

Comparison of glues, sutures, and other commercially available methods of skin closure: A review of literature

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Abstract

Objectives: Octyl-2-cyanoacrylate (Dermabond) is a soft tissue adhesive that has been approved for topical use to close traumatic lacerations and surgical incisions. We review paediatric and adult human studies that compared octyl-2-cyanoacrylate with conventional closure techniques in a variety of wounds.

Methods: Medline were searched using a combination of 'tissue adhesives', 'cyanoacrylates', 'sutures', 'surgical staplers' and 'surgical tape' for paediatric and adult studies comparing skin adhesives with other methods of wound closure. A review was performed using search results screened using predetermined inclusion and exclusion criteria.

Results: We found and summarized 17 studies comparing octyl-2-cyanoacrylate skin glue to conventional methods of skin closure.

Conclusions: Octyl-2-cyanoacrylate skin adhesive produces similar cosmetic results to sutures and other current wound closure techniques while being cost effective, quick and easy to use. Studies suggest that it may be a preferable alternative to sutures.

Keywords: Tissue adhesives; cyanoacrylates; surgical tape; sutures; wounds; surgical staplers

1. Introduction

For centuries, man has sought the ideal way to close a wound. A multitude of methods have been employed during this time. Trauma and war have long been a source of wounds, but it is only relatively recently that surgical incisions have become numerically significant. Now, more than ever, there is a need to find the ideal wound closure.

Many innovative and intriguing methods have been used in the past to close wounds. For example, reports from both India and South America describe termites being provoked to bite across an approximated wound, after which the bodies of the termites are quickly twisted off, leaving behind the clenched jaws of the insect, effectively “stapling” the wound closed; an antecedent of the familiar surgical stapler.

In East Africa, the Masai would place acacia thorns into the skin along the edges of a laceration, before securing them together (and thus closing the wound) using plaited plant fibre^{<1>}.

By the mid-19th century, there was much experimentation in the world of surgery, and many different types of material including aluminium, copper and silver wire, flex, hemp, cotton, hair, tendons, arteries, and even catgut (made from the submucosa of animal (not cat!) intestines) were used. The early to mid-20th century eventually brought us sterile, mass produced sutures, such as polyamide (Nylon), and later in the 20th century polyglactin 910 (Vicryl) and polydioxanone (PDS) that we find in operating theatres today^{<2>}.

The history of modern skin glues dates back to 1942, when cyanoacrylates were first synthesized by a Kodak scientist, Dr Harry Coover. The cyanoacrylates originally

gained fame in 1958 as a super strong, fast drying glue, marketed by Dr Coover himself.

During the Vietnam War (1955-1975) many soldiers carried 'Superglue' for quick equipment repairs on the battlefield. Inevitably, when soldiers were wounded, bleeding and necessity called. It was soon discovered that cyanoacrylate glue had an exceptional ability to hold wounds closed, as it polymerized and hardened when exposed to moisture. Eventually field surgeons started spraying it on wounds before transit to army hospitals and many lives were saved as a result.

It wasn't long until the glue was granted Food and Drug Administration approval in the United States for medical use. Octyl-2-cyanoacrylate is now used worldwide in hospitals, mostly for minor superficial wound repairs and where the use of sutures would prove impractical or difficult^{<3>}.

2. Methods

Medline was searched using a combination of ‘tissue adhesives’, ‘cyanoacrylates’, ‘sutures’, ‘surgical staplers’ and ‘surgical tape’ for paediatric and adult studies comparing skin adhesives with other methods of wound closure. Relevant literature was reviewed with the aim of creating a descriptive review and comparison of tissue adhesives, sutures, surgical staplers and tape for wound closure.

