

Fibrin Sealant: Alternative to Nasal Packing in Endonasal Operations. A Prospective Randomized Study

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Abstract

Objectives: Endonasal operations such as septoplasty, rhinoplasty, nasal septal reconstruction and conchotomy, as well as endoscopic sinus surgery, especially when combined with turbinectomy and/or submucous resection of the septum, may produce bleeding and postoperative hematoma requiring postoperative hemostatic measures. Since nasal packing may cause pain, rhinorrhea and inconvenience, a more effective and less uncomfortable hemostatic technique is needed.

Objectives: To compare the hemostatic efficacy of the second-generation surgical sealant (Quixil™ in Europe and Israel, Crosseal™ in the USA) to that of nasal packing in endonasal surgery.

Methods: We conducted a prospective randomized trial that included 494 patients (selected from 529 using exclusion and inclusion criteria and completed follow-up) undergoing the above-mentioned endonasal procedures. Patients were assigned to one of three surgical groups: septoplasty + conchotomy + nasal packing or fibrin sealant (Group 1); ESS + nasal packing or fibrin sealant (Group 2); and ESS + septoplasty + conchotomy + nasal packing or fibrin sealant (Group 3). The hemostatic effects were evaluated objectively in the clinic by anterior rhinoscopy and endoscopy and assessed subjectively by the patients at follow-up visits.

Results: Postoperative hemorrhage occurred in 22.9–25% of patients with nasal packing vs. 3.12–4.65% in the fibrin sealant groups (late hemorrhage only). Drainage and ventilation of the paranasal sinuses, which are impaired in all cases of packing, remained normal in the fibrin sealant group. There were no allergic reactions to the sealant.

Conclusions: Our results show that fibrin sealant by aerosol spray in endonasal surgery is more effective and convenient than nasal packing. It requires no special treatment, e.g., antibiotics, which are usually used if nasal packing is involved.

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The idea of using fibrinogen or thrombin, or both, for local hemostasis was introduced at the beginning of the 20th century [1,2], revived during the Second World War when it was applied mainly for burns, and remained in use for many years until the introduction of commercial glues in the late 1970s. It was first used in otolaryngology mainly for larynx repair and in otologic surgery [3–5]. It was abandoned again in the early 1980s due to its risk of transmitting blood-borne infectious agents, and resumed in the late 1980s with the addition of viral inactiva-

tion steps during the manufacturing process. In the late 1980s, the use of fibrin sealant became established in otolaryngology mainly for tympanoplasty and tonsillectomy [6–8]. In rhinology, however, the use of fibrin sealant was still insignificant, being limited primarily to neurosurgical problems such as management of cerebrospinal fluid rhinorrhea or endonasal-trans-sphenoidal pituitary surgery [9,10].

Our preliminary reports indicate that the application of fibrin sealant (Quixil™ Omrix Ltd, Israel-Belgium) to the operative sites in various endonasal procedures [11,12] or for epistaxis problems [13,14] provides effective hemostasis and sealing with good systemic and local compatibility. Additional research was needed to evaluate the use of fibrin sealing as an alternative to nasal packing in all kinds of endonasal operations. The complications of nasal packing are well known. They include pain [15], infection [16], allergy, disturbance of breathing during sleep [17] and even a decrease in nocturnal arterial PO₂ [18], mucosal lesions including septal perforations, effect on eustachian tube function, and rare toxic shock syndrome with particular reference to functional ESS [19]. In addition, it is common practice to administer systemic antibiotics for nasal packing.

The aim of this randomized prospective trial was to evaluate the efficacy and safety of the second-generation Israeli-designed fibrin sealant Quixil™ after its application to endonasal operative sites.

Patients and Methods

Patients

This prospective study was approved by the Assaf Harofeh Medical Center Ethics Committee (ENT department). The mean age of the 494 patients recruited, 250 males and 244 females, was 34.4 years. Among them were 339 patients undergoing septoplasty + conchotomy, 64 cases of septoplasty and/or conchotomy combined with endoscopic sinus surgery, and 91 patients undergoing only ESS. Our series included patients with deviated nasal septum, and hypertrophy of the inferior conchae as a result of chronic, vasomotor and allergic rhinitis. Twenty-eight patients had arterial hypertension. Difficulties in nasal breathing were found in all patients, and 171 patients complained of snoring and 75 of sleep apnea. These patients were hospitalized for sleep monitoring. Sixty-three patients suffered from chronic sinusitis, and 49 patients complained of a visibly deviated

ESS = endoscopic sinus surgery

asymmetric nose. These symptoms were evaluated before and after surgery by anterior rhinoscopy and endonasal endoscopy, and were also subjectively evaluated by the patients.

