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Efficacy of Blood Products and Photobiomodulation Therapy for Neurosensory Recovery in Patients With Inferior Alveolar Nerve Injury Following Orthognathic Surgery: A Systematic Review Study

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Abstract

Introduction: Inferior alveolar nerve (IAN) injury is among the most common complications associated with orthognathic surgery. Managing these injuries poses significant challenges due to the lack of a standardized treatment protocol. This study aimed to systematically review the literature on the efficacy of blood products and photobiomodulation (PBM) therapy for neurosensory recovery in patients with IAN injuries after orthognathic surgery.

Methods: This systematic review involved a comprehensive search of Scopus, Embase, and PubMed databases, as well as the initial 100 search results from Google Scholar, to identify relevant articles published between 2015 and 2024. The articles were selected using defined eligibility criteria.

Results: The research paper reviewed 170 articles, ultimately including 14 studies that focused on IAN injury related to surgical procedures such as genioplasty, sagittal split mandibular ramus osteotomy (SSRO), and bilateral sagittal split osteotomy (BSSO). Among these studies, five assessed the effectiveness of various blood products—specifically platelet-rich fibrin (PRF), leukocyte-rich PRF (L-PRF), advanced PRF (A-PRF), and concentrated growth factor (CGF)—all of which were found to alleviate hypoesthesia. Nine studies evaluated the efficacy of PBM, primarily utilizing wavelengths of 810 and 808 nm over 5 to 10 sessions. PBM also successfully enhanced the recovery of IAN. Moreover, one article highlighted the synergistic effect of using L-PRF in conjunction with PBM.

Conclusion: It appears that neurosensory recovery following IAN injury due to orthognathic surgery may be enhanced by blood-derived products such as PRF, CGF, A-PRF, and L-PRF, which release growth factors that facilitate tissue repair. Additionally, PBM further supports recovery by reducing inflammation in the initial weeks and stimulating cellular metabolism to promote regeneration in the subsequent weeks.

Keywords: Blood products; Low-level light therapy; Photobiomodulation; Neurosensory disturbances; Orthognathic surgery.

Introduction

Orthognathic surgery, in conjunction with orthodontic treatment, is performed to correct dentofacial deformities and establish an appropriate intermaxillary skeletal relationship in patients who have completed their growth. This surgical procedure aims to restore lost function, improve speech, and enhance aesthetics.[1]It may involve the repositioning of the maxilla, mandible, or chin. The orthognathic surgical approaches include LeFort I osteotomy and bilateral sagittal split osteotomy (BSSO), which may be performed with or without skeletal genioplasty.[2,3] Maxillary impaction, maxillary advancement, mandibular setback, mandibular advancement, and maxillomandibular (bimaxillary) surgery are among the most commonly performed orthognathic surgical procedures.[4]

Neurosensory disturbances (NSDs) are among the most common postoperative complications following orthognathic surgery.[5,6] Patients experiencing postoperative NSDs may encounter hypoesthesia or dysesthesia in the facial regions innervated by the branches of the trigeminal nerve, resulting from nerve injury.[5,7] The incidence of subjective NSDs 6 to 24 months following maxillary surgical procedures ranges from 9.8% to 16.2%. In contrast, the incidence of subjective NSDs at the same time frame after mandibular surgical procedures ranges from 34.6% to 35.4%.[7] Lower lip paresthesia resulting from inferior alveolar nerve (IAN) injury after orthognathic

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surgery can lead to speech impairment, drooling, and lip biting, significantly impacting the quality of life for patients.[1,8] Seddon[9] classified nerve injuries into three categories: neuropraxia, axonotmesis, and neurotmesis. Neuropraxia is the mildest form of nerve injury, resulting from transient stretching or compression of the nerve. In this case, nerve dysfunction occurs due to disrupted transmission, but the anatomical structure of the nerve remains intact. The prognosis for neuropraxia is typically complete recovery. Axonotmesis represents a more severe type of nerve injury in which the nerve axon is severed; however, the endoneurium remains intact, allowing for the potential for complete regeneration of the axons. Consequently, axonotmesis also has a favorable prognosis. Neurotmesis is the most serious type of nerve injury, characterized by the complete severance of the nerve.[10] It necessitates microsurgical anastomosis or nerve grafting. The majority of nerve injuries encountered are a combination of neuropraxia and axonotmesis,[11] which typically require conservative, non-invasive treatments that are more acceptable to patients. Proper management is imperative to treat nerve damage and NSDs. Treatment of IAN damage is particularly challenging, and there is currently no standardized protocol for addressing NSDs.[12,13] Nevertheless, several adjunctive modalities have been proposed for the treatment of nerve injuries. These include pharmaceutical interventions such as steroids and vitamin B, photobiomodulation (PBM) therapy, as well as the application of platelet-rich fibrin (PRF) and advanced platelet-rich fibrin (A-PRF), which may facilitate the regeneration of the injured nerve.[1,12,14] Review studies on the efficacy of PBM for the treatment of IAN injury are limited. A previous study indicated that the application of PBM resolved IAN injury following oral surgery[1]; Whereas another study could not reach a definitive conclusion regarding the optimal efficacy of PBM for the treatment of IAN injury.[13] There is also a lack of review studies addressing the efficacy of blood products for the treatment of IAN injury resulting from orthognathic surgery. Considering the scarcity of review studies on the efficacy of blood products and PBM for neurosensory recovery following IAN injury due to orthognathic surgery, this review aimed to evaluate the effectiveness of these interventions in promoting neurosensory recovery in patients with IAN injury following orthognathic surgery.