A MEDLINE and EMBASE search was conducted from the dates January 2004 to May 2017 using a combination of terms and keywords (‘tissue adhesives’, ‘cyanoacrylates’, ‘sutures’, ‘surgical staplers’ and ‘surgical tape’). In total 32 articles were identified. Inclusion criteria: Systematic review or meta-analysis of randomized controlled trials, review articles, cohort retrospective comparative reviews/studies and

case series/reports. Exclusion criteria: laboratory studies, non-English translated articles and animal studies. The literature search was repeated by two of the authors, independently. Once the searches were collated, a final review of the chosen article bibliographies were also reviewed, looking for papers that may have been omitted by the stratifications of the primary searches. In total, 21 studies met our inclusion criteria. Of these, 19 were prospective studies, and two were retrospective reviews.

3. Results

We found 17 studies comparing octyl-2-cyanoacrylate skin glue to conventional methods of skin closure; most (11 studies) compared it with sutures. The majority of those studies were on surgical wounds, but there were also studies that looked at traumatic lacerations. In addition, we found two studies that compared octyl-2-cyanoacrylate to surgical tape (Steristrip), one study that compared skin glue to staples, and a study that compared high and low viscosity versions of octyl-2-cyanoacrylate^{<4>}. We summarise and discuss the studies in chronological order by date of publication for each subtopic.

3.1. Studies comparing octyl-2-cyanoacrylate to sutures

The first study, a prospective, randomized controlled trial published in May 1997, looked at 130 patients with 136 (mainly facial) lacerations^{<5>}. Full follow-up data were available for 98 lacerations. Of these, 48 were closed by suture and 50 by octyl-2-cyanoacrylate glue. Exclusion criteria included need for debridement of soiled wounds, bites or scratches, stellate crush wounds or puncture wounds. Lacerations could be of any length or depth. Patients were randomised to closure with either monofilament sutures or octyl-2-

cyanoacrylate glue. Wound preparation was standardised.

Closure with glue was quicker (averaging 3.6 minutes for skin glue and 12.4 minutes for sutures, $p < 0.001$) and less painful (using a 100mm visual analogue pain scale, glue: 7mm, sutures: 18mm, $p < 0.001$).

Photographs of the wounds at 3 months were rated by a plastic surgeon, blinded to the closure technique, using a previously validated 100mm visual analogue cosmesis scale (VACS) (0mm representing the worst possible scar and 100mm the best). There was no significant cosmetic difference between the closure methods (suture: 68mm, skin glue: 67mm, $p = 0.65$).

The second study published in 1998 randomised 111 patients undergoing elective facial surgery by a single surgeon (mostly for benign skin lesions, with a mean wound area of 112mm^2)^{<6>}. The patients were randomly allocated to either closure by interrupted mattress sutures (with 5-0 or 6-0 Nylon), or octyl-2-cyanoacrylate glue.

Speed of closure, wound complications and cosmesis at 1 year were assessed. Follow-up was complete for 100 patients (51 in the suture group and 49 in the cyanoacrylate group).

Again, it was shown that wound closure was much faster with the skin glue (55 seconds) compared to mattress sutures which took an average of 3 minutes and 57 seconds ($p < 0.0001$). There were no infected or dehisced wounds when assessed at 5-7 days.

Two independent plastic surgeons assessed digital photographs of the wounds at 1 year using a 100mm VACS. The suture group were rated at 29.2mm (+/- 17.7mm) and the skin adhesive group 21.7mm (+/- 16.3mm). A highly statistically significant result in favour of skin glue ($p = 0.003$),

however the absolute difference is small and the standard deviation quite large suggesting the clinical difference is negligible.

In 2001 Bernard et al. published a comparison of octyl-2-cyanoacrylate with standard monofilament sutures (4-0 to 6-0) in children and adolescents ^{<7>}. This non-randomised study involved 42 consecutive patients undergoing 52 excisional dermatological procedures. They were given information about the methods of wound closure and were then allowed to choose between glue and sutures. The wounds were assessed at approximately 2 months using two different outcome scales: a 100mm VACS and the Hollander Wound Evaluation Scale (HWES) ^{<8>}. The latter assesses both the cosmetic appearance (scar width, contour irregularities, edge inversion and step-off borders) as well as inflammation beyond an acceptable threshold. Any score above 0 indicates a sub-optimal wound.

