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Original Research Article

Effect of hyaluronic acid on neurosensory disturbance after bilateral sagittal split ramus Osteotomy, pilot study

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Name of Author:
Hassan Mamand Fattah [1], Reiadh K. Al-Kamali [2], Twana Hoshyar Salem[3]

Affiliation: *[1]Department of Oral and Maxillofacial Surgery, Rzgary Teaching Hospital, Erbil, Kurdistan Region, Iraq (Training Center: Erbil Training Center, Kurdistan Higher Council of Medical Specialities).*
[2]PhD, BDS, FDS RCSEd, FFDRCSI, Department of Oral and Maxillofacial Surgery, Erbil Training Center, Kurdistan Region, Iraq; Ministry of Higher Education & Scientific Research (Assistant Professor, Oral and Maxillofacial Surgery).
[3]MD[1].
Corresponding Author:

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Abstract: ***Background and Aim:*** Neurosensory disturbance of the lower lip and chin is a common complication following bilateral sagittal split ramus osteotomy (BSSRO), primarily due to manipulation or injury of the inferior alveolar nerve. Hyaluronic acid (HA) has anti-inflammatory and anti-fibrotic properties and may support peripheral nerve healing. This pilot study aimed to evaluate the effect of locally applied hyaluronic acid on neurosensory recovery following BSSRO. ***Methods:*** This prospective controlled pilot study was conducted at Rzgary Teaching Hospital, Erbil, from May to December 2025. Twenty adult patients undergoing BSSRO were enrolled. Hyaluronic acid was applied intraoperatively to one randomly selected mandibular side, while the contralateral side served as control. Neurosensory function was assessed using the two-point discrimination (2PD) test preoperatively and at 1, 3, and 6 months postoperatively. ***Results:*** Baseline preoperative 2PD values were symmetrical between both mandibular sides ($p = 0.801$). At 1, 3, and 6 months postoperatively, the HA-treated side demonstrated significantly lower 2PD values compared with the control side ($p = 0.048$, 0.012, and 0.004, respectively). Complete neurosensory recovery at 6 months was achieved in 65.0% of HA-treated sides versus 40.0% of control sides ($p = 0.039$). Effect size increased over time, reaching a large magnitude at 6 months (Cohen's $d = 0.91$).
Conclusion: Local application of hyaluronic acid during BSSRO appears to be safe and is associated with accelerated and improved neurosensory recovery. These findings support the potential role of hyaluronic acid as an adjunctive strategy for reducing postoperative neurosensory disturbance, warranting confirmation in larger randomized trials.

Keywords: Bilateral sagittal split ramus osteotomy, Hyaluronic acid, Neurosensory disturbance, Two-point discrimination.

INTRODUCTION

Neurosensory disturbance (NSD) of the lower lip and chin is one of the most frequent and clinically relevant complications after bilateral sagittal split ramus osteotomy (BSSRO), mainly due to traction, compression, stretching, or partial injury of the inferior alveolar nerve (IAN) during splitting, mobilization, and fixation. Although many cases improve over time, a proportion of patients experience prolonged hypoesthesia, paresthesia, or dysesthesia that can affect speech, mastication, oral function, and overall quality of life. Recent clinical evidence continues to identify NSD as a key postoperative outcome in orthognathic surgery, with

multiple surgical and anatomical factors influencing risk and recovery, including nerve exposure/encounter, amount and direction of mandibular movement, and intraoperative manipulation .[1,2] Because spontaneous neural recovery is variable, there is ongoing interest in adjunctive strategies that may reduce IAN irritation and support faster or more complete sensory return. Hyaluronic acid (HA) is a naturally occurring glycosaminoglycan widely distributed in extracellular matrices and is well known for its biocompatibility, viscoelasticity, hydration capacity, and anti-inflammatory/anti-fibrotic effects.[3] Beyond serving as a passive scaffold, HA can modulate cellular behavior through receptor-mediated signaling (e.g., CD44 and RHAMM), influencing processes such as cell migration, proliferation, and tissue remodeling—mechanisms that are relevant to neural healing environments .[4,5] Importantly, experimental and translational peripheral nerve literature suggests that HA-based barriers or gels may reduce perineural adhesions and scarring, improve nerve gliding, and create a microenvironment that is more permissive for regeneration after nerve injury.[6,7] For example, biodegradable autocrosslinked HA gel has been reported to reduce neural adhesions after peripheral nerve injury in experimental models, supporting the concept that HA can limit fibrotic tethering that may otherwise delay recovery.[8,9,10] In addition, HA–carboxymethylcellulose formulations have been investigated for reducing perineural scarring and improving regeneration in peripheral nerve contexts.[11] A recent approaches also highlights HA gel among materials with scar-preventive potential after peripheral nerve injury, though outcomes appear dependent on formulation and clinical setting.[12,13] The aim of this study was to evaluate the effect of locally administered hyaluronic acid (HA) on neurosensory recovery following bilateral sagittal split ramus osteotomy (BSSRO).