Materials and Methods

In this review study, we searched Scopus, Embase, PubMed, and the first 100 search results from Google Scholar for relevant articles published between 2015 and 2024. The primary question of the study was whether PBM or the application of blood products would facilitate the recovery of NSDs in patients with IAN injury following orthognathic surgery.

The Population, Intervention, Comparison, Outcomes, and Study Design (PICOS) Components

- Population: Patients with IAN injury due to orthognathic surgery
- Intervention: PBM, or blood products, including PRF, A-PRF, leukocyte-platelet-rich fibrin (L-PRF), and concentrated growth factor (CGF) aiming to promote the recovery of NSDs and reduce the associated signs and symptoms.
- Comparison: No PBM and no use of blood products
- Primary outcome: Neurosensory recovery according to the subjective and objective tests listed in Table 1.[13]
- Secondary outcome: Side effects related to the treatment
- Study design: Randomized clinical trials (RCTs)

Eligibility Criteria

Inclusion criteria: English-written RCTs regarding the effects of PBM and blood products, namely PRF, L-PRF, A-PRF, and CGF on IAN recovery following orthognathic surgery, studies with a control group, and relevant articles published from 2015 to 2024.

Exclusion criteria: Studies lacking the PICO components and unavailability of full texts.

Search Strategy

Different databases of Scopus, Embase, PubMed, and the first 100 search results of Google Scholar were searched for articles published from 2015 to 2024 using the following keywords:

("blood products" OR "platelet-rich plasma" OR "PRP" OR "autologous blood products" OR "fibrin-rich plasma" OR "platelet concentrates" OR "blood platelets" OR "Advanced platelet-rich fibrin" OR "A-PRF" OR "platelet-rich fibrin" OR "PRF" OR "fibrin" OR "platelet" OR "blood platelets" OR "leukocyte-platelet-rich fibrin" OR "L-PRF") AND ("photobiomodulation" OR "PBM" OR "low-level laser therapy" OR "LLLT" OR " low-level light therapy" OR "Laser" OR "laser therapy" OR "red light therapy" OR "near-infrared light therapy") AND ("neurosensory recovery" OR "nerve regeneration" OR "sensory recovery" OR "nerve healing" OR "nerve repair" OR "axonal regeneration") AND ("inferior alveolar nerve injury" OR "IAN injury" OR "mandibular nerve injury" OR "nerve damage" OR "alveolar nerve trauma" OR "Neurosensory disturbance" OR "Neurosensory deficits" OR "Neurosensory disorder") AND ("orthognathic surgery" OR "jaw surgery" OR "maxillofacial surgery" OR "corrective jaw surgery" OR "bilateral sagittal split osteotomy" OR "BSSO" OR" LeFort I" OR "Sagittal split osteotomy" OR "SSO" OR "sagittal split ramus osteotomy" OR "SSRO")

Data Extraction

Two independent reviewers extracted data. In cases of

disagreement, a third reviewer was consulted. First, the titles and abstracts of the articles were assessed, followed by their full texts. The information extracted from each article is summarized in Table 2 and Table 3.[15-24]

Quality Assessment

The RoB 2 (Cochrane Risk of Bias tool for randomized trials) was used to assess the quality of clinical trial articles. This assessment included randomization bias, allocation concealment (bias during randomization, bias due to deviation from intended interventions, bias due to missing outcome data, and bias in outcome measurement), selective outcome reporting bias, and overall article quality. Studies were classified into three groups based on bias: "low risk," "uncertain risk," and "high risk." If all of the mentioned criteria for a study were assessed as low risk, that study was considered to have a "low" risk of bias. If any of the criteria were assessed as high risk, the study was considered to have a "high" risk of bias. If at least one criterion was assessed as uncertain risk, the study was

