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Comparative Evaluation of Intralesional Injection of Autologous Platelet Rich Plasma Versus Intralesional Injection of Corticosteroids in The Management of Resistant Oral Lichen Planus

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ABSTRACT

Background: Lichen Planus (LP) is a chronic mucocutaneous inflammatory disease that predominantly affects the oral mucosa, with a female predilection. The oral lesions are characterized by burning and pain which relentlessly affect the patient's quality of life. The available treatment approaches for OLP documented to have a short term effect with potential adverse effects which further increases the demand of a novel therapeutic approach for the severe resistant lesions of OLP with a malignant potential. This double-blind, split-mouth randomized controlled trial aims to evaluate and compare the effectiveness of intralesional Autologous Platelet Rich Plasma and corticosteroid for the management of resistant OLP.

Materials and methods: 28 clinically and histopathologically confirmed cases of resistant OLP were included with total 56 lesion sites divided into two groups of 28 each, in group 1 intralesional PRP and in group 2 intralesional steroid was given. The injections were repeated for consecutive 4 weeks and then kept on regular followup. Parameters recorded on every visit were according to the Modified Escudier Index.

Results: A statistically significant reduction in the lesion activity scores was found amongst the group treated with Platelet Rich Plasma as compared to the group treated with intralesional steroids.

Conclusion: The use of intralesional PRP in resistant cases of OLP showed superior results in improving clinical signs to that of intralesional Steroids, without any adverse effects.

Keywords: OLP, Platelet Rich Plasma, Intralesional Steroid

INTRODUCTION

Lichen planus (LP) is a chronic mucocutaneous inflammatory disease that frequently affects the oral mucosa, with predominance towards the middle aged female patients mostly. OLP is estimated to affect 0.5% to 2% of the general population and it tends to be more persistent and more resistant to treatment than the cutaneous

form.¹

OLP can present clinically in six different patterns: papular, reticular, plaque, atrophic, erosive and bullous, each having specific characteristics and can be found isolated or associated together. The most prevalent type of OLP is the reticular type, characterized by the presence of Wickham striae, which are typically symmetric, bilateral and mainly found on the buccal mucosa. The erosive form,

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regardless of being less frequent, has an extra medical importance because the lesions are typically symptomatic and patients usually present slight discomfort to episodes of excessive pain.²

In the pathogenesis of OLP disease, antigen-specific or non-specific mechanisms or both may be involved. Antigen specific mechanisms include antigen presentation by basal keratinocytes and antigen specific keratinocyte killing by CD8⁺ T-cells. Nonspecific mechanisms include mast cell degranulation and MMPs activation in the lesions. These mechanisms may act simultaneously to cause T-cell accumulation in the superficial lamina propria, basement membrane disruption, T-cell migration, and keratinocyte apoptosis. It has been hypothesized that the chronicity of OLP may be attributed to the TGF- β 1-mediated immunosuppression.³

Topical corticosteroids with their anti-inflammatory and anti-immunologic properties are considered as the first-line pharmacological agents for OLP.⁴ For the erosive type of LP intralesional CS are considered superior to that of topical and systemic as the high concentration of the drug can be achieved with intralesional injections with negligible systemic absorption. Yet various systemic adverse effects have been highlighted in the literature. The complications due to the long term use of corticosteroids include Hypothalamus pituitary adrenal suppression, endocrinal changes as moon face, hirsutism, striae, fungal infections as well as growth retardation. Moreover, local adverse effects including tissue atrophy, candidiasis, granuloma formation and gingival neo-vascularization also have been reported with the use of ILS.^{5,6}

Hence, in light of all the above mentioned adverse effects of CS there is necessity for an alternate treatment with lesser side effects. Platelet Rich Plasma (PRP) is a plasma concentrate of the patient's blood that predominantly contains platelets. Along with the high concentration of platelets, PRP has a very high concentration of coagulation factors. Activated platelets release different growth factors that contribute to cell migration, proliferation, differentiation, angiogenesis, removal of tissue debris and regeneration of the appropriate type of tissues.⁷ PRP helps to accelerate wound healing and improve the patient's quality of life with its anti-inflammatory, anti-oxidative and immunomodulatory action.⁸ Therefore, PRP can be a better novel substitute to the CS without any adverse effects.

To the extent of our knowledge no study has compared the therapeutic effect of intralesional steroids and PRP for the patients of OLP in a split-mouth study design.

Material and Methods

The study was double-blind split-mouth randomized controlled trial which included twenty-five patients, clinically and histopathologically diagnosed with Oral Lichen Planus according to the WHO modified diagnostic criteria (2003)⁹ who reported to the department of Oral Medicine at I.T.S CDSR Ghaziabad. The ethical clearance was provided by the I.T.S institutional ethics committee (IIEC) with protocol number ITSCDSR/IIEC/2019-2022/OMR/01.

All the patients were given a detailed explanation of the study and a signed consent was taken.

A minimum sample size of 20 for each group was calculated using OpenEpi, version 3, open source calculator and software. In our study 28 patients with a total of 56 lesion sites (right and left buccal mucosa) were included and divided into two groups, in group 1- intralesional PRP and in group 2- intralesional steroid (inj. Kenacort 40mg). The injected side for PRP was determined using coin toss method by the physician who injected and a blinded physician scored the severity, the lesion size and take the pain/burning score. The patients were also blind to the nature of injection in each side of buccal mucosa.

Inclusion and exclusion criteria- Patients presenting with a clinical picture that favors the diagnosis of oral lichen planus and histological findings confirming the diagnosis and those who received topical or systemic treatment for OLP in the last 2-4 weeks were included. Patients with Systemic disorder, severe cardiovascular diseases, history of drugs that could cause Lichenoid reaction, any dysplastic lesion, platelet count of < 150,000/mm³ and Hb < 11 g/dl were excluded. Additionally pregnant or breastfeeding females, and the patients who were on anticoagulant therapy and/or used non-steroidal anti-inflammatory drugs in the last 5 days before taking the blood sample were also excluded.

the Modified Escudier Index¹⁰ was used for lesion analysis which include the Site score- 0- absence of the lesion and 1- for the presence of lesion; the Severity score, where 0 means whitish plaque only, 1-keratosis/plaque with mild erythema, 2-marked erythema and 3-presence of ulceration; pain/burning sensation perceived by the patient (recorded using the Visual analog scale of 0-10) where 0 denotes no pain/burning and 10 denotes severe pain/burning.

