

A Randomized, Controlled Trial Comparing a Tissue Adhesive With Suturing in the Repair of Pediatric Facial Lacerations

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Study objective: To compare the tissue adhesive Histoacryl Blue® with suturing in the repair of pediatric facial lacerations.

Design: Prospective, randomized controlled trial.

Setting: Emergency department of a pediatric teaching hospital.

Participants: Eighty-one children presenting with clean facial lacerations less than 4 cm in length and 0.5 cm in width.

Interventions: Patients were allocated randomly to have their lacerations repaired with sutures or Histoacryl Blue®.

Results: The two groups were similar for demographic and clinical characteristics. Photographs taken at three months were rated by two plastic surgeons blinded to the method of closure. There was no difference between groups for appearance scores on a visual analog scale (60.5 mm for Histoacryl Blue® versus 57.2 mm for suture, $P = .45$) or on a categorical scale (Histoacryl Blue® versus sutures: unacceptable, 11% versus 13%; acceptable, 59% versus 71%; excellent, 30% versus 16%; $P = .76$). Measures of observer agreement produced Pearson correlations of .72 and .94 on the visual analog scale and κ coefficients of .46 and .73 on the categorical scale. Histoacryl Blue® was assessed as less painful on a visual analog scale (24.7 versus 43.7 mm, $P < .01$) and faster (7.9 versus 15.6 minutes, $P < .001$).

Conclusion: Histoacryl Blue® is a faster and less painful method of facial laceration repair that has cosmetic results similar to the use of sutures.

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INTRODUCTION

Lacerations are one of the most common pediatric problems seen in emergency departments.¹ Although sutures have been the standard means of laceration closure, there are a number of undesirable features associated with their use. Suturing requires the use of a local anesthetic, the injection of which is painful.² The use of instruments and a needle may further frighten an already traumatized child, and this can lead to a negative interaction with the medical profession and may have an impact on future visits.³

The topical agents tetracaine, adrenaline, and cocaine (TAC) and an eutectic mixture of local anesthetics (EMLA) have been investigated as a means of minimizing the pain of local anesthetic infiltration but are time consuming in their application, and the use of EMLA in open wounds has been questioned because of altered wound healing.^{4,5} Alternatives to suturing exist but are not free of limitations. Staples can be placed more quickly than sutures but an anesthetic is still necessary, and they cannot be used in wounds in which cosmesis is critical. Adhesive tapes are quick and easy to use but are appropriate only for superficial wounds with easily apposable edges and are limited to broad, flat, hairless body surfaces.⁶

Clearly, a method of laceration closure that is relatively painless and that does not require local anesthetic would be desirable. The closure should be fast and nontraumatic, be associated with a low incidence of dehiscence and infection, and, most important, should yield acceptable cosmetic results. The tissue adhesive *N*-2-butylcyanoacrylate (Histoacryl Blue®) may provide such a method. Two recent case series reported favorably on the use of Histoacryl Blue® in the management of lacerations in children.^{7,8} Despite being commercially available in Canada for many years, the adhesive still has not been accepted as a routine method of laceration closure.⁹ Therefore, our objective was to compare the cosmetic outcome of pediatric facial lacerations closed with sutures with those closed with Histoacryl Blue®.

MATERIALS AND METHODS

Fifteen physicians at the Children's Hospital of Eastern Ontario, a pediatric teaching hospital and referral center, participated in the study. These physicians consisted of house staff of various levels of training who were working in the ED during the study period. All 15 physicians attended a brief training session given by the chief investigator or study nurse, during which they were informed

of the study protocol and were instructed on the application of Histoacryl Blue®.

We considered for entry into the study any child, from newborn to age 18 years, presenting to the ED with clean facial lacerations that met the following criteria: length less than 4 cm, width less than 0.5 cm, and not requiring deep layer closure. Wounds caused by animal bites, lacerations on hair-bearing surfaces or crossing mucocutaneous junctions, and heavily soiled wounds requiring debridement were excluded from the study. The study period was from May 1, 1991, to July 15, 1991, between noon and 10:00 PM. The study received approval and support of the Ethics Committee and the Research Institute of the Children's Hospital of Eastern Ontario.