Table 1. Neurosensory Test for Evaluation of Inferior Alveolar Nerve

Classification	Test Category	Name	Description
Objective	Mechanoceptive	BDD	A soft brush was moved across the test area in either an anterior or posterior direction. The patient's ability to identify the direction of movement was noted as the number of correct responses out of 10 trials.
		TPD	Two pointed, but not sharp, tips of a caliper make contact with the skin simultaneously and with light pressure while the patient's eyes are closed. The distance between the two points is gradually decreased from 20 mm at the chin and 10 mm at the lips until the patient perceives them as a single point.
		Contact detection/LT	The contact detection threshold, defined as the minimum force exerted on the skin that can be felt, is assessed using a Semmes-Weinstein monofilament attached to the end of a plastic handle.
		PP	This test consists of repeating 10 touches with an explorer tip on the lip or chin skin and calculating how many times the patient reported the contact.
	Nociceptive	SBD	This is done by touching the test area randomly with a sharp or blunt head of a mechanical probe. The patients are asked to report whether the sensation was sharp or blunt.
		THD	Two small glass tubes filled with water at 50°C (warm) and 15°C (cold) were utilized. The response to each stimulus, indicating cold versus hot, was recorded.
Subjective	NA	VAS	This test is conducted using a 10-cm, 5-degree VAS marked with divisions at 2.5-cm intervals. Patients evaluate their personal perception of the affected area by choosing from five options: 1 (lack of sensitivity), 2 (almost none), 3 (reduced sensation), 4 (almost normal), and 5 (normal). During each testing session, they indicate their response by placing an "x" on the scale.

NA, not applicable; BDD, brush stroke directional discrimination; TPD, two-point discrimination; LT, light touch; PP, Pin prick; SBD, sharp blunt discrimination; THD, thermal discrimination; VAS, visual analog scale.

Table 2. Studies Related to the Use of Blood Products

Author, Year	Country	Study Design	Surgery	Nerve Injury Based on Seddon Classification	Sample Size	Mean Age (y)	Sex	Blood Product	Assessment Method	Follow-Up Duration	Conclusion	Side Effects
Behnia 2024[15]	Iran	RCT, split-mouth	Genioplasty with or without Lefort 1 osteotomy	NR	20	27.70 ± 6.67	20 F	L-PRF	TPD, PD, THD, VAS	2 days, 2 weeks, 4 weeks, and 2 months	L-PRF > Control All times	No
Zhu 2024[14]	China	RCT, split-mouth	SSRO	NR	30	23.3 ± 6.0	20 F 10 M	A-PRF	TPD	1, 2 ,5 days, 3 months	A-PRF > Control All times	NR
Wang 2022[10]	China	RCT, split-mouth	Genioplasty	1&2	26	24	26 f	CGF	TPD, VAS	1 week, 1, 3, 6, and 9 months	1 week: CGF = Control 1, 3, 6, and 9 months: CGF > Control	NR
Behnia 2023[11]	Iran	RCT, split-mouth	Genioplasty	1&2	20	28 ± 6.55	16 F 4 M	L-PRF	TPD, BDD, VAS	1, 4, 12 month	4 months: L-PRF > Control 12 months: L-PRF = Control	NR
Tabrizi 2018[16]	Iran	RCT, split-mouth	BSSO	NR	21	25.48 ± 5.16	15 F 6 M	PRF	TPD, BDD, VAS	6 and 12 months	PRF > Control All times	NR

A-PRF, Advanced platelet-rich fibrin; BDD, Brush stroke directional discrimination; CGF, Concentrated growth factor; F, Female; M, Male; NR, Not reported; LPRF, Leukocyte-rich fibrin; PD, Pain discrimination; PRF, Platelet-rich fibrin; RCT, Randomized clinical trial; Seddon classification 1: Neurapraxia, 2: Axonotmesis, 3: Neurotmesis; SSO, Sagittal split osteotomy; SSRO, Sagittal split ramus osteotomy; THD, Thermal discrimination; TPD, Two-point discrimination; VAS, Visual analogue scale.

