal represents a significant milestone in our ongoing pursuit of excellence in healthcare education, research, and practice.

The field of integrative health is witnessing a remarkable evolution as it brings together the time-honored traditions of holistic healing with the rigor of modern scientific research. At Sankalchand Patel University, we have always embraced the philosophy of blending the wisdom of the past with the innovations of the present. The launch of JIHR is a testament to this vision and reflects our unwavering commitment to fostering interdisciplinary collaboration in healthcare for the betterment of society.

I take this opportunity to extend my warmest congratulations to **Dr. J. R. Patel, Director, Health Sciences**, for his unwavering dedication and dynamic leadership in bringing this initiative to fruition. His vision of creating a platform to promote high-quality research in integrative healthcare has been instrumental in the establishment of JIHR.

A special acknowledgment and heartfelt congratulations are also due to **Dr. Vivekanand Kattimani, the Editor-in-Chief of JIHR**, for his exemplary leadership of the editorial team and expertise, tireless efforts, and commitment to uphold the highest standards of scientific rigor and ethical integrity that have been pivotal in shaping the journal into a credible and impactful platform for research dissemination.

The *Journal of Integrative Health Research* is poised to serve as a bridge between conventional and alternative medicine, creating a space for evidence-based studies, critical reviews, clinical insights, and innovative ideas. By embracing a holistic approach, the journal aims to contribute significantly to address the multifaceted healthcare challenges of the modern era, including the rise of chronic diseases, lifestyle disorders, and the need for patient-centered care.

As we celebrate this historic milestone, I invite researchers, academicians, clinicians, and policymakers from across the globe to join us in this transformative journey. Your contributions will be invaluable in building a robust body of knowledge that has the potential to redefine healthcare practices and improve lives.

Let us work together to make the *Journal of Integrative Health Research* a beacon of innovation, collaboration, and excellence in the healthcare community. I am confident that this initiative will leave a lasting impact on the future of healthcare and inspire new paradigms in integrative health research.

With best wishes for the success of JIHR and gratitude to all who have made this dream a reality, let us embark on this exciting journey to advance the frontiers of healthcare research.

Shri PrakashPatel
President
Sankalchand Patel University
Visnagar, Gujarat, India

Sankalchand Patel University Visnagar

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With best wishes for the success of JIHR and gratitude to all who have made this dream a reality, let us embark on this exciting journey to advance the frontiers of healthcare research.

Prof. (Dr.) Prafulkumar Udani
Provost
Sankalchand Patel University
Visnagar, Gujarat, India

Sankalchand Patel University Visnagar

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Inaugural Message

It is with immense pride and great pleasure that I present this inaugural message for the *Journal of Integrative Health Research (JIHR)*. This journal marks a significant milestone in the journey toward advancing interdisciplinary collaboration and promoting a holistic approach to healthcare.

The modern healthcare landscape calls for a convergence of traditional and contemporary medical practices to address the growing complexities of human health. The *Journal of Integrative Health Research* serves as a dedicated platform to bridge this gap, fostering dialogue between conventional medicine and alternative therapies such as Ayurveda, Yoga, and other traditional systems of healing. Our mission is to inspire evidence-based studies that enhance healthcare practices by combining innovation with the wisdom of age-old traditions.

I would like to take this opportunity to recognize and congratulate the efforts of the editorial team, led by **Dr. Vivekanand Kattimani, Editor-in-Chief of JIHR**. Under his visionary leadership, the team has worked tirelessly to bring this journal to fruition. Their dedication to ensuring scientific rigor, upholding ethical standards, and curating impactful research is commendable.

JIHR is committed to publish high-quality original research, review articles, clinical studies, and case reports that explore integrative health approaches. By fostering global collaboration, we aim to inspire innovative ideas and evidence-based solutions that address pressing healthcare challenges such as chronic diseases, lifestyle disorders, and rising healthcare costs.

I extend my gratitude to the editorial board, reviewers, and contributors for their relentless efforts in launching this journal. Your passion and commitment have laid a strong foundation for its success.

As we embark on this journey, I invite researchers, clinicians, and academicians worldwide to contribute their insights and discoveries to JIHR. Together, we can advance the frontiers of integrative healthcare, creating a positive impact on the well-being of individuals and communities.

With best wishes for the success of JIHR, let us move forward, united in our mission to revolutionize healthcare through integration, innovation, and collaboration.

Dr. J. R. Patel
Director, Health Sciences
Sankalchand Patel University
Visnagar, Gujarat, India

Sankalchand Patel University Visnagar

Editorial Message

With immense pride and enthusiasm, I present the inaugural issue of the *Journal of Integrative Health Research (JIHR)*, the official publication of the Sankalchand Patel University, Visnagar, Gujarat. This journal serves as a platform dedicated to integrating modern medicine and Indian systems of medicine, including Ayurveda, Homeopathy, Unani, and other traditional practices, reflecting the university's commitment to advancing interdisciplinary healthcare research.

The launch of *JIHR* comes as healthcare systems worldwide is evolving to embrace a more comprehensive, patient-centered approach. The integrative health model combines the strengths of modern medical advances with the time-tested wisdom of Indian traditional medicine. This approach not only promotes healing, but also emphasizes preventive care, wellness, and holistic treatment, offering a broader spectrum of care that meets the complex needs of patients today.

Bridging Modern and Traditional Medicine

At its core, integrative health acknowledges that modern medicine excels in diagnosing and treating acute and critical conditions through technological advancements, while Indian systems of medicine offer invaluable insights into chronic disease management, preventive care, and the promotion of overall well-being. The *JIHR* aims to bridge these two systems, encouraging dialogue, collaboration, and research that demonstrate the potential of combined approaches to healthcare.

Our vision for *JIHR* is to become a leading platform for sharing original research, reviews, clinical studies, and case reports that explore the integration of modern and traditional health practices. By fostering interdisciplinary research, we aim to advance knowledge that contributes to better health outcomes and improved patient care.

The Importance of Integrative Research

Integrative healthcare is gaining recognition not only in India but around the world. The increasing prevalence of chronic diseases, lifestyle-related health issues, and the growing demand for holistic, patient-centered care make it essential to explore all available medical systems. The combination of modern diagnostics and treatment strategies with the preventive and holistic approaches of Indian medicine systems can offer a more balanced and effective healthcare model.

At *JIHR*, we are committed to publishing high-quality, evidence-based research that highlights the benefits of such an integrative approach. Our goal is to ensure that both healthcare practitioners and researchers have access to innovative insights that promote interdisciplinary understanding and collaborative practice.

A Future of Collaboration

The establishment of *JIHR* is a testament to the vision of Sankalchand Patel University to promote integrative health research. I would like to extend my sincere gratitude to The Provost of the university and the editorial board for their dedication and support in making this journal a reality.

As we embark on this new journey, I invite researchers, clinicians, and healthcare professionals from all streams to contribute their work to *JIHR*. Together, we can shape the future of healthcare by integrating the best of modern and traditional medicine.

Warm regards,

Dr. Vivekanand Kattimani, MDS, Ph.D
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Head, Department of Clinical Research, Sibar Institute of Dental Sciences, Guntur.
Andhra Pradesh, India.

Efficacy of Low-Level Laser Therapy and Temporomandibular Joint Mobilization in subjects with Myo-facial Pain Syndrome

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Abstract

Background: Every age group is affected by myofascial pain syndrome (MPS), a regional pain illness that is typified by the presence of trigger points (TrPs) in the muscles or fascia. A distinct local and referred pain that is in line with the patient's presenting pain symptoms is produced when manual pressure is applied over an MPS. MPS can be treated with a variety of physiotherapy techniques. There are conflicting findings about the effectiveness of temporomandibular mobilization and low-level laser treatment (LLLT) in treating MPS, as evidenced by earlier research. For the treatment of MPS, there is also no comparison between LLLT and temporomandibular mobilization. The study sought to determine the effectiveness of temporomandibular joint mobilization and LLLT in treating MPS.
Results: Both methods are effective in reducing the degree of discomfort and increasing the maximum mouth opening in MPS patients.
Conclusion: TMJ joint mobilization, LLLT, and physical therapy therapies demonstrated notable clinical improvements in reducing discomfort and maximizing mouth opening in people with MPS.
Keywords: *Temporomandibular (TMJ) mobilization, low-level laser therapy (LLLT), and myofascial pain syndrome (MPS).*

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Introduction

Trigger points (TrPs) in muscles or fascia are a hallmark of myofascial pain syndrome (MPS), a regional pain disease that affects people of all ages. One of the most frequent cause of chronic regional pain in the region of temporomandibular joint is MPS, which is sometimes referred to as "muscle knots." Simon initially described MPS as a "combination of sensory, motor, and autonomic symptoms that are caused by Myo-facial trigger points". [1]

The patient's presenting pain symptoms are consistent with the unique local and referred pain that is produced when manual pressure is placed over an MPS region.[2] Although MPS is frequently combined with other pain syndromes, it differs from conditions like fibromyalgia in that it is localized, involves a taut band in skeletal muscle, and does not require numerous pain generators.

Although the precise prevalence of MPS in the general population is rarely mentioned in the literature. Currently literature demonstrates certain studies have suggested that MPS accounts for 30 to 85% of musculoskeletal pain in patients. Commonest age range of the condition is 27

to 50 years when this ailment most commonly affects people. Gender differences for the condition have not yet been identified. The pathophysiology of MPS is currently poorly understood; however, it is believed to be caused by muscle overload from either overuse or lack of exercise.

Traumatic events, ergonomic factors (such as poor or abnormal posture, overuse activities, etc.), structural factors (such as osteoarthritis, scoliosis, etc.), and systemic factors (such as hypothyroidism, vitamin D deficiency, and iron deficiency) are some of the risk factors that have been found to contribute to the development of MPS.[2]

Though MPS is very common, little is known about its pathophysiology. According to one theory, TrPs result from a malfunction of the neuromuscular junction and the connective tissue around it. Studies using electromyography have shown some indication of aberrant electrical activity at the motor endplates of neurons that terminate on TrP muscle fibers. Excessive acetylcholine (ACh) release was shown to be associated with excessive electrical activity, and both of these findings suggest potential pathways for the development of MPS and TrP activation.

Low Level Laser Therapy (LLLT) is considered as one of the conservative mode of therapy it has become more and more popular among the various physiotherapy techniques for treating MPDS. On irradiated tissues, LLLT has demonstrated analgesic, healing, and anti-inflammatory properties. Another method of treating MPS is mandibular mobilization. By theoretically exploiting reciprocal inhibition, this active-assistance strategy is used to improve mouth opening.[4]

Materials and Method

Forty MPS patients with restricted mouth opening were chosen from Nootan College of Physiotherapy's Orthopaedic Physiotherapy outpatient department. A painless, unsupported mandibular opening of <40 mm was considered limited mouth opening. Subjects who were treated for temporomandibular joint disorder in any way, including analgesics or antidepressants, were not allowed to participate in the study. The ethics committee of Sankalchand University's Nootan College of Physiotherapy gave its approval to the study. Before therapy began, each participant was informed about the study design and goal. Informed consent was obtained. Twenty patients each were randomly assigned to the LLLT and TMJ mobilization groups.

Prior to each treatment, the laser probe was cleaned with an alcohol swab and the laser was calibrated. The laser device used was gallium-aluminum-arsenide diode source (Doctor Smile Diode Laser, Italy). At 810 nm the instrument produced a continuous beam of 0.5 W peak power with a spot size of 5 mm. Light pressure was applied to the targeted muscle while the probe was held perpendicular during the procedure. To identify painful locations, the masticatory muscles were assessed bilaterally using forceful, continuous pressure. Patients in the laser group underwent 12 LLLT treatments (Table 1).

