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Efficacy of triamcinolone acetonide combined with recombinant bovine basic fibroblast growth factor in preventing scar formation after adult circumcision using a stapler device

A randomized controlled trial

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Abstract

Background: This randomized controlled trial aimed to investigate the potential benefits of local application of triamcinolone acetonide combined with topical recombinant bovine basic fibroblast growth factor in promoting wound healing and reducing scar formation after circumcision using a stapler device.

Methods: A total of 192 patients with phimosis or redundant prepuce were randomly assigned to either the observation group (n = 96) or the control group (n = 96). Both groups underwent circumcision using a stapler device. Postoperatively, the observation group received wet dressings of 2 mg/mL triamcinolone acetonide solution combined with topical recombinant bovine basic fibroblast growth factor until complete wound healing. The control group received saline wet dressings and standard postoperative wound care. Outcome measures included: postoperative edema, time to resolution of swelling at the incision edges, wound exudate, healing time, staple removal time and rate, scar formation, and patient satisfaction with penile cosmesis.

Results: The observation group demonstrated significantly faster healing times and lower incidence of edema from the seventh postoperative day compared to the control group ($P < .05$). Furthermore, the observation group exhibited superior outcomes in terms of complete staple removal time, staple detachment rate, scar hypertrophy, and cosmetic scores using the modified Stony Brook Scar Evaluation Scale ($P < .05$). Patient satisfaction with penile cosmesis was also significantly higher in the observation group ($P < .05$).

Conclusion: This study underscores the principle of "prevention over treatment" in scar management following stapler circumcision. The findings suggest that the combined use of triamcinolone acetonide and recombinant bovine basic fibroblast growth factor may be beneficial in reducing postoperative edema, improving scar formation, and enhancing patient satisfaction. However, further research is warranted to validate these findings, establish optimal treatment protocols, and ultimately assess the long-term efficacy and safety of this combined therapy.

Abbreviations: DCSD = disposable circumcision suture device, rb-bFGF = recombinant bovine basic fibroblast growth factor, SBSES = Stony Brook Scar Evaluation Scale, TA = triamcinolone acetonide.

Keywords: circumcision stapler, growth factors, penile redundancy, scar, triamcinolone acetonide

1. Introduction

The global prevalence of circumcision has witnessed a steady increase in recent years, driven in part by the United Nations' active promotion of the procedure in regions with high HIV prevalence.[1–4] However, notable variations in adult circumcision rates are observed across different countries and regions. The primary indications for circumcision encompass

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The authors have no conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

All patients were fully informed of the study's risks and provided written informed consent. The study protocol received ethical approval from the Institutional Review Board of The First People's Hospital of Kunshan City (2023-03-017-K01).

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phimosis, recurrent balanoposthitis secondary to redundant prepuce, and religious or cultural practices. Studies have indicated that patient satisfaction following circumcision is relatively low, at approximately 60%, and penile appearance can influence sexual function.[5–7] Factors contributing to patient satisfaction include variations in surgical techniques, postoperative wound dehiscence, local infection, and the extent of scar formation. Scarring, in particular, not only compromises the cosmetic appearance of the incision but can also negatively impact sexual quality of life, potentially leading to pain during erection. A recent study conducted in developed countries indicated that approximately 100 million individuals are affected by scarring and related complications annually.[8] The incidence of scar formation following circumcision is approximately 30%. Among individuals who develop incisional scars after circumcision with a disposable circumcision stapler device (DCSD), the proportion of moderate to severe scar hyperplasia is higher compared to those undergoing traditional surgical techniques. Patients frequently experience heightened anxiety regarding surgeries involving the genitals compared to analogous procedures in other anatomical locations. Although topical application of recombinant bovine basic fibroblast growth factor (rb-bFGF) after traditional circumcision can promote wound healing and inhibit scar formation, its efficacy has been shown to be inconsistent and limited to wounds without active inflammation.[9,10] Local administration of triamcinolone acetonide (TA) has been shown to suppress the release of various pro-inflammatory cytokines and growth factors. Intralesional injection of TA following circumcision has demonstrated significant short-term efficacy in scar reduction, but its use as monotherapy is often associated with local adverse effects and a higher risk of recurrence.[11,12] Therefore, this study aimed to investigate the feasibility of combining TA and exogenous rb-bFGF after circumcision using a DCSD to leverage their synergistic effects, potentially achieving both effective scar suppression and a reduction in TA-related adverse effects, ultimately minimizing the incidence of postoperative complications.

