Section A-Research paper

Brief Overview about Endoscopic sinus surgery and Possible Role of Platelet Rich Plasma

Mohamed Alshawadfy , Ramzy Tantawey , MAA EL-AHL , Islam R. Herzallah
Otorhinolaryngology Department, Faculty of Medicine , Zagazig University, Egypt.

Email: ramzytantawey@gmail.com

Article History: Received 10th June, Accepted 5th July, published online 10th July 2023

Abstract

Background: Endoscopic sinus surgery (ESS) is currently accepted as the treatment of choice for chronic sinusitis resistant to medical treatment. The concept behind sinus surgery stems from Messerklinger's studies on mucociliary clearance and its role in the pathogenesis of sinusitis. Use of Platelet-rich plasma (PRP) is of interest particularly among orthopedicians and sports medicine experts due to its regenerative and tissue healing effects. New applications of platelet-rich plasma are also being investigated. This material is particularly interesting to the ENT surgeon because of its healing properties and as a potential packing or grafting material. The contribution of platelet-rich plasma to tympanic membrane healing following bilateral tympanic membrane perforation were assessed showing promising results. Also, method for the autologous transplantation of fat and platelet-rich plasma was investigated to treat atrophic rhinitis, All patients described symptom improvement, with the disappearance of nasal crusting.

Keywords: Knowledge, Associated Factors, Polypharmacy, Elderly Patients

DOI: 10.53555/ecb/2023.12.Si12.340

Introduction

Endoscopic sinus surgery (ESS) is currently accepted as the treatment of choice for chronic sinusitis resistant to medical treatment. The concept behind sinus surgery stems from Messerklinger's studies on mucociliary clearance and its role in the pathogenesis of sinusitis. The goals of ESS in the treatment of sinusitis are to enlarge sinus ostia, restore adequate aeration of sinuses, improve mucociliary transport, and provide a better route for topical therapies **(1).** The notion behind ESS may seem straightforward, but the anatomical variability and the broad range and severity of diseases addressed in every ESS remain challenges for the surgeon in every case. Pre-operative planning for sinus surgery is the crucial step to obtain optimal results and to avoid all possible complications **(2).**

Endoscopic sinus surgery targets sinus pathology and is the gold standard for treating chronic rhinosinusitis (CRS). The boundaries of ESS are continually expanding with technological advances. At this point, the indications of ESS have surpassed the field of rhinosinusitis. The application of this procedure marked its place in the management of sinus tumors and pathologies beyond the sinuses **(3).**

Indications

Since endoscopic sinus surgery was introduced, the indications for performing this procedure have been expanding. The advances in the endoscopes, the camera, instrumentation, and navigation have laid the groundwork for an ever-expanding world of endoscopic surgery to access the skull base, optic nerve, cavernous sinus, pituitary, orbit, pterygopalatine fossa, and many other spaces and structures **(4).** The initial

and most common indication for ESS is chronic rhinosinusitis. Rhinosinusitis is an inflammatory process of the paranasal sinuses; it is categorized into different groups based on the duration of the inflammatory process **(5):**

- Acute rhinosinusitis: less than four weeks
- Subacute rhinosinusitis: between 4 to 12 weeks
- Chronic rhinosinusitis: longer than 12 weeks

CRS has a major negative implication on the quality of life of patients emotionally and physically. Diagnosis of CRS should be based on symptoms and objective findings on physical examination using anterior rhinoscopy, or nasal endoscopy, or on computed tomography scans **(6).** Based on the clinical practice guidelines, CRS is initially treated with saline irrigation, topical intranasal steroids, systemic steroids, and appropriate antibiotics. When maximal medical therapy fails, the next step is endoscopic sinus surgery. There is still no universally-accepted consensus on the criteria for what constitutes maximal medical therapy or on the timing of surgery. The role of surgery in the treatment of CRS with or without polyposis was studied for many years, and ESS has proved its role in significantly improving the quality of life of patients with CRS **(7).**

In addition to CRS, ESS plays a role in the management of complicated acute rhinosinusitis (ARS). Extracranial and intracranial complications of ARS are often categorized according to Chandler's classification. They include in order of increasing severity **(8):** pre-septal cellulitis, orbital cellulitis, subperiosteal abscess (SPA), orbital abscess (OA), and cavernous sinus thrombosis. In cases of pre-septal and orbital cellulitis, ESS is considered when there is visual impairment or increased intraocular pressure, and in situations that do not improve with medical treatment **(9).**