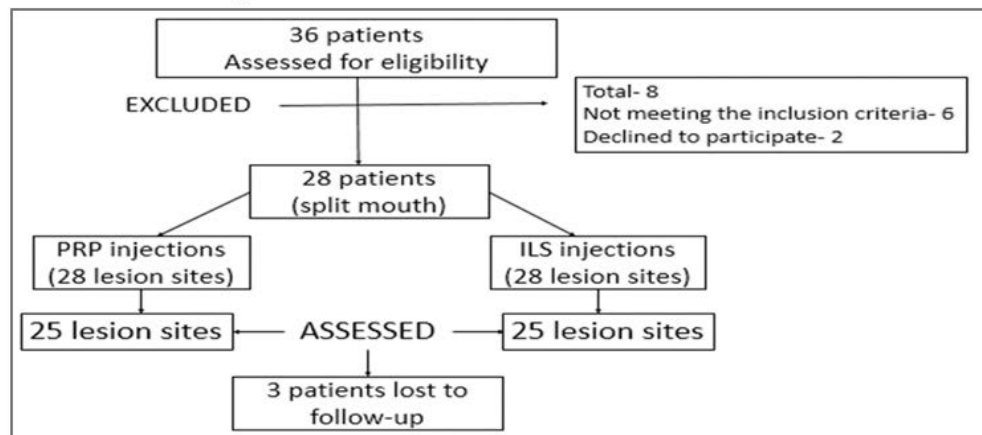
Later the activity score was calculated by multiplying the site and severity score.

For the preparation of PRP, on every visit 10ml of patient's intravenous blood was withdrawn and collected in an anticoagulant tube with the help of oral pathologist. The collected blood was then centrifuged with the regular first spin of 15 minutes which yields PPP (platelet poor plasma) and PRP (platelet rich plasma) then the PRP was transferred to another tube which undergoes a second spin of 10 minutes providing an injectable form of PRP at the bottom of tube with acellular plasma and PPP at the top. With the help of a syringe, the majority of the PPP was removed and disposed, and the rest was injected after shaking thoroughly.

A 25 gauge needle was used for the injections after topically anaesthetizing the buccal mucosa. The steroid and PRP both were injected in a volume 0.5ml per 1cm² of involved mucosa respectively on the same visit. The injections for each group were followed for every 7th day, consecutively for 4 weeks and then patients were kept on a followup for 2 months.

Results-

A total of 36 patients were assessed for eligibility out of which 8 were excluded. 28 patients were included and with the split mouth study design they were divided into 2 groups of 28 lesion sites each with a total of 56 lesions sites from right and left buccal mucosa. 3 patients were lost to follow-up before the end of the trial.



The data obtained at the end of the trial of total 25 patients was analyzed using Statistical Package for Windows; SPSS [ver 22, Armonk, IBM Corp, USA]. Various test applied include The Shapiro-Wilk, Mann Whitney U, Friedman's and Wilcoxon rank test.

Table 1 and table 2 depicts Mean and percentage difference of pain scores and the activity scores at different time intervals by study participants treated with Platelet Rich Plasma and intra lesional steroid.

Table 1: Mean and percentage difference of pain scores at different time intervals by study participants treated with PRP and intra lesional steroid

	Platelet Rich Plasma ^a				Intra-lesional Steroid ^a			
	Mean scores	MD	P value	% difference	Mean scores	MD	P value	% difference
1st visit	9.48 ± 1.0	1.64	P = 0.001*	20.3	9.52 ± 0.82	1.32	P = 0.001*	13.86
2nd visit	7.84 ± 1.45				8.2 ± 0.81			
2nd visit	7.84 ± 1.45	2.36	P = 0.001*	30.1	8.2 ± 0.81	1.76	P = 0.001*	21.46
3rd visit	5.48 ± 1.5				6.44 ± 1.08			
3rd visit	5.48 ± 1.5	1.96	P = 0.001*	35.7	6.44 ± 1.08	1.96	P = 0.001*	30.4
4th visit	3.52 ± 1.55				4.48 ± 0.82			
4th visit	3.52 ± 1.55	1.64	P = 0.001*	46.6	4.48 ± 0.82	1.6	P = 0.001*	35.7
5th visit	1.88 ± 1.13				2.88 ± 0.88			
5th visit	1.88 ± 1.13	0.96	P = 0.01*	51.06	2.88 ± 0.88	1.08	P = 0.05*	37.5
6th visit	0.92 ± 0.49				1.8 ± 0.5			
6th visit	0.92 ± 0.49	0.25	P = 0.01*	26.08	1.8 ± 0.5	0.08	P = 0.65	4.4
7th visit	0.68 ± 0.9				1.72 ± 0.84			

MD-Mean Difference; %-percentage; a-Intra group comparison are significant using Friedman test $P \leq 0.05$

level of significance at $P \leq 0.05$;

*statistically significant using Wilcoxon rank sum test

Table 2: Mean and percentage difference in activity score at different time intervals by patients treated by PRP and Intra-lesional Steroid

	Platelet Rich Plasma ^a				Intra-lesional Steroid ^a			
	Mean scores	MD	P value	% difference	Mean scores	MD	P value	% difference
1st visit	5.16 ± 1.62	0.44	$P = 0.08$	8.52	5.24 ± 1.5	1.32	$P = 0.03^*$	13.86
2nd visit	4.72 ± 1.86				4.52 ± 1.8			
2nd visit	4.72 ± 1.86	2.2	$P = 0.001^*$	46.6	4.52 ± 1.8	1.76	$P = 0.001^*$	21.46
3rd visit	2.52 ± 1.68				3.16 ± 1.8			
3rd visit	2.52 ± 1.68	1.36	$P = 0.001^*$	53.9	3.16 ± 1.8	1.96	$P = 0.001^*$	30.4
4th visit	1.16 ± 1.02				2.2 ± 1.63			
4th visit	1.16 ± 1.02	0.48	$P = 0.11$	41.3	2.2 ± 1.63	1.6	$P = 0.001^*$	35.7
5th visit	0.68 ± 0.47				0.68 ± 0.74			
5th visit	0.68 ± 0.47	0.68	$P = 0.001^*$	68	0.68 ± 0.74	0.64	$P = 0.003^*$	62.1
6th visit	0				0.04 ± 0.2			
6th visit	0	0	-	-	0.04 ± 0.2	-0.08	$P = 0.98$	-20
7th visit					0.12 ± 0.3			