Table1: LLLT irradiation protocol

Day	1st week	2nd week	3rd week	4th week
Saturday	0.5W	0.2W	0.3W	0.1W
Sunday	0.4W			
Monday	0.3W	0.3W		
Tuesday	0.2W			
Wednesday	0.1W	0.4W	0.2W	0.2W

Two methods of TMJ mobilization treatment were administered to group 2. First, there was a passive method known as "long-axis distraction." The therapist uses this approach by placing the index or middle fingers beneath the patient's distal chin and the thumb on the patient's lower posterior

molars. The opposing hand stabilized the head. The therapist extracts the mandible along the long axis of the condyle by gently pressing inferiorly with the thumb and tapping the distal chin. This method should, in our opinion, be applied gently, held for about five seconds, and then repeated three to five times, or as necessary (Fig. 1).

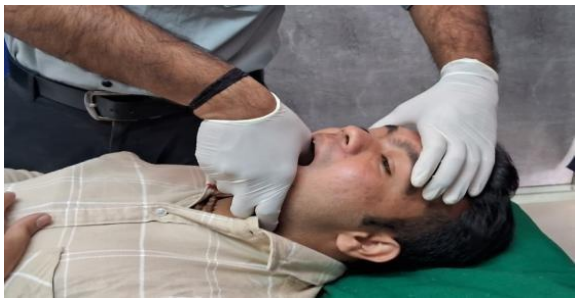

Fig1: Mobilization technique for the long-axis distraction of temporomandibular joint.

The second method of mobilization was "overpressure with an opening." This technique utilizes the same hand placement and stabilization as used for long-axis distraction. The patient was instructed to open their mouth wide - as wide as they could. After that, the therapist applies light pressure on the molars. An "overpressure" with an opening results from this. It is performed three times while being held for roughly five to ten seconds. The therapy was administered four days a week.

Fig2: Low level LASER Therapy

Results

Every participant completed the procedure during the study period. Ten patients (25%) were male, while thirty patients (75%) were female. The participants in this study were 36±12.34 years old on average. (Table 2)

Table 2: Result of both groups from 1-4 weeks.

Mean	1st week	2ndweek	3rdweek	4thweek
Changes in Mean Subjective VAS in Groups in the Whole Treatment Phase	7.25±1.51	5.65±1.69	4.80±1.79	2.75±2.19
Changes in mean subjective Maximum Painless Mouth Opening During the Treatment	31.63±7.35	33.05±5.94	33.94±5.63	39.00±8.84

Discussion

Patients with MPD may benefit from LLLT and TMJ mobilization, a non-invasive, quick, safe, and non-pharmaceutical therapeutic approach. Therefore, the purpose of this study was to determine whether mouth opening and pain intensity might be improved in MPDS patients by using LLLT or TMJ mobilization.

According to the findings, both groups experienced a 95.86% decrease in pain, and the pain did not return during the follow-up period. The release of endogenous opioids, improvement of cellular respiration and tissue healing, vasodilation, increased pain threshold by altering the action potential of cell membranes, and reduction of inflammation. This was achieved by lowering Prostaglandin E2 and cyclooxygenase 2 levels which were some of the diverse mechanisms of action underlying the therapeutic and analgesic effects.[5] Carrasco et al. (780 nm, 50/60/70 J/cm²), da Cunha et al. (830 nm, 500 mW, 100 J/cm²),

and Emshoff et al. (632.8 nm, 30 mW, 1.5 J/cm²) observed a considerable reduction in discomfort. intensity in both the laser and placebo groups, indicating that the placebo effect of laser administration was primarily responsible for the improvement. In line with our study's findings, Marini et al. hypothesized that LLLT was more effective than ibuprofen at treating TMJ disorder-related pain and that all patients who got it experienced improvements in their mandibular function and pain severity.[6]

Maximum painless mouth opening was significantly improved in both groups in this study. Results show that both groups' mouth opening increased by 33.60% beginning with the first session. According to the literature, it indicates that LLLT demonstrates the functional improvement and that the patients' objective functional metrics happened later than the reduction in pain intensity.[7,8,9] TMJ mobilization procedures demonstrated that when the patient employs the agonists (lateral pterygoid, suprahyoid, and infrahyoid muscles) to voluntarily open their mouth wide, the motor neurons to the antagonists of jaw opening (masseter, temporalis, and medial pterygoid muscles) should be repressed. Muscle guarding should be reduced with the help of this technique. [6, 10]

Conclusion

TMJ joint mobilization and LLLT, two physical therapy procedures, were found to significantly enhance clinical outcomes in terms of pain reduction and maximum mouth opening in MPS patients.

Authors do not disclose and conflict of interest.

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Evaluate the effectiveness of cryotherapy on reduction of pain during arterio-venous fistula puncturing among patients undergoing he modialysis at Amaravathi Hospital, Karur (Dt), Tamil Nadu.

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Abstract

Introduction: The study's objective was to assess how well cryotherapy reduces pain during arterio-venous fistula puncturing in hemodialysis patients.
Materials and Method: Thirty samples were chosen for the experimental group and thirty samples for the control group, totaling sixty samples. The Numerical Pain Rating Scale was used to gather the data. Cryotherapy was given to the experimental group. The post-test was administered without intervention to the control group. During the data collecting period, five to ten hemodialysis patients are evaluated every day. Both descriptive and inferential statistics were used to analyze the data.
Results: Following cryotherapy, there was a notable difference between the experimental and control groups. The degree of pain decreased. To link the post-test result to specific demographic characteristics, chi square analysis was performed. The post-test score and the experimental group's demographic characteristics are significantly correlated.
Conclusion: Arteriovenous fistula puncturing pain can be significantly decreased by cryotherapy.
Keywords: *cryotherapy, hemodialysis, and arterio-venous fistula puncture*

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Introduction

A worldwide health emergency is chronic kidney disease. The prevalence of chronic renal disease is rising globally. According to the 2015 Global Burden of illness Study, renal illness accounted for 1.1 million fatalities globally, making it the 12th most prevalent cause of death. Over the past ten years, the overall mortality rate from CKD has risen by 31.7%, making it one of the leading causes of death with the quickest rate of increase.[1,2]

In India, around 1,75,000 new patients require dialysis each year due to kidney failure. Hemodialysis patients frequently experience pain during arteriovenous fistula cannulation, which makes them less likely to adhere to the lifelong maintenance of hemodialysis.3. Despite the fact that local anesthetic is not commonly utilized because of the risk of vasoconstriction, burning sensation, scarring, and infection, arterio-venous fistula punctures are painful. Frequent fistula puncture discomfort can cause sadness, avoidance, or condensed session duration. Cryotherapy is the use of cold materials to lower tissue temperature by removing heat from the body. Through vasoconstriction, it lowers tissue blood flow, tissue metabolism, and muscle spasm.

A local anesthetic effect known as cold-induced neuropraxia is the outcome of these.[4,5]

Objectives

1. To assess how well cryotherapy works to lessen the discomfort associated with arteriovenous fistula punctures in patients receiving hemodialysis in the experimental and control groups.
2. To determine the association between hemodialysis patients' chosen demographic characteristics and their post-test arteriovenous fistula puncture pain level.

Hypotheses

H1: Patients receiving hemodialysis in the experimental and control groups have significantly different levels of arteriovenous fistula puncture pain.
H2: The degree of discomfort experienced during an arteriovenous fistula puncture is significantly correlated with the demographic characteristics chosen for hemodialysis patients.

Material and methods

An evaluative research methodology was adopted. The design of the search is one group post-test only. The Amaravati Hospital in Karur, Tamil Nadu, was the site of this investigation. The group consists of hemodialysis patients with chronic renal failure.

The director of Amaravati Hospital in Karur, the ethical committee, and the principal of Sri Aurobindo College of Nursing all formally gave the researcher permission to carry out the study. Using the convenience sampling strategy, 60 samples were chosen. The experimental group received thirty samples, while the control group received the remaining thirty. There are both males and females. The age range is 18–70 years old, and patients with peripheral vascular disease, Raynaud's disease, or cardiovascular disease are not included.

The experimental group received the cryotherapy. Ten minutes prior to the puncture, and two minutes following the procedure, Researcher filled the glove with ice cubes and began massaging the web between the thumb and index finger with ice. After two minutes, the post-test was administered. It went on for a month. The efficiency of the intervention was compared with the control group, which did not receive the intervention. Five to ten hemodialysis patients are evaluated every day.

Materials:

Tool consists of three sections.
Section A - Demographic variables,
Section B - clinical variables,
Section C - numerical pain rating scale.

Results

The majority of the experimental group experienced minor pain after receiving cryotherapy; 16 (53.33%) experienced mild discomfort, and 14 (46.67%) experienced moderate pain. (Table 1) Of those in the control group, 24 (80%) reported having severe pain, 6 (20%) reported having moderate pain, and 0 reported having no pain. This indicates that hemodialysis patients' arterio-venous fistula puncture pain scores differ significantly between the experimental and control groups (Table 2).

The post-test score of arteriovenous fistula puncture pain was compared to demographic variables such as age, gender, education, occupation, place of residence, marital status, family income, nutritional habits, bad habits, length of disease, frequency of dialysis, presence of an arm arteriovenous fistula, co-morbidity illness, arteriovenous fistula site, and duration of current arteriovenous fistula using the chi-square test. Post-test scores are significantly correlated with age ($p=0.05$), gender ($p=0.01$), and the location of the arterio-venous fistula ($p=0.03$). The experimental group's post-test level of pain score is not significantly impacted by the remaining demographic factors. None of the demographic factors in the control group were related to the posttest pain score. (Table 3)

Table1: Shows the post-test Level of pain score among the Experimental and Control group

Level of pain	Group			
	Experimental Group(n=30)		Control Group(n=30)	
	F	%	F	%
No Pain	0	0.00	0	0.00
Mild Pain	16	53.33	0	0.00
Moderate Pain	14	46.67	6	20.00
Severe Pain	0	0.00	24	80.00

Table 2: Post-test Mean,SD,and‘t’testscoreof Arterio-venous fistula puncture pain level among patients undergoing hemodialysis

Group				Meand ifferen ce	t-test	Table Value
Experimental(n =30)		Control(n =30)				
Mean	SD	Mean	SD			
3.37	1.65	7.93	1.34	4.56	t=11. 77p= 0.0 01** *(S)	2.20

post-test mean score is 7.93, SD1.34 and the mean difference is 4.56, the calculated ‘t’ value is =11.77 (p=0.001). The table ‘t’ value is 2.20. It inferences that the calculated ‘t’value is higher than the table ‘t’ value. It shows that cryotherapy is highly effective in reducing arteriovenous fistula puncture pain among hemodialysis patients. So, the research hypothesis H1 is accepted

Table3: Shows the association between post-test level of pain score with demographic variables of hemodialysis patients in the experimental group

Demographic variables	**Level of pain score**						**n**	**Chi square test**
	Mild		**Moderate**		**Severe**			
	F	**%**	**F**	**%**	**F**	**%**		
Age in years								2=8.92 P<0.05* (S)
a)18– 30yrs	1	14.29	6	85.71	0	0.00	7	
b)31–45yrs	2	33.33	4	66.67	0	0.00	6	
c)46– 60yrs	6	75.00	2	25.00	0	0.00	8	
d)61– 70yrs	7	77.78	2	22.22	0	0.00	9	
Gender								2=6.46 p>0.01** (S)
a)Male	12	66.67	4	33.33	0	0.00	16	
b)Female	4	28.57	10	71.43	0	0.00	14	
Site of AV Fistula								2=9.19 p<0.03* (S)
a) Radio-cephalic-AVF	4	100.00	0	0.00	0	0.00	4	
b) Brachio-cephalic-AVF	2	28.57	5	71.43	0	0.00	7	
c) Brachio-basilic-AVF	10	62.50	6	37.50	0	0.00	16	
d)Ulnar-basilic-AVF	0	0.00	3	100.0 0	0	0.00	3	

The post-test score of arteriovenous fistula puncture pain was compared to demographic variables such as age, gender, education, occupation, place of residence, marital status, family income, nutritional habits, bad habits, length of disease, frequency of dialysis, presence of an arm arteriovenous fistula, co-morbidity illness, arteriovenous fistula site, and duration of current arteriovenous fistula using the chi-square test. Post-test scores are significantly correlated with age (p=0.05), gender (p=0.01), and the location of the arterio-venous fistula (p=0.03). The experimental group's post-test level of pain score is not significantly impacted by the remaining demographic factors. None of the demographic factors in the control group were related to the posttest pain score. (Table 3)

Conclusion

According to the findings, cryotherapy was successful in reducing the level of pain experienced by patients receiving hemodialysis at the locations of arteriovenous fistula punctures. It is advised as a pain-relieving method for hemodialysis patients undergoing AV fistula puncture and can be utilized as a non-pharmacological intervention. Cryotherapy is a simple, low-risk technique that appears to be helpful in easing pain.

