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The use of fibrin glue as hemostatic in endonasal operations: a prospective, randomized study*

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SUMMARY

Operations like septoplasty, rhinoplasty, nasal septal reconstruction and conchotomy may produce bleeding and postoperative hematoma. Twohundredfour patients undergoing septoplasty and conchotomy operations were entered into a prospective study. Patients were randomly assigned to one of three treatment groups: Group I, septoplasty + conchotomy + nasal packing; Group II, septoplasty + conchotomy + fibrin glue; Group III, septoplasty + conchotomy + fibrin glue + transseptal suturing. To stop bleeding, we used the second generation surgical fibrin sealant Quixil and compared it with nasal packing. To increase protection against possible intraseptal hematoma we tried transseptal suturing at the end of a standard septoplasty operation. Our results show that the usage of the Quixil fibrin glue by aerosol spraying in endonasal operations is more effective and convenient than the usage of nasal packing. This combination of fibrin glue and the transseptal suturing substitutes the role of nasal packing in preventing postoperative intranasal hematoma. However, the transseptal suturing combined with the glue is not justified for the patients as no statistical difference was observed between Groups II and III in terms of occurrence of postoperative complications.

Key words: nasal septum, nasal cavity, surgery, turbinates, fibrin glue

INTRODUCTION

Deviated nasal septum and hypertrophy of inferior conchae are treated surgically using submucosal resection of the nasal septum (septoplasty, nasal septal reconstruction), and reduction of the nasal conchae (conchotomy) (Loré, 1988). All these surgical operations may produce bleeding, swelling and postoperative intraseptal hematoma. Therefore, all these operations, if not performed by laser, end with different types of nasal packing (Johnson, 1964). Despite permanent improvement of the packing materials, there is no absolute guarantee against bleeding even with nasal packing (Samad et al., 1992). In addition to that, nasal packing itself can produce various complications (Weber et al., 2000; Weber et al., 2001).

There have been several reports about the use of fibrin adhesive in otolaryngology. Some authors pointed out that fibrin tissue adhesive is not only a hemostatic, but also a bacteriostatic agent (Gleich et al., 1995). In case of endonasal operations, fibrin sealing was proposed in endonasal-transsphenoidal pituitary surgery (D'Arrigo et al., 1994). The authors did not use the fibrin glue to stop bleeding but to fix the mucoperichondrium. They admitted that a firm fixing of the margins of a mucoperichondrial laceration to the septal cartilage creates conditions for optimal healing and reduces nasal-packing time and nasal-splinting time. We successfully use the second-generation surgical fibrin sealant Quixil™ to treat epistaxis (Vaiman et al., 2002).

The current prospective, randomized study was made to prove that Quixil fibrin glue is an effective substitute for nasal packing in septoplasty, conchotomy and the other above mentioned endonasal operations.

MATERIALS AND METHODS

Approval

This study was approved by the Ethic Committee of the Asaf HaRofeh hospital.

The fibrin glue and an application device

Quixil™ is a new surgical sealant whose formulation is based on a concentrate of human clottable proteins (virus inactivated concentrated cryo) and a highly purified native human thrombin. In fact, this is a fibrin glue without fibrinogen. Unlike conventional sealants based on bovine thrombin and purified fibrinogen, collagen or synthetic compounds (first-generation

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glues), this fibrin glue attached firmly to tissue achieving instant hemostasis. Fibrin glue is a biological product of human origin (second-generation glue) which is metabolized naturally within several days without causing inflammation and crusts.

Fibrin glue is used to facilitate haemostasis and reduce operative and post-operative bleeding and oozing during surgical procedures. The amount of sealant required depends upon the area of tissue to be treated. In case of endonasal operations, the amount is small. The glue is sprayed with the help of compressed air onto the tissue in short bursts (0.1-0.2 ml) to produce a thin, even layer. If the haemostatic effect is not complete, a second layer should be applied. Quixil is metabolized by the physiological fibrinolytic system and absorbed, in the same way as an endogenous clot (Quixil: Summary, 2000).

Allergic or neurotoxic reactions to one of the constituents of Quixil™ may occur. Therefore it should not be used in neurosurgery. No other side-effects were reported. Fibrin glue is not known to interact with any other drug. There are concerns about the transmission of slow viruses through human based products. To minimize the risk of transmission of infective agents, stringent controls are applied to the selection of blood donors and donations. In addition, two consecutive virus removal and/or inactivation procedures are included in the glue production process. For clottable proteins this is Solvent/Detergent (S/D) treatment and pasteurisation; and for thrombin this is S/D treatment and firus filtration.

The new Fibrin Sealant Kit consists of reagents package and a device package. The reagent package contains two separated components: Biological Active Component (BAC, concentrate of human clottable protein plus tranexamic acid) and Thrombin (plus human albumin as an adjuvant). Several other adjuvants and excipients are added to the solutions.