2. Materials and methods

2.1. General information

This study enrolled patients who underwent circumcision using a stapler device at the Department of Urology of our hospital between September 2023 and June 2024. All participants were informed of the potential risks and benefits associated with the study and provided written informed consent prior to enrollment. The study protocol was approved by the Institutional Review Board of our hospital (approval number: 2023-03-017-K01). Inclusion criteria were: age 18 years to 60 years; diagnosis of phimosis (defined as a tight preputial orifice and inability to retract the foreskin) or redundant prepuce; a minimum follow-up of 3 months postoperatively; and availability of complete medical records and contact information. Exclusion criteria were: loss to follow-up or withdrawal of consent; significant organ dysfunction or immunodeficiency; presence of other penile conditions (e.g., phimosis combined with hypospadias, penile deformity, or balanoposthitis); and history of keloid scarring.

2.2. Sample size calculation and randomization

The primary outcome measure of this study was the overall incidence of postoperative surgical site complications. Sample size calculation was performed using the formula for comparing 2 proportions with equal sample sizes: $n_1 = n_2 = 2\ [(Z\_(\alpha/2) + Z\_\beta)/(\pi_1 - \pi_2)]^2\ \pi(1 - \pi)$, where $\alpha = 0.05$ (two-sided) and $\beta = 0.10$. Based on previous data and experience, the calculated sample size was 86 patients per group. To account for potential patient dropout due to various reasons during the study, and to minimize errors, ensure sufficient statistical power, and enhance the validity of the conclusions, a 10% dropout rate was considered. Therefore, a total of 192 patients (96 per group) were enrolled. Randomization was conducted using a random number table, with allocation performed by an independent statistician based on a pre-generated random sequence.

2.3. Surgery and intervention measures

All surgeries were performed by experienced urologists, who underwent standardized training prior to the start of the study to ensure consistency in surgical techniques. Both groups underwent circumcision using a stapler device under local anesthesia, achieved with lidocaine spray applied 20 minutes prior to the procedure. The operation steps are as follows: routine skin preparation, disinfection, and draping; selection of an appropriate stapler device based on penile diameter; application of hemostatic forceps to the redundant prepuce, placement of the bell over the glans penis, fixation of the redundant prepuce to the traction rod with a tie, insertion and rotation of the stapler device followed by removal of the safety lock; and simultaneous compression of the handles to complete the circumcision and anastomosis. Postoperatively, all patients received a 3-day course of oral antibiotics. In the observation group, precut gauze strips, the bell, and the staple cartridge of the stapler device were soaked in a 2 mg/mL TA solution prior to surgery. Following circumcision, the TA-soaked gauze strips were applied over the staple line and covered with a sterile dressing. On the first postoperative day, the dressing was removed after the application of lidocaine solution for 3 minutes. The gauze strips were then removed, and rb-bFGF was sprayed onto the staple line (Fig. 1). Subsequently, the dressing was changed and the gauze strips were removed every other day, with rb-bFGF sprayed onto the staple line twice daily until complete wound healing was achieved. In the control group, saline-soaked gauze strips were applied over the staple line and covered with a sterile dressing after circumcision. The dressing was changed on the first postoperative day in the same manner as the observation group. Subsequently, the wound was disinfected with povidone-iodine solution twice daily until complete wound healing was achieved. All medications were prepared under standardized conditions and stored in an appropriate environment to ensure their potency and efficacy.

2.4. Observation index

This study assessed several outcome measures, including wound healing time, defined as the number of days required for complete wound healing. Postoperative edema was assessed and categorized as none, mild, moderate, or severe based on the degree of elevation of the surrounding tissues and the presence or absence of skin wrinkles. Staple detachment was evaluated by recording the time to first and complete detachment, as well as the complete detachment rate. Scarring was assessed at 3 months postoperatively using the Sawada Scar Scale and the modified Stony Brook Scar Evaluation Scale (SBSES).[13–15] The Sawada Scar Scale evaluates scar color, height, pliability, vascularity, and pigmentation, assigning a corresponding grade. The SBSES assesses scar width, height, color, and incision line characteristics, with higher scores indicating less noticeable scarring. The incidence of significant wound exudate was also noted, and patient satisfaction with penile cosmesis was assessed using a questionnaire. All evaluators underwent standardized training prior to the start of the study, covering scale scoring criteria and evaluation methods.