ESS has also become the standard procedure for mucoceles, invasive and non-invasive fungal sinusitis, silent sinus syndrome, pituitary tumors, cerebrospinal fluid leaks, benign and malignant sinonasal tumors, and ventral skull base lesions, lesions of the petrous apex, or pterygomaxillary fossa. Expanded sinus surgery plays a role in cases of malignancies in the nasal and paranasal spaces, even for those that extend through the anterior skull base **(10).** Navigation-guided endoscopic sinus surgery has gained much recognition in the world of rhinology. It guides the surgeon intraoperatively based on imaging obtained before surgery. The tracking system in image-guided surgery helps achieve a more thorough and complete dissection of the sinuses, better visualization of tumor borders to obtain negative margins, and with a lower risk of complications **(11).**

Contraindications

Contraindications for ESS include patients who have general contraindications for general or local anesthesia. Also, contraindications for purely endoscopic surgery include lesions/ pathologies extending into the palate, skin/soft tissues, laterally into or above the orbit, lateral recesses of the frontal sinus, or advanced intracranial involvement. In cases with significant extensions, a combined endoscopic and open approach may be required instead **(12).**

Equipment

Equipment required in the OR includes a television monitor, navigation system (if being used), camera, sinus endoscopy tray including varied curettes, downbiters, backbiters, elevators, ball-tip probes, through-cut instruments, Kerrison rongeurs, giraffe instruments, sinus forceps with different angulations, punch instruments, endoscopes (0, 30, 45, 70 degree scopes and reverse scopes), and a powered debrider with straight and angled blades **(13).**

Technique

A thorough nasal endoscopy is performed using a 0 or 30-degree scope. Firstly, decongestion of the nasal cavity is carried out using topical xylometazoline or 1:10000 epinephrine. Subsequently, removal of middle meatal polyps is done to enhance access to the lateral nasal wall **(14).**

Uncinectomy:, where the middle turbinate is gently medialized to access the uncinate process. Retrograde uncinate removal is then conducted, with careful attention paid to avoid injury to adjacent structures**(15).**

Maxillary antrostomy: The natural ostium of the maxillary sinus is visualized after removing the uncinate. It is elliptical in shape and found in the lower part of the infundibulum. It is crucial to distinguish the natural ostium from the accessory ostium. The opening to the maxillary sinus is confirmed using a ball-tip probe and is best visualized with a 30 or 45-degree scope. Once confirmed, the natural ostium is enlarged using a through cutting instrument, punch forceps, and powered debrider. The ostium is enlarged posteriorly and inferiorly to avoid injury to the orbit superiorly and nasolacrimal duct anteriorly **(16).**

Ethmoidectomy: entails removal of ethmoid sinus cells, starting with the ethmoid bulla and progressing posteriorly through the basal lamella to clear the posterior ethmoid air cells **(17).**

Sphenoidotomy: Sphenoidotomy involves enlarging the sphenoid ostium, either transnasally or transethmoidally, to facilitate access to the sphenoid sinus.This is followed by clearance of ethmoid air cells over the skull base and lamina papyracea. **(18).**

Frontal sinusotomy: frontal sinusotomy is performed, with careful dissection of the agger nasi cells to alleviate obstruction of the frontal sinus outflow **(19).**

During all steps, sparing the mucosa decreases the risk of scarring postoperatively and of osteogenesis. The middle turbinate's vertical and horizontal attachments should be preserved to avoid destabilization of the turbinate. In the case of destabilization, there is a high risk of lateralization of the turbinate, causing scarring and obstruction of sinus drainage. In order to avoid lateralization, the anterior part of the turbinate can be removed, suturing of the turbinates to the septum can be performed, or nasal packing can be placed in the middle meatus. These options will help keep the turbinate in a medial position. At the end of the procedure, any bony septations left are removed, and hemostasis is obtained. A dissolvable nasal pack can be placed as a middle meatus spacer **(20).**

