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Fibrin glue treatment for epistaxis*

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SUMMARY

Our study was made to prove the second-generation surgical fibrin sealant Quixil™ to be an effective substitute for nasal packing, chemical coagulation and cautery in management of patients with epistaxis. Our series includes 204 patients with anterior epistaxis (186), and with posterior epistaxis (18) as results of trauma, clotting disorders, chronic and/or atrophic rhinitis and upper respiratory infections, and hypertension. Patients were randomly divided into four groups: with fibrin glue (67) (Quixil™), with electric cautery (61), with silver nitrate coagulation (60), and with foam nasal packing (16). For the fibrin glue group, hemostasis was achieved by spraying with 0.3 ml Quixil™ fibrin glue to each bleeding nostril. The results were excellent in all of the 62 (92,5%) patients of the fibrin glue group with complete and immediate hemostasis. We found good healing of bleeding sites, no swelling and secondary bleeding, no inflammation, no plaque or crists. Three months monitoring of atrophic changes of the nasal mucosa proved absence of atrophy of the nasal mucosa. In this group, the bleeding time averaged 2 min 30 sec since the moment of admittance. In the groups where cautery, coagulation, or nasal packing was used, we found local swelling, pain, and slow healing of the bleeding site with accidental atrophy of the nasal mucosa. The rates of these side effects were significantly higher in comparison with the fibrin glue group. The bleeding time was also longer. We found that the fibrin glue is more effective hemostatic in comparison with foam nasal packing, cautery and coagulation, and provides no complications usual for these types of treatment of epistaxis.

Key words: epistaxis, fibrin glue, hemostasis

INTRODUCTION

Approximately 5-10% of the population experiences an episode of active nasal bleeding each year (Jackson et al., 1988; Abelson et al., 1991; Bingham et al., 1991; Tan and Calhoun, 1999). Less than 10% of these patients visit a physician for this problem and only one of those ten requires hospitalization. The incidence increases with advancing age (Shaheen, 1967), during the winter months (Nunez et al., 1990), and epistaxis is more common in males (Juselius, 1974).

The first line of management involves the use of some form of cautery and/or nasal packing. Many patients are managed by placing packing material into the nose to either to keep the mucosa moist or tamponade the mucosal hemorrhage. Risks and complications of nasal packing, however, are well known. They include pain (Tierney et al., 1996), dehydration, infections (Weber et al., 2000), allergy, disturbance of breathing during sleep (Kalogjera et al., 1995) or decrease in nocturnal arterial PO2 (Jahannenssen et al., 1992), dislocation with possible aspiration (rare), influence on eustachian tube function (Morgan, 1995), and altered ventilation from obstructive and physiologic derangements in pulmonary mechanics. Generally, nasal packing requires administration of antibiotics and/or topical ointment to prevent dryness.

As for cautery, it is only useful for clearly visible nasal sites that are not bleeding briskly. The main risk for both cautery with silver nitrate and electrocautery is atrophy of the nasal mucosa, that can lead to septal perforation. Thus, it is necessary to avoid opposing septal sites. Secondary measures include operations or non-operative ligation of the feeding arteries of the nasal mucosa. These options are usually considered after failed initial packing-cautery management for technical reasons or because of patient morbidity. As for laser coagulation, this method can initiate metaplasia of the nasal epithelium.

There were several reports about the use of fibrin adhesive for hemostatic needs in otolaryngology (Risti et al., 1990; Moralee et al., 1994). Some authors pointed out that fibrin glue is not only a hemostatic, but also a bacteriostatic agent (Gleich, 1995). While the hemostatic properties of fibrin glue are well

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known (Radisevich, 1997), its use for treatment of epistaxis is not developed yet.

Our study was made to prove the second-generation surgical fibrin sealant Quixil™ to be an effective substitute for nasal packing, chemical coagulation and cautery in management of patients with epistaxis. In our study, the anterior epistaxis is a bleeding from anterior area of the septum (Kiessellbach or Little area), and the posterior epistaxis is a bleeding from posterior and/or superior lateral walls of the nose and septum. A trial was carried out to make a comparison between three hemostatic methods - nasal packing, cautery, and fibrin glue - in regard to their effectiveness in treatment of epistaxis. We compared the rates of side effects (local swelling, for example) and rebleeding, time needed for complete stop of hemorrhage, and rate of development of scars. We were specifically monitoring any atrophic changes of the nasal mucosa for three months since the admittance.

We did not compare amounts of blood loss since the moment of admittance to the operating room till the moment of complete hemostasis for two reasons. First, the amount of blood loss before the moment of admittance is almost always not known. Therefore, the total blood loss is not known, and the partially known blood loss is of small importance. Second, physiological reactions on blood loss vary significantly among different patients and there is no direct correlation of amount of blood loss with severity of these reactions. Furthermore, easily controlled bleeding, profuse nosebleed, continual hemorrhage, and other types of epistaxis are generally treated with the same devices. For us, the time needed for complete stop of hemorrhage is more important.