Table 3. Studies Related to the Use of Low-Level Laser Therapy

Author, year	country	Study design	surgery	Sample size	Mean Age (years)/ sex	Wavelength (nm)/ Power (mW),	Energy density (J/cm²)/ spot size (cm²)	Irradiation mode	Radiation Time per point, Irradiation points	Radiation Time per point, Days of laser therapy	Assessment Method	Follow-up Duration	Conclusion	side effects
Behnia 2024 [15]	Iran	RCT, split-mouth	Genioplasty with or without Lefort 1 osteotomy	20	27.70 ± 6.67/ 20 F	880/ 500 W	15 / 0.5	continuous	15 s , **Extra-oral**: six points in the chin area, and six points in the buccal region **Intra-oral**: two points at the mesial and distal of the mental nerve	1, 3, 7, 14, 21, and 28 days	TPD, PD, THD, VAS	2 days, 2 weeks, 4 weeks, and 2 months	TPD, PD: laser > control THD, VAS: laser = control	**No**
Esteves 2020 [17]	Brazil	RCT, split-mouth	SSRO	12	30/ 6 F 6 M	808, 100	100/ NR	continuous	28s, From the mandibular foramen to the chin and lip region	started 48 hours after surgery, a minimum of 10 sessions (two sessions per week)	VAS	6 weeks	laser > control	**No**
Sharifi 2020[18]	Iran	RCT, split-mouth	SSRO	18	23 ± 5/ 14 F 4 M	980nm, /100	12/0.5	continuous	60s, six points in the chin area, and six points in the buccal region from the oral commissure to the lingula	one day preoperatively, 1, 3, 7, 14, 21, 28	VAS, TPD, PD, THD	Immediately after operation, 1&2 months	VAS, TPD, PD : laser > control after 30 and 60 days THD: laser = control	**No**
Santos 2019[19]	Brazil	RCT, split-mouth	SSRO	20	35.6 ± 11.6/ 13 F 7 M	780 nm, NR	157.5/ 0.04	continuous	90s, 29 points: an extraoral point (the mandibular ramus and along the entire course of the inferior alveolar nerve to the mental region) and an intraoral point (in the mental foramen region	5 times, 3-to-4-week intervals between sessions	SWMF	30 days, 6 months, 1 year	laser > control after the 4th laser therapy session	**No**
Guarini 2018 [20]	Chile	RCT, split-mouth	SSRO	42	Laser: 25.8 ± 22 control: 29.8 ± 24/ 33 F 9 M	810/100	31.8/ 0.283	continuous	90s, **Intraoral:** mandibular and mental foramen and osteotomy site (buccal side in relation to mandibular second molar)	1, 2, 3, 5, 10, 14, 21, 28	VAS, TPD, THD	6 months, 1 & 2 years	VAS, TPD: laser > control after 6 months, 1 & 2 years THD: laser = control	**No**

Table 3. Continued.

Author, year	country	Study design	surgery	Sample size	Mean Age (years)/ sex	Wavelength (nm)/ Power (mW),	Energy density (J/cm²)/ spot size (cm²)	Irradiation mode	Radiation Time per point, Irradiation points	Radiation Time per point, Days of laser therapy	Assessment Method	Follow-up Duration	Conclusion	side effects
Esmaeelinejad 2018 [21]	Iran	RCT, split-mouth	SSRO	40	26.52 ± 3.78/ 22 F 18 M	810/ 70	8.4/0.5	continuous	60 s , **Extraoral**: 3 points of vermilion, median chin area, paramedian chin area, **Intraoral**: mental foramen	0, 1, 2, 3, and then every other day for two weeks (10 sessions in total)	TPD, THD, PP	1 year	TPD, THD, PP: laser > control After 1 year	**No**
Eshghpour 2017 [22]	Iran	RCT, split-mouth	SSRO	16	23.1 ± 4.4/ 11 F 5M	660 + 810/200	1.5(660), 7 (810)/1.3(660), 0.028(810)	continuous	**Intraora**l: 4 points located 1 cm away from the surgical site, **Extraoral**:8 points located on ramus and body of the mandible along the distribution of the inferior alveolar nerve	10s, 1, 2, 3 days and then twice a week for 3 weeks	TPD	45 & 60 days	laser > control After 45 & 60 days post-operation	**No**
Mohajerani 2017 [23]	Iran	RCT	SSRO	20	23.45 ± 4.05/ 12 F 8 M	810 (laser) + 632 (LED) /NR	5(810), 2(632)/ NR	NR	90s, entrance of the mandibular foramen, along the osteotomy line, the lips, and the chin region	1 , 2, 3, 7, 14, 28 days	VAS, BDD, TPD, PP, THD	1, 3, 7, 14, days 2 , 6 months	VAS, BDD: laser > control LED > control 2 week, 2 & 6 months	**No**
Buysse Temprano 2017 [24]	Brazil	RCT, split-mouth	SSRO	12	30/ 6 F 6 M	808 nm, /100	100/ 0.0028	NR	28s, 25 points: length of the inferior alveolar nerve starting at its entrance in the mandible foramen to the chin area and the external lip, and the oral area before the molars to the internal side of the lip	2 sessions per week (10 sessions)	THD, VAS	6 weeks	laser > control	**No**

BDD: brush stroke directional discrimination, F: Female, M: Male, PD: pain discrimination, PP: Pin prick, RCT: randomized clinical trial, SSRO: sagittal split ramus osteotomy, SWMF: Semmes-Weinstein monofilament test, THD: thermal discrimination, TPD: two-point discrimination, VAS: visual analogue scale.

classified as having an "uncertain" risk of bias.[25]

Results

Search Results

A total of 170 articles were retrieved through electronic database searches. After the elimination of duplicates, 95 articles remained; 65 articles were excluded following the screening of titles and abstracts. Additionally, 16 articles were excluded after reviewing the full texts and applying the eligibility criteria. Finally, 14 articles were included in the review (Figure 1).

