Original Article

Efficacy of Fibrin Sealant as Waterproof Cover in Improving Outcome in Hypospadias Surgery

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Abstract

Background: This prospective comparative study aims to assess the efficacy of fibrin sealant to improve outcomes in paediatric patients operated for hypospadias. **Materials and Methods:** Forty consecutive patients with hypospadias were randomised into two groups of twenty patients each. The first group underwent hypospadias repair, technique depending on the type of hypospadias, whereas in the second group, fibrin sealant was used to reinforce the urethroplasty. Assessment was done with respect to the type of hypospadias, type of repair done, operative time, immediate post-operative complications (early ooze and skin flap-related complications), intermediate complications (urethra-cutaneous fistula) and delayed post-operative complications (penile torsion and poor cosmetic outcome) at follow-up. We also compared the overall improvement in outcome among the two groups. **Results:** First Group: The mean operative time was 1 h and 45 min. Complications were seen in nine patients: Early ooze (n = 2); skin flap-related complications (n = 3); fistula (n = 7); poor cosmetic outcome (n = 7) and penile torsion (n = 4). Second Group (Fibrin Sealant): The mean operative time was 1 h and 30 min. Post-operative complications were observed in five patients: Coronal fistula (n = 3) and poor cosmetic outcome (n = 3). On comparing, the differences in outcomes of ooze, skin flap-related complications and torsion were found to be statistically significant with $P < 0.05$. The differences in the urethra-cutaneous fistula and cosmetic appearance were not found to be statistically significant. The difference in overall improvement in complications was found to be statistically significant. **Conclusion:** Fibrin sealant, when applied over the urethroplasty suture line as a waterproof cover, may help to improve the outcome in patients with hypospadias.

Keywords: Fibrin sealant, hypospadias, outcome, repair

Introduction

Hypospadias is a congenital condition wherein the urethral meatus is located ventrally at a location from the tip of the glans to the perineum.[1] Urethrocutaneous fistulae are the most common post-operative complication (10%–40%) after hypospadias surgery; other complications being skin flap-related complications such as flap necrosis, suture-line breakdown, ascent of the testis and penile torsion.[2-5] Fibrin glue used as a hemostat, wound sealant and sometimes to avoid the use of conventional sutures has been found to minimise the formation of urethrocutaneous fistula after hypospadias surgery.[1] In this prospective study, the efficacy of fibrin sealant (human plasma-derived fibrin sealant, manufactured by Ethicon) applied over the subcutaneous urethroplasty suture line to reduce complications and improve the overall outcome in hypospadias was assessed.

Materials and Methods

This is a prospective comparative study on forty consecutive patients of hypospadias operated in the Department of Paediatric Surgery of a tertiary care centre, over a period of 1 year. The aim of the study was to evaluate if application of a fibrin sealant over the urethroplasty suture line for waterproofing instead of vascular cover to reduce complications and improve the outcome in hypospadias repair. The study was approved by the Ethical Committee of the Institute and written and informed consent was obtained from the parents of all included patients for being a part of the study and also for publication of data and images of their children.

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All patients with hypospadias, irrespective of the type were included in the study. The exclusion criteria were congenital urethrocutaneous fistula, post-traumatic urethrocutaneous fistula and patients of hypospadias with associated disorders of sexual differentiation.

Forty consecutive patients with hypospadias were randomised (using a computer-generated list of random numbers) into two groups of twenty patients each. The first group underwent hypospadias repair, technique depending on the type of hypospadias, whereas in the second group, fibrin sealant was used to reinforce the urethroplasty.

Operative technique

All hypospadias repairs were performed using loop magnification. The neo-urethra was created by a subcuticular running Vicryl 6.0 round body suture. In the first group of patients undergoing (Tubularised Incised Plate [TIP] Urethroplasty) repair, a dartos vascularised pedicled flap was created to cover the neo-urethra. Patients with more proximal hypospadias requiring staged repair, chordee correction was followed by transposition of the inner preputial pedicled flap on the ventral aspect of the penis. The second-stage urethroplasty was performed after 6 months. In the second group of patients, fibrin sealant was applied on the suture line of the neo-urethra and no vascular cover was used [Figures 1-3]. A 6 or 7 Fr urethral catheter was kept for 10 days post-operatively, for patients in both study groups. Figure 4 shows a child voiding in good stream from neomeatus after removal of urethral catheter just before discharge.