Postoperative Complications

- **Epistaxis**

Epistaxis is a common complication, occurring in 2% of patients after ESS. It usually occurs on the day of surgery; it may also occur 5–7 days after surgery, but this is relatively rare. The most common sites of postoperative bleeding are the middle turbinates, posterior fontanelle of the middle antrostomy, and inferior margin of the ostium of the sphenoid sinus. The blood vessels responsible for bleeding arise from different branches of the sphenopalatine artery, including the branch of the middle turbinate located in the posterior part of the root of the middle turbinate, branch of the posterior fontanelle arising from the branch of the inferior turbinate, posterior nasoseptal artery traversing the lower margin of the sphenoidal ostium, and one of the main branches of the sphenopalatine artery. Thus, the site most prone to bleeding after maxillary sinus surgery is the posterior lower part of the maxillary sinus opening window, while that after sphenoidal sinus surgery is the external lower part of the sphenoidal sinus opening window **(21).**

- **Cavity Synechiae**

Adhesions or synechiae usually develop 2–3 weeks after surgery. Minor adhesions within the surgical cavity generally do not cause symptoms and do not require management. However, severe adhesions or synechiae

secondary to mucosal scarring can be a source of postoperative anosmia, recurrent sinusitis, and mucocele formation. Although a silicone spacer or packing material placed at the time of surgery may decrease the incidence of adhesion formation, a partial middle turbinectomy, outfracture of the inferior turbinate, or septoplasty should be performed prospectively. If adhesions are noted at the time of outpatient endoscopy examination during the first postoperative week, they can usually be divided with minimal patient discomfort. However, resection of synechiae in the outpatient department is more difficult when it is severe or when the nasal cavity has become very narrow. Even for mild adhesion, revision surgery is definitely required under general anesthesia **(22)**

Platelet Rich Plasma

Platelet-rich plasma (PRP) (also called platelet-concentrated plasma or platelet-rich growth factors), is an autologous blood product having a large concentration of platelets suspended in a small volume of plasma, above the baseline. The initial description and clinical application of PRP were in cardiac surgery and hematology but owing to its versatile anti-inflammatory and immunomodulatory actions, PRP found wide interest in a variety of clinical fields, including dentistry and ophthalmology. Use of PRP is of interest particularly among orthopedicians and sports medicine experts due to its regenerative and tissue healing effects. New applications of platelet-rich plasma are also being investigated. This material is particularly interesting to the ENT surgeon because of its healing properties and as a potential packing or grafting material **(23).**

Platelet-rich plasma preparations

Platelet-rich plasma preparations have traditionally been produced by dual-speed centrifugation. The first 'soft spin' separates blood into red blood cells, platelet-poor plasma and a buffy coat. The second 'hard spin' separates platelet-rich plasma from platelet-poor plasma. The isolated platelet-rich plasma is then mixed with thrombin and calcium chloride to form a gel-like product with five to eight times the platelet concentration of whole blood **(24).**

Mechanism of action

Platelets are anucleated cytoplasmic fragments of megakaryocytes that differentiate down the myeloid cell lineage. They contain α-granules, often thought of as the storage units of platelets, which studies suggest contain an abundance of growth factors (GFs). **(25).** These are believed to influence inflammation, angiogenesis, stem cell migration and cell proliferation. Platelets are well known to be the initiators of the healing process; however, not all tissues have a rich blood supply, for example tendons, ligaments and cartilage. This results in relatively low levels of GFs being available to these tissues to enact effective healing (89). Application of PRP to these, and other, areas can therefore introduce supra-physiological levels of GFs to theoretically stimulate resolution of chronic pathological processes. Commercial ELISA (Vector Laboratories, Burlingame, CA; Quantikine Immunoassay, R&D Systems, Minneapolis, Minnesota) and Luminex kits (Luminex Corporation, Austin, Texas) were used to accurately quantify GFs in software based statistical analysis **(26).**

Once recruited to an area of injury, platelet adhesion is facilitated through adhesive glycoproteins secreted by α-granules, including vitronectin, fibronectin, thrombospondin and von Willebrand factor. Once the clot is formed the platelets are activated, allowing the release of the GFs from α-granules to stimulate healing. There are myriad GFs contained within α-granules, of which the complex interchange amongst them is hypothesized to be of additional benefit to the healing process beyond simply introducing a higher concentration of platelets at hypovascular sites **(27).**