MD-Mean Difference; %-percentage; a-Intra group comparison are significant using Friedman test $P \leq 0.05$ level of significance at $P \leq 0.05$;

*statistically significant using Wilcoxon rank sum test

Statistically no significant difference was found in the distribution of activity scores between 1st to 2nd visit and between 4th to 5th visit in the group treated with Platelet Rich Plasma. But there was a significant difference

Figure 1 and 2- showing Group-1 treated with Intralesional PRP



Fig. 1- Baseline/ Pre-Treatment



Fig. 2- After 4 therapies by intralesional PRP

Figure 3 and 4- showing Group- 2 treated with Intralesional triamcinolone acetonide



Fig. 3- Baseline/ Pre-Treatment



Fig. 4- After 4 therapies by Intralesional Steroids

Discussion

LP is a defect of the stratified squamous epithelia which affects a large number of population.¹¹ The lesions of LP involving the skin generally improve within a duration of two years, but in OLP it could last up to 20 years or even more.¹² The oral mucosa is a common site of involvement, and it may be the only representing site in 0.5 to 2% of the population.

OLP is a chronic disorder with predictable flare-ups and symptom-free periods where each patient's disease behavior can differ.¹³ Hence, the goal of different available treatments is to alleviate unpleasant symptoms, curtail ulcerative lesions, extend symptom-free periods, and mitigate the risk of oral cancer. In the mild cases of OLP various topical preparations of steroids can be used but in the cases of erosive OLP systemic steroids are prescribed extensively which has the major limitation of potential adverse effects. Another treatment options are immunosuppressant and immunomodulatory drugs, which can have a major drawback of promoting malignant transformation with prolonged use, theoretically.¹⁴ In comparison to corticosteroids, PRP has a stronger safety profile with little or no side effects.^{15,16} In the present study, patients were recalled every week till the 5th visit for PRP then for monthly follow-up for next 2 months.

The activity scores were found to be significantly reduced in the group treated with PRP as compared to the one treated with intralesional steroid which is in contrary to the results of the studies conducted by Ahuja US et al. where they compare the efficacy of ILS and PRP for the management of erosive LP and reported a comparative efficacy of both intralesional steroids and PRP for the treatment/management of OLP.¹⁷ This variation could be due to the larger sample size of our study.

Merigo et al. in their case report used platelet rich plasma rinses for the patient with non- responding erosive lichen planus after trying all other modalities including the topical and systemic steroids, low-level laser therapy etc and advocated the efficiency of PRP over other modalities.¹⁸

Lore et al. compared the effects of PRP gel with cyclosporine mouthwash and retinoic acid lotion in various types of OLP in a pilot study and came to the conclusion that the use of PRP could be effective in the management of erosive form when applied weekly.¹⁹

In our study, none of the patients report any adverse effect during the follow-up period. Five patients report recurrence in the form of slight burning sensation on the side treated with intralesional steroids on the 7th visit.

Conclusion-

The present study promotes the use of intralesional PRP for the management of resistant OLP, as its results are superior to that of intralesional steroids with no side effects. Further research with a larger sample size and longer follow-up is needed to validate the PRP as a standard treatment in OLP.

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Conflict of interest- NIL

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Sleep Apnea and Dental Implications -A Review

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Abstract

Obstructive sleep apnea (OSA) is an increasingly common, chronic, sleep-related breathing disorder. The prevalence of obstructive sleep apnea (OSA) continues to rise due to change in life patterns. The most common presenting symptom of OSA is excessive sleepiness and is associated with a 2- to 3-fold increased risk of cardiovascular and metabolic disease. The key contributors to OSA pathogenesis include a narrow, crowded, or collapsible upper airway “anatomical compromise” and “non-anatomical” contributors such as ineffective pharyngeal dilator muscle function during sleep, a low threshold for arousal to airway narrowing during sleep, and unstable control of breathing. Effective treatments include weight loss and exercise, positive airway pressure, oral appliances that hold the jaw forward during sleep, and surgical modification of the pharyngeal soft tissues or facial skeleton to enlarge the upper airway. This review summarizes the latest knowledge on different contributors to OSA with a focus on emerging clinical tools.

Key words - Obstructive sleep apnea, upper airway physiology, positive airway pressure; snoring. Oral appliances

Introduction

Sleep disordered breathing (SDB) is a term which includes simple snoring, upper airway resistance syndrome (UARS), and sleep apnea. Obstructive sleep apnea (OSA) is characterized by recurrent episodes of partial or complete collapse of the upper airway during sleep, resulting in reduced (hypopnea) or absent (apnea) airflow lasting for at least 10 seconds and associated with either cortical arousal or a fall in

blood oxygen saturation. Patients present with various symptoms, although almost all complain of snoring, witnessed breathing pauses, and excessive day time sleepiness. Simple snoring is a common complaint affecting 45% of adults occasionally and 25% of adults habitually and is a sign of upper airway obstruction. ⁽¹⁾ OSA is approximately 25% of adults in the US and is a major cause of excessive sleepiness, contributing to reduced quality of life, impaired work performance,

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and increased motor vehicle crash risk.(2)OSA is associated with an increased incidence of hypertension, type 2 diabetes mellitus, atrial fibrillation, heart failure, coronary heart disease, stroke, and death.(3)OSA can be diagnosed with either home- or laboratory-based sleep testing, and effective treatments are available. This review provides an update on the epidemiology, pathophysiology, diagnosis, and management of OSA.

Epidemiology

The prevalence of OSAS is around 4% for men and 2% for women in the age-group of 30-60 years. OSA is associated with overweight and obesity.(4) Among individuals aged 30 to 49 years with a body mass index (BMI) less than 25, the prevalence of OSA among men is 7.0% and among women is 1.4%,

compared with 44.6% among men and 13.5% among women with a BMI of 30 to 39.9.7.(5,6)

Pathophysiology

OSA is characterized by repetitive partial or complete collapse of the upper airway during sleep, resulting in episodic reduction (hypopnea) or cessation (apnea) of airflow despite respiratory effort. Contraction of upper airway dilator muscles is necessary to maintain airway patency during inspiration. The most important upper airway dilator muscle is the genioglossus muscle, which contracts with each inspiration to prevent posterior collapse of the tongue, assisted by the levator and tensor palatini muscles (advancing and elevating the soft palate) and the geniohyoid and stylopharyngeus muscles (opposing medial collapse of the lateral pharyngeal walls). (7) Most people with OSA have a narrow upper airway, typically caused by fat deposition in the parapharyngeal fat pads and pharyngeal muscles,(8)or abnormalities in craniofacial structure (**Figure 1**).