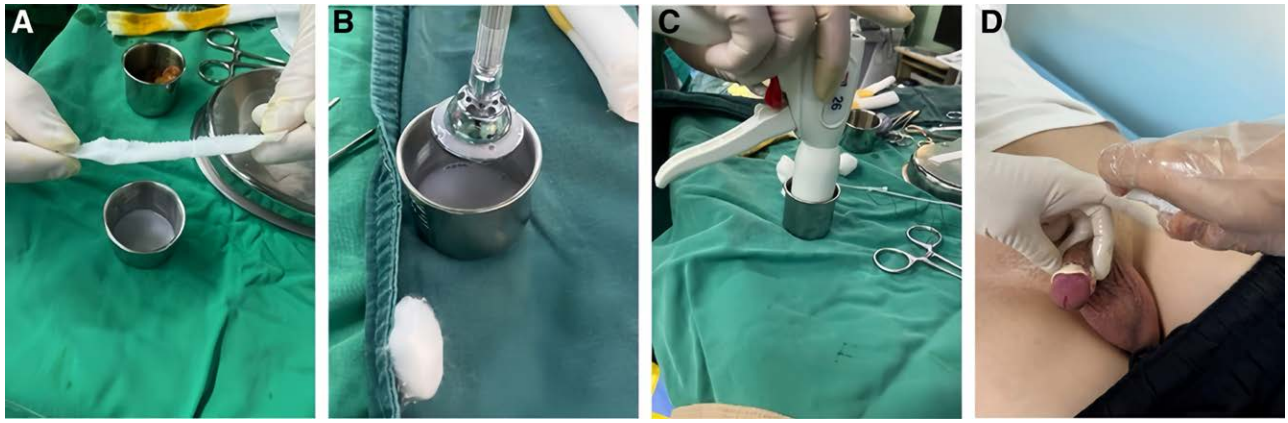

Figure 1. Interventions applied to the observation group. (A) Small gauze strips soaked in TA solution. (B) Bell-shaped covers soaked in TA solution, with nail slots filled with the solution. (C) Stapler cartridge immersed in TA solution. (D) Surgical incision sprayed with rb-bFGF postoperatively. rb-bFGF = recombinant bovine basic fibroblast growth factor, TA = triamcinolone acetonide.

A blinded approach was used to assess scars, ensuring that evaluators were unaware of the patients' group assignments during the evaluation.

2.5. Statistical analysis

Data were analyzed according to the per-protocol principle using SPSS version 27.0 software. Continuous variables are presented as mean ± standard deviation. Between-group comparisons for normally distributed data were performed using independent-samples *t* tests, while non-normally distributed data were compared using the Mann–Whitney *U* test. Categorical variables are presented as frequencies (percentages) and were compared using the chi-square test or Fisher's exact test, as appropriate. Ordinal data were compared between groups using the Mann–Whitney *U* test. Statistical significance was set at a $P < .05$.

3. Results

Initially, 215 individuals were screened for eligibility in this study. Ultimately, 192 participants meeting the inclusion criteria and providing informed consent were enrolled. The recruitment flowchart is presented in Figure 2. In the control group, 2 participants were lost to follow-up and consequently classified as dropouts, while one participant was excluded due to the self-administration of concomitant scar treatment medications. One participant in the observation group was lost to follow-up and subsequently excluded. Therefore, the final analysis included 95 participants in the observation group and 93 participants in the control group (Fig. 2). The mean age was 29.10 ± 7.17 years in the observation group and 29.75 ± 9.27 years in the control group. The mean BMI was 23.63 ± 2.65 in the observation group and 23.56 ± 2.88 in the control group. There were no statistically significant differences in age or BMI between the 2 groups ($P > .05$).