Study Characteristics

Blood Products

The studies retrieved were conducted between 2018 and 2024, with the number of patients ranging from 20 to 30. These studies evaluated IAN injury following genioplasty,[11,15,26] SSRO,[14] and BSSO.[16] Different blood products, including L-PRF,[11,15] A-PRF,[14] CGF,[10] and PRF[16] were applied among studies.

In two studies, L-PRF was applied on the intervention side as a loop around the mental nerve following the fixation of the osteotomy segment.[11,15] Another study applied a CGF membrane to the mental nerve following osteotomy and prior to fixation.[10] Additionally, A-PRF was utilized at the intervention site prior to rigid fixation.[27] In a separate investigation, PRF was employed at the osteotomy site following the procedure and before fixation.[16] The NSD tests employed in these studies included the two-point discrimination (TPD) test (5 studies),[11,14-16,26] pain discrimination (PD) (1 study),[15] thermal discrimination (THD) (1 study),[15] visual analog scale (VAS) (3 studies),[10,15,16] and brush stroke directional discrimination test (BDD) (2 studies).[11,16]

In all studies, the administration of blood products led to the recovery of hypoesthesia, and no adverse effects were reported (Table 2).

Photobiomodulation

Studies on PBM were published between 2017 and 2020, with the number of patients ranging from 12 to 42. The cause of IAN injury in all studies was SSRO.[17,19-24]

The light source varied among the studies and included the use of laser at wavelengths of 660 nm,[22] 780 nm,[19] 808 nm,[17,24] 810 nm,[20-23] 880 nm,[15] 980 nm,[18] and a combination of laser 810 nm and LED 632 nm.[23] The number of laser irradiation sessions was also highly variable, ranging from 5 to 10 sessions. The energy density reported in the

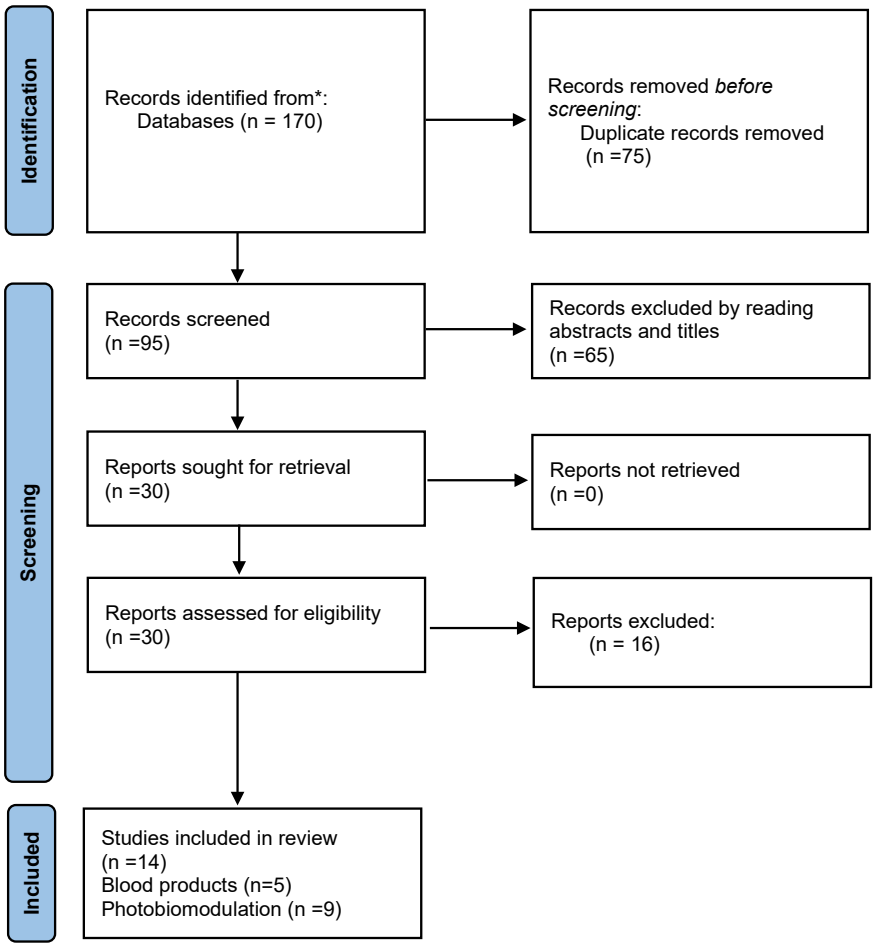

Figure 1. PRISMA Flowchart

articles varied and included 1.5 and 7 J/cm^2,[22] 2 and 5 J/cm^2,[23] 8.4 J/cm^2,[21] 12 J/cm^2,[18] 15 J/cm^2,[15] 31.8 J/cm^2,[20] and 100 J/cm^2,[17,24] and 157.5 J/cm^2.[19]