The glue was applied through a pre-assembled application device featuring the MixJect vital transfer mechanism. This is a dual-syringe delivery system. Unlike previously used dual-syringe systems (Redl et al., 1986), the MixJect is connected to an air regulator capable of delivering 2-4 bars of pressure. The air pressure helps to distribute the glue in an aerosol form over the operative site. The syringe itself is designed in such a way that all clottable proteins and the thrombin concentrates are mixed passively in a syringe hub connector, just prior to contact with the repair site. It ensures quick aspiration of the reagents into the application device. The MixJect system is clog-free and allows for needle-free aspiration of the reagents into the application device, enhancing safety to hospital staff. We used Merocel foam packing made of polyvinylacetal for nasal packing in the control non-fibrin glue 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 thus leading to absorption of blood and at the same time to wound compression.

Table 1. Distribution of patients: age, sex, and affected part of nasal septum.

Total	Sex		Age			affected part	
cases	M	F	18-25	26-45	46-62	anterior	posterior
204	104	100	62	79	63	177	27

Patients

Two hundred and four patients undergoing septoplasty + conchotomy were entered into a prospective study. Our series includes patients with a deviated nasal septum (105), and hypertrophy of the inferior conchae (99) as a result of chronic, vasomotor, and allergic rhinitis. Patient data, such as age, sex, and affected part are shown in Table 1. One hundred of the patients were female, and 104 were male. One hundred eighty patients had no prior nasal or sinus surgery, 24 patients were operated before. Fourteen patients suffered with arterial hypertension. Difficulties in nasal breathing were found in all 204 patients. Fifty-one patients complained of snoring, 25 patients complained of sleep apnea. These patients were hospitalized for sleep monitoring. Thirty-three patients suffered from chronic sinusitis. Twenty-seven patients complained of a visibly deviated, asymmetric nose. These symptoms were evaluated before and after surgery by using anterior rhinoscopy and endonasal endoscopy, and also subjectively evaluated by the patients.

The patients were randomly assigned to one of three treatment groups:

Group I: septoplasty + conchotomy + nasal pakcking
Group II: septoplasty + conchotomy + fibrin glue
Group III: septoplasty + conchotomy + fibrin glue + transseptal suturing (suture-supporting sealing)

Surgical Technique

The surgery was performed under local anesthesia by using nasal packing soaked in a cocaine solution for 10 to 15 minutes. Then the nasal mucosa was injected with 0.1% Mercaine with Adrenaline (1:100,000).

The Killian incision was made on the anterior part of the septum. The mucopechondrium was elevated from one side. After the ridge was removed, the chondroplasty was performed. Our technique is based on a plastic of a deviated portion of the quadrangular cartilage. We used resection only in cases when the nasal septum was severely deformed. After that, for Groups II and III, the fibrin glue was sprayed between the mucoperichondrium and the cartilage to fix these parts and to prevent bleeding and intraseptal hematoma.

In 27 cases, when the nasal septum was severely deformed and bent in the posterior part, the perichondrium was elevated from both sides of the septum. In these cases in Groups II and III, the fibrin glue was sprayed onto the operative site from

Table 2. Number of postoperative bleeding episodes in three groups.

	Group I	Group II	Group III
scanty bleeding after nasal pack removal	18(26,46%)	-	-
significant bleeding after nasal pack removal	3(4.38%)	-	-
bleeding through nasal packing	2(2.92%)	-	-
late bleeding after opeartion	1(1.46%)	0	1(1.46%)
intraseptal hematoma	1(1,46%)	0	0
TOTAL	25(36,5%)	0	1(1,46%)

both sides to fix the mucoperichondrium and to stop intraseptal bleeding. Although the fibrin glue prevents bleeding and postoperative intraseptal hematoma, for additional security transseptal suturing was used (Group III). Any cavity left in the intraseptal space could accumulate blood. For Group III, to fix the mucoperichondrium and to avoid hematoma in intraseptal cavities, the anterior portion of the septum was approximated with three to five through and through sutures (septal mattress sutures) in all cases. The surgical incision was closed with absorbable sutures. We used 4-0 Vicryl or catgut for the suturing. In cases with deformity of the posterior part, suturing of the posterior portion of the septum was hard to perform and a small incision in the mucoperichondrium was made from one side at the basis of the septum.

A standard technique was used for conchotomy (turbinectomy) in all the groups. In these operations the glue spray (Groups II and III) was applied beneath a mucosal flap elevated for an open rhinoplasty approach. After that, in all types of operations in these groups, the fibrin glue was sprayed in an amount of 0.5 cc into each nostril to achieve complete hemostasis in every part of the operation site. Bearing in mind the anatomy of the nasal passages, we inserted the applicator tube to the posterior portion of the nose through the nasal valve towards the turbinates. The nozzle should not touch the tissue. Then we started depositing the aerosol glue in the region of the turbinates moving the applicator tube outward. Only by moving the nozzle out could we achieve a good and even intranasal distribution of the glue.

For Group I, the surgical operations ended with Merocel foam nasal packing. Moxipen (Amoxicillin) was administered 500 mg 3 times a day until the packing was removed. In Groups II and III, intraoperative bleeding was stopped by the fibrin glue aerosol spray. Because of the absence of postoperative hemorrhage, a nasal packing was not necessary for patients in these groups. (In this study intraoperative bleeding is defined as bleeding that occurs during the operation. Primary postoperative hemorrhage is defined as bleeding that occurs within the first 24 hours of surgery, whereas secondary hemorrhage occurs after the first 24 hours.)

