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Use of fibrin glue in preventing urethrocutaneous fistula after hypospadias repair

Saroj C. Gopal *, Ajay N. Gangopadhyay, T. Vittal Mohan, Vijai D. Upadhyaya, Anand Pandey, Ashish Upadhyaya, Dinesh K. Gupta

Department of Pediatric Surgery IMS, BHU, Varanasi 221005, India

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Abstract

Urethrocutaneous fistula is one of the most common complications after hypospadias surgery.The incidence of fistula development has varied from 4% to 20% in larger series. We sought to investigate the role of fibrin glue (Tisseel manufactured by Baxter India Pvt Ltd, Chennai, India) to reduce the chances of fistula formation in cases in proximal penile hypospadias.

Method: A total of 120 patients with proximal penile hypospadias (patients having urethral meatus at posterior third of penile shaft and at penoscrotal junction) were included in the present study. Patients were randomly allocated into 2 groups of 60 each by using Strata 9 software random number table. In group A, fibrin glue was used as a sealant after hypospadias surgery, whereas in group B, no sealant was used. All the operations were performed by single surgeon using transverse preputial tubularized island flap urethroplasty.

Result: Fistula formation occurred in 6 cases in group A (10%) and 19 cases in group B (32%) (P = .027). The fistulae observed in fibrin glue group A were single and small in size (<1 mm). Multiple (≥2 fistulae) and larger fistulae (>2 mm) were observed in group B. Overall complication was significantly higher in group B (P = .006).

Conclusion: Fibrin glue in hypospadias repair does not eliminate fistula formation. However, it seems that it minimizes the incidence of fistula formation.

Hypospadias is a congenital abnormality occurring in 1 of 300 live births. Recent studies suggest an increase of the incidence with considerable variation in different countries [1]. The surgical goal for hypospadias repair is to construct a cosmetically appealing straight penis with a terminally situated oval meatus, which will facilitate a well-directed full urinary stream and normal coitus. Although more than 200 reported original methods of urethral reconstruction were described, the quest for an ideal procedure to minimize the complications continues. The incidence of complications of hypospadias repair is directly related to the complexity of the repair: it is generally less than 2% with meatal-based advancement and glanduloplasty, 5% to 10% with meatal-based flaps, and 6% to 30% with more extensive reconstruction [2].

Well-known aspects of the modern hypospadias surgery (eg, delicate tissue handling, instruments, point coagulation, and maintaining the vascularity of tissues) probably play a

* Corresponding author.
E-mail address: upadhyayavj@rediffmail.com (S.C. Gopal).

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role in the outcome of hypospadias surgery especially in terms of complication such as urethrocutaneous fistula and proximal stricture formation. In an attempt to minimize the fistula and overall complications, various suture materials and techniques have been tried.

Few studies advocated the role of fibrin glue in various surgical problems and in hypospadias repair [3,4]. This study was conducted with a view to seek out the role of fibrin glue in reducing the chances of fistula formation after hypospadias surgery.

1. Materials and methods

This is a prospective study, carried out in the Department of Paediatric Surgery, University Hospital, Institute of Medical Sciences, Banaras Hindu University (Varanasi, India) from May 2004 to June 2006. One hundred twenty cases of proximal penile hypospadias (patients having meatus at the posterior third of penile shaft, although we have also included the patients with meatus at penoscrotal junction) with or without chordee were selected for single-stage urethroplasty. Patients were randomized based on random number table using Strata 9 software (120 random numbers from 1 to 120 without replacement were randomized into 2 groups or block based on random number table); 60 cases (group A—study group) underwent transverse preputial tubularized island flap urethroplasty (Duckett urethroplasty), performed with application of fibrin glue. The control group, group B (60 cases), underwent the same procedure without application of fibrin glue by the same surgeon. The study was permitted by the ethical committee of our institute.

Fibrin glue has the advantage of being biodegradable; and it does not result in significant inflammation, tissue fibrosis, or foreign-body reaction [5]. Fibrin glue may promote angiogenesis, local tissue growth, and repair [6]. Conventional synthetic hemostatic agents, for example, cyanoacrylate, may be associated with an increased incidence of infection, fibrosis, and chronic inflammation if left in situ [7].

Fig. 1 Inner preputial layer is marked for urethral tube after proper degloving of penis.