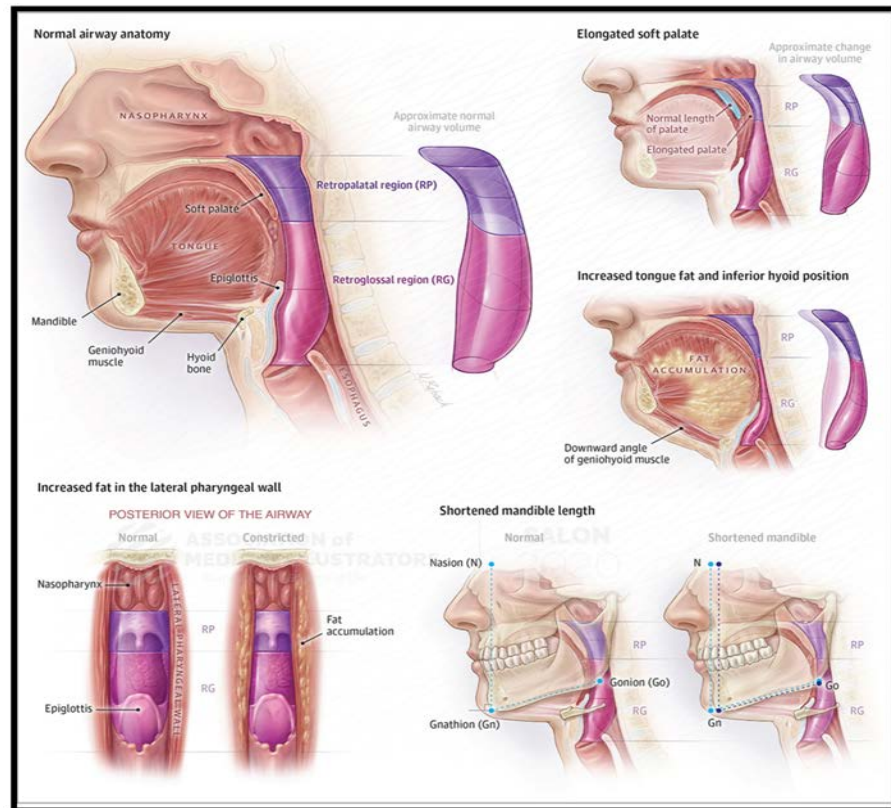


Figure -1 Anatomical features contributing to OSA

These abnormalities include both clinically evident anatomic abnormalities, such as micrognathia and retrognathia, or subtle radiographic findings, such as inferior positioning of the hyoid bone and shorter mandibular and maxillary length, which result in a small maxillomandibular volume.(9) Obstructive apneas and hypopneas result in large changes in

intrathoracic pressure, intermittent hypoxemia, and arousal from sleep. Although these arousals generally do not wake the patient, this sleep fragmentation is the primary cause of excessive sleepiness in individuals with OSA. Intermittent hypoxemia, particularly with concomitant hypercapnia, activates the sympathetic nervous system

system and is the major contributor to both acute and chronic elevation of blood pressure. Repetitive episodes of hypoxemia increase reactive oxygen species, which may further contribute to vascular disease, metabolic abnormalities, and inflammation.⁽⁷⁾

Clinical Features

Excessive sleepiness is reported by 15% to 50% of people with OSA identified through general population screening.⁽¹⁰⁾ While some patients experience awakenings accompanied by gasping or choking, awakenings without accompanying symptoms are more typical.⁽¹¹⁾ Patients with OSAS may have memory problems, excessive day time sleepiness, difficulty in concentrating, night drooling of saliva, depression, irritability, xerostomia, gasping for breath at night, and witnessed apneas. Poor work performance, occupational accidents and a reduction in social interactions and other aspects of quality of life appear to be associated with untreated OSA. There have been reports of exacerbations of epilepsy, asthma and hypertension in patients with untreated or undiagnosed OSA. Motor vehicle accidents in untreated OSAS patients is reported to be two or three times higher than in matched control drivers.^(12,13)

Assessment and Diagnosis

OSA can be made on History, Examination, various

modalities like Questionnaires, Imaging modalities, Polysomnography, AHI, Split-night testing, Oximetry, Home sleep apnea testing etc...intensive and inconvenient for the patient.⁽²¹⁾

A complete history obtained regarding snoring, day time sleepiness, association with systemic complications was obtained and evaluated. Questionnaires like Berlin Questionnaire (developed for use in the primary care setting) and the STOP-Bang questionnaire (developed for preoperative screening) helps in preoperative assessment. The Epworth Sleepiness Scale is widely used in both clinical practice and research to assess sleepiness, but has low sensitivity for OSA.⁽¹⁴⁻¹⁷⁾

Examination of oral and upper airway may include identification of anatomic abnormalities, such as tonsillar hypertrophy, macroglossia, or retrognathia, occlusion, periodontal status, tooth mobility, parafunctional habits, wear facets (generalized / isolated), DMFT, charting, recording of the sensitivity of teeth, tori, and the amount of overbite and overjet present. The dental, skeletal midlines, and temporomandibular joint (TMJ) status have to be recorded prior to analysis of sleep apnea. The Mallampati score (**Figure-2**)