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Aversive Conditioning: Hand-over-Mouth Technique & Physical Restraint

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Abstract

It is widely accepted that behavior control is crucial when it comes to giving children dental treatment. In fact, if a child's behavior in the dental office is not managed, it is difficult, if not impossible, to provide any necessary dental care. In the field of Pediatric dentistry, children are typically treated using a variety of psychological behavior management techniques. However, when all psychological behavior management strategies are ineffective at calming the child, physiological strategies such as physical restraint and hand-over-mouth exercises are used to stop the child's inappropriate behavior and provide dental treatment with the parents' permission.

Keywords: *Hand-over-mouth technique, Physical restraint, Children, Pediatric Dentistry*

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Introduction

According to the American Academy of Pediatric Dentistry (AAPD), dental care is medically required to prevent and treat oro-facial diseases, infections, and pains; to restore the dentition's structure and function; and to treat face deformities or dysfunctions.[1] Any action that is observable, quantifiable, and recordable is considered behavior.[2]

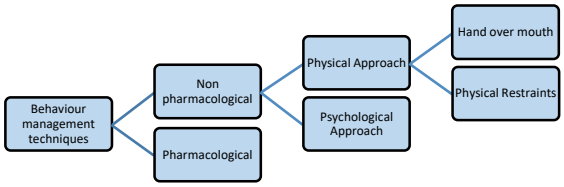
A child's good behavior is not a miracle; it requires a variety of encouragement techniques to support them during their difficult times. A dentist's ability to constructively manage a youngster while meeting their dental needs is one of their primary attributes. Consequently, they will develop a favorable dental attitude and maintain good oral health.[3] Wright et al. (1975) defined behaviour management as the method by which the dental health team treats a young patient effectively and efficiently while also fostering a healthy dental attitude.[2,3]

Objectives of behaviour management:[2] According to Snowder (1980),

• To provide a calm, pleasant environment for the child;
• To build trust between the child and parent regarding dental care;
• To instill in the child a favorable attitude toward preventative dental care;

Classification of behavior management techniques:[2]

In 2002, the Royal College of Surgeons (England) released the first national clinical recommendations on non-pharmacological behavior management strategies online.[3,4]



Hand–over–Mouth Technique (Home):

It was Dr. Evangeline Jordan who initially reported this method in 1920.

Dr. Evangeline Jordan wrote: "Hold a folded napkin over the child's mouth and gently but firmly hold the mouth shut if a typical child will not listen but still cries and struggles." When his mouth is kept shut, there is minimal sound and he quickly starts to reason, but his scream made his hysteria worse.[2]

Table 1: Types of mechanical aids for protective stabilization:[1]

PART	AID	FEATURES
Mouth	Tongue blades Open wide mouth prop	Use these to open mouth directly. It features a tongue depressor with a sturdy foam core on the outside. i t is long-lasting, Simple to use, and comes in two different sizes.
	Molt mouth prop	For a long time, it can be quite beneficial when managing a challenging patient. Different sizes are available It makes the other side of the mouth accessible. If Improperly applied, It cuts palatal and lip as well as cause tooth luxation It is best to avoid pushing the patient's mouth above its natural boundaries because doing so would make them uncomfortable and anxious, which could compromise their airway.
	Rubber bite blocks	Different sizes are available to fit on the occlusal surfaces and keep the mouth open. To make it easier to retrieve the bite blocks in the event that they become dislodged in the mouth, floss should be tied to them.
	Finger guards	Used directly to open mouth
Body	Papoose Board	Easy to use and store Both large and small children can be accommodated there Head stabilizers attached Reusable If taken in along with sedation, it is essential to monitor respiration. Any patient who is confined needs ongoing attention and supervision since a very resistive patient could become hyperthermic if immobilized for an extended period of time.
	Triangular sheet	Mink explained how to manage a child that is very resistant by utilizing a triangle sheet. It enables the patient to stand up straight for radiography tests. Its drawbacks include the potential for airway impingement, the difficulty of using it on little patients, and the frequent requirement for straps to keep the patient in the chair. Another issue that could arise during extended immobility is hyperthermia. It is stressed that continuous supervision is necessary to prevent these issues.
	Pedi-Wrap	Comes in different sizes Permits some mobility while keeping the sufferer confined. Its mesh material keeps you from getting too hot. Straps are necessary to keep the body in the dental chair. Continuous monitoring to stop the patient from getting out of the chair
	Beanbag dental chair insert	Reusable and washable. It was created to comfortably accommodate hypnotic and severely spastic individuals who require more support and less immobility in a dental setting. In this environment, many individuals with physical limitations feel more at ease.
	Safety belt and extra assistant	Used to control movements
Extremities	Posey straps Velcro straps Towel and tape Extra assistant	Attach to the dental chair's arms and permit a restricted amount of movement. frequently stops patients who are aggressive or resistant from overreacting. Beneficial for a patient with athetoid-spastic cerebral palsy who makes a valiant but unsuccessful effort to control their body motions
Head	Head positioner Plastic bowl Extra assistant	Used to stabilize head

According to Craig (1971), the technique's goal is to grab a child's attention so that they can communicate.[5] Rombom et al. (1981) contended that rather than being an unpleasant approach, the technique is better understood psychologically as response prevention, a flooding procedure.[6]

According to Barton (1993), HOME could be better explained in terms of negative reinforcement, in which the child's behavior of being silent and putting an end to the protest is reinforced by the removal of the unpleasantness associated with being unable to protest loudly and having his or her limbs constrained. It has been discovered that youngsters are not impacted by or recall hand-over-mouth or restraining events. [7] Types of mechanical devices for protective stabilization are displayed in Table 1.[1]

Other terminologies: Emotional surprise therapy by Lampshire, HOM Airway Restricted (HOMAR) by Levitas (1947), Aversion by Crammer (1973), Aversive Conditioning by Lenchner and Wright (1975)[2]

Objectives:
• To capture the child's interest and facilitate discussion with the dentist in order to communicate acceptable behavior expectations.
• To create a suitable learnt response and get rid of improper avoidance behavior related to dental care.
• To boost the child's self-assurance in handling dental stimuli that cause anxiety.
• To guarantee the safety of children while providing high-quality dental care.[2]

Indications:
• A healthy children who can comprehend and participate yet behaves hysterically, defiantly, or obstinately after receiving dental care. [2]
• Mostly used with children who can communicate effectively and in the age range of 3 to 8 years old. [8]

Contraindications:
• Any children whose mental capacity and command of language make effective conversation difficult;
• When it stops the child from breathing;
• When the dentist is emotionally attached with the child.[8]

Technique:
• A hand is put over the child's lips as necessary, and the expectations for behavior are calmly communicated.
• The child is informed that as soon as the proper behavior starts, the hand will be taken away.
• The hand is taken away when the child reacts, and the proper behavior is rewarded.
• The process is repeated if the youngster exhibits unfavorable behavior once more.[2]

Legality of use of home:
• It has been noted that when HOME is used appropriately and with parental approval, the patient will not hold the dentist liable.
• Using Hand Over Mouth Airway Restricted (HOMAR) is more or less illegal and could make the dentist liable. [2]

Review of literature:
Association of Pedodontic Diplomates (1970) found out that 80% Pediatric Dentist used HOME technique frequently.[2]
Acs G et al (1990) suggested that HOM was indicated in situations other than for the control of hysterical and tantrum-like behaviour.[9]
Carr et al. (1999) found out the number of clinicians who did not practice HOME was around 57%.[10]
Adair et al. (2004) observed that 79% of the clinicians did not use HOME.[11]
Hassan SQ et al (2010) did the survey to check the alternative behaviour management techniques that might be utilized by pediatric dentists in place of HOME after its elimination from the

clinical guidelines of the AAPD. He found that 50% pediatric dentist believed that HOME is an acceptable behaviour management technique, and 41% believed it should be continued to be recognized by the AAPD. Only 7% believed that HOME elimination affected access to care for some children.[12]

Desai SP et al (2019) conducted study to assess the attitudes of parents of children towards Behaviour management techniques used by pediatric dentists. He found tell show do, positive reinforcement, and live modeling were the most accepted techniques, while the least accepted techniques were HOME and voice control technique.[13]

Segarra Ortells C et al (2021) did the survey of members of the Spanish Society of Pediatric Dentistry about behaviour modification techniques and He found the most common techniques were Tell Show Do and positive reinforcement, while the most abandoned HOM because it was rejected by parents and because of potential legal problems and psychological consequences for the patients.[14]

Variations of the techniques: Airway uninstructed, hand over both nose and mouth (HOMAR), towel held over mouth only, dry towel over nose and mouth, wet towel over nose and mouth.[2]

Protective stabilizers: In certain cases, diagnosing and treating individuals who require assistance with controlling their extremities may require partial or total immobilization of the patient. In order to prevent harm to the patient, the dentist, or other dental personnel while treatment is being given, immobilization is especially helpful when dealing with belligerent, resistant patients. Before immobilization is employed, the parents must be fully informed, their consent must be recorded, and they must understand the sort of immobilization to be utilized, its purpose, and its duration.[2]

According to the May 1996 revision of the American Psychological Association's Standard of Care for Behavior Management, immobilization must be justified by the necessity to diagnose and treat the patient as well as to ensure the practitioner's and patient's safety. The patient's emotional development, physical and medical factors, dental needs, other alternative behavioral modalities, and the standard of dental care should all be taken into account while making this decision. Since we are not only strapping the youngster to the chair to limit his movement, the terms medical immobilization and protective stabilization have replaced the previous vocabulary of physical restraints. The youngster and the dentist will both benefit and be protected if the child is rendered immobile. [2]

When a parent, dentist, or dental assistant restricts a person's movement, this is known as active immobilization. In passive immobilization, a restraining device is used. [11] In the context of dentistry, restraint is defined by Frankel et al. (1991) as the act of physically restricting a kid's movements to facilitate dental treatments and reduce the risk of harm to the child and/or dentist.[15]

In order to help patients with physical or mental disabilities avoid involuntary movements of their limbs or heads, whole-body restraint is frequently used in conjunction with sedation. It can also be used as an alternative to sedation or general anesthesia in very young children.[8]

Objective:

- Used to control unwanted physical movement of the child, both to facilitate treatment and also to prevent harm to the child and dental staff.[8]
- Facilitate delivery of quality dental treatment.[16]

Indications:

• A patient who needs diagnosis or treatment but is unable to comply due to immaturity;

- A patient who needs diagnosis or treatment but is unable to cooperate due to physical or mental impairments.
- A patient who, after previous behavior control strategies have failed, refuses to participate and needs a diagnosis or treatment.
- When the practitioner's or patient's safety would be in jeopardy if immobilization weren't used for protection.[2]
- To control involuntary movement with sedated patients,
- When sedation or general anaesthesia are not available or permitted by parents.[8]

Contraindications:

- A patient who is compliant;
- A patient whose underlying medical or systemic issues prevent them from being safely immobilized
- As a kind of discipline;
- Not just for the staff's convenience.[2]
- A patient with a history of physical or psychological trauma, including physical or sexual abuse or other trauma that would place the individual at greater psychological risk during restraint.[16]

Connicket al (2000) distilled 5 salient points on use of restraint:[17]

i. It should only be used when absolutely necessary
ii. The least restrictive alternative should be chosen
iii. It should not be used as punishment
iv. It should not be used solely for the convenience of the dental team
v. Staff should closely monitor its use.