Growth factors enact their functions primarily via ligand binding to associated extracellular cell surface

receptors, which signal intracellular cytoplasmic proteins to attach to phosphorylated tyrosine. This is followed by multiple phosphorylation and activation steps of protein kinases within the cytoplasm, finally leading to translocation of a phosphorylated kinase to the cell nucleus. This phosphorylates transcription factors enabling gene transcription and ultimately the execution of the encoded function **(28).**

Growth factors contained within α-granules thought to be crucial to the efficacy of PRP include platelet-derived growth factor (PDGF), VEGF, the transforming growth factor-β superfamily (TGF-β), fibroblast growth factor (FGF) and insulin-like growth factor (IGF). PDGF is able to initiate callus formation via chemotaxis and mitogenesis of fibroblasts and chondrocytes, along with chemotaxis of mesenchymal stem cells (MSCs). The promotion of endothelial cell proliferation by PDGF also has an important role in angiogenesis. VEGF is involved in neovascularization through its strong endothelial chemokine and mitogenic properties **(29).** TGF-β is well established as a promoter of chondrogenesis, but has also been shown to **(30):** stimulate osteogenic MSC differentiation and undifferentiated mesenchymal cell proliferation; regulate the mitogenic effects of other GFs; and inhibit macrophage and lymphocyte proliferation. The FGF family is involved in multiple biological processes including osteoblastogenesis, growth and differentiation of chondrocytes and MSCs. IGF regulates the proliferation and maturation of chondrocytes and IGF-1 may down-regulate expression of programmed cell death 5 (PDCD5), thereby inhibiting apoptosis of osteoarthritic chondrocytes **(31).**

In addition to GF release following platelet activation, PRP also forms a fibrin gel, which acts as a conductive bio scaffold to allow incorporation of migrating cells for tendon healing. Entrapment of GFs within a fibrin matrix may hold the key to controlled release of GFs at the intended site of action. However, it is important to note that cellular response to GFs is limited by number of target receptors available on cell surfaces, therefore high platelet concentrations and subsequent GF release may not be of benefit. This may explain why PRP preparations with GFs over six times the physiological concentration may have an inhibitory effect **(32).**

Platelet-rich plasma in rhinology surgery

A number of reports describing the use of platelet-rich plasma in rhinology were identified. A method for the autologous transplantation of fat and platelet-rich plasma was investigated to treat atrophic rhinitis. Five patients had an autologous lipoaspirate applied to both nasal cavities, specifically the inferior turbinate, middle turbinate, floor and septum. Platelet-rich plasma was injected into the same areas. All five patients described symptom improvement, with the disappearance of nasal crusting. Clinical examination confirmed the presence of glistening nasal mucosa and no signs of atrophy. Six months after the intervention, Sino-Nasal Outcome Test 20 scores had improved from an average of 36 to an average of 8. In addition, the nasal mucociliary clearance time was significantly shorter after (960 seconds) than before (1995 seconds) surgery. The authors concluded that this method achieved encouraging subjective and objective outcomes **(33).**

The quality of life of 16 patients who underwent packing with platelet-rich plasma was evaluated after endoscopic sinus surgery. Their results were compared with retrospectively collected data from another group of 16 control patients who had undergone traditional packing. Each group completed two Sino-Nasal Outcome Test 16 questionnaires related to quality of life before and after surgery; the mean scores before and after surgery were converted into an absolute change score. The control group scored 0.938 and the platelet-rich plasma group scored 0.957, indicating more improvement in the platelet-rich plasma group. However, the difference between the groups was not significant because of the small population size **(34).**

The early results of a prospective study published into the use of platelet-rich plasma as packing material after endoscopic sinus surgery. The first 13 patients experienced no significant benefit of platelet-rich plasma, with some experiencing a worse post-operative course. As a consequence of these discouraging results, the

study was not completed **(35).**

a group of 30 patients with a platelet-rich plasma injection was treated into the inferior turbinates following submucosal diathermy. Patients treated with platelet-rich plasma showed significant improvements in crusting, bleeding and mucociliary clearance compared with a saline-treated control group (n = 30) **(36).**

Conclusion:

Based on the limited number of studies, we cannot draw safe conclusions about the value of platelet-rich plasma in endoscopic sinus surgery . Nevertheless, the available literature suggests that platelet-rich plasma holds promise for future research and may have a number of clinical applications.