[1] Wound Healing Time: All patients in both groups achieved complete wound healing. In the observation group, 91 patients achieved Grade A healing and 4 achieved Grade B healing, with a mean healing time of 9.58 ± 1.70 days. In the control group, 90 patients achieved Grade A healing and 3 achieved Grade B healing, with a mean healing time of 12.14 ± 1.14 days. Although there was no significant difference in healing grade between the 2 groups, the observation group demonstrated significantly faster healing ($P < .05$).

[2] Postoperative Edema: No significant differences in edema severity or incidence were observed between the 2 groups during the first 3 postoperative days. However, on postoperative days 7 and 10, the control group exhibited significantly higher edema scores and incidence compared with the observation group ($P < .05$) (Table 1).

[3] Staple Detachment: All patients in both groups achieved complete staple detachment. There was no significant difference in the time to first staple detachment between the 2 groups; however, the observation group demonstrated a significantly shorter time to complete detachment and a higher rate of complete detachment ($P < .05$) (Table 2).

[4] Postoperative Scar Healing and Patient Satisfaction at 3 Months: Postoperative assessments at 3 months revealed significant advantages in the observation group compared with the control group. Specifically, the observation group demonstrated significantly less scar hyperplasia, improved surgical incision quality, significantly higher SBSES scores for cosmetic appearance, and significantly higher satisfaction scores and overall satisfaction rates regarding penile appearance (all $P < .05$) (Table 3).

[5] Combined Safety and Wound Exudation Evaluation: The combined use of triamcinolone acetonide and recombinant bovine basic fibroblast growth factor appeared safe for the treatment of surgical incisions following DCSD circumcision, with no local or systemic adverse events observed in either group. Although the incidence of severe wound exudation (associated with Grade B healing) was slightly higher in the observation group (4 cases) compared with the control group (3 cases), this difference was not statistically significant.

4. Discussion

Despite advancements in surgical techniques and devices that have contributed to a reduction in the incidence of complications associated with circumcision, challenges such as postoperative edema, scar formation, and staple detachment remain. Studies have indicated that patients' primary preoperative concern is safety, with concerns shifting postoperatively to wound-related issues, including wound healing, scarring, staple detachment, penile appearance, and pain during dressing changes.[2,5] Incomplete staple detachment is a significant concern for patients undergoing DCSD circumcision, as it can adversely affect penile cosmesis and, in severe cases, result in pain during erection and intercourse. Staples that fail to detach spontaneously necessitate manual removal in an outpatient setting, a procedure often associated with pain due to the absence of specialized removal tools.[7] Studies and our institutional data indicate that the rate of incomplete staple detachment after adult