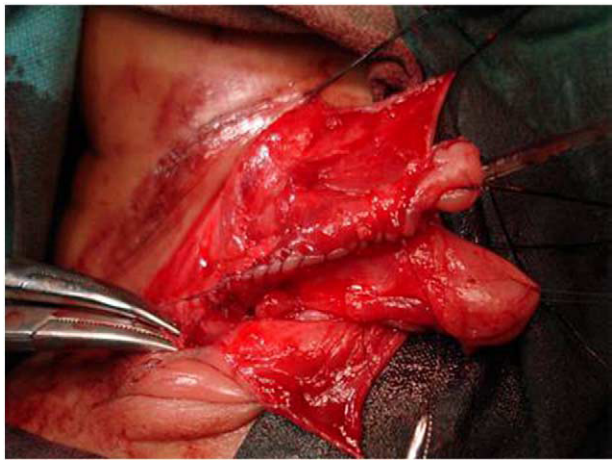

Fig. 2 Neourethra is prepared from inner preputial tube, and proximal anastomosis is completed.

In the present study, the hypospadias was repaired with tubularized transverse preputial island flap technique by a single surgeon (pediatric surgeon having experience of >25 years). The penis was degloved up to the root (Fig. 1). Chordee and rotational deformity were corrected properly and confirmed by artificial penile erection test. Transverse island flap was raised form the inner preputial skin and tubularized on a no. 6F feeding tube using 6.0 Vicryl suture (Fig. 2). The length of reconstructed tube was meticulously measured with the help of vernier caliper. In group A, the suture line of the neourethral tube was sealed with fibrin glue (Tisseel manufactured by Baxter India Pvt Ltd) containing fibrinogen and thrombinogen (Fig. 3) and then on to the dartos layer (Fig. 4) sutured over the urethral tube, whereas in group B, the procedure was the same but fibrin glue was not applied. The dressing was done using Sofratulle wrap (Aventis Pharma, Ltd., Ponda Goa, India). The catheter was usually removed after 10 days of operation.

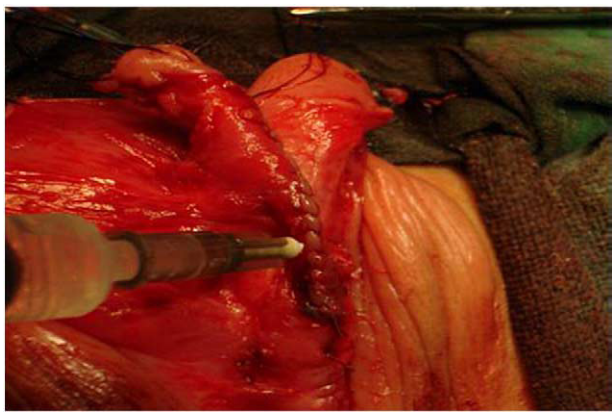

Fig. 3 Fibrin glue is applied on the proximal anastomosis site and over the suture line of neourethra.

Fig. 4 Fibrin glue is applied on the dartos layer covering the neourethral tube.

All cases were evaluated and compared for complications especially for fistula formation by the staff nurse and resident of the department (both of them were unaware of the study, making the study blind). Statistical analysis was done using Fisher's Exact test.

All patients were followed after 2 weeks of surgery and then 3 monthly follow-ups for the first year and then 6 monthly follow-ups for next 5 years. The range of follow-up time was 14 to 30 months in the present study.

Patients presenting with urethrocutaneous fistula were taught to close the fistula manually during micturition. Patients with fistula were assessed regularly and operated after 1 year of previous surgery. More than 90% of fistulae responded to redo operation in the follow-up period of 8 to 18 months. In all cases, the fistula was treated with excision of fistulous tract and layered closure of the tissue. Most of the patients with proximal urethral stricture and meatal stenosis responded to the urethral dilatation; none of them required reoperation.

2. Results

In present study, most of the patients were younger than 3 years; the mean age in group A was 28.02 months (range, 16-54 months; SD, 9.56 months) and that for group B was 28.00 months (range, 18-56 months; SD, 10.30 months). Mean length of reconstructed urethra in group A was 26.17 mm (range, 14-32 mm; SD, 4.25) and 25.22 mm in group B (range, 14-29 mm; SD, 3.92 mm). The various complications noted after hypospadias repair were described in Table 1. Postoperative edema was observed in 10 cases in group A and in 21 cases in group B, and the difference was found to be statistically significant (P = .039). Fistula formation occurred in 6 (10%) cases in group A and 19 cases in group B (31%). The incidence of fistula in group B was significantly higher than that in group A (P = .027). The fistulae observed in group A were single and minute in size (<1 mm) Table 2. Multiple (≥2) and bigger fistulae were observed in group B. Meatal stenosis, proximal urethral stricture, and diverticulum were the other complications observed in few patients. Twenty-five percent of cases in group A and 52% of cases in group B developed one or the other complications. Overall complications were less in the fibrin glue group, and the difference was found to be statistically significant (P = .003).

Table 1 Overall complication

Complication	Group A (n = 60)	Group B (n = 60)	P
Postoperative edema[a]	10	21	.039
Fistula	6	19	.027
Diverticulum	0	3	.1
Infection[a]	4	2	
Meatal stenosis	3	3	.1
Proximal stricture	3	10	
No. of cases developed complications	12/60 (20%)	34/60 (56%)	.003

[a] Not included in main complication.