Photographs of the wounds were assessed blindly by two dermatologists. In addition, early complications were evaluated at 2 weeks by an attending dermatologist, who inspected the wounds for dehiscence and infection, and asked standardised questions about infection, pain and adverse reactions. They found no difference in early complications between the closure methods. When it came to evaluating cosmesis, however, a statistically significant difference in favour of glue was shown by the VACS at 2 months (suture group: 63mm, skin adhesive group: 48mm; $p = 0.02$, with 0mm representing an optimal scar). With the Hollander Wound Evaluation Scale, again the cyanoacrylate group had a lower median score of 5, versus 6 for the suture group ($p = 0.09$). Another statistically insignificant finding was that the skin glue group had a higher occurrence of hypertrophic scars ($p = 0.45$). It must be stressed that this was not randomized study – however the groups

were well matched for site and surgical procedure, but there were more women and non-caucasians in the suture group.

In 2004, Gennari et al. carried out a prospective randomized study investigating the use of tissue adhesives in superficial wound closure after breast surgery ^{<9>}. 133 patients were randomized to octyl-2-cyanoacrylate closure (69 patients) or monofilament suture closure (64 patients). The groups were well matched for age, length of incision, procedure type and length of stay in hospital. The results obtained included assessments by both blinded plastic surgeons and patients, rating cosmetic appearance after 6 months and 1 year. A scale of 1-10 was used, with ten corresponding to optimal cosmetic appearance. Early follow-up was performed at 5-10 days to assess wound erythema. In addition, economic outcome was compared. At six months, both patients and physicians rated the wounds in both groups an average 8.9. At one year, again there was very little difference between the groups, with plastic surgeons rating both glue and sutures at 8.8, and patients 8.6 and 8.9, respectively. In terms of early follow-up assessment of wounds by plastic surgeons, it was reported that the skin adhesive group showed less erythema and inflammation. For patient satisfaction scores (on a scale of 1-10, with 10 being optimal) the skin glue group appeared to be significantly more satisfied with their wound healing than the monofilament suture group (9.5 vs. 7.45, $p < 0.0001$). Finally, for economic outcome, it was found that overall it was significantly more economical to use skin adhesive (20.3 Euros) than sutures (29.3 Euros) ($p < 0.001$). The authors conclude that there was little to choose between the methods of closure in terms of outcome but economically glue had the edge over sutures.

A randomized, controlled study from

2005, compared octyl-2-cyanoacrylate to monofilament sutures, and staples, in total hip (102 patients) and total knee arthroplasties (85 patients)^{<10>}. Patients were randomised after closure of the deeper layers using traditional methods. The hip and knee arthroplasty groups were analysed separately. The authors noted that the amount of wound discharge was decreased in the initial 24 hours in both knee and hip arthroplasties closed with glue (a similar observation was made by Gennari et al. in their study^{<9>}).

The study showed that stapled closure was significantly faster in both types of arthroplasty than the other two methods of skin closure.

Cosmesis was assessed using the HWES^{<7>}. No statistically significant difference was found between the different wound closure methods for either type of arthroplasty. Early and late wound complications were also remarkably similar in all groups (although occurrence was very low overall). Patient satisfaction was also similar for all three methods of wound closure for both types of arthroplasty. The authors conclude that staples should be the closure method of choice.

Another randomized prospective study from 2005 by Handschel et al. compared octyl-2-cyanoacrylate to sutures in standardised facial wound closure^{<11>}. The advantage of this study as with the one above is that the incisions were essentially the same each time which benefitted the direct comparison of closure techniques. In this study, 45 Caucasian patients undergoing orbital floor reconstructions via an infraorbital incision were randomised. An early follow-up was performed 10 days postoperatively to check for wound dehiscence and infection, during which no patients in either group were found to have any complications. The wounds were

assessed for cosmesis at three months by three cranio- and maxillofacial surgeons, as well as by the patients themselves, using a 100mm VACS. The results showed a better cosmetic outcome for the suture patients [mean 84 +/- 8.3mm for the suture group and 71 +/- 4.1mm for the skin glue group (p<0.05 for surgeons' rating of cosmetic outcome)]. Striving for more detail, this study also included phase-shifting profilometry at 3 months post-procedure to assess, mainly, the depth of wounds closed with sutures and octyl-2-cyanoacrylate. The results showed that the incisions closed with skin adhesive healed producing deeper results at 0.47mm +/- 0.51mm compared to 0.21mm +/-0.10mm for the suture group.