Our ESS series included patients with persistent or recurrent sinusitis of different locations, and polypoid rhinosinusitis [Table 1]. Sixty-eight patients had no prior nasal or sinus surgery, and 23 patients had been operated before (13 ESS, 20 polypectomy). Seventeen patients had arterial hypertension. Difficulties in nasal breathing were found in all 91 patients. Thirty-nine patients complained of snoring and 25 of sleep apnea. These patients were hospitalized for sleep monitoring. Sixty-four patients had chronic sinusitis, which was combined with polypoid degeneration in 36 cases. The diagnosis had been made on a basis of clinical evaluation, anterior rhinoscopy, endonasal endoscopy, and computer tomography.

Altogether, 529 were allocated for intervention, 16 were excluded, 513 were randomized, 19 were lost to follow-up, and 494 completed follow-up and were analyzed.

Due to the type of surgical intervention, the patients were distributed into three groups: Group 1 (n=339): septoplasty + conchotomy; Group 2 (n=91): ESS; and Group 3 (n=64): ESS + septoplasty/conchotomy. Within these groups, patients were randomly assigned, by sealed envelopes, to one of two hemostatic methods: nasal packing or fibrin sealant. Randomization was done before the surgery in groups 1 and 2, and for the ESS patients randomization was performed during or after surgery for those who suffered excessive intraoperative and/or immediate postoperative bleeding (inclusion criteria). The resulting subgroups were as follows:

- Group 1A (n=182): septoplasty + conchotomy + nasal packing
- Group 1B (n=157): septoplasty + conchotomy + fibrin sealant
- Group 2A (n=48): ESS + nasal packing (middle meatus)
- Group 2B (n=43): ESS + fibrin sealant
- Group 3A (n=32): ESS + septoplasty/conchotomy + nasal packing
- Group 3B (n=32): ESS + septoplasty/conchotomy + fibrin sealant.

Materials

Quixil™ (Omrix Ltd., Israel) is a second-generation fibrin glue whose formulation is based on a concentrate of human clottable proteins and a highly purified human thrombin. It was developed in the early 1990s in Israel by a research group led by Prof. Uri Martinowitz. Since 1999 it has been licensed in Israel and several other countries, and was approved in the UK. It is licensed as Crosseal™ in the United States. The fibrin sealant attaches firmly to tissue, achieving instant hemostasis, and metabolizes naturally within several days without causing inflammation, plaques and crusts [20].

Quixil is used to facilitate hemostasis and prevent or reduce operative and postoperative bleeding and oozing during surgical procedures. The amount of sealant required depends on the area of tissue to be treated. In endonasal procedures the amount is small (0.5–1 ml). Using a dual-syringe delivery spray device with a triple lumen catheter the sealant is sprayed onto the tissue in short bursts (0.1–0.2 ml) to produce a thin, even layer. Allergic reactions to any of the constituents of Quixil

rarely occur. A rare neurotoxic effect was described upon application of Quixil on the meninges, caused by tranexamic acid contained in the sealant. No other side effects were reported. Quixil is not known to interact with any other drug.

We used Merocel™ foam packing (USA), which is made of polyvinylacetyl, for nasal packing in the control non-fibrin sealant group of patients. In the dry state the packs of Merocel are considerably smaller than after hydration at the site of action in the nose. Uptake of blood during the operation caused a rapid increase in volume, leading to absorption of blood and at the same time to wound compression.

Surgical technique

The surgery was performed under generally accepted local anesthesia. Our series included conchotomy, septoplasty, polypectomy, Cuidwell Luc operation, rhinoplasty, and ESS (155 sides operated) [Table 1]. A standard technique was used for polypectomy and septoplasty. Various approaches were used for functional rhinoplasty. In the group with fibrin sealant, we applied additional suturing of the septum to avoid intraseptal hematoma.

