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Posisep Versus PureRegen Gel for Post ESS Nasal Packing – A Randomized Blinded Prospective Study

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Objective: Endoscopic sinus surgery (ESS) is the procedure of choice for chronic rhinosinusitis (CRS). Adhesions are the most common postoperative complications, causing recurrent disease and revision surgery. Postoperative care is thus essential for the healing of the operated cavity. A wide variety of packing materials are used to prevent bleeding and adhesions postoperatively. Two main absorbable packing materials are used: Foam-based packs (e.g., Posisep and Nasopore) and gel-based packs (PureRegen Gel – PRG). The current study is a randomized, blinded, prospective analysis of cavity healing using Posisep and PRG in ESS, aiming to compare the pros and cons of the two.

Methods: Patients with bilateral symmetric CRS were recruited for the study. At the end of surgery, one side was randomly packed with Posisep, whereas the other was packed with PRG. The postoperative cavity cleaning was video recorded and a blinded physician evaluated the mucosal healing.

Results: The side packed with Posisep had significantly less middle turbinate (MT) lateralization and adhesions yet dissolved significantly slower than the PRG, causing more mucosal edema. Severe MT scarring requiring recurrent medialization and adhesiolysis was exclusively observed in the PRG group. All differences were observed in the early postoperative period (up to 12 weeks after surgery). By that time, only the MT position was significantly different between groups, despite recurrent adhesiolysis and medialization.

Conclusion: The authors recommend using Posisep for MT support only when it is unstable or lateralized. Packing the surgical cavity in other cases with PRG is more beneficial.

Key Words: chronic rhinosinusitis, nasal surgical procedure, paranasal sinus disease, quality of life, respiratory mucosa.

Level of Evidence: 2

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INTRODUCTION

Messerklinger pioneered nasal endoscopy in Germany throughout the 1960s; later on, it became more popular in the 1980s when Keneddy practiced diagnostic and surgical nasal endoscopy in the united states.[1,2] Nowadays, endoscopic sinus surgery (ESS) is the gold standard surgical treatment for chronic rhinosinusitis (CRS) with a marked positive impact on quality of life.[3-5] More than 500,000 procedures are performed annually in the United States.[6] ESS aims to create adequate passage connecting the sinuses and the nasal cavity to achieve unobstructed mucociliary transport and to enable postoperative administration of topical treatment.[7,8] Adhesions are the most common postoperative complications, causing recurrent disease and revision surgery. Surgical cavity cleaning is thus essential for optimal outcomes. Bugten found that postoperative debridement resulted in faster resolution of nasal congestion and fewer middle meatal adhesions.[9] Later, Vlastarakos demonstrated that nasal packing at the end of endoscopic surgery reduced the postoperative adhesion rate.[10]

A wide variety of commercial nasal packs are available: typically, they are grouped into absorbable and non-absorbable materials. Verim et al. did not find differences in surgical outcomes between biodegradable and non-degradable packing. However, with biodegradable packing, pain, bleeding, nasal blockage, and facial edema were less frequent.[11] Shoman et al. showed that an absorbable pack was associated with significantly slower mucosal healing and did not significantly reduce the risk of bleeding compared with non-absorbable packs.[12] The authors routinely use absorbable packing in all ESS cases and believe that this lessens the risk of bleeding and prevents blood clot formation (which are more difficult to remove). Absorbable packs also obviate the need for removal, which might be painful.

Ideally, the absorbable packing material should act as a spacer in the immediate postoperative period, prevent bleeding and adhesions, and dissolve rapidly to enable early aeration and effective topical treatment of the sinus cavity. Although a pack that acts as a spacer tends to be more stable and thus dissolves slowly, a substance that degrades faster may not provide the adequate support required to prevent adhesions.

Among absorbable packs, the two most commonly used types are synthetic fragmenting foam (e.g., NasoPore (Polyganics, Groningen, The Netherlands),

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Posisep (N, O-carboxymethyl chitosan, Hemostasis LLC, Minnesota, USA)), and gel-based materials (e.g., PureRegen gel [PRG], Self-Crosslinked Hyaluronic Acid Hydrogel, Bio-Regen Biomedical, Changzhou, Jiangsu, China).

The former inflates when exposed to liquid and is more stable in the first postoperative days. It tends to act as a spacer as well, thus lowering the risk of adhesions. The latter is a liquid gel injected into the cavity that dissolves faster yet lacks the supporting properties of the fragmenting foam. Many articles compare absorbable to non-absorbable packs, but there is a lack of literature about the impact of different absorbable packing materials on mucosal healing and cavity outcome.