MATERIAL AND METHODS

Biodegradable surgical adhesive and sealant for wound closure, Quixil™, is made from human plasma cryoprecipitate. It was invented in 1997. Since 1999, it has been licensed in Israel and several other countries, and was approved in the UK. Fibrin glue was recently approved by the U.S. Food and Drug Administration for use in the United States. Based entirely on enzymes and other proteins derived from human blood plasma, Quixil™ binds itself to severed or damaged blood vessels and tissues, stopping bleeding. Quixil™ has two liquid components which when sprayed together on a bleeding site form an elastic material which mimics natural clotting.

Currently Quixil™ is used to facilitate hemostasis and reduce operative and post-operative bleeding and oozing during surgical procedures. The amount of Quixil™ required depends upon the area of tissue to be treated. In case of epistaxis, the amount is usually small. Quixil™ is sprayed with the help of compressed air onto the bleeding site in short bursts (0.1-0.2 ml) to produce a thin, even layer. If the hemostatic 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.

Allergic and neurotoxic reactions to one of the constituents of Quixil™ may occur. Quixil™ should not be used in surgical operations where contact with the cerebrospinal fluid or dura mater would occur. Quixil™ is not known to interact with any other drug.

Quixil™ was applied through a pre-assembled application device featuring the MixJect vital transfer mechanism (Figure 1). This is a dual-syringe delivery system. It 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 the hospital staff.

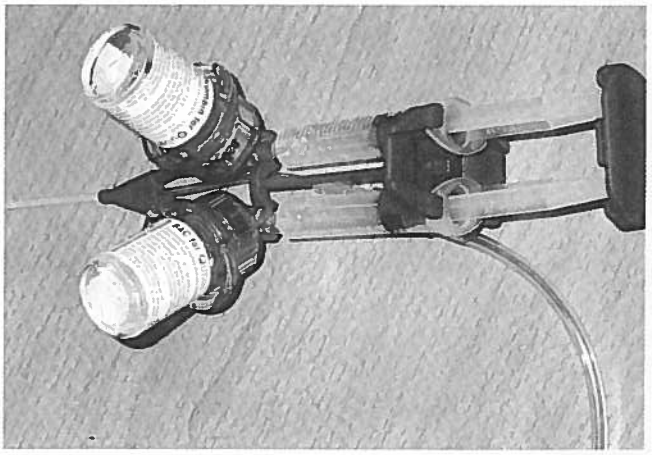

Figure 2. MixJect - a dual-syringe delivery system for the Quixil fibrin glue. It was used in all types of our endonasal operations.

Our series includes --204 patients with anterior epistaxis (186), and with posterior epistaxis (18) as results of trauma, clotting disorders (22), chronic and/or atrophic rhinitis and upper respiratory infections, and hypertension (40). Among patients with clotting disorders, seven suffered from primary diseases of the clotting system, and 15 presented secondary clotting disorders, usually after aspirin or anticoagulant treatment. Three patients presented epistaxis as a secondary postoperative hemorrhage after nasal operations. These three patients were treated with fibrin glue. Finally, cases of idiopathic epistaxis presented as well.

Arbitrarily, anterior bleeding sites are those anterior to the maxillary sinus ostium and posterior sites lie behind the ostium. Patient data, such as age, sex, etiology and type of bleeding were recorded and are shown in Table 1. All patients presented active bleeding at the time of admittance. Ninety of patients were female, and 114 were male. Twenty patients had no prior incidents of epistaxis, 104 patients presented epistaxis as a recurrent problem. After clots were evacuated with suction, all patients were examined by anterior rhinoscopy and endonasal endoscopy before treatment.

Table 1. Distribution of patients: age, sex, and type of epistaxis.

Total	Sex		Age				type of epistaxis	
cases	M	F	3-15	16-25	26-45	46-81	anterior	posterior
204	104	90	52	33	34	85	186	18

At the time of admittance patients were randomly divided into four groups for the first choice treatment:

(1) 67 patients were treated with Quixil™ fibrin glue (60 – anterior epistaxis, 7 – posterior epistaxis)
(2) 61 patient - with electrocautery (56 – anterior epistaxis, 5 – posterior epistaxis)
(3) 60 patients - with silver nitrate coagulation (all anterior epistaxis);
(4) 16 patients - with foam packing (10 – anterior epistaxis, 6 – posterior epistaxis).

As a rule, foam packing is rarely used in our outpatient department because of various side effects. There were no significant differences between the three groups with respect to age, sex, distribution of pathologic condition, and causes of bleeding. Usually patients were assessed while seated bleeding anteriorly into a dish. For the control groups, hemostasis was achieved by needle point electrocautery (group 2), by silver nitrate coagulation (group 3), and by nasal packing with Merocel packs (group 4). For the fibrin glue group (group 1), hemostasis was achieved by spraying 0.3 ml Quixil™ fibrin glue to each bleeding nostril. For the electrocautery group, cases of posterior bleedings were treated under microrhinoendoscopic control.

RESULTS

The results of the treatment were assessed objectively by the surgeon by using anterior rhinoscopy and endoscopy of the nasal cavity and assessed subjectively by the patients at the above mentioned follow-up visits. All patients were advised to avoid nonsteroidal anti-inflammatory drugs and situations likely to increase blood pressure like hot showers, hot beverages, and vigorous exercises.