A standard technique was used for conchotomy (turbinectomy). In these operations the sealant spray (Groups 1B and 1B) was applied beneath a mucosal flap elevated for an open rhinoplasty approach. After that, in all types of procedures in these groups, the fibrin sealant was sprayed in amounts of 0.5 ml into each nostril to achieve complete hemostasis in every part of the operation site. Bearing in mind the anatomy of the nasal passages, we insert an applicator tube to the posterior portion of the nose through the nasal valve towards the turbinates, depositing the aerosol sealant in the region of the turbinates, while moving the applicator tube outward [Figure 1].

We used standard types of ESS [21] to remove sinus pathology with general (53 cases) or local anesthesia (11 cases). The fibrin sealant was sprayed in short bursts, starting from the

Table 1. Types of operations performed: endonasal (groups 1 and 3), and endoscopic sinus (group 2)

Endonasal surgery	(Groups 1 and 3)	
Septoplasty + conchotomy	265	
Conchotomy	9	
Septo-rhinoplasty	25	
Rhinoplasty + conchotomy	26	
Polypectomy	3	
Cuidwell Luc + polypectomy	2	
Cuidwell Luc + conchotomy	1	
Cuidwell Luc + polypectomy + septoplasty	8	
ESS + conchotomy	28	
ESS + septoplasty	12	
ESS + septoplasty + conchotomy	24	
Endoscopic sinus surgery (Group 2)	Group 2A	Group 2B
Sphenoidectomy	19	22
Ethmoidectomy	62	63
Frontotomy	19	18
Maxillary sinusotomy	53	47
Polypectomy	38	46



Figure 1. MixJect: dual-syringe delivery system for fibrin sealant application to small operative sites.

posterior part of the operative site and then moving the nozzle towards the ostiomeatal complex to achieve complete hemostasis in every surgically affected part. If one side was completely operated, it took 0.7–1.0 ml of the fibrin sealant to achieve complete hemostasis.

For nasal packing patients, the surgical procedure ended with Merocel foam packing of the middle meatus. Antibiotics were given according to standard protocol in all cases with packing, with slight variations in cases of purulent discharge or when nasal packing was in place for more than 2 days (rare).

Results

The results of the surgical procedures were assessed objectively in the clinic by anterior rhinoscopy and endoscopy of the nasal cavity and operated sinuses, and subjectively by the patients at follow-up visits. The observers were the authors and two independent judges. The follow-up visits were scheduled for the day after discharge, the third day, 2 weeks, 1 month and 3 months after surgery. Nineteen patients were lost to follow-up. The data were statistically evaluated by one-dimensional analysis of variance (bleeding x hemostatic technique), SPSS, Standard version 10.0.5 (SPSS, Chicago, USA, 1999), and chi-square criterion using 95% confidence interval. The level of significance for all analyses was set at $P < 0.05$.

The results were excellent in all patients treated with the fibrin sealant, with complete resolution of the major symptoms. Endoscopic evaluation did not demonstrate any atrophic changes or adhesions. We found good tissue approximation, and no hematomas, swelling, bleeding, synechia, or displacement. There were no any other complications in these series. Because of the absence of postoperative hemorrhage due to the biophysical properties of the sealant, nasal packing was not necessary. The patients in these groups left hospital immediately after the surgical procedure. They did not complain of pain or other inconvenience. None of them required postoperative care.

Nine cases (3.88%) of late postoperative bleeding occurred in the fibrin sealant groups 30–48 hours after the operation. The hemorrhage was stopped by additional application of the fibrin sealant onto the bleeding site. There were no allergic reactions or other adverse events of the sealant in our study.

Table 2. Number of postoperative bleeding episodes in groups

	Group 1A	Group 1B	Group 2A	Group 2B	Group 3A	Group 3B
A.	29	–	8	–	6	–
B.	6	–	1	–	1	–
C.	2	–	2	–	0	–
D.	6	6	0	2	1	1
Total	43 (23.6%)	6 (3.82%)	11 (22.9%)	2 (4.65%)	8 (25%)	1 (3.12%)

A = scanty bleeding after nasal pack removal

B = serious bleeding after nasal pack removal

C = bleeding through nasal packing

D = late bleeding after operation.

Patients with foam packing presented various complications of packing as well as postoperative bleeding. These patients complained of breathing disturbances during sleep (93%), lacrimation (26%), and pain caused by nasal packing (47.2%). In general, for these subgroups mucous discharge was usual, but we did not check this inconvenience in the fibrin sealant subgroups.