Precautions: [18,19]

The following precautions are recommended:

The patient's medical history must be reviewed carefully to ascertain any medical conditions or medications that can compromise physiologic function, may contra indicate the use of protective stabilization, or are associated with specific risk factors including: Cardiac instability, Pulmonary and respiratory instability, Musculoskeletal alignment issues or weakness, Joint hypermobility, Bone fragility, Cutaneous vulnerability to mechanical stress, Psychological instability, Thermoregulation disorders, Psychotropic medications, Tightness and duration of the stabilization must be monitored and reassessed at regular intervals, Stabilization around extremities or the chest must not actively restrict circulation or respiration;

Observation of body language and pain assessment must be continuous to allow for procedural modifications at the first sign of distress; and stabilization should be terminated as soon as possible in a patient who is experiencing severe stress or hysterics to prevent possible physical or psychological trauma.

Review of literature:

Association of Pedodontic Diplomats (1972) conducted a survey and found out that 84% of the pediatric dentist's used physical restraints in selected patients.[2]

Nathan JE (1989) observed that only 4% of the pediatric dentist's employed immobilization technique. [2]

Newton JT et al (2004) did the questionnaire survey of pediatric dentist and found a large proportion of practitioners (62%) felt that the use of physical restraint was appropriate with certain disabled patients. The most commonly anticipated psychological sequeala which may accompany the use of these techniques was subsequent fear of dental treatment.[3]

Boka V et al (2014) examine the acceptance by Greek parents of nine behaviour-management techniques and he found least accepted techniques were passive restraint and General Anaesthesia.[20]

Guinot F et al (2021) compare the acceptance of behaviour management techniques used in pediatric dentistry by Spanish and Portuguese parents. From the 8 different behaviour management techniques the least accepted techniques in both countries were active and passive restraint.[21]

Ramadevi RP (2024) did the study to elicit parents' opinion and record their response to their children's experience who underwent dental treatment with an extra assistant for protective stabilization. In result she found the dental assistant was most preferred as the extra assistant to provide active stabilization. An overwhelming 98% of the parents agreed to protective stabilization with an extra assistant as advantageous and a good 88% of the parents recommended its use for further appointments of their children.[22]

Conclusion

The several modalities that are available in a clinical setting have been outlined in this review of the literature. Nonetheless, it is important to give psychological techniques priority first. Physiological approaches to behavior management should only be used when absolutely required because they may affect a child's behavior in the future. Safely completing treatment modalities while avoiding legal ramifications would be made possible by the prudent application of physical restraints with parental approval.

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Minimally Invasive Periodontal Therapy: A Paradigm shift

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Abstract

Periodontitis is a complex term that affects all supporting tissues of the teeth and can be treated non-surgically as well as surgically. Periodontal therapy success is contingent on adequate case selection, patient cooperation, accurate diagnosis, and treatment plan. From a clinical standpoint, improved visualization during periodontal operations is required to achieve better results. Minimally invasive periodontal therapy (MIPT) explains need of utilizing minimally invasive techniques and provides information on how to improve visualization using a minimally invasive approach. Also, the reasons for minimally invasive periodontal procedures as well as numerous strategies for minimally invasive nonsurgical and surgical periodontal procedures in this Review will be explored.
Keywords: *Illumination, Microsurgery, Magnification, Periodontitis*

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Introduction

For decades, the traditional non-surgical and surgical procedures for treating chronic periodontitis remained constant. We treat chronic periodontitis cases with these techniques by using all the blind non-surgical ways to rely on tactile perceptions to locate and remove subgingival deposits. For example, in nonsurgical periodontal therapy, root planing entails removing some structure of the teeth during periodontal instrumentation to obtain a 'hard' and 'smooth' root surface. Because it requires the removal of some tooth structure, it is an intrusive treatment. However, in early 1980s concluded that the purposeful removal of cementum during the technique of root planning was not justified[1,2] and therefore a new idea was established for the treatment of damaged teeth. There is evidence suggesting that extensive surgery may be necessary to address underlying bony defects in cases where the pockets are deeper.

Traditional surgical procedures for periodontal disease often involve creating a large flap to access the affected area, resulting in bone exposure. To address the shortcomings of traditional procedures, Minimally Invasive Surgery (MIS) was introduced in 1995 by Harrel and Ress.[3] MIS aims to minimize incisions and flap reflection, making it less time-consuming, less painful, more acceptable, beneficial, and cost-effective. This newer technique involves using micro incisions design to obtain all surgical therapies that were previously done through larger surgical access for the treatment of periodontal diseases. MIS allows for a gentler handling of both soft and hard tissues during surgery.

Objectives of Minimally Invasive Periodontal Therapy:[4]

- Minimum surgical trauma
- Increase stability of flap/wound
- Primary wound closure stability
- Less time on operating
- Reduce patient pain and discomfort while minimising side effects

Types and Principles of Magnification System:

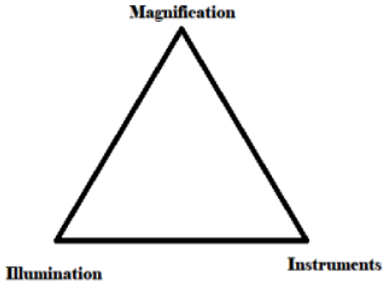
Precision is essential to the art of dentistry, and while the naked eye can detect fine details, enhancing and enlarging images can yield even better results. Despite the interest in microsurgery among dental professionals, many lack the necessary skills to perform such procedures, indicating a lack of understanding of its potential.[5] Periodontal microsurgery entails utilising a microscope to improve visual acuity at magnifications greater than 10x, and the use of loupes, surgical operating microscopes, and micro tools has elevated periodontal surgery to a new level of precision.

Application of periodontal microsurgery in procedures such as periodontal flap and recession coverage, periodontal regeneration, and implant surgery. The microsurgical triad, consisting of magnification, illumination, and refined surgical skills, is essential to achieving improved accuracy in surgical interventions **(Belcher et al. 2001).**[6] without any one of these elements, microsurgery is not possible. Enhancing the micro-surgical triad through the use of surgical microscopes and micro instruments can refine basic surgical techniques and improve surgical outcomes.

Dentists now have access to a wide selection of basic and complex magnifying systems, allowing them to improve the precision of their clinical abilities.

Fig.1 Magnification Triad

There are two types of optical magnification available to dentists which includes, Surgical Loupes and Surgical Operating Microscope



Surgical Loupes: Magnification loupes represent the most frequently employed magnification technique in the field of dentistry. These loupes consist of two separate monocular microscopes positioned next to each other to focus on a specific object. Dentistry commonly utilizes three distinct types of loupes, all employing convergent optics. These loupes are as follows: [7,8] Simple loupes, Compound loupes and Prism loupes

Surgical Operating Microscope: The Operational Microscope that enhanced adaptability and ease of use when compared to magnifying surgical loupes. However, comes with a significantly higher cost and a steeper learning curve initially. In the realm of dentistry, operational microscopes are designed based on Galilean principles. These scopes combine magnifying loupes with a magnification changer and a binocular viewing system, creating binoculars that work in parallel to minimize eye strain and fatigue. With fully coated optics and achromatic lenses, operational microscopes deliver higher quality of resolution and high colour contrast stereoscopic vision.

Working of Surgical Microscope:

To appreciate the working of surgical operating microscope one needs to have knowledge about the following.[9] Magnification, Illumination, Documentation, Accessories

Effective microsurgical procedures demand precise instruments. A typical toolkit comprises all types of micro surgical instruments. In the field of Periodontics, various ophthalmic knives, such as the crescent, lamellar, blade breaker, sclera, and spoon knife, find application. Their distinct advantage lies in their exceptional micro sharpening ability and diminutive size. This combination reduces tissue trauma and expedites the healing process. Notably, these sharp instruments are etched rather than conventionally honed, ensuring a more precise wound edge.[10]

Instruments for Periodontal Microsurgery[11]

In the field of Periodontology, a variety of ophthalmic knives, including the curved shaped, lamellar, blade breaker, sclera, and spoon knife. Ophthalmic knives have the advantage of being both extremely sharp and small in size. This reduces tissue stress and speeds up healing. Ophthalmic knives' sharper blades generate a more precise wound edge because they are chemically etched rather than honed. The reduced size of the ophthalmic blades, when compared to the normal No.15 blade typically used in Periodontics, streamlines surgical work. Micro-instruments are placed in a sterile container or tray to avoid damage. During sterilisation or transit, the tips of the instruments must not come into contact with each other. Needle holder, they come in a variety of sizes and are designed to grab very thin needles. Their jaws are smooth, resulting in a straightforward and controlled knot. The most popular needle holders are 14 cm and 18 cm.[11] The needle holder tip should be 1mm for suturing 5-0 and 6-0 sutures, and 0.3 mm for suturing 8-0 and 10-0 sutures. Sutures and microsurgical needles to prevent breaking, needles have high flexural and ductile strength. Curved needles fit better into small areas. In periodontal surgery, needles with a 3/8 or 12 curve circular and an arc length of 8-15 mm are preferable. Needles ranging from 6-0 to 9-0 are commonly used.[12]

Indications: Microsurgical Periodontal Surgery:[13,14.] Minor Surgical Procedure, Flap Surgery, Regenerative surgery, Muco-gingival / Perio-plastic surgery.

Passive wound closure represents one of the three fundamental principles in microsurgery. Achieving precise primary closure of the wound edges is crucial for obtaining the desired outcome. Ideally, incisions should be nearly imperceptible, and they should be closed using meticulously positioned, small sutures that minimize tissue trauma and bleeding. Advances in suture materials and techniques have led to the development of sutures tailored for specific procedures across various surgical specialties, with dental procedures benefiting from these innovations.