Scott et al. retrospectively reviewed 255 consecutive bilateral reduction mammoplasties performed by a single surgeon, closed with octyl-2-cyanoacrylate^{<12>}. These cases were compared to a previously reviewed consecutive series 415 reduction mammoplasties in which standard sutures were used. Patients were reviewed at 5-7 days. He noted 13.4% of the skin adhesive patients had a complication of wound healing (including cellulitis, hypertrophic wound healing, medial symmastia, unilateral necrosis and wound dehiscence) compared to 18.5% of the suture patients. This difference was not found to be statistically significant. The review noted that the average procedure time was 20% shorter for the glue closure patients (93 minutes as opposed to 118 minutes), which was a significant cost-saving. Patients were also more satisfied with the skin glue as there was no need to have sutures removed. The authors contend that using glue closure will simplify postoperative care.

Nipshagen et al. published a randomised controlled trial in 2008 of patients undergoing bilateral reduction mammoplasties^{<13>}. 50 women between the

ages of 18 and 70 were used as their own control with each patient having one breast closed with sutures and the other with Dermabond (octyl-2-cyanoacrylate), the order of closure being decided by the flip of a coin. Patients with a personal or family history of hypertrophic scar formation were excluded.

The study protocol was explained to each patient and formal written consent obtained. The surgical incision was standardized to result in an inverted-T scar (Strombeck's method ^{<14>}) with the same surgeon performing every procedure to prevent bias. Patients were followed up at 1 week, 6 weeks, and 6 months post procedure. At the first follow-up a standardized list was used to rate erythema and infection. The cosmetic appearance of the scar was assessed at the next 2 visits. The wounds were photographed by a professional photographer and subsequently blindly rated by a panel of 5 plastic surgeons and 5 residents in plastic surgery. A VACS and the HWES were completed by the panel. Patients also completed visual analogue scales for scar comfort and cosmetic appearance for each breast. The study reported that both patients and panellists found the wound closed with adhesive to be more aesthetically pleasing after 6 weeks and this was sustained at 6 months. The difference was statistically significant ($p < 0.05$). The HWES scores by the panellists were congruent with this ($p < 0.02$). Overall, this study suggested that skin adhesive produced a slightly better aesthetic outcome than sutures, and the authors recommended glue for skin closure in reduction mammoplasty in the future.

Knott et al. compared Dermabond to traditional skin sutures for patients undergoing cleft lip and palate correction ^{<15>}. The trial was a case-control study enrolling 11 patients and 11 age matched

controls. The skin that was glued ran from the nasal sill superiorly to the inferior margin of the red zone of the lip. Photographs taken at least 9 months after the procedure were analysed for cosmetic outcome by three plastic surgeons, blinded to the closure method used. A 100mm VACS was used together with the HWES. Dermabond treated patients had an overall mean score of 70 +/- 9.5mm and those treated with sutures 68.3 +/- 13.4mm ($p=0.46$). The HWES scores were also not significantly different. The study has shown that cyanoacrylate adhesives can be used effectively on the partially keratinized mucosa of the red zone of the lip with similar cosmetic results to sutures. Dermabond is not recommended for internal mucosal closure as it uses moisture to catalyze its hardening. If used on an internal 'wet' surface premature hardening would result in an ineffective join.