Informed consent was acquired for all patients, who then were randomly allocated to have their wounds repaired with Histoacryl Blue® or sutures. Lacerations randomized to the suture group were anesthetized with 1% lidocaine and were closed with 5-0 or 6-0 non-absorbable monofilament sutures under sterile conditions, using chlorhexidine as a cleansing solution. Lacerations in the Histoacryl Blue® group were cleansed with chlorhexidine, and hemostasis was achieved with dry gauze and pressure. Gloves were used, and the wound edges were apposed manually in a desirable fashion. A thin film of the tissue adhesive then was applied on the apposed edges. Manual approximation of the wound was maintained for 30 seconds until full polymerization had taken place. Wounds in both groups were covered with an Elastoplast® bandage. Patients and parents were asked to keep the wound dry for at least three days and to return to the ED on day 5 after repair for either suture removal or a wound check. The management of infection was determined by individual physicians. Dehiscence was managed by delayed primary closure.

Parents were asked to fill out a data information sheet and to rate the pain intensity that they perceived their child had experienced during the procedure. This was done using a visual analog scale that consisted of a 100-mm line with "No pain" at the right end of the line and "Worst pain" at the left end of the line.¹⁰ The parents were asked to mark on the line the amount of pain they thought their child was suffering during the procedure. The scale has been shown to be an accurate measure of pain in children when used by third parties.¹¹ Time of laceration repair was recorded by the study physicians and was recorded from when the physician donned gloves to repair the wound until the time when the bandage was applied. On day 5, after the repair, the presence or absence of erythema or discharge was observed and

FACIAL LACERATIONS

Quinn et al

recorded. The wound was considered infected if both were present. The presence of dehiscence also was noted and was defined as wounds requiring delayed primary closure.

Patients were contacted at three months by the study nurse who arranged for a photograph of the healed laceration. Photographs were taken in a standardized fashion by the audiovisual department or by the study nurse by home follow-up. The photographs of the scars at three months were reviewed by two plastic surgeons on two occasions. They were blinded to the method of closure and were asked to independently rate the healed lacerations on two recently developed appearance scales.

The scales, a categorical scale and a visual analog scale, have been demonstrated to be reliable and valid outcome measures of cosmesis.¹²⁻¹⁴ The visual analog scale is a 100-mm line with "Worst scar" at the right end of the line and "Best scar" at the left end. Using the line as a continuous entity, the surgeons were asked to mark on the line where they thought the scar fit. The categorical scale is a three-category scale for which the surgeons were provided criteria for ranking the wounds: an "unacceptable" scar was defined as a wide, unsightly, hypertrophic scar that was probably in need of revision or extended follow-up; an "adequate" scar was a clearly visible scar neither exceedingly wide nor hypertrophic that was acceptable in its present form; and an "excellent" scar was defined as faint or not evident.

Patient characteristics were compared as appropriate with the χ^2 and unpaired *t*-tests. The cosmetic outcomes at three months were considered the primary endpoints. The visual analog scale scores were compared with the unpaired *t*-test, and the categorical scale scores were compared with the Mann-Whitney test. Interobserver and intraobserver agreements were measured using the Pearson coefficient for the visual analog scale and κ coefficient for the categorical scale. Secondary outcomes included time of repair and pain (compared with unpaired

t-test) and proportion of patients with infection and wound dehiscence (compared with the χ^2 test).

RESULTS

Of 90 patients meeting entry criteria during the study period, 81 were enrolled into the study. The most common reasons for refusal to enter the study were the parents' unwillingness to commit to follow-up and concerns of their child being used as a study subject. Three patients were lost to early follow-up and six were unavailable for the three-month assessment, four in the Histoacryl Blue® group and two in the suture group. The Histoacryl Blue® group (41) and suture group (40) were similar for age (mean, 4.7 and 4.5 years; age range, 0.7 to 16 years and 0.5 to 15 years, respectively), sex (58% and 42% male, respectively), and length of laceration (mean length, 1.53 and 1.52 cm; length range, 0.5 to 3.5 and 0.5 to 3.5 cm, respectively).