MATERIAL AND METHOD

Patients and Methods

This research was planned as a prospective controlled clinical pilot trial employing a split-mouth model. The use of the split-mouth method made it possible for every patient to function as his or her own control, thus reducing inter-individual differences in neurosensory results to a large extent. The trial was held at the Department of Oral and Maxillofacial Surgery, Rzgary Teaching Hospital, Erbil Governorate, Kurdistan Region, Iraq. The recruiting of participants and monitoring their progress lasted from May 2025 to December 2025. Through a consecutive sampling technique, the patients were selected. Any person meeting the eligibility criteria and coming to the department during the study period was asked to participate. The number of patients who participated in this pilot study was 15.

Trial participants who were aged 18 and older and scheduled for bilateral sagittal split osteotomy as part of orthognathic surgical correction for mandibular deformities were eligible. The pilot study had the objective of preliminary clinical evidence generation and data provision for the future sample size calculation necessary for larger randomized trials. The sample was chosen based on the possibility of conducting a pilot investigation and using a paired comparison framework. The theoretical sample size determination was done according to the formula for a paired t-test in split-mouth designs:

$$n = \left(\frac{(Z_{\alpha/2} + Z_{\beta}) \times \sigma}{\delta} \right)^2$$

Where:

- $Z_{\alpha/2} = 1.96$for a 95% confidence level
- $Z_{\beta} = 0.84$for 80% statistical power
- σrepresents the standard deviation of paired differences
- δrepresents the minimum clinically significant difference in two-point discrimination values

Due to the absence of robust local baseline data, a pragmatic pilot sample of 20 patients was selected to assess feasibility, safety, and preliminary efficacy.

Inclusion Criteria

Participants were eligible for inclusion if they were 18 years of age or older and scheduled to undergo bilateral sagittal split ramus osteotomy as part of orthognathic surgical management. Only patients with normal preoperative neurosensory function of the mandible and lower facial region were included to ensure accurate postoperative assessment of sensory changes. Individuals with any history of neurological or neurosensory disorders affecting the distribution of the inferior alveolar nerve were excluded at baseline. All participants were required to be capable of providing written informed consent, demonstrate a clear understanding of the study objectives and procedures, and agree to regular postoperative follow-up visits throughout the study period.

Exclusion Criteria

Patients were excluded if they had undergone previous mandibular orthognathic surgery, as prior surgical intervention could confound neurosensory outcomes. Individuals with syndromic craniofacial anomalies known to affect neurosensory function were also excluded. Additional exclusion criteria included the presence of pathological lesions, severe infections, or traumatic mandibular fractures unrelated to iatrogenic nerve injury. Patients who experienced intraoperative complications not directly associated with neurosensory disturbance, as well as those who were unwilling or unable to comply with

postoperative follow-up, were not included in the study.

Surgical Operation

Patients were operated for the procedure under general anaesthesia with a bilateral sagittal osteotomy of the skin using bone splitting to mobilize the mandible. This procedure was done by experienced maxillofacial surgeons, using a standardized technique that followed proper surgical landmarks with the utmost preclusions from damage to the inferior alveolar nerve through the clear steps of cutting, splitting, and mobilization of the jaw segments. To rule out possible variations in surgical results, the same surgical technique and instruments were applied to all patients.

Hyaluronic Acid Use

Upon completion of the osteotomy, and after the final mandibular repositioning had been checked, the application of local HA was carried on a randomly selected side in close proximity to the inferior alveolar nerve canal. No HA was used on the other side, which served as a control. Side selection for random treatment was done only once intraoperatively to eliminate selection bias. The same HA product and dose were used in all cases to ensure that the results were strictly comparable without any procedural inconsistencies.

Neurosensory Evaluation.