In 2009, Krishnamoorthy et al, studied octyl-2-cyanoacrylate versus subcuticular sutures in the closure of bridged saphenous vein harvest incisions, for use in coronary artery bypass grafting ^{<16>}. 106 patients were enrolled on the trial, with 53 patients randomized to each group. On day 7 the HWES was used to assess the wounds, and at 6 weeks the Vancouver scar scale was used to assess scar pigmentation, vascularity, the height of the scar and pliability ^{<16>}. The total operating time and vein harvest wound closure time was also recorded. The time for vein harvest wound closure was reduced significantly ($p=0.017$), but total operating time was not significantly reduced ($p=0.43$). In terms of cosmetic outcome at 7 days, assessed by 2 blinded surgeons, using the Hollander scale, all of the patients whose wounds were closed with skin adhesive scored 0 whereas those closed by suture all scored 1 or more ($p < 0.001$). The Vancouver scar scale at 6 weeks also showed significantly better results for the scar appearance for the group whose incisions

were closed with glue ($p = 0.001$). Patients were also significantly more satisfied with their glued leg wounds at 6 weeks ($p < 0.001$).

3.2. Studies comparing octyl-2-cyanoacrylate to staples, Steristrips and possible improvements to the current commercially-available octyl-2-cyanoacrylate formulas

A number of other non-suture skin closure techniques are employed in modern day surgery. Metal staples are a fast way to close wounds, and various devices are available commercially. Another popular method used for closing small low tension wounds are adhesive paper tapes such as Steristrips. Steristrips were developed by 3M and are widely used throughout the world. They can be used alone or in conjunction with other closure techniques to give additional wound support.

3.2.1. Staples

In a study published in 2007 by Ridgway et al. ^{<17>}, 30 patients due to undergo thyroid and parathyroid surgery were randomized to skin closure with Dermabond or skin staples. Time taken for closure was recorded. The patients were assessed at 48 hours and 1 week for neck mobility. Cosmesis was assessed at 6 weeks postoperatively. One of the glue patients suffered a wound dehiscence when the dressing was changed as the glue had become adherent to the dressing.

In terms of neck mobility after surgery, the results were similar in both groups at 48 hours and at 1 week.

The time for wound closure was significantly reduced with the use of staples. Compared to Dermabond, staples took an average of 67s +/- 42s less time.

Cosmetic results at 6 weeks were similar for both groups as assessed by the surgeons, a blinded assessor and the patient.

N-butyl-2-cyanoacrylate (Histoacryl blue) is a skin glue similar to octyl-2-cyanoacrylate which hardens slightly faster and is thus said to be easier to use on scalp wounds. It was studied in patients undergoing an elective supratentorial neurosurgical craniotomy procedure ^{<18>}. Forty patients were randomized to receive either glue closure or traditional closure with sutures or staples, with 20 patients in each group. Two nurses, one blinded to the closure method, completed a HWES (modified to include patient and surgeon satisfaction scores). Patients were followed up three times in the first week, at two weeks, then at 3, 6 and 12 months after the procedure. There were no wound complications in either of the groups, and there was no significant difference in cosmetic outcome. However, patient satisfaction was significantly higher in the glue group (9.4/10 vs. 7.1/10; $p < 0.005$). In terms of the time taken for wound closure, it was found that the skin glue took roughly the same time as staples, but significantly less time than subcuticular sutures ($p < 0.001$).

3.2.2. Surgical tape (3M Steristrips)

A study from 2002 compared Steristrips with octyl-2-cyanoacrylate for the closure of traumatic lacerations of less than 5cm in 60 children ^{<19>}. The children involved were aged between 1 and 14 years old, with 30 children randomized into each of two groups. Parents and nurses were asked to complete a 100mm VAS assessing the distress caused by the procedure (0mm for most distressing and 100mm for no distress). Furthermore, standardized photographs were taken of the scars between 3 and 12 months after the procedure. These photographs were categorised by a blinded

consultant plastic surgeon using a VACS. Full follow-up data was available for 44 children (19 in the tissue adhesive group and 25 in the Steristrips group). There was no significant difference in patient distress as judged by parents ($p=0.96$) or nurses ($p=0.07$). There was also no difference in cosmetic outcome score from a blinded consultant plastic surgeon, or the children's parents.