The purpose of the current study is to prospectively compare two commonly used absorbable packing, representing the two major packing groups of materials used in ESS. The study design compares the left side to the right side of the same patient in symmetric bilateral disease, thus eliminating most confounders related to disease severity and other patients' as well as environmental factors. Blinded prospective study design prevents errors regarding compliance, surgical field evaluation bias, and retrospective chart analysis errors. Thus, any difference in mucosal healing between the two sides can be mainly attributed to the different packing used.

MATERIALS AND METHODS

The study was approved by the ethical committee of the Shaare Zedek Medical Center. Patients were recruited from the Rhinology service outpatient clinic. During the study period (September 2021–June 2022), all patients meeting the criteria for CRS by the EPOS guidelines[13] who did not respond to maximal medical therapy (systemic antibiotics and systemic and local steroid treatment) were referred for ESS.

Inclusion criteria for the study were signed informed consent and symmetric disease (LMS difference ≤2). Excluded from the study were patients with asymmetric disease, non-CRS etiology (tumor, antrochoanal polyps, and endoscopic dacryocystorhinostomy), and patients who did not complete all three postoperative visits.

Upon completion of the surgical procedure, one side was randomly assigned for Posisep packing and the contralateral side was packed with PRG. If septoplasty was done for septal deviation, additional Posisep packs were placed anterior to the middle turbinates (MT) on both sides for septal cartilage support without impact on the sinus cavity pack.

Postoperative treatment regimen in all patients included prednisone 20 mg once daily for 1 week, followed by 10 mg once daily for an additional week, Amoxicillin with clavulanic acid 875 mg twice daily for 10 days, and FLO CRS (ENT Technologies Ltd, Victoria, Australia) nasal wash three times daily for 1 month.

The patients were also blinded to the packing material used on each side. They were scheduled for three postoperative cavity cleaning visits (2, 6, and 12 weeks post-operation) as is routinely done in the rhinology service in our institution. All visits were video-recorded for data collection and blinded analysis by the senior resident. The cavity status was graded using the validated Lund-Kennedy outcome score (LKS) described elsewhere.[14] Each sinus cavity (maxillary, anterior ethmoids, posterior ethmoids, sphenoid, and frontal) was graded for Polyps, mucosal edema, crusting, secretions, and adhesions and given a 0–2 grade for each side (maximum of 10 points for each side). In the first postoperative visit, the presence of residual nasal packing was also graded for each sinus (maxillary, anterior ethmoid, posterior ethmoid, sphenoid, and frontal sinus). Each cavity was given 0–2 points (0 – no residual packing, 1- packing filling less than 50% of the cavity, 2- packing filling more than 50% of the cavity). The total residual packing score range was 0–10 on each side.

MT position/adhesions were also analyzed and subdivided into: Grade 0 - no lateralization (4 mm suction can easily pass into the ethmoid cavity). Grade 1 - Mild lateralization (suction can enter the cavity with gentle pressure on the MT) with or without adhesions (less than 1/3 of the MT adhered to the lateral nasal wall). Grade 2 - severe lateralization (suction cannot enter the ethmoid cavity) with or without adhesions (more than a third of the MT adhered to the lateral nasal wall).

A senior resident, blinded to the packing choices on each side, recorded the Lund-Kennedy cavity grading on each side, the presence of packing in the different sinuses, and cleaning time.

Patients were asked to rate the level of pain/discomfort after surgery and at each postoperative visit according to the Visual Analog Scale (VAS) score. Patient demographic risk factors (asthma, allergies) and radiologic data were also recorded.

RESULTS

Between September 2021 and June 2022, 137 endoscopic sinus and skull base surgeries were performed by the senior author at Shaare Zedek Medical Center. In 75 patients, the indication was CRS (excluding 52 cases of skull base and sinus tumors, endoscopic dacryocystorhinostomy, orbital decompression, and cerebro-spinal-fluid leak repair). Of those 75 cases, 37 cases were excluded for asymmetric disease (CRS with LMS≥3). Thirty-eight patients were eligible for the study. Of those cases, one patient refused to sign an informed consent, and three had insufficient follow-up. A total of 34 cases were included in the study.

The mean age was 47 years (range 17-75), with 15 females and 19 males. The average LMS score was 19.15. Five patients had asthma and had a higher LMS (average of 22.8).

In 18 patients, Posisep was placed on the right side and PRG on the left; in the remaining 16 patients, Posisep was placed on the left side, whereas PRG was inserted on the right.

1st visit results – 2 weeks postop, Table I:

LKS and MT position, residual packing and cleaning time are summarized. The amount of residual packing was significantly greater for Posisep compared to PRG ($p < 0.001$). After removal of the remaining pack, the average total LKS did not differ between Posisep and PRG groups ($p = 0.2312$). Breaking down the different LKS variables revealed that the edema score was significantly higher in the "slower absorbing" Posisep ($p < 0.001$), whereas the scarring score was significantly higher in the "less robust yet fast-absorbing" PRG compared to Posisep. ($p < 0.001$).