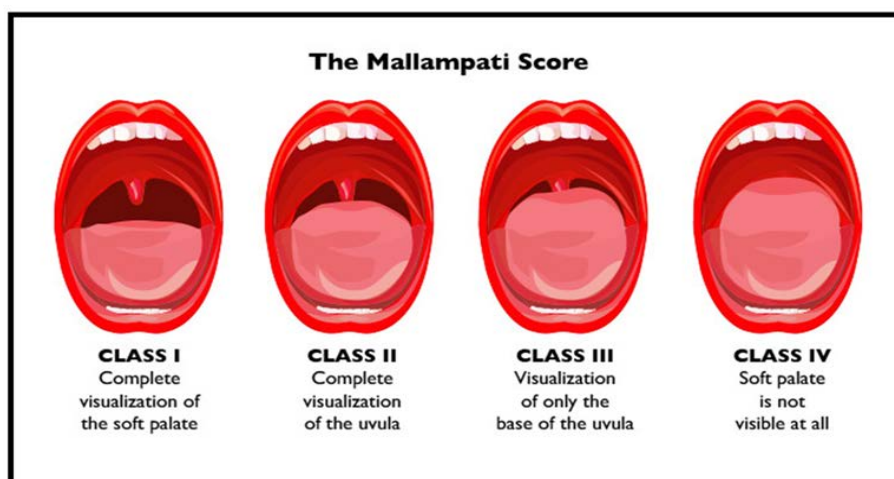


Figure-2 Mallampati Score

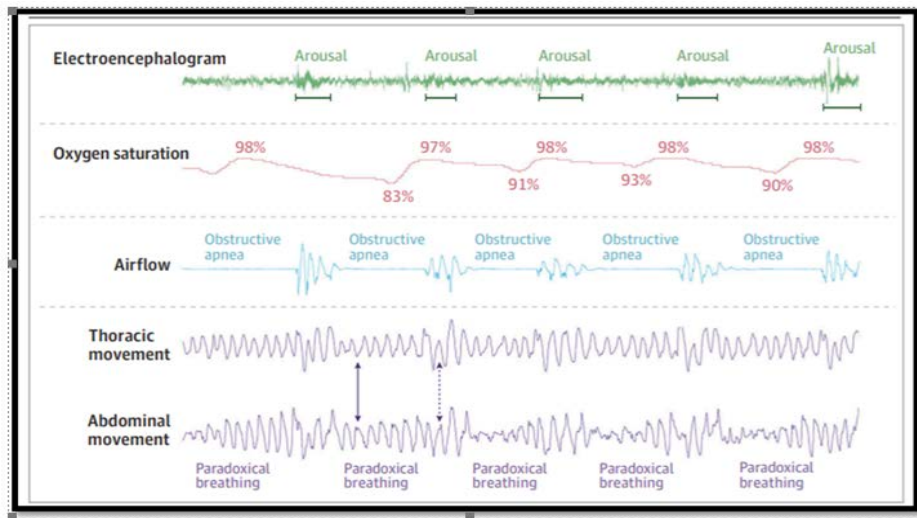
(Grades 1-4) can be used as a predictor for determining the severity of sleep apnea, particularly in cases where an enlarged tongue may seem to be the cause for airway obstruction.¹⁸⁻¹⁹

A number of Imaging modalities like acoustic reflexion, fluoroscopy, nasopharyngoscopy, cephalometry, MR imaging, and both conventional and electron-beam CT scanning have been used to assess the airway. When specific problems like TMJ dysfunction are present and an oral appliance is being planned, specific imaging of the

TMJ should be done. Cephalometrics could be used if the practitioner wishes to evaluate the airway dimension, evaluate cranial or skeletal structures, or plan for orthognathic surgery; for example, SNA and SNB angles and posterior airway space are decreased and PNS-P (length of soft palate) are increased in OSAS.⁽²⁰⁾

If the clinical and radiographic evaluation suggests OSA, diagnostic confirmation requires overnight testing.

The standard diagnostic test is laboratory-based Polysomnography, during which both sleep and respiratory parameters are monitored (**Figure 3**).



A typical laboratory-based polysomnogram includes measures of (1) Airflow through the nose using a nasal cannula connected to a pressure transducer or through the nose and mouth using a thermal sensor; (2) Respiratory effort using thoracic and abdominal inductance bands; (3) Oxygen hemoglobin saturation by finger pulse oximetry; (4) Snoring using a microphone affixed over the trachea or by filtering out low-frequency signals from the nasal cannula-pressure transducer system; (5) Sleep stage and arousal using electroencephalogram, electrooculogram, and chin electromyogram; (6) Electrocardiogram findings; (7) Body position; and (8) Leg movement. Laboratory-based testing is labor-intensive and inconvenient for the patient.⁽²¹⁾

OSA severity is typically quantified using the AHI. An AHI less than 5 events per hour is considered normal, 5 to 14.9 is considered mild, 15 to 29.9 is considered moderate, and at least 30 is considered severe OSA. Differences in how hypopneas are defined affect the AHI value and a lack of consistency in event definition complicates the interpretation of sleep test results and highlights the importance of considering symptoms and comorbid illnesses when making treatment decisions.⁽²²⁾

Home sleep apnea testing is increasingly used to diagnose OSA, and consists of measures of airflow, respiratory effort, and oxygen saturation, but not measures of sleep or leg movements. The sensors are self-applied by the patient at home following instruction from a technologist or via an instructional video. Home sleep apnea testing has both high sensitivity (79% [95% CI, 71%–86%]) and specificity (79% [95% CI, 63%–89%]).⁽²³⁾

Treatment Options

Various treatment modalities are proposed based on the severity of the sleep disorder, preference of the patient, the patient's general health, and the preference and experience of the team members the first and simplest option is behavior modification; this would be followed by insertion of oral devices suited to the patient, especially in those with mild to moderate OSA. CPAP and surgical options are chosen for patients with moderate to severe OSA.

BEHAVIOR MODIFICATION

Behavioral measures include abstinence from alcohol, avoiding supine sleep position, regular aerobic exercise, and weight loss. Changing the sleep position from the supine position to the side position; by placing a tennis ball or by positioning a pillow such that they cannot roll on to their back (positional training). The avoidance of alcohol and sedatives for 3 h before sleep causes a depressing effect on the central nervous system. They also act as muscle relaxants, reducing airway patency.^(24–26)

CONTINUOUS POSITIVE AIRWAY PRESSURE (CPAP)

Positive airway pressure (PAP) is the primary therapy for individuals with symptomatic OSA of any severity. PAP devices deliver pressure to the airway through a mask worn over the nose or the nose and mouth.