Neurosensory competency was measured using a Two Point Discrimination (2PD) test, a validated and objective test for indexing sensory nerve integrity and recovery. These tests were obtained bilaterally at specified anatomical points in the distribution area of the inferior alveolar nerve. A neurosensory preoperative baseline test was taken for validation of any normal sense of sensation. Sensory tests were performed postoperatively at set intervals, to show the patient's sensory regeneration over time and most probably its progress as well.

Figure 1: Hyaluronic acid injection drug of choice used for the study

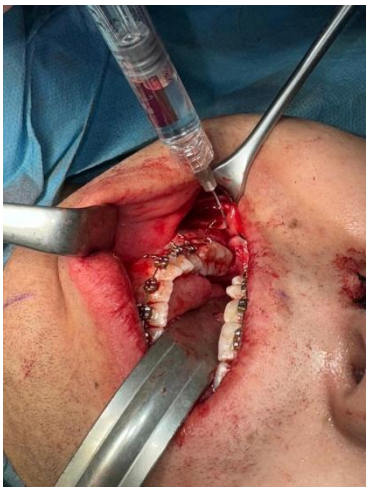

Figure 2: Intra-operative hyaluronic acid injection applied to selected site of surgical field of sagittal split ramus osteotomy

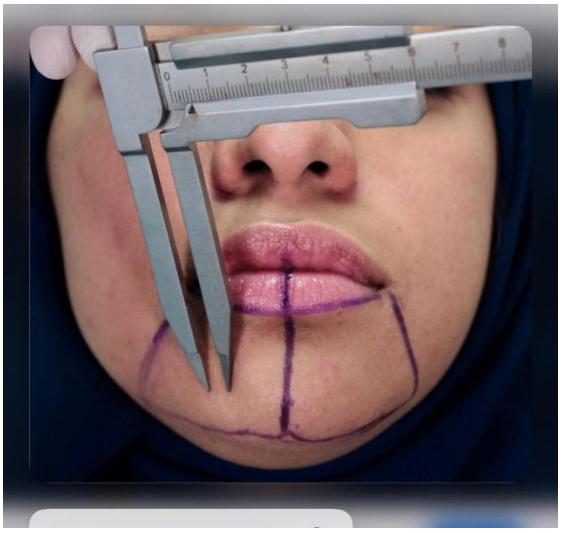

Figure 3: Measuring the result of study by two point discrimination test

Outcome measures

The primary outcome measure was the difference for the two-point discrimination values between the application of hyaluronic acid on a side and the untreated side before they increased during a follow-up at the postoperative stage. The secondary outcomes were the pattern of neurosensory recovery, sensory improvement over time during the stages of the follow-up period, and—if present—any local adverse reaction related to the application of hyaluronic acid.

Safety evaluation

Post local and systemic side effects suspected to be related to the administration of hyaluronic acid, all patients were examined on a regular basis within the stipulated time frame, particularly looking at inflammation, infections, delayed healing, allergic reactions, or any other unanticipated post-op complications.

Ethical considerations

The study protocol was reviewed and approved by the Kurdish High Council of Medical Specialties (KHCMS) Medical Research Ethics Committee. Informed consent was solicited from all participants before participating in the study. Also, it was made clear to the participants that they could refuse to participate or withdraw at any time without affecting their medical routine.

Statistical analysis

Data were analyzed with SPSS version 26 (IBM Corp., Armonk, NY, USA) as a main tool for the analysis. The Shapiro-Wilk test was used for the assessment of data normality. The paired t-test was utilized to compare baseline preoperative two-point discrimination (2PD) values between the right and left mandibular sides. Thereafter, postoperative comparisons of 2PD values on the hyaluronic acid-treated and control sides at 1, 3, and 6 months were made using the paired t-test, which suited the split-mouth design. Cohen's d was calculated for the effect size. Categorical neurosensory outcomes were analyzed via the McNemar test and a Pearson's correlation coefficient examined the relationship between early postoperative deficit and 6-month recovery. All the tests were conducted in both directions, and a threshold value of $p < 0.05$ was treated as a statistically significant result.