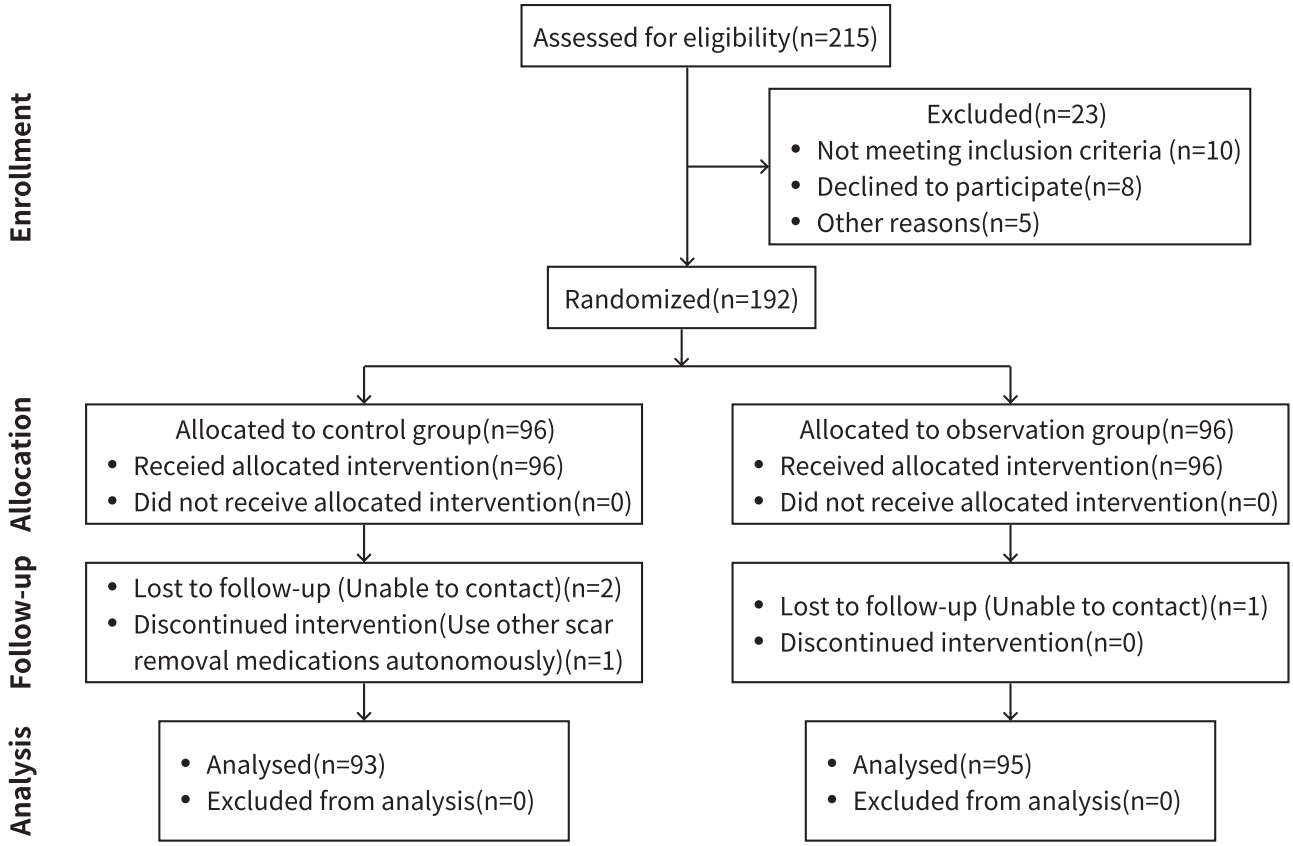

Figure 2. Participants' flow chart.

Table 1

Comparison of postoperative edema severity and incidence between the 2 groups

Postoperative time	Degree of edema	Observation group (n = 95)	Control group (n = 93)	Z/χ^2	*P* value
Day 3	No Edema	16 (16.8%)	14 (15.1%)	0.112	.738
	Mild	51 (53.7%)	39 (41.9%)	1.731	.084
	Moderate	24 (25.3%)	31 (33.3%)		
	Severe	4 (4.2%)	9 (9.7%)		
Day 7	No Edema	39 (41.1%)	25 (26.9%)	4.203	.040
	Mild	39 (41.1%)	37 (39.8%)	2.667	.008
	Moderate	16 (16.8%)	27 (29.0%)		
	Severe	1 (1.1%)	4 (4.3%)		
Day 10	No Edema	56 (58.9%)	37 (39.8%)	6.903	.009
	Mild	32 (33.7%)	44 (47.3%)	2.632	.009
	Moderate	7 (7.4%)	12 (12.9%)		
	Severe	0 (0%)	0 (0%)		

Categorical data were compared between groups using the chi-square test, while ordinal data were compared using the Mann–Whitney *U* test.

DCSD circumcision is approximately 20%.[16] The mechanism of staple detachment is thought to be related to a cutting effect between the staple and the healed skin, primarily influenced by the device itself and postoperative inflammation, rather than surgical technique. The severity of scar formation after DCSD circumcision is strongly correlated with the duration of staple retention. Staples, acting as foreign bodies, can exacerbate the inflammatory response and foreign body reaction at the incision site, thereby increasing the risk of infection and promoting the formation of extracellular matrix. This, in turn, hinders staple detachment, leading to a vicious cycle. In this study, the control group exhibited a significantly longer average staple detachment time and a higher incidence of scarring compared to the observation group. The observation group demonstrated significantly lower scar severity and incidence, with no cases of severe hypertrophic scarring observed. Conversely, 2 cases of severe hypertrophic scarring occurred in the control group, necessitating surgical excision and revision of the circumcision. The favorable outcomes in the observation group may be attributed to the early application of local TA to suppress inflammation and reduce extracellular matrix formation, as well as the protective effect of topical rb-bFGF on the wound. This low-inflammatory environment likely contributed to a reduced risk of infection and accelerated wound healing. Furthermore, recognizing the heightened sensitivity of the circumcision wound and the potential for pain during dressing changes due to medication irritation, which could negatively affect patient compliance and potentially lead to bleeding and wound dehiscence, we utilized lidocaine solution soaks prior to dressing changes to minimize discomfort and facilitate easier removal of the gauze.

