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Prospective Randomized Trial

The role of 2-octyl cyanoacrylate in prevention of penile adhesions after circumcision: A prospective, randomized trial

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ABSTRACT

Purpose: Penile adhesions are the most common complication after circumcision, although strategies to decrease them are poorly studied. We conducted a prospective, randomized trial comparing the use of 2-octyl cyanoacrylate (glue) skin adhesive to hydrophobic ointment after circumcision.
Methods: Patients <7 years old undergoing circumcision were randomized to glue around the sutures and corona of the penis or antibiotic ointment. The primary outcome variable was postoperative penile adhesions. Utilizing a power of 0.8 and an alpha of 0.05, 168 patients were calculated for each arm. Because of high attrition, we planned to include up to 500 patients. Presence/absence of adhesions was evaluated 2–4 weeks postop. Parents subjectively scored happiness, comfort, distress, and concern on a Likert scale 1–5.
Results: From 11/2012 through 7/2016, 409 patients were enrolled. Adhesion data were available on 243 patients. There was no difference between glue (16.8%) and those with antibiotic ointment (15.2%) ($p = 0.88$) or in parental satisfaction across all areas measured. 165 patients were lost to follow-up, evenly distributed between the two groups (38% vs. 42%, $p = 0.49$).
Conclusion: The placement of 2-octyl cyanoacrylate skin adhesive does not decrease the rate of postoperative penile adhesions after circumcision. Parent satisfaction outcomes are similar.
Type of study: Treatment study.
Level of evidence: Level II.

Circumcision is one of the most common procedures performed around the world [1]. The most common complication after circumcision is penile adhesions followed by bleeding, infection, incomplete circumcision, excessive skin removal, recurrent phimosis, epithelial inclusions cysts and meatal stenosis [1].

There are two etiologies of postoperative adhesions. First is incomplete release of the natural adhesions, which is rare with freehand circumcisions. The second occurs when the raw surfaces on the glans and preputial collar fuse postoperatively [1]. These may be treated with steroids, in office adhesiolysis, or may require another procedure [2–5].

The most recent circumcision opinion from The American Academy of Pediatrics (AAP) comments that the rate of postcircumcision complications, including adhesions, is largely unknown because of the paucity of literature on the subject, and variability in the reported adhesion rate [1].

In our institution, some surgeons have utilized skin glue placed on the sutures and corona of the penis after circumcision in an attempt to prevent adhesions. To date there has been no literature on the use of 2-octyl cyanoacrylate skin glue to prevent recurrent adhesions after circumcision. The objective of this study is to evaluate whether application of 2-octyl cyanoacrylate skin adhesive decreased the incidence of adhesions after circumcision. We hypothesized that the incidence of adhesions will be decreased with use of 2-octyl cyanoacrylate skin adhesive. The secondary objective was to assess parent satisfaction and comfort level after circumcision with and without the use of 2-octyl cyanoacrylate skin adhesive.

1. Methods

Approval was obtained from the institutional review board (IRB #1290443) prior to enrolling patients in this study. Children were subsequently enrolled after obtaining informed permission from the legal guardian. Assent was waived as all patients included were younger than 7 years and therefore unable to assent. The enrollment process occurred prior to the time of the operation. The permission forms and consent process were audited by the IRB on a continuing basis. The

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study was registered with clinicaltrials.gov in February, 2013 (NCT01794221). There was no funding.

1.1. Participants

The study population consisted of males younger than 7 years undergoing elective operative circumcision. Those found to have had a previous circumcision or attempted circumcision, those undergoing plastibell circumcision, or those found to have an anatomic anomaly such as hypospadias or chordee at the time of the operation were excluded. Non-English speaking patients were also excluded.

1.2. Interventions

All operations were performed by 1 of the 8 institutional staff surgeons and booked electively via the clinic or from the neonatal intensive care unit. All were either freehand circumcisions or performed using the Gomco clamp. All were performed with use of an absorbable monofilament suture to reapproximate the preputial collar to the shaft skin. If the patient was randomized to placement of 2-octyl cyanoacrylate (GLUE group), then the skin adhesive was applied at completion of the circumcision. If the patient was randomized to no placement of 2-octyl cyanoacrylate (NO GLUE group), then skin adhesive was not placed at completion of the circumcision, and bacitracin ointment used.

1.3. Sample size

This was a superiority trial using postoperative penile adhesions as the primary outcome. Secondary outcomes evaluated were parental satisfaction, postoperative complications, and unplanned admission rate. Parental satisfaction included data regarding parents' satisfaction with circumcision appearance, parent comfort with postoperative care, parent distress caring for the circumcision and parent concern with further issues with the circumcision.