Results

Demographic and clinical characteristics of the 20 patients, who participated in the study, are summarized in Table (1). The study population was predominantly male, as among the participants 12 (60.00%) were males and 8 (40.00%) were females. The patients' mean age was 26.9 ± 5.8 years, which reveals that the majority of the participants were young adults, and this is likewise the age group that usually comes for orthognathic surgical correction. The surgical indication was the case of mandibular prognathism, which was the most frequent diagnosis, and 13 (65.00%) of patients were diagnosed accordingly, while 7 (35.00%) had the opposite condition of mandibular

Table (1): Demographic and clinical characteristics of the study participants

Variable	Category	n (%)
Sex	Male	12 (60.00%)
	Female	8 (40.00%)
Age (years)	Mean ± SD	26.9 ± 5.8
Indication for Surgery	Mandibular Prognathism	13 (65.00%)
	Mandibular Retrognathism	7 (35.00%)
Type of Osteotomy	BSSRO	20 (100%)

Table (2) shows the initial preoperative two-point discrimination (2PD) test results for both sides of the mandible. The average 2PD score was 6.1 ± 0.9 mm on the right side of the mandible and 6.2 ± 0.8 mm on the left side. The difference between the two sides was not statistically significant (p = 0.801), which means that the neurosensory functions were symmetrical and similar before the operation.

Table (2): Baseline Preoperative Two-Point Discrimination (2PD) Values (mm) for Both Mandibular Sides

Side	Mean ± SD (mm)
Right Mandibular Side	6.1 ± 0.9
Left Mandibular Side	6.2 ± 0.8
p-value	0.801 (NS)

Table (3) shows how the recovery of neurosensory function progressed during the follow-up period after surgery in terms of two-point discrimination (2PD) values on the sides treated with hyaluronic acid (HA) and those controlled (untreated). The side treated with HA was confirmed significantly earlier in the recovery of sensitivity when it presented at one month postoperatively 2PD values that were lower than those of the control side (10.4 ± 1.6 mm vs. 11.6 ± 1.7 mm, p = 0.048). The difference became even more evident at three months, where the HA-treated side continued to show better recovery (8.2 ± 1.3 mm vs. 9.6 ± 1.4 mm, p = 0.012). By the sixth month, neurosensory function had further improved on both sides; however, the HA-treated side remained significantly better off (6.7 ± 0.9 mm vs. 7.9 ± 1.1 mm, p = 0.004).

Table (3) Mean two-point discrimination (2PD) values (mm) on HA-treated and control sides at follow-up

Follow-up Time	HA-Treated Side (Mean ± SD)	Control Side (Mean ± SD)	p-value
1 Month	10.4 ± 1.6	11.6 ± 1.7	0.048
3 Months	8.2 ± 1.3	9.6 ± 1.4	0.012
6 Months	6.7 ± 0.9	7.9 ± 1.1	0.004

As shown in Table (4), the distribution of the various categories of neurosensory recovery was recorded six months after surgery and based on two-point discrimination (2PD) measurements. On the side treated with hyaluronic acid, a greater number of patients were able to complete the neurosensory recovery, 13(65%) with 2PD values ≤ 6 mm, while only 8(40%) were the same on the control side. The HA-treated side had 5(25%) showing partial recovery while 7(35%) were the same on the control side. Interestingly, persistent neurosensory deficit (≥ 10 mm) was found to occur less often on the HA-treated side, afflicting just 2(10%), whereas it hit 5(25%) on the control side.

Table (4): Distribution of neurosensory recovery based on 2PD categories at 6 months

Recovery Category	HA-Treated Side n (%)	Control Side n (%)
Complete Recovery (≤ 6 mm)	13 (65%)	8 (40%)
Partial Recovery (7–9 mm)	5 (25%)	7 (35%)
Persistent Deficit (≥ 10 mm)	2 (10%)	5 (25%)
Total	20 (100%)	20 (100%)

Table (5) summarizes the overall neurosensory gain in the treated with hyaluronic acid (HA) and control sides 6 months after the operation. The extent of neurosensory function recovery was 18 patients (90%) on the side of HA treatment and 14 patients (70%) on the side of no treatment. On the other hand, only 2 cases (10%) of the HA side were recorded as non-responders, whereas in the control arm, 6 patients (30%) were found non-responders. The difference between the sides was statistically significant (p = 0.046), which means that the local use of hyaluronic acid was related to the higher overall rate of neurosensory improvement after the bilateral sagittal split ramus

osteotomy.

Table (5): Comparison of overall neurosensory improvement between HA-treated and control sides at 6 months

Outcome	HA-Treated Side n (%)	Control Side n (%)	p-value
Improved	18 (90%)	14 (70%)	0.046
Not Improved	2 (10%)	6 (30%)	
Total	20 (100%)	20 (100%)	

Table (6) presents an overview of the safety profile and local tissue reaction after the intraoperative use of hyaluronic acid. The vast majority of patients, 17 out of 20 or 85.00%, did not experience any adverse events, thus showing that the intervention was well tolerated. One patient (5.00%) experienced mild local inflammation and two patients (10.00%) experienced transient postoperative swelling; however, both events were self-limiting and resolved without further intervention. Importantly, no cases of infection, delayed wound healing, or allergic reactions were recorded. The local application of hyaluronic acid during the bilateral sagittal split ramus osteotomy is safe and well-tolerated, according to these findings, and there are minimal, if any, local tissue reactions that are not clinically significant.