In microsurgery, fine-gauge needles, ranging from small to extremely small, are used. These needles are designed to provide optimal stability when held by a needle holder, a critical factor influencing the entire suturing process. It's essential for the surgeon to have complete control over the procedure, particularly when passing the needle through the tissue. Therefore, the needle holder must be appropriately sized to match both the needle and the selected suture material. This ensures that the surgeon maintains the highest level of control and precision throughout the suturing process.

To facilitate passive wound closure, microsurgery relies on meticulous, minimal invasive entry incision design and dissection. The site is then closed utilising the proper fundamental techniques, with the aim of achieving both primary and passive wound site closure. (Price PB, 1948).[15]

In Mucogingival Surgery:

All these techniques yield varying degrees of therapeutic benefits due to their sensitivity to the operator's skill and the

specific technique employed. Microsurgical approaches, which require an extended period of learning and practice to achieve desired treatment outcomes, offer a more compatible method for complete successful muco-gingival surgical treatment results.

In the field of periodontics, microsurgery has proven to be a valuable approach for improving the predictive results of gingival transplantation techniques used in root coverage treatment. It also helps in reducing surgical damage and postoperative discomfort. When combined with accurate diagnosis, microsurgical techniques significantly enhance the predictability of achieving complete root coverage in various cases of mild to moderate marginal tissue recession abnormalities. Moreover, even in cases of class III and class IV marginal recession, where conventional surgery often yields partial root coverage results, microsurgery can lead to substantial improvements in outcomes.

Papillary Reconstruction Procedure:
The restoration of missing interdental papillae remains difficult. Microsurgical treatment is an atraumatic approach for positioning donor tissue under a deficient interdental papilla. Surgical magnification and microsurgical devices are important because to the small size of the interdental papilla and the limited access.[16]

Root Coverage Procedures:
The success of the root covering operation is dependent on the surgeon's dexterity, excellent visualisation of the working region, and, of course, an atraumatic surgical technique. A surgical microscope can meet all these requirements. To maximise treatment outcomes, it is necessary to regulate aspects impacting the degree of coverage, such as root preparation, sensitive tissue handling, tissue biotypes, and thorough plaque control.[17]

Minimal Invasive Surgery in Implant Therapy:
Techniques that give function, aesthetics, and comfort using a minimally invasive surgical approach are widely recognised among clinicians and patients in the modern era. Many clinicians suggest trans-gingival (flapless) implant surgery to meet this need. This method can be utilised to ease the implant placing procedure.[18]

The one-piece implant technique promotes improved tissue recovery by improving gingival mucosal adhesion to build a collar that is adequate for healing and adapting to the surface of implant, so eliminating a second surgical treatment (Prithviraj DR, et al 2013).[19] Single unit implant prosthetic approach allows the normal structure of the Peripheral tooth tissues to be preserved by allowing a endline preparation that follows the contour of the gingival margin, resulting in a better keeping of the mucosal seal (Barrachina-D'ez JM et al in 2013).[20] The success rate of single unit immediate loading implants is comparable to that of delayed loading implants (Shigehara S, et al in 2014).[21]

Sinus Floor elevation:
Numerous authors have proposed modifications to conventional techniques, leading to the rise in popularity of "Minimally Invasive Techniques". One notable advancement in the realm of sinus augmentation is the "Sinus Lift System" an example of minimal invasive indirect sinus lift tools. When combined with Platelet-Rich Plasma (PRP) and Tricalcium Phosphate (TCP), this procedure becomes even more reliable, potentially accelerating bone production and sinus elevation.

It is reasonable to assert that elevation of sinus floor using the "sinus-lift system" is a dependable method for getting significant sinus lift during augmentation procedures. This approach, involving sinus lift prior to implant placement, is poised to play a more prominent role in the future due to its evident advantages. Minimal invasive technique provides successful implant

procedure and maximize the augmentation. This proposed technique is minimally invasive, reduces procedural time, enhances the precision of implant dentistry with predictable outcomes, and enhances the comfort of implant patients.[22]

Wound Healing in MIPS

Microsurgery promotes a healing process. Reduces the formation of granulation or scar tissue. Research suggests that wounds treated with microsurgery typically heal within 2 days. In contrast secondary wound healing takes longer as new tissue needs to be generated to fill the gaps at the wound's edges. The reduced surgical trauma, during microsurgery leads to cell damage, necrosis, inflammation and pain.

Microsurgery promotes healing with granulation or scar tissue formation. Studies indicate that wounds treated with microsurgery typically heal within 48 hours. In contrast secondary wound healing takes longer as new tissue needs to be generated to cover the gaps at the wounds edge. The advantage of microsurgery is that it causes cell damage due, to reduced trauma.

The Transition Sequence:

Periodontists are now able to receive training in periodontal microsurgery. However, microsurgery training differs from other types of continuing education courses. First and foremost, the courses are practical rather than academic. Their primary educational emphasis is on the clinical skills required for excellent microsurgical technique. To guide students' skills from beginner to advanced levels, a programme requires at least two days of rigorous training with direct one-on-one instruction. Movement education focusses the mind and enhances the neurobiology of learning to new heights of performance and achievement. As the twenty-first century progresses, such learning approaches will play an increasingly essential role in teaching periodontists for microsurgery as it enters the mainstream of periodontal therapy.[23]

A practitioner who aspires to learn microsurgery must become visually acclimated to the microscope. Visual movement of the instruments without reference to surrounding cues (known as kinaesthetic movement) necessitates a slower, more nuanced movement. New microsurgical skills, such as tool grip and posture, must be learned by the practitioner. Structured training creates an optimal setting for developing these abilities. After training, the practitioner might gradually integrate microsurgery into his or her office practise.

Common errors in the use of surgical microscope are using magnification that is too high, inadequate task sharing between surgeon and assistant, Lack of practice. The technology currently considered cutting-edge for both non-surgical and surgical minimally invasive periodontal therapy is likely to be seen as primitive or outdated in the next 30 years. The potential for advancements in periodontal therapy seems boundless, with a strong likelihood that treatment procedures will become progressively more effective and less invasive.[24]

Conclusion

Minimally invasive periodontal surgery (MIPS) is becoming increasingly important as medicine and dentistry pursue less invasive treatment options. The use of microscopes allows for precise and detailed information for diagnosis and treatment. MIPS has many benefits, such as improved aesthetics, faster healing, and less patient discomfort. Utilizing endoscope-assisted root planning and regenerative surgery is proving to deliver superior results with reduced patient morbidity when compared to conventional techniques. The goal of any treatment is the regeneration of lost tissue with minimal post-operative issues, which

MIPS is proving effective in achieving. Specific training, instruments, and materials are required for a successful minimally invasive approach. Further studies are necessary to determine if MIPS can substitute conventional methods while accomplish similar or better results.

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Comparison of Layers of Twak and Layers of Skin

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Abstract

'Twak' as per Ayurvedic science means which encloses the whole body. Joseph Listre said, 'Skin is best dressing'. Twak is updhatu of Mamsa which forms the outer covering of the body and protects the body from external factors such as heat & cold. It is an important organ of integumentary system which envelops underlying tissues & organs. Ayurveda mentions twak as sparshanaindriya and different layers of twak are mentioned by Acharyas. Understanding each layer is still unclear with reference to layers of skin mentioned by contemporary science. There is a need to understand the different layers of twak & skin, their structural, functional and developmental interpretation and to correlate between them.

Keywords: *Twak, Sparshanaindriya, Updhatu*

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Introduction

In Ayurveda, the term Twak refers to the skin, named so because it envelops the body. Acharya Sushruta explained the formation of Twak during fetal development. He compared it to the layer of scum (Santanika) that forms on boiling milk, which gradually thickens; similarly, seven layers of skin develop on the surface of the fetus.[1] During fetal formation (Garbha), the skin layers differentiate and are influenced by all three doshas, especially Pitta. Charaka described Twak as a Matruja Bhava (maternal factor), one of the six essential elements for fetal growth. On the other hand, Vagbhata suggested that Twak originates from Rakta (blood) through the action of Rakta Dhatu Agni, drying and forming the skin much like cream deposits on boiling milk. Charaka mentioned six layers of Twak, with only the first two layers specifically named: Udakadhara and Asrugdhara.[2]

Acharya Sushruta detailed seven layers of Twak, describing their thickness and the conditions that affect each layer.[3] Vagbhata also mentioned seven layers similar to Sushruta but did not provide detailed descriptions; commentators Arunadatta and Hemadri followed Sushruta's classification.[4] Sharangadhara described seven layers as well, aligning the first six with Sushruta's layers and adding a seventh layer called Sthula, identified as the site of Vidradhi (abscess).[5] There are differing opinions regarding the exact number of skin layers in Ayurveda. The layers of twak explained by different Acharyas have been tabulated (Table 1).

Table 1: Layer of Twak as per different Acharyas

Layers	Charaka[6]	Sushruta [7]	Vagbhata [8]	Arunadatta [8]	Sharangadhara [9]	Bhavaprakash a [10]
Prathama	Udhakadhara	Avabhasini	1st	Bhasini	Avabhasini	Avabhasini
Dwitiya	Asrugdhara	Lohita	2nd	Lohita	Lohita	Lohita
Tritiya	Sidhma, Kilasasambhava adhistana	Shwetha	3rd	Shwetha	Shwetha	Shwetha
Chaturtha	Alaji, Vidradhisambhav aadhistana	Tamra	4th	Tamra	Tamra	Tamra
Panchami	Dadru, Kushtasambhava adhistana	Vedini	5th	Vedini	Vedini	Vedini
Shashthi	If this layer is injuired, leads to Andhatwa and Tama pravesha	Rohini	6th	Rohini	Rohini	Rohini
Sapthami		Mamsadhara	7th	Mamsadhara	Sthula	Sthula

The skin is the body's largest organ, covering an area of about 20 square feet and weighing between 4.5 to 5 kilograms, making up roughly 7% of total body weight. Known as the "First Line of Defence," the skin protects against microbes and other harmful external agents. It is part of the integumentary system, which helps maintain homeostasis by shielding the body and regulating body temperature. Additionally, the skin allows us to perceive various external sensations, including pleasure and pain. The skin and its structures originate entirely from the ectoderm and mesoderm layers of the embryo. It consists of three main layers: the outer Epidermis, the Dermis, and the Hypodermis,[6,7] as outlined in Table 2.