There was no difference for cosmetic outcome at three months between the Histoacryl Blue® and suture groups on the visual analog scale (60.6 mm versus 57.2 mm, *P* = .45). The sample size afforded 80% power to detect a difference of as little as 9 mm between groups. Similarly, there was no difference in cosmetic outcome between groups on the categorical scale (Histoacryl Blue® versus sutures: unacceptable, 11% versus 13%; acceptable, 59% versus 71%; excellent, 30% versus 16%; *P* = .76) (Table 1). Both plastic surgeons showed good intraobserver and interobserver agreement (visual analog scale, .94 and .75; categorical scale, .72 and .46; 95% confidence interval, .57 to .89 and .27 to .66, respectively) for rating the cosmetic outcomes of the scars.^{13,14}

The treatment with Histoacryl Blue® was rated as less painful by parents (24.7 mm versus 43.7 mm; *P* < .01) and the application of the tissue adhesive took less time (7.9 minutes versus 15.6 minutes; *P* < .001) when

Table 1

Cosmetic outcomes at three months for the two study groups

	Histoacryl (N = 37)	Suture (N = 38)	<i>P</i>
Mean visual analog scale score (mm)	60.6	57.2	.45
Categorical scale score (%)			.76
Unacceptable	4 (11)	5 (13)	
Acceptable	22 (59)	27 (71)	
Excellent	11 (30)	6 (16)	

Table 2

Other outcomes for the two study groups

	Histoacryl (N = 37)	Suture (N = 38)
Mean pain intensity (mm)	24.7	43.7 [†]
Mean time of repair (min)	7.9	15.6 [‡]
Wound healing (%)		
Infection	1 (2.7)	1 (2.6)*
Erythema	1 (2.7)	4 (11.5)*
Dehiscence	3 (8.1)	2 (5.3)*

**P* = NS.
[†]*P* < .01.
[‡]*P* < .001.

FACIAL LACERATIONS

Quinn *et al*

compared with sutures (Table 2). Short-term follow-up revealed one infection in each group. The suture group had four wounds with erythema noted, whereas the Histoacryl Blue® group had one such wound. True complete dehiscence requiring delayed primary closure occurred three times in the Histoacryl Blue® group and twice in the suture group. Physical trauma was the cause of dehiscence in two Histoacryl Blue® wounds and in one of the suture wounds. One wound from each of these subgroups received a poor categorical scale score.

DISCUSSION

The cyanoacrylates were discovered in 1949, and the first reported use of these agents as adhesives was described ten years later.¹⁵ They are created through the reaction of cyanoacetate with formaldehyde, with variations in the alkyl group resulting in different compounds of the cyanoacrylate family. The cyanoacrylates are liquid monomers, similar to water in their appearance and viscosity. When exposed to water, they polymerize rapidly, releasing heat in the process. The cyanoacrylates are thought to degrade through hydrolysis, the rate of which is determined by the length of the alkyl chain.¹⁶ Studies using radioactively labeled cyanoacrylates have shown that small amounts are absorbed through the skin and excreted in the urine.^{17,18}

Extensive experience with the cyanoacrylates exists in many surgical fields. They have been used on skin, bone and cartilage grafts, middle ear surgery, repair of cerebrospinal fluid leaks, and repair of corneal ulcers.¹⁹⁻²² Methyl-2-cyanoacrylate was initially the most widely used compound, but in the early 1970s its histotoxicity was recognized and it is no longer used.²³ Longer alkyl chain derivatives were developed and were found to promote a smaller acute inflammatory response with faster polymerization. The optimal derivative has become Histoacryl Blue®, which has shown little or no histological difference with less inflammatory response when compared with sutures in cutaneous wound repair.^{24,25} Analysis of the use of Histoacryl Blue® for closing skin wounds has revealed no risk of carcinogenic potential.²⁶

Considerable clinical experience exists with Histoacryl Blue® in the management of skin wounds. Kamer *et al* closed 225 surgical facial wounds with Histoacryl Blue® and reported normal healing in all.²⁷ Other studies involving use of Histoacryl Blue® on surgical cutaneous wounds have shown similar results.²⁸⁻³⁰ All of these studies are limited, however, in that they lack control groups and blinded valid outcome measures.