Table (6): Safety and local tissue response to hyaluronic acid application

Adverse Event	n (%)
Mild Local Inflammation	1 (5%)
Transient Swelling	2 (10%)
Infection	0 (0%)
Delayed Wound Healing	0 (0%)
Allergic Reaction	0 (0%)
No Adverse Events	17 (85%)

Data from Table (7) reveal the mean differences in two-point discrimination (2PD) values between the control and chemically (hyaluronic acid) treated sides during the whole follow-up period after surgery. The mean difference at the first month was 1.2 ± 0.6 mm, and it was statistically significant ($p = 0.048$), which indicates an early advantage of the HA-treated side in terms of neurosensory recovery. At three months the mean difference rose to 1.4 ± 0.7 mm ($p = 0.012$), showing that the intermediate phase of nerve recovery was more impacted by hyaluronic acid. By six months, the mean difference decreased only slightly to 1.2 ± 0.5 mm, but even then the difference was still very significant ($p = 0.004$).

Table (7): Mean Difference in two-point discrimination (2PD) between HA-treated and control sides during follow-up

Follow-up Time	Mean Difference (Control − HA) ± SD (mm)	p-value
1 Month	1.2 ± 0.6	0.048
3 Months	1.4 ± 0.7	0.012
6 Months	1.2 ± 0.5	0.004

Cohen's d was used to quantify the effect size of hyaluronic acid on neurosensory recovery at different postoperative follow-up intervals, which is shown in Table (8). A month later, there was a moderate effect size ($d = 0.52$) which pointed to the early impact of hyaluronic acid on sensory improvement to be clinically meaningful. At three months the effect was ($d = 0.78$) which means there was a moderate to large therapeutic benefit as neurosensory recovery was taking place. A large effect size ($d = 0.91$) was then noted at six months showing that hyaluronic acid had a huge and clinically important impact on the long-term neurosensory outcomes.

Table (8): Effect size (Cohen's d) of hyaluronic acid on neurosensory recovery

Follow-up Time	Cohen's d	Interpretation
1 Month	0.52	Moderate effect
3 Months	0.78	Moderate to large effect
6 Months	0.91	Large effect

Table (9) presents a comparison of the time intervals needed for the complete neurosensory recovery, which is defined as the attainment of a two-point discrimination (2PD) value of ≤ 6 mm, between the sides treated with hyaluronic acid (HA) and the control sides. At the end of three months postoperative period, 9 patients (45.00%) in the HA-treated group had recovered completely while only 4 patients (20.00%) in the control group had done so,

and this difference was found to be statistically significant (p = 0.041). By the end of six months, the number of patients with complete neurosensory recovery had increased in both groups, but it was still significantly greater in the HA-treated side, seen in 13 patients (65.00%) versus 8 patients (40.00%) on the control side (p = 0.039).

Table (9): Time to complete neurosensory recovery (2PD ≤ 6 mm) in HA-treated and control sides

Follow-up Time	HA-Treated Side n (%)	Control Side n (%)	p-value
3 Months	9 (45.00%)	4 (20.00%)	0.041*
6 Months	13 (65.00%)	8 (40.00%)	0.039*

Table (10) presents the relationship between early postoperative neurosensory deficit and long-term recovery on the hyaluronic acid (HA)–treated side. The correlation between two-point discrimination (2PD) values at one month and those at six months was found to be statistically significant and positive (r = 0.62, p = 0.003), which implies the existence of a moderate-to-strong association.