MT position was significantly more lateralized in the PRG group than in the Posisep group ($p < 0.001$). Severe scarring was seen only in the PRG side of 5 patients, requiring adhesiolysis and Posisep positioned in the axilla to prevent recurrent adhesion.

TABLE I.
Comparison of Residual Packing, Lund Kennedy Score (LKS) for Cavity Healing, MT Position, Cleaning Time, and VAS Scores Between Posisep and PureRegen Gel (PRG) Groups. Significantly More Residual Packing was Observed in the Posisep Group, Causing Edema. On the Other Hand, Significantly more MT Lateralization and Scaring were seen in the PRG Group.

1st visit					
	Posisep		PureRegen gel		
	Total Score	Mean (+/-SD)	Total Score	Mean (+/-SD)	*p*-value
Total pack	230	6.76 (+/− 4.06)	79	2.32 (+/− 3.24)	***< 0.001***
Total LKS	82	2.41 (+/− 0.82)	70	2.05 (+/− 1.04)	0.23121
Edema	65	1.91 (+/−0.28)	40	1.17 (+/− 0.62)	***< 0.001***
Scarring	1	0.02 (+/−0.17)	20	0.59 (+/− 0.82)	***<0.001***
Polyp	1	0.02 (+/−0.17)	0	0	0.32096
Discharge	7	0.20 (+/− 0.47)	5	0.14 (+/−0.36)	0.56857
Crusting	8	0.23 (+/− 0.6)	5	0.14 (+/−0.36)	0.49302
MT lateralization	3	0.08 (+/− 0.28)	29	0.85 (+/− 0.85	***<0.001***
Cleaning time (Minuets)	85.95	2.53 (+/−0.86)	104.43	3.07 (+/− 3.30)	0.35627
VAS	148	4.35 (+/−1.76)	160	4.71 (+/− 2.22)	0.1779

No significant differences were observed between the Posisep and the PRG groups regarding polyps, discharge, or crusting.

The average cavity cleaning time on the 1st visit was not significantly different for the two groups.

The total VAS score of the Posisep was 148, whereas for PRG it was 160, no statistical significance was found. ($p = 0.1779$).

2nd visit results – 6 weeks postop, Table II:

The differences in total LKS, edema, scarring, and MT lateralization between the two groups were still significant. Total polyp/discharge/crusting scores and cleaning time were not significantly different.

In two patients in the PRG group, recurrent adhesiolysis and medialization of the MT were needed to gain access to the surgical cavity.

3rd Visit – 12 weeks postop – Table III:

On the third postoperative visit, none of the parameters measured were significantly different between the two groups except for the MT position, which was more lateralized in the PRG group ($p < 0.001$).

There were no major complications in our study population (CSF leak, intra-cranial infection, eye complications, major bleeding). Three patients complained about minor headaches responding to over-the-counter pain medication, and facial pressure/pain was documented in five patients; this complaint was resolved with time and after the first postoperative visit. In all patients, no minor postoperative bleeding was documented, neither early nor late.

DISCUSSION

ESS is a common operation for the treatment of CRS. Postoperative care is essential to prevent complications (e.g., bleeding, adhesions) and revision surgery.

Packing the surgical field at the end of ESS is important, and many types of packs exist. Lately, absorbable packs are gaining popularity, obviating the need for removal while temporarily filling the surgical cavity.[11,12]

In this prospective blinded study, we aimed to compare the clinical outcomes of using two types of

TABLE II.
Significantly More Edema was Still Present in the Posisep Group, While Significantly More MT Lateralization and Scaring on the PRG Group.

2nd visit					
	Posisep		PureRegen gel		
	Total score	Mean (+/-SD)	Total score	Mean (+/-SD)	*p*-value
Total pack	0	0	0	0	1
Total LKS	62	1.82 (+/−1.29)	37	1.11 (+/−1.06)	***0.015***
Edema	45	1.32 (+/−0.68)	13	0.41 (+/−0.65)	***<0.001***
Scarring	2	0.05 (+/−0.23)	14	0.41 (+/−0.60)	***0.003***
Polyp	2	0.05 (+/−0.23)	0	0	0.164
Discharge	11	0.32 (+/−0.68)	8	0.23 (+/−0.49)	0.571
Crusting	2	0.05 (+/−0.23)	2	0.05 (+/−0.23)	1
MT lateralization	8	0.23 (+/−0.49)	23	0.67 (+/−0.63)	***<0.001***
Cleaning time (Minuets)	51.27	1.50 (+/−1.29)	56.03	1.64 (+/−1.17	0.64

Table III.
12 Weeks Following Surgery no Differences were seen Between the Groups, Except for MT Position Which was Still More Lateral in the PRG Group.