Table 2

Comparison of staple removal time and complete staple removal rate between the two groups.

Group	Observation group	Control group	t/χ^2	*P*-value
Time to first nail removal (d)	7.46 ± 1.36	7.12 ± 1.43	1.696	.092*
Time to complete nail removal (d)	18.34 ± 2.55	25.74 ± 2.26	−10.423	<.001†
Complete nail removal rate [n (%)]	95.40%	74.60%	38.72	<.001‡

* Continuous variables were analyzed using the independent-samples *t*-test if normally distributed.

† Continuous variables were analyzed using the Mann–Whitney *U* test if non-normally distributed.

‡ Categorical variables were analyzed using the chi-square test.

Table 3

Comparison of scar characteristics and patient satisfaction between the two groups at 3 months postoperatively.

Outcome measure	Observation group (n = 95)	Control group (n = 93)	Statistic	*P*-value
Scar severity at 3 mo			$z = 3.881$	.000‡
Smooth	84 (88.4%)	60 (64.5%)		
Mild	8 (8.4%)	22 (23.7%)		
Moderate	3 (3.2%)	9 (9.7%)		
Severe	0 (0%)	2 (2.2%)		
SBSES	7.56 ± 1.14	7.02 ± 1.50	$z = -3.218$	.001†
Satisfaction with penile appearance			$z = 3.310$	.001‡
Unsatisfied	1 (1.1%)	11 (11.8%)		
Basically satisfied	22 (23.2%)	31 (33.3%)		
Very satisfied	72 (75.8%)	51 (54.8%)		
Satisfaction rate with penile appearance	98.9%	88.2%	$\chi^2 = 9.131$	.003*

* Categorical data for between-group comparisons were analyzed using the Chi-square test.

† For ordinal data, the independent samples *t*-test was employed for normally distributed data, while the Mann–Whitney *U* test was used for non-normally distributed data.

‡ The Mann–Whitney *U* test was used to compare grade data.

Corticosteroids, particularly glucocorticoids, are considered the first-line therapy for scar prevention and management. Glucocorticoids exert significant anti-inflammatory effects throughout the wound healing process. In the early inflammatory phase, they increase local microvascular tone, reduce capillary permeability, and decrease the release of cell adhesion molecules and cytokines, effectively mitigating inflammatory exudation and edema.[17] TA, a synthetic long-acting corticosteroid, is frequently used clinically for scar treatment. A previous study demonstrated the efficacy of prophylactic intralesional TA injection in preventing scar formation after penile scar excision.[18] However, this study was limited by its small sample size, lack of a control group, and exclusive focus on post-scar excision application. Moreover, local TA injection can lead to adverse effects such as hypopigmentation, hyperpigmentation, atrophy, and even impaired wound healing. These adverse effects are potentially attributed to the suppression of both positive and negative regulators of scar formation, hindering local microvascular formation, as well as individual patient sensitivity and unintentional injection into surrounding healthy tissue. Therefore, researchers recommend combining TA with other preventative measures to mitigate these adverse effects. The concentration of the drug and the method of administration are crucial factors in minimizing adverse reactions. This study employed a novel approach of applying a 2 mg/mL TA solution via local wet compresses following circumcision with a stapler device to reduce the incidence of wound complications. This method was chosen because the staples act as conduits, guiding the medication directly to the wound edges, achieving a localized effect comparable to injection while minimizing uneven drug distribution and leakage into surrounding healthy tissue. Currently, there is no consensus on the optimal concentration of TA solution for local injection in scar prevention and treatment. Based on established guidelines and relevant literature, this study utilized a concentration of 2 mg/mL, aiming to balance therapeutic efficacy with minimal disruption to normal wound healing. TA exerts its effects within hours of application, reaching peak efficacy within 1 to 2 days, and maintaining its effects for 2 to 3 weeks.[19]