This pressure acts as a splint to prevent airway collapse during inspiration. PAP normalizes AHI in more than 90% of patients while wearing the device. Benefit depends on adherence to therapy, with more hours of use per night associated with greater symptom improvement and greater blood pressure reduction.⁽²⁷⁻²⁸⁾

ORAL APPLIANCES

Oral appliances were used by Robin to treat glossoptosis in infants with micrognathia as early as 1905. There is sporadic mention of dental devices for prevention of snoring in patent records before 1980. In 1991, The American Academy of Sleep Dentistry was formed for the education and certification of dental sleep-disorders specialists. In 2000, a section on oral appliances was created in the Academy of Sleep Medicine.⁽²⁹⁻³⁰⁾

The American Academy of Sleep Medicine (AAOSM) has recommended oral appliances for use in patients with primary snoring and mild to moderate OSA. It can also be used in patients with a lesser degree of oxygen saturation, relatively less day time sleepiness, lower frequency of apnea, those who are intolerant of CPAP, or those who refuse surgery.⁽³¹⁾

Oral devices are basically thermoplastic materials with retainers and supports and are usually custom made.

A. Mandibular repositioning or advancement devices (MRD/MAD)

E.g., Herbst appliance / snoreguard / silencer.³²

Which may be titratable. They function by engaging one or both of the dental arches to modify mandibular protrusion; Fabrication of appliance requires dental impressions, a centric relation record, and protrusive record.

B. Tongue repositioning or retaining devices (TRD),
E.g., snorex.⁽³³⁾

C. Soft-palatal lifters.

D. Tongue trainers.⁽¹²⁾

E. A combination of Oral Appliance and CPAP

The combination of CPAP with Oral appliance helps in eliminating the disadvantages of CPAP. This combination helps in delivering the pressurized air directly into the oral cavity and eliminates the use of head gear or nasal mask and avoids the problems of air leaks and the claustrophobia.⁽³⁴⁾

How the Oral Appliances Work

Oral appliances are worn only during sleep and work to enlarge the airway by moving the tongue (anteriorly) or the mandible to enlarge the airway. It is hypothesized that these appliances may also affect upper airway muscle tone and thus decrease their collapsibility. Movement of the tongue or **Mandible anteriorly** can increase the cross-sectional size of the airway and hence oral appliances help in increasing the airway size (**Figure-4**).

Activation of the upper airway dilator muscles by the appliance could cause a decrease in airway collapsibility and this may contribute to preservation of airway patency during sleep, A Tongue-retaining device (**Figure -5**)

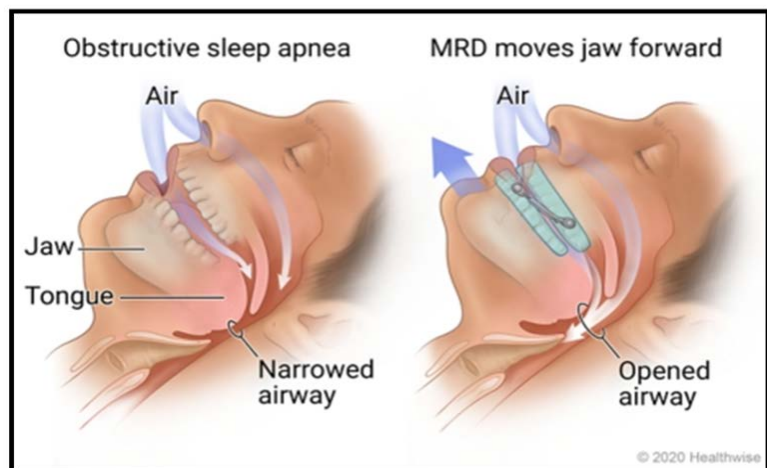


Figure-4 Oral Appliance -MAD



Figure -5 Tongue Retaining Device

is a custom-made soft acrylic appliance that covers the upper and lower teeth and has an anterior plastic bulb. It uses negative suction pressure to hold the tongue in a forward position inside the bulb. By holding the tongue in a forward direction through its attachment to the genial tubercle, it stabilizes the mandible and hyoid bone, thus preventing retrolapse of the tongue. These devices, reverse pharyngeal obstruction both at the level of the oropharynx and the hypopharynx, thereby enlarging the airway and reducing snoring and the related apnea. (35) Soft palate trainers and tongue posture trainers are rarely used. (12)

Goals of Oral Appliance

The treatment goal should be a decrease of about 50% of the initial AHI or to less than 10 events/hr. Oral appliances improve the blood oxygen saturation levels as they relieve apnea in 20-75% of patients. They reduce AHI to < 10 events per h or bring about 50% reduction in AHI. Oral appliances also reduce the AHI to normal in 50-60% of patients.

Advantages

The main advantages of using oral appliances are that there is good patient compliance and the appliances are noninvasive and relatively inexpensive; they can also be easily carried anywhere by the patient.

Side effects and complications

Dental malocclusion (21%), TMJ pain (15%), and TMJ dislocation (<5%) are the side effects of MRDS. Other side effects include excessive salivation, tongue dryness, tooth pain, posterior open bite, and insomnia. The overall incidence of side effects with MRDs is reported to be 25-60%, though these side effects were often mild and resolved with adjustment of the device. (32) Complications with oral appliances include limited degree of lateral freedom during jaw movements. Recalls are necessary at a minimum at 2 weeks, 1 month, and thereafter every 6 months. The appliances are retained tightly by the remaining dentition and place almost orthodontic like forces on the teeth. They may also become loose or can distort or break and hence maintenance is mandatory. (36)

SURGICAL PROCEDURES

The most common surgical procedures for managing OSA modify upper airway soft tissue, including palate, tongue base, and lateral pharyngeal walls. The most extensively studied procedure is Uvulopalatopharyngoplasty, which involves resection of the uvula and part of the soft palate. Other procedures include lateral wall pharyngoplasty and tongue reduction procedures. The bony

structures of the face can also be modified to manage OSA.

Maxillomandibular advancement, in which the upper airway is enlarged via Lefort I Maxillary and Bilateral Mandibular Osteotomies with forward fixation of the facial skeleton by approximately 10 mm causes mean reduction of 80% in AHI, consistent with a mean (SD) change of -47.8 (25.0) events per hour. Hypoglossal nerve stimulation is a newer surgical procedure that increases pharyngeal dilator muscle tone during sleep. (37-41)

FUTURE STUDIES

OSA is common and the prevalence is increasing. Daytime sleepiness is among the most common symptoms, but many patients with OSA are asymptomatic. The treatment of sleep apnea requires a skilled multidisciplinary team. The dentist can also identify a patient with symptoms of snoring and OSA and refer him/her for medical and sleep evaluation. Dentist can treat OSA either by surgical procedures or oral appliance. As oral appliance is noninterventional, it is most accepted by patients. The Association of American Sleep Disorders has published guidelines about the appropriate use of oral appliance therapy and defines the respective roles of the physician and the dentist in this type of care. Further research is necessary for advancement of newer Oral Appliances allow greater lateral jaw movement, cover all of the dentition, and provide better retention. Adjustable (titratable) appliances allow the clinician to titrate the amount of mandibular protrusion in order to obtain an adequate treatment response.