Shamiyeh et al. published a randomized controlled trial in 2001, comparing octyl-2-cyanoacrylate to Steristrips and sutures ^{<20>}. 79 patients undergoing phlebectomies for varicose veins were randomised into the 3 groups. Surgical closure time, wound/scar cosmesis, and costs were studied. The results showed that at day 10 of follow-up, the wounds showed no significant statistical difference in terms of wound dehiscence. The cosmetic results, as determined by patient satisfaction with their healing wounds and a blinded dermatologist's examination (at 8-14 months after the operation), also showed no significant difference between techniques. This study found that closing incisions with skin adhesive proved more expensive than the other two methods of closure.

Steristrips were the fastest method of closure compared to sutures and tissue adhesive closure, but this was not statistically significant. In this study however, miniphlebectomy was performed using the Muller technique ^{<21>} and a very small incision, taking a short time to close overall. This leaves room for error in timing and accurately assessing how long the closure procedure took, as the time differences were, in real terms, very small, but percentagewise seem larger.

3.3. Possible adverse effects associated with the use of octyl-2-cyanoacrylate skin glue

Contact allergic dermatitis has been reported with octyl-2-cyanoacrylate, although it seems to be rare. In one case, a 32-year old woman had her abdominoplasty wounds closed using octyl-2-cyanoacrylate. One week later, the glued skin and surrounding area became pruritic, eczematous and erythematous. This resolved after 48 hours of topical corticosteroid treatment. Three months later she was patch tested and a strongly positive reaction to the glue obtained ^{<22>}.

A 7-year old boy had a 1.5cm laceration above his right eye closed with octyl-2-cyanoacrylate. After 4 days, he returned with discomfort and oedema of the wound. The wound was explored and cultured. No foreign body or infection was found. Patch testing to the glue was negative but the authors concluded that the wound problem was caused by a foreign body reaction to the glue within the wound ^{<23>}.

4. Public health issues and conclusions

It is more important than ever to take the total cost of an intervention into consideration when deciding on the best treatment for our patients. Many of the studies discussed above show that using tissue adhesive for wound closure can save time when compared with traditional sutures. Time in a health care setting is an expensive commodity, particularly when it is spent in an operating theatre.

A study from Texas, USA, included an economic evaluation of the cost of closing laparoscopic wounds with either 4-0 Monocryl/Vicryl or cyanoacrylate glue ^{<24>}. They found a mean cost saving of \$303 per patient in the cyanoacrylate group, resulting

from time saved during surgery. As this was published in 2003 the savings are likely to be ever greater today.

Any cost comparison with non-absorbable sutures or staples must include the cost of their removal. Another factor often ignored (and certainly not costed) is the anxiety and discomfort to the patient of suture or staple removal.

If skin glue was used more widely in publicly-funded health services, time and cost savings could be significant and could impact positively on Government targets such as the 18-week waiting time target set in 2000 ^{<25>}.

It is easier to learn to close wounds with glue than it is to learn to suture wounds. This could have implications for training third world care providers. Eliminating the need to remove sutures would be another benefit in this setting.

Cosmetic outcome, particularly on the face, is another important factor to consider. A poor cosmetic result could result in problems with confidence and other psychological disorders such as anxiety and

depression. Wounds closed with glue have been shown to match or exceed the short and longer term results of other closure methods, and thus increased use could help to reduce the psychological burden associated with sub optimal scars.

Moy et al. described the ideal wound closure in 1992 ^{<26>}. It should be a simple technique that is quick to perform, it should hold the wound edges together precisely, provide a degree of wound eversion and maintain tensile strength for the duration of the healing process. The technique should also leave no marks once the wound has healed. The studies above have shown that staples, Steristrips and skin glue closure are fast and easy to perform. Suturing is a more complex technique than the others available. In terms of maintaining tensile strength throughout wound healing, Steristrips can struggle in this regard and are best for wounds with low stresses and tension.

Tissue glue fulfils many of the properties of ideal wound closure as propounded by Moy et al. With wider use a lot of these benefits would be realised.

5. References

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