References

1. Smith TL, Schlosser RJ, Mace JC, Alt JA, Beswick DM, DeConde AS, et al., editors. Long-term outcomes of endoscopic sinus surgery in the management of adult chronic rhinosinusitis. International forum of allergy & rhinology; 2019: Wiley Online Library.
2. Abdelnaseer U, El Sayed Salem A, Shawky BH, Yousef A. Assessment of Nasal Obstruction Symptoms and Pulmonary Function Following Functional Endoscopic Sinus Surgery (FESS) in Chronic Rhinosinusitis with Nasal Polyps. Indian Journal of Otolaryngology and Head & Neck Surgery. 2023:1-7.
3. Bachert C, Zhang N, Hellings PW, Bousquet J. Endotype-driven care pathways in patients with chronic rhinosinusitis. Journal of Allergy and Clinical Immunology. 2018;141(5):1543-51.
4. Homsi MT, Gaffey MM. Sinus endoscopic surgery. 2020.
5. Öçal R, Cingi C, Friedman O. Acute and Chronic Rhinosinusitis: Pathophysiology, Symptoms and Treatment. Airway diseases: Springer; 2023. p. 1-17.
6. Nyaiteera V, Nakku D, Nakasagga E, Llovet E, Kakande E, Nakalema G, et al. The burden of chronic rhinosinusitis and its effect on quality of life among patients re-attending an otolaryngology clinic in south western Uganda. BMC Ear, Nose and Throat Disorders. 2018;18(1):1-9.
7. Behiry EA, Elshazly HM, Abdel-Shafy IA, Adel Hussein H. Evaluation of quality of life after Functional Endoscopic Sinus Surgery (FESS) in chronic rhinosinusitis patients in Menoufia Governorate. Egyptian Journal of Ear, Nose, Throat and Allied Sciences. 2019;20(3):131-6.
8. Snidvongs K, Chitsuthipakorn W, Akarapas C, Aeumjaturapat S, Chusakul S, Kanjanaumporn J, et al. Risk factors of orbital complications in outpatients presenting with severe rhinosinusitis: a case-control study. Clinical Otolaryngology. 2021;46(3):587-93.
9. Pawar S. Study of Effectiveness of Functional Endoscopic Sinus Surgery (FESS) in Patients with Chronic Rhinosinusitis (CRS) Using Sino Nasal Outcome Test 22 (Snot-22): Rajiv Gandhi University of Health Sciences (India); 2018.
10. González C, Callejas C. Indications of Frontal Sinus Surgery. Atlas of Frontal Sinus Surgery: A Comprehensive Surgical Guide: Springer; 2022. p. 37-57.
11. Samarakkody ZM, Sran HS, Shukri NM, Abdullah B. Registration accuracy and surface marking of an electromagnetic navigation system for use in endoscopic sinus surgery. Egyptian Journal of Ear, Nose, Throat and Allied Sciences. 2019;20(2):67-73.
12. Saxena A, Nekhendzy V. Anesthetic considerations for functional endoscopic sinus surgery: a narrative review. Journal of Head and Neck Anesthesia. 2020;4(2):e25.
13. Bong JH, Song Hj, Oh Y, Park N, Kim H, Park S. Endoscopic navigation system with extended field of view using augmented reality technology. The International Journal of Medical Robotics and Computer Assisted Surgery. 2018;14(2):e1886.
14. El Ahl MAAS, Elnashar IS, El-Malt AE, Fareed MTM. Intact Bulla Technique versus Classic Technique as an Endoscopic Approaches to Frontal Sinus. The Egyptian Journal of Hospital Medicine. 2022;89(2):6329-35.
15. Mekhiemer S, Kadah S, El-gaber A, Abd-Elghaffar A. Total versus partial uncinectomy in functional endoscopic sinus surgery. Journal of Recent Advances in Medicine. 2020;1(2):75-9.
16. Kim AS, Willis AL, Laubitz D, Sharma S, Song BH, Chiu AG, et al., editors. The effect of maxillary sinus antrostomy size on the sinus microbiome. International forum of allergy & rhinology; 2019: Wiley Online Library.
17. Liu M, Jin K, Sun J, Lou Z. Postoperative ethmoid sinus mucoceles: Late complication of endoscopic ethmoidectomy and MWA management in outpatient. American Journal of Otolaryngology. 2021;42(5):103120.
18. Grayson JW, Cavada M, Wong E, Lien B, Duvnjak M, Campbell R, et al., editors. Effects of sphenoid surgery on nasal irrigation delivery. International forum of allergy & rhinology; 2019: Wiley Online Library.