Declarations

Ethics approval and consent to participate

Obtained from institutional ethics committee

Consent for publication:- I hereby give the consent for publication on behalf of all the authors

Availability of data and material: The data and material was obtained from the department after obtaining the permissions from authorities

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Narrative Review on Prosthetic Reconstruction of Neurofibromatosis Cases Undergoing Hemi-Mandibulectomy

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ABSTRACT

Neurofibromatosis (NF) is an autosomal-dominant inherited syndrome with teeth retention and complex tooth deficiencies which can affect swallowing, speech, esthetic, and airway patency. That's where the rehabilitation of structures, functions, esthetics deformities, and life quality with different prosthetic choices should be considered. The present literature review inspected the prosthetic treatment plans to rehabilitate NF type 1 after hemi-mandibulectomy. By an extensive literatures search, some articles were chosen. The prosthetic treatment options for dental reconstruction of the hemi-mandibulectomy can be conventional removable prostheses, implant-supported fixed prostheses, and implant-supported removable prostheses. Ultimately, choosing among prosthetic treatment plans is made based on clinician opinion, patient preference, and ridge condition in each case.

Keywords: Bone deformity; Mandibular reconstructions; Neurofibromatosis

INTRODUCTION

A neurocutaneous disease called neurofibromatosis (NF) is an autosomal-dominant inherited syndrome with three different types.^{1,2} NF1 occurs almost 20 times more than NF2.^{3,4} NF1 discovered by Von Recklinghausen^{3,5} shows symptoms such as café-au-lait macules, Lisch nodules of the iris, and intertriginous freckling.⁶⁻⁸ Different malformations and tumors manifest with this syndrome however, neurofibroma, the benign nerve sheath tumor is more common among them.^{9,10}

NF1 can act as a bone disease and cause jaw deformity if the plexiform of neurofibroma

cells (PNF) are involved.¹¹ This jaw deformity can cause significant problems in the dental procedure and surgical approach.¹² Also, in the facial region, tumors can disfigure the soft tissue extensively, usually unilateral.⁽¹³⁾⁽¹⁴⁾ Teeth retention and complex tooth deficiencies are the syndrome's oral manifestation.^{(13),15}

NF2, in contrast to NF1, is characterized by bilateral schwannoma involvement of the superior vestibular branch of the eighth cranial nerve and it doesn't have oral features.¹⁶ That's why NF2 wasn't included in this review.

To treat the neurofibroma tumor, still, no significant approach is introduced. Surgical

removal is the gold standard treatment plan.^{1,12} However, it can affect swallowing, speech, esthetic, and airway patency.^{11,17} This is the point where the rehabilitation of structures, functions, esthetics deformities, and life quality with different prosthetic choices is brought out.¹⁸ The present literature review inspected the prosthetic treatment plans to rehabilitate five cases of NF type 1 which went through hemi-mandibulectomy.

MATERIAL AND METHODS

An extensive literatures search had been carried out by combing through the Embase, Medline, and PubMed databases.

Inclusion criteria were met if (1) abstract topic related to NF1 and prosthetic rehabilitation; (2) article was in English language; and (3) full-text article was available.

Records were then excluded if one of the following criteria pertained: (1) inadequate patients' information was provided (age, sex,

type of NF, jaw lesion location, clinical and radiographic findings); (2) no oral involvement was mentioned. The collected data organized and analyzed. Table 1 presenting the data of the investigated 5 cases.

FINDING

The study was based on 5 patients, 3 females and 2 males. The youngest case was 21 years old and the oldest was 65 years old. Based on the location of the jaw lesions, all cases were in the mandible along with maxillary lesions in 4 cases. (Table1)

The Clinical, radiographic, and pathological characteristics were evaluated and listed on table 2.

The radiographic appearance was radiolucent in all cases. When the effect of tumors on the mandibular canal was assessed, the enlargement of the canal was seen in Abraham et al²², Schneider et al²⁰, and Kokovic et al²³ case reports and the involvement of canal was

Table 1: Characteristics of the studied cases.

Case number	age	sex	Lesion location	Frequency	Age at diagnosis of NF 1	Familial history	References
1	58	Female	<ul style="list-style-type: none"> Maxilla: In right maxillary sinus Mandible: All over the arch 	Multiple	15	None	Tosios et al 2018 ¹⁹
2	21	Female	<ul style="list-style-type: none"> Maxilla: In the left side Mandible: In the left side 	Multiple	21	Not mentioned	Schneider et al 2017 ²⁰
3	45	male	<ul style="list-style-type: none"> Left posterior part of the mandible crossing the midline 	Single	Not mentioned	Not mentioned	Narang et al 2017 ²¹
4	65	Female	<ul style="list-style-type: none"> Maxilla: All over the arch Mandible: All over the arch 	Multiple	4	None	Abraham et al 2016 ²²
5	57	Male	<ul style="list-style-type: none"> Maxilla: In the right and left sides (not anterior portion) Mandible: All over the arch 	Multiple	Not mentioned	Not mentioned	Kokovic et al 2012 ²³

stated in Narang et al study.(21) However, in Tosios et al study the mandibular canal and mental foramen were not identifiable.(19) Teeth displacement was observed on Narang et al case report. One of the patient suffered

from left hemi-facial paralysis due to the tumor.(20)

The surgical procedure and prosthesis treatment plan in these articles were listed in table 3. As can be seen, different cases have