Discussion

Acharyas such as Sushruta, Vagbhata, Bhavprakasha, and Sharangadhara described seven layers of Twak. In contrast, Charaka, Bhela, and Astanga Sangraha referred to six layers. These differences in opinion stem from the distinct perspectives of surgeons and physicians.[8,9]

Prathama Avabhasini: Acharya Sushruta referred to the outermost layer of the skin (Twak) as Avabhasini, describing its thickness as 18/20th of a unit called Vreehi. This layer is associated with diseases like Sidhma and Padmakantaka. Dalhana noted that this layer influences skin color variations such as Gaura (paleness) and Shyamadhi (darkness), as well as five types of skin radiance (Prabha) and shading (Chaya), through the action of Bhrajaka Pitta. Meanwhile, Acharya Charaka and Vriddha Vagbhatta named this outermost layer Udakadhara, meaning it holds the skin's moisture (Udakadhatu) and prevents its loss, maintaining surface hydration. Vagbhatta also called this layer Bhasini, aligning with Charaka and the Astanga Sangraha. Since layers above Malpighi are opaque, the skin's visible complexion is mainly due to the Stratum corneum, which corresponds to Avabhasini. This layer consists of flattened, scale-like keratinized cells that provide resistance to water loss, hence Charaka's term Udakadhara.[10]

Table 2: Layers of Skin and thickness

Layer of Skin	Sub-layers	Thickness
Epidermis	Stratum corneum	10-30mm
Thin skin –4 layers, 0.1mm	Stratum lucidum	100 mm
Thick skin – 5 layers 1-2mm	Stratum granulosum	100mm
	Stratum spinosum & S. basale	100mm
Dermis	Papillary layer	100 mm
	Reticular layer	

Dwitiya Lohita: The second layer, according to Sushruta, is called Lohita, with a thickness of 16/20th of Vreehi, and is the site of marks such as Tilakalaka, Nyaccha, and Vyanga. Charaka and Vriddha Vagbhatta referred to it as Asrugdhara, meaning the layer that holds blood and prevents its leakage. Hemadiri named it Lohini. This corresponds to the Stratum lucidum, a translucent layer with evenly distributed cells that lack clear boundaries, giving it a clear appearance. Changes in blood components like hemoglobin and bilirubin affect the skin's pallor or jaundice visible through this layer, justifying its association with blood by the Acharyas.[10,11]

Tritiya Shweta: Sushruta called the third layer Shweta, about 12/20th of Vreehi in thickness, which serves as the base for skin conditions like Charmadala, Ajagalika, and Mashaka. Charaka and Vriddha Vagbhatta described it as the site of Sidhma and Kilasa, while Astanga Hrudaya identified it as the site of Sidhma and Shwitra. In modern terms, this matches the Stratum granulosum, which consists of 2-5 layers of flattened cells filled with keratohyaline granules that bind keratin filaments.[12]

Chaturthi Tamra: Sushruta identified the fourth layer as Tamra, lying below Shweta, with a thickness of 8/20th of Vreehi, and associated with diseases like Kusta and Kilasa. Charaka described it as the site of Dadrukushta, and Astanga Sangraha and Hrudaya labeled it the location for Sarvakushta. Sharangadhara and Bhavaprakasha linked Tamra to Kilasakushta. This layer likely includes both Stratum spinosum and Stratum basale, as melanocytes residing here release melanin, which determines skin color.[13,14]

Panchami Vedini: The fifth layer, Vedini, according to Sushruta, is about 5/20th of Vreehi thick and is involved in sensing touch, pain, heat, and cold. It is also linked with diseases such as Kusta and Visarpa. Charaka and Vagbhata identified it as the site of Alaji and Vidradhi, while Hemadiri called it Twagvedini and Rogakarini. Sharangadhara and Bhavaprakasha associated it with Sarvakushta and Visarpa. This layer corresponds to the papillary dermis, rich in sensory receptors such as Meissner's corpuscles and free nerve endings, and its involvement in skin disorders affects the papillary layer's structure.[10,15]

Shasthi Rohini: The sixth layer, Rohini, is described by Sushruta as one Vreehi thick and is linked with conditions like Granthi, Apachi, Galaganda, Arbuda, and Shleepada. Charaka termed it the site of Arumshi, and Chakrapani noted that injuries to this layer could cause temporary blindness or loss of consciousness sensations. Vagbhata called it Pranadhara, with injuries here being life-threatening. This layer plays a vital role in wound healing (Vrana Ropana) by aiding the formation of granulation and fibrous tissue. It corresponds to the reticular layer of the dermis.[16]

Saptami Mamsadhara: The seventh and thickest layer, Mamsadhara, measures about 2 Vreehi and is the site of diseases like Bhagandhara, Vidradhi, and Arsas. Sharangadhara and Bhavaprakasha refer to it as Sthula, highlighting its role as the location of Vidradhi. This layer can be correlated with the hypodermis, containing blood vessels, lymphatics, and fat tissue. It acts as the superficial fascia, enveloping muscles and supporting them, hence the name Mamsadhara.[14]

Formation of Twak: Twak is considered the Upadhatu (secondary tissue) of Mamsa (muscle). Sushruta explained that after fertilization of Shukra and Shonita (sperm and ovum), the skin develops similarly to the formation of scum (Santanika) on boiling milk, accumulating layer by layer to form the seven layers of skin. Vagbhata believed Twak originates from Rakta (blood), which, after being processed by the

body's metabolic fire (Dhatwagni), dries up to form the skin, analogous to scum forming on boiling milk.[12,15]

The skin consists of two main layers: the epidermis (superficial epithelial tissue from surface ectoderm) and the dermis (deeper connective tissue from mesenchyme). Skin structures vary by body area. At 4-5 weeks of embryonic development, the skin starts as a single layer of surface ectoderm over the mesoderm. During the first and second trimesters, the epidermis thickens as ectodermal cells proliferate, forming layers including the periderm and basal layer. The periderm cells keratinize and shed until about the 21st week, when the Stratum corneum appears. Epidermal ridges form from proliferating basal cells, extending into the dermis. The multi-layered epidermis results from this transformation, and skin is classified as thick or thin based on epidermal thickness.[15]

Melanoblasts (pigment-producing cells) originate from the neural crest and migrate to the Stratum basale. Langerhans cells come from bone marrow and migrate into the epidermis. Merkel cells, of uncertain origin, associate with nerve endings.[16]

The dermis mainly develops from mesenchyme derived from the somatopleuric lateral mesoderm and dermatomes of somites. By week 11, mesenchymal cells produce collagen and elastic fibers. As epidermal ridges form, the dermis projects upward to form dermal ridges, interlocking with epidermal ridges. Sensory nerve endings, tactile receptors, and blood vessels develop within these ridges.[17]

During fetal development, the skin forms gradually in distinct layers. Two types of skin develop on the fetus's body: thick skin, which covers the palms and soles, consists of five epidermal layers, lacks hair follicles, arrector pili muscles, and sebaceous glands, but contains sweat glands; and thin skin, which covers most other areas, lacks the Stratum lucidum layer in the epidermis, and includes hair follicles, arrector pili muscles, sebaceous glands, and sweat glands.

Table 3: Layers of Skin as per Ayurveda and possible modern correlation

Layers	Twak layer	Subdivision of layer of Skin	Skin layer
Prathama	Avabhasini	Stratum corneum	Epidermis
Dwitiya	Lohita	Stratum lucidum	
Tritiya	Shweta	Stratum granulosum	
Chaturthi	Tamra	Malpighian layer	
Panchami	Vedini	Papillary layer	Dermis
Shasthi	Rohini	Reticular layer	
Saptami	Mamsadhara	Subcutaneous tissue and Muscular layer	Hypo-dermis

Measurement of Twak Layers:

Dalhana described the total thickness of the skin (Twak) as equivalent to the combined thickness of six barley grains (Shad Yava Pramana), roughly the size of a thumb or a fist. This measurement applies mainly to fleshy areas and not to bony regions such as the forehead or fingertips. The reason for specifying the thickness of each skin layer is to aid in surgical procedures—for example, abdominal tapping should be performed within this thickness using instruments like the Vrihimukha Yantra in Jaludhara. While the classical measurements add up to six barley grains in thickness, aligning these with modern scientific measurements proves challenging. Similarly, correlating diseases that affect specific skin layers with modern anatomy remains complex and requires further research.[18]

Conclusion

Based on comparative analysis, the seven layers of Twak described in Ayurveda—Avabhasini, Lohita, Sweta, Tamra, Vedini,

Rohini, and Mamsadhara—can be correlated respectively with the Stratum corneum, Stratum lucidum, Stratum granulosum, Stratum malpighianum, papillary dermis, reticular dermis, and hypodermis. These correlations are drawn considering similarities in their structure, function, and clinical significance. Regarding skin formation, all layers do not develop simultaneously; rather, they form gradually during fetal development, akin to the way cream layers accumulate on boiling milk, as described by the ancient Acharyas.

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Revolutionizing Drug Discovery: The Role of Artificial Intelligence in Modern Drug Design

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Abstract:

The traditional drug discovery process is slow, expensive, and prone to high failure rates, with timelines of 10–15 years and costs reaching $1–2 billion. Recent advancements in artificial intelligence (AI) have revolutionized drug design by enabling the analysis of vast biomedical datasets, identifying patterns, and making predictions that streamline and optimize the drug discovery pipeline. This article explores the transformative role of AI methodologies, including Machine Learning (ML), Deep Learning (DL), Natural Language Processing (NLP), and generative models, in accelerating target identification, lead compound optimization, and predicting drug toxicity or efficacy. AI applications in drug repurposing, de novo drug design, and the prediction of drug-target interactions are discussed, showcasing significant reductions in time and resource requirements. The article also highlights critical challenges, such as data quality, model interpretability, and regulatory concerns, which must be addressed to fully realize the potential of AI in drug discovery. With continued advancements and collaboration between computational and pharmaceutical sciences, AI promises to revolutionize drug development, paving the way for personalized and precision medicine.

Keywords: *Artificial Intelligence (AI), Deep Learning (DL), Natural Language Processing (NLP), Drug Repurposing, Lead Compound Optimization, Drug-Target Interactions, De Novo Drug Design.*

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1. Introduction

The traditional drug discovery process is notoriously slow, expensive, and has a high failure rate. On average, bringing a drug from the initial discovery phase to market approval takes around 10-15 years and costs between $1-2 billion.[1] The complexity arises from several factors, such as identifying suitable drug targets, designing compounds with desired therapeutic effects, and conducting multiple phases of clinical trials to ensure safety and efficacy.

AI has emerged as a revolutionary tool in drug design, offering the ability to analyze vast amounts of biomedical data, recognize patterns, and make predictions that were previously unattainable.[2] By leveraging computational power, AI can expedite target identification, optimize lead compounds, and even predict drug toxicity or efficacy, all while cutting down the time and resources required.[3] This section introduces the growing role of AI in transforming how new drugs are designed and the promise it holds for the pharmaceutical industry.

2. Methodologies in Drug Design

2.1 Machine Learning (ML)

Machine Learning (ML) involves using algorithms that allow computers to learn from historical data and make predictions or decisions without being explicitly programmed. In drug design, ML algorithms are particularly effective for analyzing large datasets from biochemical assays, clinical trials, or genomic studies to predict drug-target interactions, identify off-target effects, or optimize compounds for improved potency and reduced side effects.[3]

For example, supervised learning algorithms can be trained on datasets of known drug molecules and their biological activities to predict whether a new compound will likely bind to a particular target. Similarly, unsupervised learning can cluster chemical compounds based on their properties, aiding in drug classification and repurposing.

2.2 Deep Learning (DL)

Deep learning (DL), a subset of ML, is ideal for processing more complex data, such as 3D molecular structures and protein-ligand interactions. DL models, like convolutional neural networks (CNNs) or recurrent neural networks (RNNs), learn multiple layers of representation from raw data, allowing them to model more intricate biological systems.[4]

DL models have revolutionized tasks like structure-based drug design,[5] where 3D models of molecular interactions are used to predict how well a drug molecule will bind to its target protein.[6] These models can also screen vast chemical libraries, analyzing millions of potential drug candidates much faster than traditional methods.[6]

2.3 Natural Language Processing (NLP)

Natural Language Processing (NLP) enables AI to process and analyze vast amounts of unstructured data, such as scientific papers, patents, or clinical trial records. NLP algorithms extract key information from texts, such as new drug targets, mechanisms of action, or side effects, providing insights that can guide the drug discovery process.[7]

NLP is particularly useful for drug repurposing, where AI systems scan existing literature and clinical data to identify new uses for approved drugs, shortening development timelines by bypassing early-phase testing.[8]

2.4 Generative Models

Generative models, such as Generative Adversarial Networks (GANs) or Variational Autoencoders (VAEs), are used to create novel drug molecules. These models can explore vast chemical spaces to suggest entirely new compounds that meet predefined criteria, such as binding affinity, solubility, or toxicity profiles.[9]

For instance, VAEs can learn the underlying distribution of drug-like molecules and generate new, chemically valid compounds, while GANs can create novel molecular structures by pitting two

neural networks against each other to refine output quality.[10]

3. Applications of AI in Drug Design

3.1 Lead Compound Identification

Identifying lead compounds is one of the most critical steps in drug design, where AI significantly accelerates the process. AI-based algorithms use data from high-throughput screening (HTS) experiments to identify molecules that can potentially interact with a biological target. Virtual screening powered by AI models allows the evaluation of large chemical libraries, reducing the need for extensive laboratory-based testing.