19. Chen PG, Levy JM, Choby G, Smith K, Yao WC, Halderman A, et al., editors. Characterizing the complexity of frontal endoscopic sinus surgery: a multi-institutional, prospective, observational trial. International forum of allergy & rhinology; 2021: Wiley Online Library.
20. Elwany S, Askar M. Basic Endoscopic Sinus Surgery. Rhinology Review: Springer; 2023. p. 173-96..
21. Wang L, Wang X, Ba Y. Clinical analysis of delayed epistaxis following endoscopic sinus surgery. American Journal of Otolaryngology. 2022;43(3):103406.
22. Ali M, Kandoth JJ, George S. A Study on the Cavity Problems in Patients Who Have Undergone Functional Endoscopic Sinus Surgery. National Journal of Medical Research. 2020;10(02):97-104.
23. Le AD, Enweze L, DeBaun MR, Dragoo JL. Platelet-rich plasma. Clinics in sports medicine. 2019;38(1):17-44.
24. Etulain J, Mena HA, Meiss RP, Frechtel G, Gutt S, Negrotto S, et al. An optimised protocol for platelet-rich plasma preparation to improve its angiogenic and regenerative properties. Scientific reports. 2018;8(1):1513.
25. Stavrakas M, Karkos P, Markou K, Grigoriadis N. Platelet-rich plasma in otolaryngology. The Journal of Laryngology & Otology. 2016;130(12):1098-102.
26. Alves R, Grimalt R. A review of platelet-rich plasma: history, biology, mechanism of action, and classification. Skin appendage disorders. 2018;4(1):18-24.
27. Collins T, Alexander D, Barkatali B. Platelet-rich plasma: a narrative review. EFORT open reviews. 2021;6(4):225-35.
28. Anitua E, Cugat R, Sánchez M. Platelet Rich Plasma in Orthopaedics and Sports Medicine: Springer; 2018.
29. Misiura M, Guszczyn T, Oscilowska I, Baszanowska W, Palka J, Miltyk W. Platelet-Rich plasma promotes the proliferation of human keratinocytes via a progression of the cell cycle. A role of prolidase. International Journal of Molecular Sciences. 2021;22(2):936.
30. Harsini SM, Oryan A. Growth Factor of Platelet-Rich Plasma and its Application in Trauma and EOrthopedic Surgery. EC Orthopaedics. 2018;9:139-46.
31. 94. Everts P, Onishi K, Jayaram P, Lana JF, Mautner K. Platelet-rich plasma: new performance understandings and therapeutic considerations in 2020. International journal of molecular sciences. 2020;21(20):7794.
32. Kumar A, Runu R, Kumar S, Kashyap N, Subhash A, Khemka G, et al. The effect of intra-articular PRP (platelet rich plasma) injection in knee osteoarthritis-A short term results. Journal of Indira Gandhi Institute Of Medical Science. 2020;6(1):57-61.
33. Tabrizi AG, Asadi M, Mohammadi M, Yekta AA, Sohrabi M. Efficacy of platelet-rich plasma as an adjuvant therapy to endoscopic sinus surgery in anosmia patients with sinonasal polyposis: a randomized controlled clinical trial. Medical Journal of the Islamic Republic of Iran. 2021;35.
34. Hassan O, Ibrahim M, ElFarouk A, El Garem A. Platelet-rich plasma nasal packing in endoscopic sinus surgery. Pan Arab Journal of Rhinology. 2020;10(2):94-9.
35. Sari H, Karaketir S, Kumral TL, Akgun MF, Gurpinar B, Hanci D, et al. The effect of platelet-rich fibrin (PRF) on wound healing, adhesion, and hemostasis after endoscopic sinus surgery in patients with nasal polyposis. American Journal of Otolaryngology. 2021;42(5):103010.
36. Jeong E, kyung Yoo I, Cakir OO, Kim HK, Kim WH, Hong SP, et al. Effectiveness of autologous platelet-rich plasma for the healing of ulcers after endoscopic submucosal dissection. Clinical Endoscopy. 2019;52(5):472-8.