All patients from all three groups were observed in the hospital during 48 hours. We feel, however, that the patients treated with fibrin glue could leave the hospital immediately after the surgical procedure. They needed no postoperative care. Follow-up visits were scheduled the next day after discharge, the third day, two weeks, and one month after surgery.

RESULTS

We investigated the properties of Quixil™ since 1998. Our series included conchotomy (189) and septoplasty (167). The results of these surgical procedures were assessed objectively in the clinic by anterior rhinoscopy and endoscopy of the nasal cavity and assessed subjectively by the patients at the above mentioned follow-up visits.

The results in all of the patients in Groups II and III showed complete resolution of the major symptoms. We found good tissue approximation, no hematomas, swelling, synechia, atrophic changes or adhesions, and no displacement. No postoperative bleeding occurred except for one episode of late bleeding in Group III. There were no other complications in this series. We found no statistical difference between Groups II and III in terms of occurrence of any postoperative bleeding and complications. There were no allergic reactions to the glue in our study.

In Group I, where foam packing was used, we observed various complications of nasal packing as well as cases with postoperative bleeding. All 68 patients complained of disturbance of breathing during sleep, 30 patients complained of lachrymation, and 45 complained of pain caused by nasal packing. In general, for this group, mucous discharge was usual, while we did not check this inconvenience in both fibrin glue groups.

Hemorrhage after nasal pack removal was observed in 25 patients (36,5%) in Group I. Eighteen patients had scanty reactionary bleeding immediately after nasal pack removal that stopped spontaneously (26,46%). Two patients (2,92%) presented bleeding through the nasal packing. In three cases (4,38%), nasal bleeding related to pack removal was significant and replacement of the nasal pack was needed. One patient (1,46%) had late bleeding 30 hours after pack removal that stopped spontaneously. One patient (1,46%) presented with intraseptal hematoma 48 hours after the nasal packing was removed. He was treated by incision, drainage, and repeated nasal packing. One patient (1,46%) presented with postoperative synechia. The incidence in postoperative bleeding is shown in Table 2.

DISCUSSION

The surgical treatment for chronic, vasomotor, and allergic rhinitis with hyperthrophy of inferior conchae is proposed when medical therapy is unsatisfactory. Surgical treatment for a deviated nasal septum is the only treatment possible.

Already in 1987, Hayward and Mackay successfully used fibrin glue in nasal septal surgery (Hayward and Mackay, 1987). These authors, however, used the glue mostly as a sealant, by injecting it between the layers of the mucoperichondrium to fill the position from which cartilage had been removed. They used a Duploject applicator, which cannot be connected to a pressed air regulator and, therefore, a pressure-driven aerosol spray cannot be achieved. That is why they were unable to use the glue as a main hemostatic agent for the whole operative site. These authors used Telfa pack during the operation and mentioned "some spotting of fresh blood from the nose" during the first two post-operative days.

Our main innovations were the use an aerosol form of the fibrin glue to avoid bleeding both with and without additional suturing of the septum to avoid intraseptal hematoma in nasal septal operations. The surgical technique was relatively easy to perform and was done after achievement of local anesthesia. The convalescence was uneventful, and nasal ventilation was possible immediately after the operation. In the technique used for Group I, nasal ventilation was only possible when the nasal packing was removed on the second or the forth post-operative day.

The most recent review on packing in endonasal surgery stresses importance of patient comfort and ease of removal if packing was used (Weber et al., 2001). As we did not use any packing at all in Groups II and III, the patient comfort is secured from the very beginning and there is no need to remove anything.

Our observations proved previous reports that the dual-syringe delivery system is especially useful for applying the fibrin sealant onto small body surfaces (Radisevich et al., 1997). In case of endonasal operations, the aerosol spraying technique helps to stop the bleeding in all parts of the nasal cavity.

In contrast with nasal packing, the usage of fibrin glue does not require administration of antibiotics. Indeed, in the Groups II and III, there were no transient or chronic infections. We feel this is due to the properties of the human fibrin sealant and the modified surgical technique. In our cases, there was no need to apply a second layer of the glue and no crusts were detected. In fact, the Quixil glue produces no plaques, therefore there is no danger for their aspiration. In addition, the nasal packing was not used at all, thus avoiding discomfort and reducing the chance of sinonasal infection or other complications.

CONCLUSION

We found the results of this series to be encouraging. The human fibrin sealant is well suited to stop bleeding after septoplasty and conchotomy operations if used in aerosol form. It is readily available and relatively inexpensive. This sealant is safe and easy to use. It does not only stop bleeding but being a human blood product also stimulates healing of the operated area. The transseptal suturing combined with the glue is not justified for the patients as no statistical difference was observed between Groups II and III in terms of occurrence of postoperative complications.

The surgical procedure is relatively simple to perform and can be done with local anesthesia, reducing the cost and duration of hospital stay. In addition to laser usage in endonasal operations, the usage of the new fibrin glue is a convenient and simple method to avoid nasal packing.

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