Although TA is widely used in clinical practice, its efficacy varies significantly, with reported scar regression rates ranging from 50% to 100%. However, recurrence rates remain high, approximately 33% at 1 year and up to 50% at 5 years.[20,21] Moreover, the side effects of TA limit its long-term application. Studies have shown that combining TA injections with surgical excision of keloid scars does not significantly reduce the recurrence rate of keloids, with a pooled risk difference of 0.06 (95% CI, −0.16 to 0.28).[22] To mitigate the potential adverse effects of corticosteroids on the skin, this study incorporated the use of exogenous growth factors. The fibroblast growth factor family comprises 23 members, with basic fibroblast growth factor being one of the most extensively studied and possessing a wide range of biological activities. Basic fibroblast growth factor promotes tissue remodeling and wound healing by regulating angiogenesis and cell mitosis. Research has demonstrated that TA solution can stimulate basic fibroblast growth factor secretion from fibroblasts and reduce transforming growth factor-β1 production in vitro, contributing to its anti-scarring effects.[23] We believe that the combined application of TA and rb-bFGF offers significant complementary advantages. TA rapidly suppresses inflammatory responses and collagen synthesis, effectively controlling the early development of scars. Meanwhile, rb-bFGF promotes angiogenesis and tissue regeneration, accelerating wound healing and repairing damaged tissue. This combined strategy may help reduce the dosage and frequency of TA, thereby minimizing its side effects and ultimately improving therapeutic outcomes. Fu et al's study demonstrated that rb-bFGF intervention enhances wound healing rates and reduces the expression of inflammatory factors such as TNF-α and IL-6, further supporting the role of rb-bFGF in promoting wound healing.[24] Therefore, this study employed a combined treatment approach: soaking the staples and staple cartridge in TA solution during surgery, followed by the immediate application

of TA solution wet compresses to the penile wound post-circumcision. Given the rapid onset and sustained action of TA, the TA-soaked gauze was removed on the second postoperative day, after which topical rb-bFGF spray was applied to supplement exogenous basic fibroblast growth factor and further reduce the incidence of wound complications.[25]

While stapler circumcision offers advantages, the prevention and management of subsequent scar formation remain a challenge with limited evidence-based strategies. This study investigated a novel approach incorporating TA and rb-bFGF for post-stapler circumcision care, emphasizing a proactive "prevention over treatment" paradigm. Our findings demonstrate a statistically significant reduction in mean staple detachment time and scar formation incidence in the intervention group compared to the control group. Notably, no severe hypertrophic scarring was observed in the intervention group, while 2 patients in the control group developed severe hypertrophic scars necessitating surgical excision. Moreover, patient satisfaction with penile appearance was significantly higher in the intervention group. These preliminary results suggest that intraoperative soaking of the stapler device and cartridge in TA solution, coupled with post-operative application of TA solution compresses and topical rb-bFGF, may effectively promote wound healing, potentially reducing postoperative edema, accelerating staple detachment, and enhancing patient satisfaction.

However, this study has several limitations, including a relatively small sample size, potential biases due to subjective outcome assessments, and the possibility that variations in age and BMI among participants may have confounded the results. Despite these limitations, the positive outcomes observed in this trial support further investigation. Future studies should focus on larger, multi-center trials to confirm these findings and assess the influence of surgical techniques, postoperative wound care protocols, local infection rates, patient age at the time of circumcision, and BMI on satisfaction with penile appearance. These findings could contribute to the development of personalized surgical and postoperative care strategies aimed at improving the quality of life for patients undergoing circumcision.

5. Conclusion

This study provides evidence that the combined application of TA and rb-bFGF offers significant advantages in reducing edema, promoting wound healing, minimizing scar formation, and ultimately improving patient satisfaction following adult stapler circumcision. These findings merit further investigation to confirm their long-term efficacy and safety, as well as to establish the optimal treatment protocol for this combined therapy.

Author contributions

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Software: Yunlong Li.
Supervision: Bing Wang, Yunlong Li.
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Visualization: Yang Yuan, Shihao Zhang, Dingli Hu, Yunlong Li.
Writing – original draft: Yang Yuan, Shihao Zhang, Yunlong Li.
Writing – review & editing: Yang Yuan, Shihao Zhang, Yunlong Li.

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