Table 2: Clinical, radiographic, and pathological characteristics of the studied cases.			
1	Intra oral clinical assessment	<ul style="list-style-type: none"> • Maxilla: Well-defined brown tumors in labial, Palatal expansion • Mandible: An indurated, yellow-colored mass extended from the alveolar ridge to the floor of the mouth 	Tosios et al 2018 ¹⁹
	Radiographic assessment (Panoramic view and CBCT)	<ul style="list-style-type: none"> • Maxilla: A radiolucency with indiscrete borders • Mandible: Poorly defined, multilocular radiolucencies all over the arch 	
	Pathological assessment	<ul style="list-style-type: none"> • Not mentioned 	
2	Intra oral clinical assessment	<ul style="list-style-type: none"> • Maxilla: Narrow and deformed ridge, hyper plastic soft tissue • Mandible: Narrow and deformed ridge, hyper plastic soft tissue 	Schneider et al 2017 (20)
	Radiographic assessment (Panoramic view)	<ul style="list-style-type: none"> • Maxilla: A radiolucency. • Mandible: A radiolucency, shortening of the ramus, narrowing of the mandible body, and rarefaction of the coronoid and articular process. 	
	Pathological assessment	<ul style="list-style-type: none"> • Not mentioned 	
3	<ul style="list-style-type: none"> • Intra oral clinical assessment 	<ul style="list-style-type: none"> • Irregular shaped swelling with firm consistency from the left third molar region to the central incisor of the opposite side crossing the midline. 	Narang et al 2017 ²¹
	<ul style="list-style-type: none"> • Radiographic assessment • (Panoramic view) 	<ul style="list-style-type: none"> • Irregular radiolucency, teeth displacement, and teeth missing 	
	<ul style="list-style-type: none"> • Pathological assessment 	<ul style="list-style-type: none"> • Hyper cellular connective tissue stroma consisting of spindle shaped cells, with wavy nuclei arranged in fascicular and storiform patterns 	
4	<ul style="list-style-type: none"> • Clinical assessment 	<ul style="list-style-type: none"> • Multiple soft nodular masses on the tongue, maxillary and mandible edentulous arches 	Abrahan et al 2016 ²²
	<ul style="list-style-type: none"> • Radiographic assessment • (Panoramic view) 	<ul style="list-style-type: none"> • Enlargement of the mandibular canal 	
5	<ul style="list-style-type: none"> • Clinical assessment 	<ul style="list-style-type: none"> • Maxilla: Narrow residual ridge on left and right side (without involvement of anterior portion), buccal soft tissue of the right cheek • Mandible: Narrow residual ridge 	Kokovic et al 2012 ²³
	<ul style="list-style-type: none"> • Radiographic assessment • (Panoramic view and CT) 	<ul style="list-style-type: none"> • Maxilla: Increase in bone density • Mandible: Lateral bowing of the mandibular ramus, increase in dimensions of the coronoid notch, and a decrease in the mandibular angle 	
	<ul style="list-style-type: none"> • Pathological assessment 	<ul style="list-style-type: none"> • Not mentioned 	

Table 3: Surgical procedure and prosthetic treatment plan of the studied cases.

	Surgical procedure	Prosthetic treatment plan	Follow up
1	Was not performed due to patient desire.	<ul style="list-style-type: none"> • Maxilla: Tissue-supported removable complete denture • Mandible: Tissue-supported removable complete denture 	Patient refused.
2	Hemi-mandibulectomy to remove the lesion and impacted teeth.	<ul style="list-style-type: none"> • Maxilla: Screw-retained implant-supported fixed partial prosthesis • Mandible: Screw-retained implant-supported fixed partial prosthesis 	Several years
3	Left hemi-mandibulectomy along with the dissection of supra-omohyoid lymph nodes	<ul style="list-style-type: none"> • Mandible: Implant-supported fixed partial prosthesis 	Not mentioned
4	Hemi-mandibulectomy was performed before referring.	<ul style="list-style-type: none"> • Maxilla: Tissue-supported removable complete denture • Mandible: Tissue-supported removable complete denture 	Not mentioned
5	Hemi-mandibulectomy was performed before referring.	<ul style="list-style-type: none"> • Maxilla: Implant-supported removable partial prosthesis • Mandible: Implant-supported removable complete denture 	2 years

different treatment plans. In none of the studied cases, recurrence of the lesion was reported.

DISCUSSION

The prosthetic treatment options for dental reconstruction of the hemi-mandibulectomy can be conventional removable prostheses, implant-supported fixed prostheses, and implant-supported removable prostheses.

Conventional prostheses may not be appropriate ⁽²⁴⁾⁽²⁵⁾ because they are incompatible with excessive soft tissue contour and defective bone morphology.⁽²⁴⁾ this is where implant-supported prostheses are more welcomed.^{26,27} However, in two studied case reports, the conventional removable prostheses were delivered.^{19,22}

Despite the long-term success of the implant-supported fixed prostheses, the placement of sufficient numbers of implants can be restricted by severe bone resorption and financial limitation.⁽²⁸⁾⁽²⁹⁾ In these conditions, Implant-supported removable prostheses become bold.³⁰

Implant-supported removable prostheses are of great advantages in terms of improvement of mastication, speaking ability, and quality of life.⁽³⁰⁾⁽³¹⁾ Also, implant-supported overdentures will create pink interdental papilla better than implant-supported fixed prostheses ⁽³²⁾⁽³³⁾⁽³⁴⁾ and as well, they have flanges to rehabilitate the supportless soft tissue.⁽³⁰⁾⁽³⁴⁾ In deviated mandible cases where the forces on implants are angled, and in cases with the restricted mouth opening, removable prostheses perform better.³⁰

To avoid peri-implantitis, in patients with poor oral hygiene, implant-supported removable prostheses have been mostly indicated because it's easy to keep them clean.^{26,30}

It is worth noting that, implant-supported removable prostheses offer very significant improvement for patients with systemic diseases because of the fewer implants required compared to implant-supported fixed prostheses.^{30,35} Only in one of the studied cases, implant-supported removable prostheses were delivered.²³

Along with the dental reconstruction, the reconstruction of the resected bone is important.⁽³⁶⁾ The jaw reconstruction is a challenging approach which can be more complicated if the fibrosis and scarring of soft and hard tissue happen due to delayed reconstruction.⁽³⁸⁾⁽³⁷⁾ A sound and healthy bone graft with a titanium reconstruction plate is an ideal choice to restore the segmented mandible.⁽³⁹⁾⁽⁴⁰⁾ In none of the cases reviewed in this manuscript, the bone reconstruction were conducted.

CONCLUSION

Ultimately, choosing among prosthetic treatment plans is made based on clinician opinion, patient preference, and ridge condition in each case. This statement is of great importance in hemi-mandibulectomy cases where the rehabilitation approaches are more challenging.

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