The patients were assessed for the following variables: type of hypospadias, type of repair done, operative time, immediate post-operative complications (early ooze and skin flap-related complications), intermediate complications (urethra-cutaneous fistula) and delayed post-operative complications (penile torsion and poor cosmetic outcome) at follow-up. All patients were reassessed 7 days following discharge, followed by 1 month, 3 months, and 6 months. Chi-square and fischer exact test were used for statistical evaluation, with a $P < 0.05$ considered as being statistically significant. The overall improvement in outcome was also calculated by comparing the total possible complication events among the two groups and calculating the *P* value for statistical significance.

Results

First (routine hypospadias repair) group

The mean age at operation was 4.6 years. The types of hypospadias were as follows: Coronal (4), subcoronal (5), distal penile (1), mid-penile (7), proximal penile (1) and penoscrotal (2). Eighteen patients underwent Snodgrass repair (TIP urethroplasty) and two patients with penoscrotal hypospadias underwent ThierschDuplay repair. The mean operative time was 1 h and 45 min. Complications were seen in nine patients: Early post-operative ooze in two patients which resolved by compression dressing; skinflap-related complications in three patients; urethra-cutaneous fistulae in seven patients-coronal (3), mid-penile (3) and penoscrotal (1). The cosmetic outcome was poor in seven patients and penile torsion was observed in four patients on follow-up.

Second group (fibrin sealant)

The mean age at operation was 3.8 years. The types of hypospadias were as follows: Coronal (1), subcoronal (9), distal penile (4), mid-penile (4), proximal penile (1) and penoscrotal (1). Eighteen patients underwent Snodgrass repair (TIP urethroplasty) and two patients (proximal penile and penoscrotal hypospadias) underwent ThierschDuplay repair. The mean operative time was 1 h and 30 min. Post-operative complications were observed in five patients. There were no immediate complications of the early post-operative ooze and skin flap-related complications. At follow-up, coronal fistula was observed in three patients. The cosmetic outcome was poor in three patients but there was no penile torsion in any of these patients.

Comparison was made between both groups on the basis of early and late complications and Chi-square test and Fisher's exact test were applied and *P* values were calculated as stated above [Table 1]. On comparing, it was observed that the differences in early post-operative ooze, skin flap-related complications and torsion were found to be statistically significant with $P < 0.05$. Although the number of patients with urethra-cutaneous fistulae and poor cosmetic appearance was less in fibrin sealant group, the difference between them was not found to be statistically significant. The overall improvement in outcome was also calculated by comparing the total possible complication events ($n = 100$) among the two groups. This was found to be statistically significant [Table 2].

Discussion

Urethrocutaneous fistula is a common complication of hypospadias repair varying from 10 to 40% as reported in various studies depending on the degree of hypospadias and the surgical technique used.[1-5] The other common complications are urethral stricture, wound breakdown, skin flap necrosis, penile torsion and ascent of the testis.[6]

Table 1: Comparison of complications in both groups

Complications	Group 1 (routine)	Group 2 (fibrin sealant)	*P*
Ooze and hematoma formation	2	0	0.0121
Skin flap-related complications	3	0	0.0112
Fistula	7	3	0.144
Unsatisfactory cosmetic appearance	7	3	0.144
Penile torsion	4	0	0.0265

Table 2: Comparison of overall improvement in outcome

Total possible complication events ($n=100$)	Group 1 (routine)	Group 2 (fibrin sealant)	*P*
Adding up all complication events	24	6	0.000761

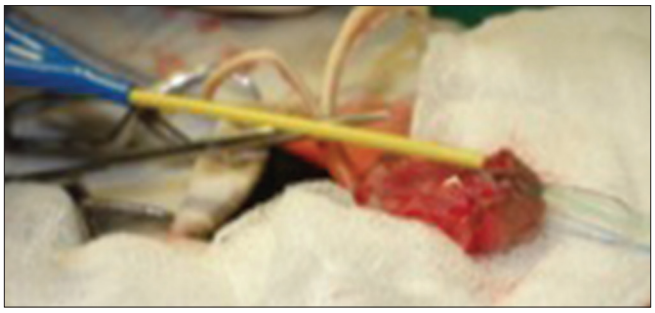

Figure 1: Intraoperative image showing application of fibrin sealant

Figure 3: Intraoperative image showing completed repair

Figure 2: Intraoperative image showing completed urethroplasty after application of fibrin sealant

Figure 4: Post-operative image showing voiding in single-stream from the tip of neo-meatus before discharge of the child from hospital

The techniques for hypospadias repair have evolved in recent decades and TIP urethroplasty or TIP repair has currently emerged as one of the most popular procedures in the surgical repair of hypospadias (utilised in 85% of all hypospadias cases).[7] The result of this technique is the creation of a slit-like meatus, which meets aesthetic demands, in contrast to the less satisfactory cosmetic results of other techniques as reported.[8,9] However, the rate of reported complications is around 20%–30%, common being urethrocutaneous fistula, meatal stenosis and glans breakdown.[10] There have been ongoing efforts to reduce these complications.