The studies utilized various laser power levels, including 70 mW,[21] 100 mW,[17,18,20,24] 200 mW,[22] and 500 mW.[15] In two studies, the laser power was not specified.[19,23] Seven studies employed the continuous emission mode,[15,18-22] whereas two studies did not report the emission mode.[23,24]

In a study conducted by Behnia et al,[15] improvements in NSD were reported at all time points: 2 days, 2 weeks, 4 weeks, and 2 months, according to the PD and TPD tests. However, the VAS and THD tests did not show any significant improvement. Esteves et al[17] reported enhancements in VAS results following 10 sessions of PBM. Sharifi et al[18] observed improvements in VAS, PD, and TPD test results after 1 and 2 months. The THD test results were higher in the laser group compared to the control group after 30 days; however, no significant difference was observed after 60 days. Santos et al[19] performed PBM 15 days after surgery in one group and 6 months to 1 year after surgery in the other group. The group that initiated treatment earlier demonstrated a significantly faster recovery than the group that began treatment later. Overall, notable recovery was observed starting from the fourth treatment session in the laser group, in contrast to the control group. Guarini et al[20] observed NSD recovery at 6 months, 1 year, and 2 years post-treatment as measured by the VAS, and at 1 and 2 years according to the TPD test. However, no significant difference was identified between the test and control groups based on the results of the THD test. Esmaeelinejad and Kalantar Motamedi[21] assessed NSD recovery after one year and demonstrated significantly greater improvements in all test results for the PBM group compared to the control group. Eshghpour et al[22] demonstrated that the TPD result was lower in the PBM group compared to the control group at 45 and 60 days post-surgery. Mohajerani et al[23] reported that the application of PBM with laser and light-emitting diodes (LEDs) resulted in IAN recovery, as indicated by VAS, BDD, and TPD test results at 2 and 6 months post-surgery. However, the PP test results did not show a significant difference between the two groups, and THD test results returned to baseline in both groups after 7 days. No side effects were reported (Table 3).

Combination of Blood Products and Photobiomodulation

In a study conducted by Behnia et al,[15] the effectiveness of L-PRF combined with 880 nm PBM at an energy density of 15 J/cm^2 was evaluated for recovering from NSDs of the mental nerve following genioplasty. After the surgery and application of PRF, the intervention side received diode laser irradiation at designated intervals. Sensory recovery was assessed using a visual analog scale and discrimination tests at different time points. The findings showed that the intervention group had significantly improved sensory function compared to the control group, especially in two-point discrimination and brush tests. Although time had a positive impact on recovery, the interaction between time and treatment was not significant. Overall, the combination of L-PRF and PBM was found to be beneficial in enhancing recovery after genioplasty.

Risk of Bias Assessment

The summary of the risk of bias assessment for the included RCTs is illustrated in Figures 2 and 3.

Discussion

Orthognathic surgery is a significant surgical procedure typically performed to correct dentofacial anomalies through invasive techniques.[1] IAN injury following orthognathic surgery is a common complication. Although cone-beam computed tomography is conducted for all patients preoperatively, certain anatomical variations in the mandible and IAN intrabony course, along with the surgeon's experience, surgical approach, type of fixation, and the presence of third molars, can elevate the risk of postoperative NSDs.[1] This review study aimed to evaluate the efficacy of adjunctive treatments, such as the application of blood products and PBM for the recovery from NSDs following IAN injury due to orthognathic surgery.

PRF has gained increasing attention in recent years due to its potential for successfully inducing hard and soft tissue regeneration as well as angiogenesis.[28] One advantage of PRF over platelet-rich plasma (PRP) is the absence of anticoagulants. This absence leads to the formation of a robust fibrin matrix and the generation of substantial amounts of growth factors, which may be released over a period of 10 to 14 days.[28] Increasing preclinical and clinical evidence indicates that PRP and its fibrin scaffolds possess significant potential as neurogenic and modulatory systems for enhancing neurosensory and motor neuromuscular functions.[29,30]

According to neurobiological science, the survival of nerve cells following injury depends on the presence of an optimal environment enriched with growth factors, cytokines, hormones, and extracellular matrix components. Therefore, the application of growth factor products at the site of nerve injury can enhance the regeneration of nerve cells.[10] In all five reviewed studies, the application of blood products resulted in NSD recovery compared to the control group. Behnia et al[11] utilized L-PRF for the treatment of IAN paresthesia following genioplasty and found that the application of L-PRF was effective in promoting nerve sensory recovery after 4 months, but not after 12 months, when compared to the control side. Since NSDs often arise from neuropraxia and axonotmesis, these types of injuries typically heal within approximately 4 months post-injury.[11] In another study, Behnia et al[15] used L-PRF followed by 880 nm LLLT for