The results were excellent in 62 (92,5%) patients of the fibrin glue group with complete and immediate hemostasis. We found good healing of the bleeding sites, but no swelling, scars, atrophy, nor inflammation, nor plaques or crists. There were no other complications in this series, except a few cases showing excessive nasal discharge. Quixil™ absorbs completely. It does not form plaques, and there is no danger for aspiration of plaques. For five patients in this group we were unable to stop bleeding by spraying the fibrin glue. Among them, three patients with anterior epistaxis due to clotting disorders were then treated with electrocautery. However, only one of these patients stopped bleeding after cauterization. The two others were then treated with nasal packing after which the bleeding finally stopped. Two other patients presented posterior bleeding and their bleeding was stopped with cautery (1) and Merocel nasal packing (1). In this group bleeding time averaged 2 min 30 sec since the moment of admittance. Three months monitoring of atrophic changes of the nasal mucosa proved absence of atrophy of the nasal mucosa.

In the groups where electrocautery, coagulation, or nasal packing were used, we found local swelling, pain, and slow healing of the bleeding site with accidental atrophy of the nasal mucosa. The rates of side effects are presented in Table 2. It took 12 min, 2 min 45 sec, and 6 min to stop bleeding, respectively. The incidence of post-treatment bleeding (rebleeding) in these groups were 14.7 % (9 patients) for the cautery group, 26.7% (16 patients) for the chemical coagulation group, and 12.5% (2 patients) for the nasal packing group. The incidence of rebleeding in the fibrin glue group was 14.9% (10 patients). All these patients returned to the operating room for hemorrhage revision.

Table 2. Incidence of complications and the bleeding time in four investigated groups.

	Electro cautery group	Silver nitrate group	Nasal packing group	Fibrin glue group
local swelling	61(100%)	19(31.6%)	-	0(0%)
rebleeding	9(14.7%)	16(26.6%)	2(12.5%)	10(14.9%)
scars	49(80.3%)	41(68.3%)	0(0%)	0(0%)
atrophy of nasal mucosa	3(4.9%)	3(5%)	1(6.25%)	0(0%)
synechia	2(3.2%)	0(0%)	1(6.25%)	0(0%)
infection	0(0%)	0(0%)	1(6.25%)	0(0%)
excessive nasal discharge	54(88.5%)	42(69.9%)	16(100%)	2(3%)
time needed for complete stop of hemorrhage	12 min	2'45"	6 min	2'30"

DISCUSSION

Epistaxis is a frequent problem in rhinology and general practice. It presents as an emergency, as a chronic problem of recurrent bleeds or may be a symptom of a generalized disorder. Current practical guidelines for the management of patients with epistaxis are not successful and an innovative approach is essential.

It is obvious that in cases of recurrent epistaxis or continual hemorrhage cautery or chemical coagulation can cause even more disturbance to a patient than epistaxis itself. In case of trauma-induced epistaxis, if the nose is crooked or flattened, it is safe to say it has been fractured and reduction is required. Fractured noses will bleed from a mucosal tear inside the nose but packing can be very painful and sometimes impossible to apply. In these cases fibrin glue has the obvious advantage because of its painless method of application by spraying. No anesthesia is needed before spraying the fibrin glue. Generally, nasal packing requires administration of antibiotics. This is not the case for fibrin glue treatment.

We found a statistically significant difference between the incidence of complications observed in the Quixil™ fibrin glue group and the other groups of patients. Indeed, fibrin glue use did not produce swelling, scars, synechia, infection, nor atrophy of the nasal mucosa. At the same time, the incidence of rebleeding is almost similar in the fibrin glue, electrocautery, and nasal packing groups. The highest incidence of rebleeding was observed in the chemical (silver nitrate) coagulation group.

The absence of side effects after fibrin glue usage is remarkable. Even when opposing septal sites are treated, there is no danger of perforation. Absence of mucosal atrophy or skin necrosis is a very stimulating effect for fibrin glue usage in epistaxis treatment. Dryness is not developed either, and there is no need to apply topical ointment.

As it was mentioned above, for five patients in the Quixil™ group we were unable to stop bleeding by spraying fibrin glue. Among them were three patients with anterior epistaxis due to clotting disorders. Two other patients presented intensive posterior bleeding. In regard to epistaxis due to clotting disorders, additional research with more cases should be performed. As for the cases with posterior bleeding, the problem might be connected with peculiarities of the nasal distribution of fibrin glue aerosols and highly intensive bleeding.

CONCLUSION

Our results indicate that the Quixil™ fibrin glue application to the bleeding sites in epistaxis provides effective hemostasis and sealing with good systemic and local compatibility. With the help of Quixil™, we minimized surgical trauma and achieved effective hemostasis at the same time. We completely avoided post-treatment atrophy of the nasal mucosa. We found this fibrin glue to be a more convenient intranasal hemostatic sealant in comparison with nasal packing, chemical (silver nitrate) coagulation and needle point electrocautery.

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