	3rd visit				
	Posisep		PureRegen gel		
	Total score	Mean (+/-SD)	Total score	Mean (+/-SD)	*p*-value
Total pack	0	0	0	0	1
Total LKS	36	1.06 (+/− 1.25)	34	1.00 (+/− 1.26)	*0.8493*
Edema	26	0.764 (+/−0.88)	19	0.558 (+/−0.74)	*0.2808*
Scarring	1	0.03 (+/−0.17)	2	0.06 (+/−0.24)	*0.3246*
Polyp	1	0.03 (+/−0.17)	2	0.058 (+/− 0.28)	*0.5717*
Discharge	6	0.176 (+/−0.45)	8	0.235 (+/−0.55)	0.6615
Crusting	2	0.06 (+/−0.34)	3	0.09 (+/−0.38)	0.7382
MT lateralization	6	0.176 (+/−0.38)	22	0.647 (+/−0.59)	***<0.001***
Cleaning time (Minuets)	30.80	0.905 (+/−0.40)	34.03	1.00 (+/−0.5)	0.3258

biodegradable nasal packs (Posisep and PRG) with different physical properties.

As mentioned earlier, every patient in our cohort was randomly packed with Posisep and PRG, each on one side of the nose. The amount of pack used from each type was between 1.5 and 3 units for each side (for PRG 1 unit = 1 ml), the cost of Posisep is 65$ per unit, whereas PRG costs 100$ per unit.

On the 1st postoperative visit, significantly more residual packing was observed in the Posisep group; another significant result was more edema that lasted more than a month (subsiding toward the third visit) found in the same group. Reviewing these results, we pursue an explanation for the interaction effect between the sino-nasal mucosa and the different packing materials. We assume that because Posisep applies pressure to the mucosa for a longer time, resulting in local irritation and less nasal wash delivery, the mucosa was more edematous and much fewer adhesions were seen compared to PRG. We could not explain why 4 weeks after cleaning the cavity from the remaining Posisep, the mucosa was still significantly more edematous compared to the side packed with PRG, and 10 weeks after cleaning there was a difference, though not significant. From our insight, we know that PRG is degraded fast. In some patients, no residual PRG was found 2 weeks post-surgery, and in most patient's, a minimal amount of PRG was seen. This, and the fact that it is gel based and does not have mechanical strength nor apply pressure, explains the higher number of adhesions compared to Posisep and significantly less edema of the mucosa.

The lesson learned from the data is that whenever possible, PRG is the preferred packing to achieve faster clearing and healing of the operative cavity. When postoperative care is not feasible (young children or anxious patients), PRG is more reliable to dissolve in 2 weeks, preventing edema and infection.

Another issue to consider is MT support and adhesions. The MT position was significantly less favorable using PRG because the gel does not provide support to the MT and, if not stabilized, it may adhere to the nasal wall. The relatively longer presence of Posisep significantly reduced this complication and prevented severe adhesions that may have resulted in tedious and painful postoperative medialization. Posisep in the axilla is thus recommended when MT is lateralized or unstable to provide support and avoid lateralization and scarring, which is challenging to treat.

Apart from the MT position, no other factor was significantly different between the two groups at the 3rd visit (3 months postop).

Cleaning time did not differ between the groups, probably because longer suctioning of the Posisep on one side was equalized with longer time for medialization and adhesiolysis on the other side.

Another important point that should be discussed is that although mucosal healing is significantly higher with PRG compared to Posisep, and it is clear that Posisep negatively affects mucosal healing, our study cannot provide evidence related to the positive effect (if there is one) of PRG on the sino-nasal mucosa, that is to say, is PRG have qualities that enhance mucosal healing.

Nonetheless, a recent systematic review and pooled analysis published in 2021 by Huang, Z., & Zhou, B.,[15] compared different absorbable nasal packs (including gel-based and chitosan-based packs) to No-packing. In this analysis, no difference was seen in 2, 6, and 12 weeks after surgery between the packing arm and non-packing arm concerning mucosal edema, granulation formation, and infection. From that, we can carefully conclude that the gel-based packs do not affect mucosal healing positively or negatively.

The limitations of the present study are that it is a single-institution study, and only two materials were used. More comparative studies are needed on other packing materials to better define the optimal material for nasal packing in ESS.

CONCLUSION

The data in this study demonstrate that using PRG for packing in ESS results in faster mucosal healing at the expense of MT lateralization and scarring. Therefore,

the authors recommend PRG be applied in the sinus cavity whenever possible. Posisep should be used when the MT is unstable or has a lateral position to prevent lateralization and adhesions.

The authors changed their packing protocol accordingly and do not routinely use Posisep in the ethmoid, sphenoid, and frontal recesses. Posisep is mainly used for support in areas where adhesions are anticipated.

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