Figure 2. Risk of Bias Based on the RoB2 Tool for Blood Products Studies

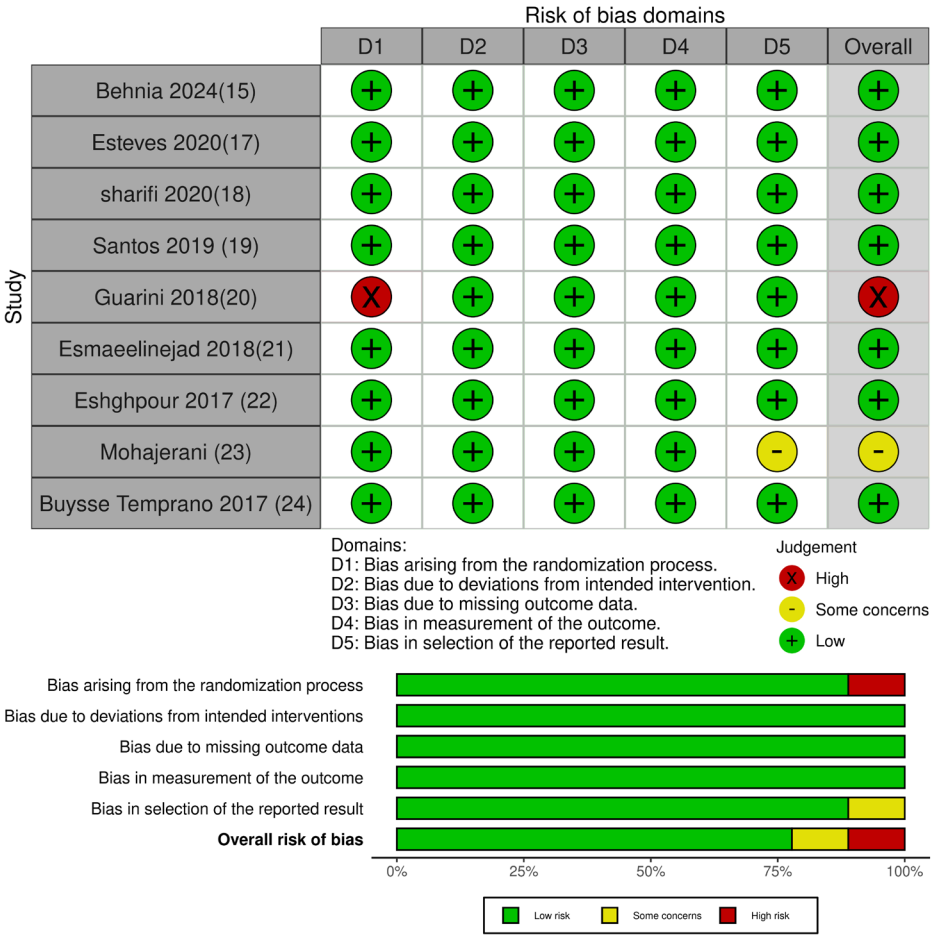

Figure 3. Risk of Bias Based on the RoB2 Tool for Low-Level Laser Therapy Studies

NSD recovery of IAN injury after genioplasty and found that it was effective at all-time points of 2 days, 2 and 4 weeks, and 2 months. They used L-PRF in all patients, irrespective of the test and control sides.

The most significant difference between PRF and L-PRF lies in the concentration of leukocytes. Leukocytes influence the inherent biological properties of platelets. The immunological and antibacterial characteristics of leukocytes are crucial in the wound healing process.[31,32] L-PRF influences peripheral nerve regeneration in cases of inflammation and nerve damage.[26] It exhibits anti-inflammatory properties and can reduce the level of inflammation in injured tissues.[33] Unlike other platelet concentrates, L-PRF does not require anticoagulants or thrombin. It is prepared through blood centrifugation without additives, making its application in clinic straightforward.[11]

A study conducted in 2022 reported that the application of a CGF membrane enhanced IAN recovery following genioplasty.[10] CGF is a derivative of Leukocyte-Platelet Rich Fibrin (L-PRF). There is no significant difference in the active to total platelet ratio in CGF compared to other derivatives, such as A-PRF and horizontal-PRF. Furthermore, active platelets exhibit a homogeneous distribution in CGF.[34] It appears that no clear consensus exists regarding the differences between CGF and other PRF matrices.[10]