For example, AI models can predict the binding affinity of drug candidates to target proteins, significantly reducing the number of compounds that need to be synthesized and tested in the lab.[11]

3.2 Drug Repurposing

AI excels in drug repurposing by analyzing existing drugs and their interactions with various targets, predicting new therapeutic applications. Repurposing approved drugs for different diseases saves time and resources since much of the safety testing has already been completed.[11]

Using AI tools like deep learning models and NLP, researchers have repurposed existing drugs for conditions ranging from rare diseases to cancer, significantly reducing the overall time to market.[12]

3.3 Prediction of Drug-Target Interactions

Predicting drug-target interactions is a fundamental aspect of drug design. AI-driven models, such as structure-based or ligand-based approaches, predict how small molecules (drugs) will interact with biological macromolecules (proteins or DNA). AI can model these interactions based on known structures of the drug and target, helping researchers to identify the best candidates for further development.[13] For example, structure-based models predict the interaction by docking simulations, where the AI algorithm fits a drug molecule into the binding site of a target protein and calculates the interaction strength.[14]

3.4 Optimization of Drug Properties

AI is used to optimize pharmacokinetic (PK) and pharmacodynamic (PD) properties of drug candidates. These properties include how a drug is absorbed, distributed, metabolized, and excreted (ADME), as well as its toxicity.[15] AI models can predict these parameters early in the drug development process, ensuring that only the most promising compounds move forward. For example, AI tools are used to predict a compound's solubility, permeability, and potential for toxicity, all of which are critical for successful drug candidates.

3.5 De Novo Drug Design

AI models, particularly generative algorithms, are now capable of performing de novo drug design, where they generate entirely new molecular structures from scratch. The algorithms explore vast chemical spaces and propose new molecules that have specific therapeutic properties. For example, AI-generated molecules for cancer treatments can be designed with predefined properties such as high affinity for a particular target and minimal toxicity.[16]

4. Challenges in AI-Driven Drug Design

4.1 Data Quality and Availability

AI systems are only as good as the data they are trained on. In drug design, high-quality, diverse, and comprehensive datasets are critical for building accurate AI models.

However, access to such datasets can be limited due to privacy concerns, proprietary restrictions, or inconsistencies in data collection methodologies. Additionally, biases in data can lead to poor model generalization, reducing the accuracy of predictions.[17]

4.2 Interpretability of AI Models

One major challenge with AI, especially deep learning models, is their "black box" nature. These models are often difficult to interpret, meaning that researchers may not fully understand how or why a particular prediction is made. To gain wider acceptance, AI models need to offer greater transparency, so that their predictions can be trusted and validated by experts in the field.[18]

4.3 Regulatory and Ethical Concerns

As AI becomes more integrated into drug design, regulatory agencies like the FDA will need to establish frameworks for evaluating AI-generated results. Ethical concerns, such as the ownership of AI-designed molecules and the responsibility for AI-driven decisions, must also be addressed.[19]

4.4 Integration with Experimental Validation

While AI models can make accurate predictions, these predictions must be validated in the lab through biochemical assays, animal models, and eventually clinical trials. The integration of AI predictions with experimental validation is critical to ensure the safety and efficacy of AI-designed drugs.[20]

5. Discussion

The integration of artificial intelligence (AI) in drug discovery marks a paradigm shift in the pharmaceutical industry. Traditional drug design is fraught with challenges, including extensive timelines, exorbitant costs, and high attrition rates. AI technologies, by contrast, offer solutions that enhance efficiency, reduce costs, and improve success rates across various stages of drug development.

5.1Key Contributions of AI

AI's ability to analyze complex datasets, uncover hidden patterns, and make accurate predictions has revolutionized target identification, lead compound optimization, and drug property prediction. Machine Learning (ML) and Deep Learning (DL) have been particularly impactful in predicting drug-target interactions and optimizing molecular structures. Similarly, Natural Language Processing (NLP) and generative models have streamlined processes like literature analysis and de novo drug design, respectively.For instance, DL's capacity to interpret 3D molecular structures and simulate protein-ligand interactions has significantly enhanced structure-based drug design. Generative models, such as GANs and VAEs, have expanded the scope of chemical space exploration, enabling the generation of novel compounds with desired therapeutic properties. Furthermore, AI-driven virtual screening reduces the need for extensive experimental assays by prioritizing promising candidates early in the pipeline.

5.2 Applications and Benefits

AI-driven tools have successfully expedited drug repurposing, identifying new therapeutic applications for existing drugs and bypassing early-stage safety testing. In predictive toxicology and pharmacokinetics/pharmacodynamics (PK / PD), AI has proven invaluable for anticipating adverse effects and optimizing drug profiles, ensuring only viable candidates progress to clinical trials. These advancements not only accelerate drug

development but also enhance the precision of therapies, particularly in the context of personalized medicine.

5.3 Challenges and Limitations

Despite its transformative potential, several challenges limit the widespread adoption of AI in drug design. Data quality and availability remain significant obstacles, as AI models require large, diverse, and unbiased datasets for training. Additionally, the interpretability of AI predictions, especially in deep learning models, remains a hurdle, as their "black-box" nature raises concerns about the reliability and transparency of results.

Regulatory and ethical concerns also need attention. Clear frameworks for evaluating AI-generated outputs, data privacy considerations, and questions of intellectual property ownership for AI-designed molecules must be addressed. The integration of AI predictions with experimental validation is another critical aspect to ensure the robustness of outcomes.

5.4 Future Directions

The future of AI in drug discovery is promising, with opportunities for real-time drug optimization, improved automation in laboratories, and the development of precision therapies for rare and complex diseases. Continued advancements in algorithms, coupled with interdisciplinary collaboration and robust regulatory frameworks, are essential to unlocking the full potential of AI.

6. Conclusion

AI has emerged as a powerful tool, addressing many limitations of traditional drug discovery processes. While challenges persist, the ongoing evolution of AI technologies, supported by collaborative efforts, can transform the landscape of drug development, ultimately benefiting both pharmaceutical research and global healthcare.

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A Rare Case Report of Congenital Adrenal Hyperplasia: 46XX at Tertiary Care Centre, Visnagar, North Gujarat.

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Abstract

This report presents a rare case of pure classical congenital adrenal hyperplasia (CAH) due to 21-hydroxylase deficiency in a 22-year-old woman with a 46 XX genotype. The patient exhibited virilism, excessive hair growth, and primary amenorrhea with absent secondary sexual characteristics. The diagnosis was confirmed by 17-hydroxyprogesterone testing and the Synacthen test. Treatment with hydrocortisone and spironolactone was followed by feminization surgery, leading to the development of secondary sexual characteristics, including breast development, a reduction in hirsutism, and the onset of regular menstruation.

Keywords: *Congenital adrenal hyperplasia; 21-hydroxylase deficiency; Virilism; Syacthen test; Feminizing surgery; Hydrocortisone; Spironolactone*

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Introduction

The most prevalent type of congenital adrenal hyperplasia (CAH), which is a collection of autosomal recessive illnesses, is 21-hydroxylase deficiency, which is defined by enzyme abnormalities in the adrenal steroidogenesis pathway. The disorder is caused by mutations in the CYP21A2 gene, that codes for an enzyme called 21-Hydroxylase[1] which results in a high level of adrenal androgens or inadequate synthesis of cortisol and aldosterone. Due to excessive testosterone exposure during pregnancy, females with the severe type of classic 21-hydroxylase deficiency have virilized external genitalia at birth. This illness can have serious long-term health effects and potentially fatal adrenal crises if left untreated.

The uncommon appearance of a 22-year-old woman with pure classical virilizing CAH is described in this case report, underscoring the difficulties in diagnosis, treatment, and clinical care. To guarantee transparency and completeness, the report is prepared in accordance with the CARE criteria.[2]

Case Presentation

In her adult life, a 22-year-old woman from a non- consanguineous marriage visited our outpatient department. Her preliminary consultation with our team was for atypical sexual development (excessive hair growth) amenorrhea and unclear genitalia which dates back to the time her mother found a genital bud at birth. Upon reviewing her medical history, no evidence of maternal exposure to androgens during pregnancy or salt loss syndrome was discovered. She

visited numerous gynecologists for her issue, but she never obtained a satisfactory response. She eventually came to us about her issue. The clinical examination revealed excessive amounts of body hair growth, no breast growth, and a male morphotype.

The genital examination demonstrated a pair of distinct orifices below the clitoris (Prader II), non-fused smooth pigmented and symmetrical genital folds, clitoromegaly with peniform aspect that measured broadly around 5.5 cm in length and 2 cm in width, and no evidence of gonad palpation at the inguinal and fold levels (Fig 1 and 2). Her subjective Ferriman and Galleway Score of 29 indicated significant hirsutism, which was linked to virilization symptoms.

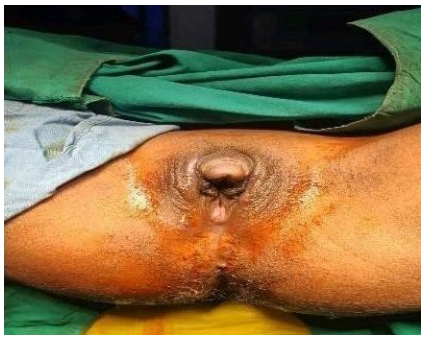

Fig 1 Pre-treatment photograph showing symmetrical, non-fused, pigmented vaginal folds, clitoromegaly with penniform appearance, and two distinct orifices beneath clitoris.

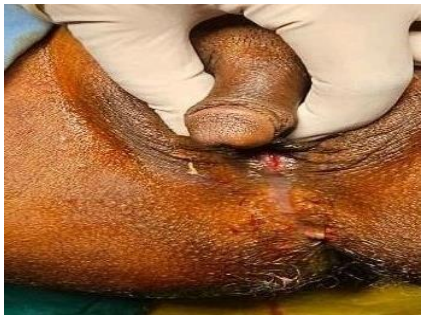

Fig 2: Pretreatment Photograph showing clitoromegaly and Pinniform appearance.

On 50 mitoses, the biological exploration using modal of karyotypes demonstrated a karyotype 46, XX, with testosterone levels of 367.55 ng/ml (CMIA), progesterone was 23.3ng/ml and estrogen (E2) was 3.3 pg/ml while DHEA 752.5 µg/dl (CMIA), and 17OH Progesterone subsequently synacthene stimulation T60 min: 354 ng/ml (VN< 10 ng/ml, radioimmunology), cortisol level was low, measuring 52 g/ml (CMIA). A hypoplastic uterus with uniform contours measuring 42 x 21 x 17 mm and macropolycystic ovaries measuring 23 mm on the left and 24 mm on the right were discovered by pelvic ultrasonography. An abdominal MRI scan revealed hypertrophy of the adrenal glands but no other abnormalities.