Table 2 Incidence of fistula formation

	No. of fistulae			Size of fistula (mm)		
	Total	Single	Multiple	<1	1-2	>2
Group A	6 (10%)	6	0	5	1	0
Group B	19 (32%)	13	6	0	7	12

3. Discussion

Fibrin sealant has been used during many surgical procedures as a topical agent for hemostasis and as an adhesive in tissue approximation. Current Food and Drug Administration–approved uses include cardiac surgery, splenic trauma, and colonic sealing. The use of fibrin sealant has increased in numerous surgical fields, including urological surgery. The 2 major areas of fibrin sealant application are as a topical agent for hemostasis and as an adhesive for tissue approximation. The most formidable complication of hypospadias surgery is formation of fistula. In this study we used fibrin glue as a sealant to reduce fistula formation, based on some studies, indicating that fibrin glue improves wound healing [8-11]. The application of fibrin glues in urology mainly relates to its sealing power. Diner et al [12] recently described its use to strengthen vesicourethral anastomotic patency after radical prostatectomy. Hick and Morey [13] used fibrin glue as a sealant to enhance wound healing in penile urethroplasty. Ambriz-González et al [14] concluded that the incidence of urethrocutaneous fistula after hypospadias surgical repair can be reduced by applying fibrin sealant over the site of surgery and the suture lines. Barbagli et al [4] used fibrin glue in bulbar urethroplasty and stated that the use of fibrin

glue represents a slight but significant step toward perfecting the surgical technique of bulbar urethral reconstruction using dorsal buccal mucosal graft.

Dodat [15] used fibrin glue in various pediatric urological procedures and stated that it probably helps in reducing fistula formation. The local hemostatic effect seems to be very useful in urethroplasty for hypospadias. Its application in vesical, ureteral, or urethral sutures probably prevents fistulae.

In present series we observed that postoperative edema was seen in 10 cases (15%) in group A vs 20 cases (31%) in group B, which was similar to other reported series. Kinahan and Johnson [3] in their series (Mustardé repair) observed that postoperative edema was significantly lower with application of fibrin glue; it was 29% and 42%, respectively, for the glue group and the no-glue group for proximal penile hypospadias. Our hypothesis is that early postoperative edema occurs because of unrecognized microscopic leak in the tissue spaces in between the suture line, which may latter lead to fistula formation. Postoperative edema was found to be significantly higher in the nonglue group. This seems that the fibrin glue helps in improved wound healing by forming an additional layer over the urethral tube, sealing the minute cervices present between the suture and hence reducing the edema formation after surgery. These data suggest that fibrin glue improves the wound healing.

Incidence of fistula formation was lower in group A (10%) as compared to group B (31%). Kinahan and Johnson [3] in their series reported a fistula rate of 13% and 38% in the glue and non-glue groups, respectively, for proximal penile hypospadias. The fistulae developed in 10% cases in group A were single and of very small size (<1 mm), whereas the fistulae that developed in 27% of cases in group B and were large (> 2 mm) and in some cases they were multiple (>2 fistulae). Incidence of fistula formation was less in the glue group, and the difference was statistically significant. Our hypothesis is that "fistulae are initiated by microscopic leaks at the sutures sites and fibrin glue forms an additional layer over the urethral tube sealing the minute cervices present between the sutures hence reducing the chances of fistula formation." Thus, these data suggest that fibrin glue help in preventing fistula formation after hypospadias surgery, although does not eradicate it completely.

Incidence of proximal urethral stricture was lower in group A, but the difference was not found to be statistically significant. Fibrin glue helps in wound healing with minimal fibrosis, which may be the factor for lesser number of proximal urethral strictures in glue group. All these findings suggest that fibrin glue helps in better healing of the tissue.

Meatal stenosis was observed in 2 cases (5%) in group A. The incidence of meatal stenosis in group B was 8%. Meatal stenosis usually results from the retraction of the meatus or scab formation after surgery or it may occur because of faulty technique (too many sutures applied for meatoplasy or sutures are applied tightly or deeper glans tissue is used for meatoplasty).

Urethral diverticulum was observed in 2 cases in group B (5%). Weiner et al [16] reported diverticulum formation in 12% of the tubularized island flap repairs in their series of 132 patients.

The number of cases, who developed complications, was significantly lower in group A (20%) than (56%) in group B. In the present study, all cases were done by single pediatric surgeon having experience of more than 25 years, although quite a number of patients developed complications.

4. Conclusion

Use of fibrin glue in hypospadias repair does not eliminate fistula formation. However, it seems that it reduces the incidence of fistula formation. Fibrin glue is an additional armamentarium in hypospadias.

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