Zhu et al found that A-PRF injection significantly reduced lower lip paresthesia at 2 days, as well as at 3 and 5 months, in thirty patients undergoing mandibular setback orthognathic surgery. They noted that A-PRF can facilitate early recovery IAN.[14] The substantial improvement in nerve sensory disturbance (NSD) recovery attributed to A-PRF, compared to the control group, can be linked to its ability to prevent apoptosis,[35] stimulate angiogenesis,[36] regulate inflammatory micro-environment,[37] and enhance axon growth along with its neural conductivity.[27] Tabrizi et al[16] conducted an RCT to evaluate the efficacy of PRF for IAN recovery after SSRO. They discovered that PRF may improve paresthesia.[16] PRF protects the nerve by enhancing axon growth capacity, inducing angiogenesis, and preventing apoptosis. Additionally, it mitigates the inflammatory microenvironment and promotes peripheral nerve regeneration.[16]

Of the nine studies that assessed the efficacy of PBM, all reported positive outcomes for nerve injury recovery. It is important to note that the penetration depth of each laser is dependent on its wavelength.[1]

The laser wavelengths varied and included 632 nm,[23] 660 nm,[22] 780 nm,[19] 808 nm,[17,24] 810 nm,[21-23] 810-820 nm,[20] 880 nm,[15] and 980 nm,[18] all of which fall within the PBM spectrum. There is currently no consensus on the PBM protocol, and the frequency of treatment sessions varied significantly, ranging from five to ten sessions. Although PBM has demonstrated efficacy in facilitating the recovery from paresthesia,[1,38] the effects of PBM include accelerated wound healing, pain relief, recovery of neural function, bone regeneration and remodeling, regulation of hormonal function, stimulation of endorphin release, and modulation of the immune system. Furthermore, because phototherapy can reduce the production of inflammatory mediators from the arachidonic acid family in injured nerves, it may enhance the regeneration of damaged neural tissue.[39] Two strategies can be employed for NSD recovery following IAN injury: the regeneration of nerve fibers after Wallerian degeneration and collateral reinnervation through the ingrowth of adjacent intact nerves.[40] Some researchers propose that PBM exerts its effects by enhancing the release of nutritional factors at the treatment site, which subsequently stimulates collateral reinnervation from inactive adjacent tissues.[41,42] Other potential mechanisms by which PBM influences neurosensory recovery include the reduction of prostaglandins and acute-phase inflammatory factors, such as tumor necrosis factor-alpha, interleukin-1, and interstitial metalloproteinases,[43] as well as the synthesis of growth factors.[44] It is important to note that time has a statistically significant impact on the recovery of all sensory parameters, with sensation often improving over time.[15]

We identified a single study that highlighted the synergistic effect of PBM and L-PRF on neurosensory recovery of IAN after genioplasty.[15] The combination of PRP and PBM has been discussed in earlier research related to periodontal regeneration[45] and arthritis.[46] The findings indicate the need for further studies to reinforce these data.

The reviewed studies employed various techniques and assessments to evaluate inferior IAN function, ranging from IAN based on subjective patient reports or clinical sensory examinations. However, the results of these tests are inherently subjective, and the lack of objectivity represents a significant limitation in the clinical examination and diagnosis of NSDs.[16,47] Subjective reports of perceived NSDs following SSOs may be either overestimated or underestimated initially. Patients may acclimate to these changes, ultimately perceiving them as in the long term. Such patient reports can significantly influence the outcomes of studies on this subject.[16] The primary objective of sensory diagnostic tests is to determine whether an NSD has occurred, quantify its severity, monitor NSD recovery, and assess the necessity for microsurgery.[48] Clinical neurological examinations can be categorized into two groups: mechanical assessments and pain assessments related to specific receptors activated by cutaneous contact. Mechanical assessments include TPD test, light touch, and BDD. THD and pinprick tactile discrimination tests are classified as pain assessments.[49]

Double-blind RCTs (with blinding both the patient and the examiner to group allocations) are recommended.

Additionally, a split-mouth design, computerized randomization of the test and control sides, and control of confounding factors—such as postoperative intake of anti-inflammatory medications that may influence surgical outcomes—are essential. Standardization of the surgical process on both sides is also crucial. A limitation of the reviewed studies was their small sample size. Future research should involve larger sample sizes and incorporate other clinical neurosensory tests, such as THD.

Considering its optimal biological effects, cost-effectiveness, and ease of preparation, PRF appears to be a promising product for application in orthognathic surgery. Its potential indications in the operating room and clinical settings include the reduction of NSDs, alleviation of pain and edema, and enhancement of bone healing.[14,16] Therefore, PRF may serve as a valuable adjunctive intervention in orthognathic surgical procedures.

Conclusion

It appears that nerve regeneration following IAN injury due to orthognathic surgery may be facilitated by the application of blood products, such as PRF, CGF, A-PRF, and L-PRF in the short term. Moreover, PBM has also shown a promising effect on sensory recovery in NSD cases, and it can mitigate the inflammatory response during the initial weeks following the injury and subsequently promote nerve regeneration by modulating cellular metabolism to favor regenerative processes in the weeks that follow.

Authors' Contribution

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Competing Interests

None.

Ethical Approval

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