The incidence of postoperative bleeding is shown in Table 2. In most cases the patients had scant reactionary bleeding after pack removal, which stopped spontaneously in most cases but the supervision of the physician was needed. Four patients (in groups 1A and 2A, 1.74%) presented with bleeding through the nasal packing. In eight cases (groups 1A, 2A, 3A, 3%), nasal bleeding related to pack removal was significant and necessitated replacement of the nasal pack. Seven patients from these groups (2.67%) had late bleeding 24–30 hours after pack removal, which stopped spontaneously. In addition to bleeding episodes, two patients in group 1A presented with intraseptal hematoma 48 hours after the nasal packing was removed. They were treated by incision, drainage, and repeated packing. Three patients from the same group presented postoperative synechia.

There were no major complications in any of our groups. Follow-up visits at 3 postoperative months did not reveal any problems.

Comparison between postoperative bleeding episodes in the sealant and the packing groups showed a statistically significant decrease in groups where the sealant was used. For all types of bleeding $P < 0.05$; for serious or scant bleeding after nasal pack removal, and bleeding through nasal packing, $P < 0.0001$; the difference in late bleeding (30–48 hours) was not significant, $P > 0.1$.

Discussion

Fibrin sealant is used to facilitate hemostasis and reduce operative and postoperative bleeding and oozing during surgical procedures. The amount of fibrin sealant required depends on the area of tissue to be treated. In endonasal operations, the amount is usually small. Our observations support previous reports on the advantage of fibrin sealants to improve local hemostasis [22]. Furthermore, the dual-syringe delivery system is useful for applying the fibrin sealant to small body surfaces, especially sites unreachable by other applicators. In ESS, the aerosol spraying technique helps to stop the bleeding in all

operated sinuses because aerosol can reach any distant hidden "cell" of a sinus (e.g., the ethmoidal complex). The hemostatic technique is relatively easy to perform and does not require special skills or lengthy training. The convalescence was uneventful, and nasal ventilation was possible immediately after the operation. With the technique used for groups with nasal packing, normal nasal ventilation was only possible when the packing was removed on the second postoperative day.

In contrast to nasal packing, fibrin sealant does not require administration of antibiotics because of the lack of foreign body (a pack) in the nasal cavity. In our patients, there was no need for additional hemostatic procedures and no crusts were detected. In fact, since the sealant does not produce plaque, there is no danger of its aspiration. In addition, the nasal packing was not used at all, thus avoiding discomfort and reducing the risk of sinonasal secondary infection or other complications.

Post-ESS bleeding may have been secondary to Merocel packing removal, but that is not the case when fibrin sealant is used. Some other packing materials like, for example, Rapid Rhino™ nasal dressing with gel knit (Tampa, FL, USA) do not have the disadvantages of Merocel products. Due to a moist gel environment they can minimize postoperative oozing and reduce synechia formation and/or crusting. Naturally, the presence of a pack, irrespective of the design, affects nasal ventilation and causes discomfort.

In our study, aerosol-sprayed sealant formed a very thin layer and did not affect ventilation. Our research supports previous observations [23] that fibrin sealant is beneficial in ESS especially when the risk of hemorrhage or synechia is increased. The current research confirmed our previous studies of fibrin sealant in endonasal operations and in the treatment of epistaxis [11–14]. We conclude that fibrin sealant is an effective substitute for nasal packing in all types of endonasal surgery.

In cases of trauma-induced endonasal surgical interventions, if the nose is crooked or flattened, it is safe to say it has been fractured and reduction is required. Fractured and later-operated noses will bleed from a mucosal tear inside the nose, but packing can be very painful and sometimes impossible to apply. In such cases fibrin sealant has the obvious advantage that its method of application by spraying is painless. No anesthesia is needed before the spraying of fibrin sealant.

Conclusion

The aerosol application of fibrin sealant can be readily performed in endonasal surgery and ESS, it requires no special treatment (antibiotics), and appears to have an adequate hemostatic effect. The best way of applying fibrin sealant is with a pressure-driven aerosol spray. This second-generation sealant for endonasal surgery and ESS is well suited to stop nasal postoperative bleeding; it is safe and more convenient than nasal packing. It may well be the technique of choice for post-traumatic endonasal surgery.

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