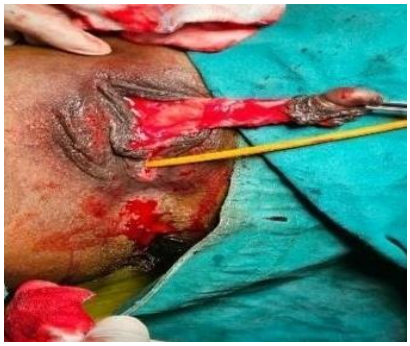

Fig 3: Illustrates the size of the clitoris, with a peniform aspect measuring 5 cm by 2 cm,

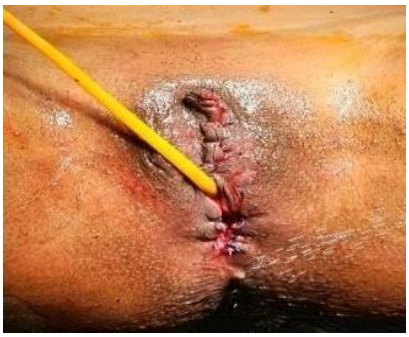

Fig 4: Clitoris appearance following clitoroplasty

Therapeutically, hydrocortisone replacement at a dosage of 10 mg at 8 am and 5 mg at 5 pm was to be administered in addition to dexamethasone at a dose of 0.5 mg/d at night. After three months she observed breast growth which was corresponding to stage S2 of Tanner, the clinical examination revealed a minor decrease in hirsutism, a Ferriman and Gallaway score of 25 versus 29, and smaller in size clitoris measuring 5.5 cm against 5 cm. On a biological level, the 17 OHP went back to 168.6 ng/ml, and the

testosteronemia dropped to 1.12 ng/ml from 3.69 ng/ml. At this point, the patient was admitted for vaginoplasty and clitoroplasty procedures. The surgery went smoothly and efficiently (Fig 3 and 4). Normal anatomical communication was established between the cervix and vagina. To avoid vaginal restenosis, she was encouraged for self-introduction of vaginal mold once a day.

Discussion

A collection of autosomal recessive illnesses known as congenital adrenal hyperplasia are brought on by total or partial abnormalities in one of the numerous steroidogenic enzymes that the adrenal glands use to synthesize cortisol from cholesterol. Steroid 21-hydroxylase, an enzyme encoded by the CYP21A2 gene, is deficient in over 95–99% of all CAH patients.[3] According to data from millions of babies screened globally, 1 in 10,000 to 1 in 20,000 live births had classic CAH.[4,5] With an estimated prevalence of one case per 200 people to one case per 1000 people, non-classic CAH is widespread throughout the world.[6]

The ambiguous genitalia associated with genetic females (46,XX) in neonates (Classical CAH) exemplify clitoromegaly and labioscrotal fusion. Signs and symptoms of dehydration, vomiting, weight loss, and shock (in extreme cases) are typical during a salt-wasting crisis. Early pubarche and advanced bone age are present in children, who have tall stature initial stages but subsequently short as a result of early epiphyseal closure. Adolescents and adults with non-classical CAH exhibit hyperandrogenism symptoms and indicators, including female infertility, hirsutism, acne, and irregular menstruation.

Lack of 21-hydroxylase, a cytochrome P-450 enzyme necessary for the adrenal cortex's synthesis of cortisol and aldosterone, is caused by mutations in the CYP21A2 gene. This enzyme's deficit causes a domino effect. The overproduction of pituitary corticotropin, which results from low cortisol, causes the adrenal cortex to enlarge and increases the release of cortisol precursors, specifically 17OHP, and adrenal steroids, the primary one being D4-androstenedione. In the target cells, this androgen can subsequently undergo metabolism to produce testosterone and dihydrotestosterone.[7]

A complicated genomic structure is intimately linked to the genetic pathways causing 21-OH deficiency. Although there are more than 200 known CYP21A2 gene mutations, over 90% of HCS cases are caused by a small number of these changes, either by gene conversion or uneven recombination. CYP21A2 point mutations account for 70–75% of cases. Large deletions connected to an uneven recombination process or abnormal segregation during meiosis account for 20% of cases. De novo mutations are linked to 21-OH deficiency in 1%–2% of instances. Real-time quantitative PCR is used for molecular diagnosis, employing distinct primer pairs that are unique for the CYP21A2 gene and not the CYP21A1P pseudogene. Point mutations are then found by sequencing.[8]

Two phenotypes, simple virilizing (SV) and salt wasting (SW), are indicative of the classic form. The age of finding, sex, and type of HCS all affect the clinical presentation. Ambiguous external genitalia are present in all patients with classic 21-OHD.[9] Rarely, like with our patient, the diagnosis of the classic pure virilizing type is established late in childhood, adolescence, or adulthood. In most cases, the diagnosis is made at birth. Because hyperandrogenism disrupts the gonadotropic axis, it can lead to anovulation or dysovulation, which can cause irregular menstruation, irregular cycles, or even infertility.[10] Any patient who presents with oligomenorrhea and/or hyperandrogenism should have the diagnosis brought up. With

severe hirsutism, a male morphotype, primary amenorrhea, no breast development, and a peniform clitoris, the clinical picture in our patient was highly suggestive. The ovaries, fallopian tubes, and uterus all develop normally. In addition to confirming the existence of female genitalia, pelvic ultrasonography often reveals the emergence of micropolycystic ovaries as a result of hyperandrogenism. This should not be confused with micropolycystic ovary syndrome, which is an elimination diagnosis. In our instance, macropolycystic ovaries measuring 23 mm on the left and 24 mm on the right were discovered by pelvic ultrasonography beside this evaluation of bone age was done using a left- hand's X-ray.

Serum 17-hydroxyprogesterone, usually stimulated by synthetic ACTH, is still the gold standard for diagnosing CAH. Therefore, the diagnosis is confirmed by a baseline 17 OH progesterone value greater than 2 ng/ml or a concentration >10 ng/ml in the synacthen test.[4] When diagnosing the condition, CYP21A2 genotyping is seen to be a useful supplement to biochemical tests.[3] But in our case because of the patient's financial issues, the genetic investigation could not proceed.

Blocking hyperandrogenism and preventing or managing complications of classic form and its therapy are the two goals of managing it throughout adolescent and adulthood.[11] The most widely used glucocorticoid is hydrocortisone. Other glucocorticoids, including dexamethasone, prednisone, or prednisolone, have longer half-lives and offer a stable replacement action all day. Unfortunately, without a sufficient dosage of glucorticoids, it is difficult to achieve androgen secretion suppression, and as a result, there is a substantial risk of iatrogenic hypercortisolism. Regardless of the regimen, the choice between long-acting glucocorticoids, which have a higher risk of adverse effects, and physiological hydrocortisone, which is well tolerated but has limited control on androgen secretion, remains problematic. Plenadren, a novel slow-release glucocoticoides formulation, was just released, while Chronocort, another, is presently being researched. Although the medication has not yet received approval, this is another modified-release hydrocortisone formulation that is being developed. It is taken twice a day, at bedtime and at waking, and has been demonstrated to imitate normal circadian cortisol levels. In patients with congenital adrenal hyperplasia, a phase II trial showed greater suppression of morning 17-OH progesterone levels (and, consequently, nightly androgen output). Phase III trial results are still pending.[12] In our case, in addition to dexamethasone at a dose of 0.5 mg/d at night, hydrocortisone replacement was to be given at doses of 10 mg at 8 am and 5 mg at 5 pm.

The antiandrogenic effects of spironolactone, an aldosterone antagonist, are seen at doses between 100 and 200 mg/day. It works by blocking androgen receptors and inhibiting 5-α-reductase activity.[11] In our instance, we decided to use 100 mg of spironolactone each day for treatment. A reduction in hirsutism, a reduction in the size of the clitoris, and the onset of breast development were observed as improvements in the symptomatology following three months of carefully managed replacement therapy and anti-androgenic medication.

Apart from this for proper dehydration and electrolyte imbalance in an acute crisis (salt-wasting CAH), intravenous fluids should be administered. IV hydrocortisone should be used for stress dosage to replenish cortisol. Beside this for the management of mineralocorticoid deficit in acute crises, sodium supplementation and fludrocortisone are recommended. Along with mineralocorticoids, glucocorticoids are used in chronic care to replenish cortisol and inhibit excessive androgen production

(e.g., hydrocortisone in children, prednisone in adults). Bone age, blood pressure, and growth are periodically monitored. When it comes to surgical management, femaleizing genitoplasty—ideally done during infancy in females with ambiguous genitalia. Growth abnormalities, puberty progression, and metabolic consequences of steroid medication all necessitate for continual observation. For concerns related to gender identity and quality of life, psychosocial help is crucial.

Complications include - Growth abnormalities spurred by the overt or insufficient usage of glucocorticoids, stress or illness-induced adrenal crisis and psychological effects associated with ambiguous genitalia and fertility. Patients can live normal lives with early diagnosis and proper care. Because of early intervention, newborn screening programs have greatly improved outcomes.

Conclusion

We describe a 22-year-old female patient who sought our consultation due to a sexual development abnormality, primary amenorrhea, and ambiguous genitalia. The diagnosis of congenital adrenal hyperplasia in its classic pure virilizing form remains unchanged at this age, necessitating challenging and specialized medical attention. In order to permit proper growth, female puberty, and good fertility, it is crucial to make the diagnosis as soon as feasible.

Consent: The patient's parents gave their written informed consent for this case report and its associated photos to be published.

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Abbreviations:

CYP21-gene encoding 21-hydroxylase Cytochrome P-450 enzyme
CMIA-Chemiluminescent microparticle immunology
DHEA-dehydroepiandrosterone sulphate
17OPH-17 hydroxyprogesterone
ACTH - Adrenocorticotropic Hormone

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Manuscript Preparation and Submission Guidelines

Detailed Instructions for Authors

1. Types of Submissions:

- Original Research Articles: Present new findings and contribute to the existing body of knowledge in integrative health.
- Systematic Reviews and Meta-Analyses: Summarize and synthesize existing research on a specific topic.
- Clinical Studies: Describe investigations that evaluate the effectiveness and safety of integrative health interventions.
- Case Reports: Detail individual cases that highlight unique health challenges and responses to integrative practices.
- Commentaries and Editorials: Offer insights into emerging trends, challenges, and opportunities within the field.

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- Technical Notes (Surgical techniques, new instruments, technical innovations): Maximum 1500 words, 10 references, and 2 figures.
- Case Reports: Maximum 1500 words, 10 references, and 2 figures.
- Book Reviews
- Letters to the Editor: Refer to detailed guidelines provided at the end of the main guide for authors.
- General Announcements

Please Note: Case reports are considered for publication only if they add new information to existing knowledge or present new perspectives on known diseases. All authors must have contributed to the paper, not necessarily patient treatment. Technical notes and case reports are limited to a maximum of four authors: in exceptional circumstances, five.

2. Formatting Guidelines:

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Title Page: Title, author names, affiliations, and corresponding author contact information.
Abstract: A concise summary (250 words max) of the study's objectives, methods, results, and conclusions.
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• Include background, methods, results, and conclusion.

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• **Materials and Methods:** Full details, technical specifications, quantities, generic names, statistical methods, and no results.
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• **Discussion:** Discuss results, exceptions, lack of correlations, implications, and conclusions.

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