Table (10): Correlation between early postoperative neurosensory deficit and recovery at 6 months on the ha-treated side

Variables Compared	Correlation Coefficient (r)	p-value
2PD at 1 Month vs 2PD at 6 Months	0.62	0.003*

DISCUSSION

Neurosensory disturbance of the inferior alveolar nerve (IAN) is still one of the most common and most important complications that occur after bilateral sagittal split ramus osteotomy (BSSRO). The present pilot study evaluated the effect of locally applied hyaluronic acid (HA) on neurosensory recovery using objective two-point discrimination (2PD) testing in a split-mouth design. The results indicate that application of HA is associated with an earlier, faster, and more complete neurosensory recovery, along with a good safety profile.(12,13) The demographic characteristics of the current cohort, mainly young adults with an average age of 26.9 years and a greater number of males, are in accordance with populations that usually undergo orthognathic surgery across the globe .(6,14,15) The reason for the surgery in most of the cases was mandibular prognathism, which corresponds to the data that skeletal Class III deformities are a leading cause of BSSRO in young adults .(16,17) The distribution of age and sex in the sample is clinically relevant since younger patients typically have better neural plasticity and regenerative capacity, which might be a factor in the variation of neurosensory recovery rates .(18,19,20) Within the context of split-mouth BSSRO, the symmetry of cortical mandibular responses is used to validate the lack of pre-existing neurosensory dysfunction. Various prospective and retrospective studies have indicated the symmetry in the functioning of the IAN before the BSSRO .(21,22) This methodology addresses interindividual variability, leaving internal validity without contradiction due to disparities of objective between treatment effects postoperatively. Low 2PD values after surgery at months of thirds and one confirm that accelerated neurosensory recovery lies during the early and intermediate healing phases. This is a realistic medical insight when judgments are made during the earliest phase of the postoperative period because nerve stretching, compression, and transient ischemia which comes during alteration of the mandible's structure and fixation maximally impair the sensory abilities .(7,23) Because of this, the longer healing effect of HA is theoretically consistent with HA's known biological activity in modulating inflammation, reducing edema, and reducing fibrotic adhesion formation critical to the perineural healing environment .(12,17,24) However, the HA side remained significantly preferable with regard to complete recovery; the number of patients who achieved a full return to sensation was higher (65% in comparison to 40%). This is in line with long-term monitoring studies showing that while spontaneous recovery is an option, there is still quite a large subset of patients that have permanent sensory degradation. The large effect size (Cohen's d = 0.91) at six months, recognized in the present context, demonstrated the clinical significance. An effect size analysis is especially beneficial for pilot studies since it offers information beyond mere statistical significance, thus providing guidelines for use in future trial design .(21) Comparable magnitudes of benefit have already been reported in peripheral nerve studies using HA-based barriers, where Fibrosis reduction translated into improved functional outcomes .(24,25,26) The categories of grading the neurosensory recovery indicated that HA significantly reduced the risk of persistent neurosensory deficits. Perineurium fibrosis, ischemia, or axonal disruption are often cited as plausible culprits for persistent deficits following BSSRO .(25,27) By engulfing the nerve in a wet, unsticky shell, HA may cushion it from these insults. Various systematic reviews on barrier materials for nerves indicate HA as one of only a tiny few material groups with both anti-fibrotic capability and biocompatibility present for perineural application .(15,29) The HA intervention on its side provided further support with the time to complete neurosensory recovery being significantly shorter.

Early recovery becomes significantly important from a clinical perspective, as prolonged numbness will adversely affect speech, mastication, oral hygiene, and patient satisfaction after orthognathic surgery .(50,30) The implications from the current data are that HA is able to shift the recovery curve toward an early period without making alterations to the surgical technique or increasing operative risk. The findings strongly support our hitherto position, reported consistently in the literature, that early postoperative functional 2PD correlates positively with the final outcome at 6 months .(4,19,31) The fact that, in all patients with early changes, both sides known to be HA treated had more optimal recovery speaks to the potential promising intervention of normalizing some of the nerve dysfunction by HA. Safety of local HA was further affirmed by the near absence of severe adverse effects. Mild inflammation and transient swelling were seen in a few cases and resolved naturally, in keeping with HA safety when used in the oral and maxillofacial region .(16) This would be found in the frame of systemic reviews, which certify the safe handling of HA when used within the surgical field, including oral, orthopedics, and neurosurgical .(12,15)

Study Limitations and Future Directions

The pilot design and small sample size have been the key limitations of this study. However, the parallel split-mouth design has increased the power level of statistics and the internal validity. Future trials that employ larger cohorts, longer follow-up, and multimodal neurosensory assessment (with electrophysiological testing) would be needed to verify and set the limits of these data and formulations and dosing strategies of HA.

Conclusion: Local application of hyaluronic acid during BSSRO appears to be safe and is associated with accelerated and improved neurosensory recovery. These findings support the potential role of hyaluronic acid as an adjunctive strategy for reducing postoperative neurosensory disturbance, warranting confirmation in larger randomized trials.

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