Similar problems exist with reports on its use in ED. Mizrahi *et al*, from Israel, reported on their experience with the adhesive over a five-year period.⁸ Some 1,500 minor lacerations were closed, and very low dehiscence and infection rates (0.7% and 1.9%) were reported. No control group was compared and cosmetic outcome was not evaluated. Another series reported on its use on 50 scalp lacerations up to 6 cm in length. Five-day follow-up revealed no infections and only one small dehiscence that did not require further treatment.³¹ In a British study, Histoacryl Blue® was used to close facial lacerations in 50 patients.⁷ Forty of the 50 patients returned for follow-up three months later. The author claimed that the cosmetic results were "excellent" in 35 patients and reported five complications. There was no objective measurement of cosmesis and no control group.

Histoacryl Blue® is supplied in plastic vials containing 0.75 mL of the adhesive to which a dye, 1-hydroxy-4-*p*-toluidion-antrachion has been added to impart a blue color. Each vial costs approximately \$30.00 and is manufactured for a single use, although it has been suggested that one vial may be safely reused multiple times.^{8,28} In a technique described by Ellis,²⁸ the vial can be cut off at the hub and attached to a 25-gauge needle, which fits snugly. This allows for fine control of the application of the adhesive and prevents the application of surplus glue onto the wound. To avoid contamination, the needle is not to make contact with the wound and is changed with each application. This allows one to repair ten to 12 lacerations with each vial at an approximate cost of \$3.00 per patient. Histoacryl Blue® has been approved for use in Canada and has been available since 1975 with no adverse effects reported to date.⁹ The Food and Drug Administration in the United States has not yet approved its use.

We have demonstrated through a prospective, blinded, randomized controlled trial that no difference exists in the cosmetic outcomes of minor facial lacerations treated with Histoacryl Blue® or suturing. Significant effort went into developing reliable and valid scales for cosmesis before the study because no such outcome measures existed in the literature. The reliability coefficients of the scales in this study were excellent. The results are similar to those found when the scales were developed and were determined to be reliable and valid measures of cosmesis.¹² Plastic surgeons rated the scars because their opinions were considered to be the gold standard.

Pain as an outcome measure had some limitations in this study. The patients could not be blinded to the treatment groups, and this may have led to some bias. Some

parents also reported having difficulty using the visual analog scale because they were unable to distinguish pain from anxiety and fear, and although the visual analog scale has been used by parents to rate pain in children more than 7 years old, it may have been presumptuous to assume that this correlation exists for younger children.¹¹ Nonetheless, we believed that pain should be included as a secondary outcome measure because some discomfort has been reported with the use of Histoacryl Blue®. A burning sensation can be caused by the heat released during polymerization. This is a particular problem when hemostasis is not adequate and a large amount of glue is applied too quickly. Applying a large amount of glue also is not desirable for apposing wound edges. In this study, particular care was taken to achieve hemostasis before the application of the glue. As described earlier, we now recommend cutting the vial at the hub near its base and attaching a 27-gauge needle, which allows more control over the amount and speed of application of the adhesive. Despite the potential problems of reporting pain as an outcome, it is evident that the application of glue can be painless and is less painful than injecting local anesthetic, especially when these precautions are taken.

Of the 15 physicians involved in the study, none had prior experience with the use of the glue, although all were experienced with suturing. The application of the tissue adhesive is a manual skill that is likely to improve with practice. If we had provided a practice period so that all of the physicians in the study could have become technically proficient in the application of the adhesive, the cosmetic outcomes in the Histoacryl Blue® group may have been better.

Further investigation must be done to further elucidate which types of wounds can be closed with Histoacryl Blue®. The authors believe that the adhesive is adequate for closing clean, simple facial lacerations described in the study. The use of a local anesthetic should be used for wounds needing debridement, and adequate debridement must not be sacrificed where indicated for a quick and virtually painless closure. Histoacryl Blue® is bacteriostatic and causes less foreign body reaction and clinical inflammation than does suturing.^{21,25} It may be beneficial in closing dirty wounds after debridement, but further study is needed in this area. As well, further study is needed to determine on what areas Histoacryl Blue® may be used. We used it on low tension areas of the face, but dehiscence may become a problem when it is used in wounds under more tension. This did not appear to be a problem in a large case series by Mizrahi et al, but their methods, follow-up, and cases were not well described.⁸

CONCLUSION

Histoacryl Blue® provides a faster and less painful method of laceration closure than does the use of sutures. It yields similar cosmetic results when compared with suturing in the management of clean, simple facial lacerations in children, and we recommend its use in these circumstances.

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FACIAL LACERATIONS

Quinn et al

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