Power calculations were based on an estimated incidence of 15% for penile adhesions after circumcision, based on previous institutional experience. We hypothesized a decrease in the incidence of recurrent adhesions of 5% for patients in the GLUE group. Using these numbers with an $\alpha = 0.05$ and a power of 0.8, we calculated a sample size of 336 patients with 168 patients in each study arm. Given an expected high attrition rate we planned on enrolling up to 500 patients.

1.4. Assignment

A computer generated individual unit of randomization was utilized in a nonstratified sequence in blocks of four. After consent for study enrollment was obtained, a sequentially numbered opaque envelope was accessed to obtain the next allotment, ensuring allotment concealment. All data were analyzed on an intention-to-treat basis, and patients remained in their assigned group.

1.5. Protocol

Preoperative evaluation was performed in surgery or urology clinic, or the neonatal intensive care unit by pediatric surgeons, pediatric urologists, fellows or allied health professionals. Patient's parents were approached for study enrollment on the day of surgery, and randomization occurred prior to the operation. Parents of patients in the GLUE group were instructed not to place any topical ointments until the skin adhesive had flaked off, and to begin routine care with retractions of the foreskin with each diaper change thereafter. If the patient was randomized to the NO GLUE group then parents were instructed in routine care with retractions of the foreskin with each diaper change and application of antibiotic ointment. Other routine preoperative and postoperative care was the same in both groups. Follow-up appointments were made at the time of the operation and instructions given to the parents postoperatively and included in the discharge documentation. At the time of follow-up, the patient is evaluated by a nonblinded pediatric surgeon, pediatric urologist, fellow or allied health personnel dedicated to pediatric surgery and urology. Penile adhesions were defined as the presence of any bands of thin or thick tissue between the preputial collar and glans obliterating the coronal sulcus from view at the site of the tissue band.

1.6. Data collection

Two research coordinators who had no role in the clinical care, collected all data prospectively. Demographics collected included age, weight, height, and BMI. Concurrent procedures, operative time, postoperative complications, unplanned readmissions, recurrent adhesions and parents' satisfaction were also recorded. Recurrent adhesions were documented at the time of follow-up using a data collection form addressing presence of adhesions, location of adhesions on a provided clock face, and ability of adhesions to be manually reduced. Parental compliance with postoperative manual foreskin retractions and parental satisfaction were evaluated with a survey provided to the parents at the time of follow-up visit. Parental satisfaction was evaluated using a 5 point Likert scale. In patients lost to follow-up, an attempt to obtain parental satisfaction data was made by administering the satisfaction survey via telephone, however adhesion data were not collected unless the patient was physically evaluated by a surgical team member at follow-up.

1.7. Statistics

All data were analyzed on intention-to-treat basis. Descriptive statistics including means, standard deviations, medians, interquartile ranges, counts, and percentages were analyzed. Continuous variables were compared using Student's 2-sample t-test and Mann–Whitney U test. Discrete variables were compared using chi square test with Yates correction, or Fisher Exact test where appropriate. Statistical significance was set at $p < 0.05$, and all reported p values are two-tailed.

2. Results

From November, 2012 to September, 2017, 409 boys were enrolled in the study and randomized to either receive 2-octyl cyanoacrylate or no 2-octyl cyanoacrylate (Fig. 1). During this time frame, 1282 patients were identified to have undergone circumcisions. Six hundred fifteen patients' parents were considered for enrollment in the study. Nineteen declined to participate. One hundred eighty-seven patients did not meet inclusion criteria. Six hundred eighty-six patients were not approached for enrollment because of guardianship issues, inability or unwillingness to follow-up, their planned follow-up was at a satellite location, or planned plastibell circumcision. Two hundred three were allocated to the intervention arm and 206 to the nonintervention arm. One patient in the nonintervention arm received the intervention. In the allocation arm 78 patients were lost to follow-up, and in the nonallocation arm 87 patients were lost to follow-up. A total of 244 patients (125 in the GLUE arm and 119 in the NO GLUE arm) were analyzed.

2.1. Patient characteristics

Table 1 shows the demographics and hospital outcomes of the study population. There was no difference in age (17.6 ± 18.2 vs. 16 ± 15.2 months; $p = 0.35$) or weight (10.2 ± 4.5 vs. 9.9 ± 4.3 years; $p = 0.55$). Both groups had similar operative times (20 ± 9 vs 20 ± 13 min, $p = 0.55$) and early complication rates (10% vs 8%, $p = 0.75$). There was no difference in compliance rate for manual retractions (76% vs. 88%, $p = 0.28$) or length of follow-up (23 ± 18 vs 20 ± 15 days, $p = 0.31$).