The use of interposition layer supports the urethroplasty and acts as a waterproof layer and is being commonly used to reduce urethra-cutaneous fistula rates. Each interposition layer has its own advantages as well as disadvantages. Various available options are dartos fascia, corpus spongiosum and tunica vaginalis (TV).[5-12] Local dartos flap can be obtained easily without a second incision; its main disadvantage being occasional devascularization of penile skin during dartos dissection leading to increased incidence of urethrocutaneous fistula.[13] TV flap though easy to harvest, may sometimes need an extra incision to obtain the flap and complications such as ascent of the ipsilateral testis, scrotal hematoma, and even abscess have been reported.[14] The incidence of urethrocutaneous fistula varies from 5.7% to 11.7% in different series reporting the use of TV flap.[12,15,16] Despite these techniques, complication rates following TIP repair with regards to fistula rate and glans breakdown are high as reported in some studies.[10]

Recently, a number of tissue sealants have also been proposed to provide a better sealing effect during urethroplasty.[1] Commercially, available fibrin sealant is prepared from pooled cryoprecipitated fibrinogen from multiple screened plasma donors and is processed with heat treating, use of solvent and detergent suspension and are usually safe to use, there is possible risk of transmission of infections and allergic reactions (though theoretical).[17] Hosseinpour *et al*., in their study on 400 patients with hypospadias repair, used autologous cryocalcium glue prepared from the patient's plasma and reported low incidence of fistulae.[17] They reported that this autologous cryocalcium glue is safe, cost-effective, and can be prepared during urethroplasty procedure and used immediately.[17] Kinahan and Johnson reported benefit of using Tisseel, a fibrin glue preparation, to augment hypospadias repairs in children. The fistula rate was significantly lower (9% vs. 28% in a control group) in hypospadias repair done using the sealant.[18] Hick *et al*. reported

that fibrin sealant promotes early catheter removal and enhanced wound healing after pendulous urethral reconstruction.[19] Barbagli *et al*. reported the use of fibrin glue in the buccal mucosa graft urethroplasty for bulbar urethral stricture with a shortened overall operative time and decreased early post-operative leakage.[20] In a prospective randomized trial of 120 boys with proximal hypospadias undergoing Tubularized Incised plate urethroplasty (TIPS) procedure, Gopal *et al*. reported reduction of fistula rate using fibrin glue-fistulae were seen in 10% of cases with the use of fibrin glue versus 30% without glue.[21]

Contrary to the above results, Kocherov *et al*., in their study, failed to demonstrate BioGlue's benefit in decreasing incidence of fistula formation.[22] Furthermore, patients from BioGlue group had unsatisfactory cosmetic appearance and had severe fibrotic skin reaction.[22] This suggests that a foreign body reaction may be triggered in some patients. Schmeeckle *et al*. reported that patients in whom fibrin glue was used had a >6-fold increased incidence of fistula formation suggesting that fibrin glue may disrupt normal tissue incorporation in the post-operative healing phase.[23]

In our study, we observed that patients in whom fibrin sealant was used had better outcomes in form of no early post-operative ooze or flap-related complications such as flap necrosis or penile torsion. This is similar to findings observed by Hick and Morey[19] Hafez *et al*. suggest that cellular and angiogenic regeneration of the tunica albuginea defect may play a role in this.[24] The number of patients with urethra-cutaneous fistulae and poor cosmetic outcome was also less in the fibrin sealant group; however, the differences were not found to be statistically significant. This is in contrast to observations made in recent studies.[21-23,25] However, similar to the observations by Ambriz-González *et al*., we also observed that overall improvement in outcome was statistically significant.[1]

This study presents a relatively small number of patients. All types of hypospadias were included in the study and different repair techniques were used which may add to the bias. Furthermore, availability of commercial fibrin sealant and its expense cannot be totally ignored.[17] Fibrin sealant being a blood-derived product carries a theoretical risk of allergy and transmission of infection which cannot be overlooked. Although we found less patients with urethrocutaneous fistulae in the fibrin sealant group, but overall outcome was improved. Basic studies on wound healing with fibrin sealant and larger clinical prospective, randomized trials including homogenous patients and same techniques would be needed to help in defining the role of fibrin sealant in hypospadias surgery in near future.

Conclusion

As observed in our study, fibrin sealant may help to provide an effective water-proof cover when applied over the urethroplasty suture-line and improve outcome in hypospadias repair.

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Conflicts of interest

There are no conflicts of interest.

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