A clinical trial of tissue adhesive (histoacryl) in skin closure of groin wounds

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Summary
The use of tissue adhesives has been widely studied since the 1960s. Since then they have found use in specialities like plastic surgery, neurosurgery, ENT surgery and dental surgery. Several papers have reported their safe use, both clinically and experimentally, particularly of the newer homologue n-butyl/2-cyanoacrylate (Histoacryl). In this study 43 patients (46 wounds) whose operations involved a groin incision were randomised into two groups for skin closure either with Dexon subcuticular suture (23 wounds) or Histoacryl glue (23 wounds). We found that both sets of wounds healed well with no wound infections or excessive inflammation when assessed at one week and four weeks. However the glued wounds had consistently better cosmesis scores (meanscore 4.71 at four weeks) compared to the subcuticular Dexon wounds (meanscore 4.00 at four weeks) and P value of less than 0.05. We feel that there is a place for tissue adhesives in skin closure for some general surgical wounds.

Key words: Tissue adhesives, cosmesis scores, skin closure.

Introduction
The use of cyanoacrylates as tissue adhesive, first described by Coover, et al, in 1959, was widely studied in the 1960s. The earlier homologues (Methyl 2 – cyanoacrylate and isobutyl-cyanoacrylate) were used experimentally mainly in ENT surgery and dentistry in the United States.

Butyl 2 – cyanoacrylate (Histoacryl) was developed in the early 1970s and this has largely replaced the others because it caused far less tissue inflammation and toxicity. Tissue adhesives are now used in a large variety of situations in plastic surgery (skin grafts), casualty (minor lacerations), ENT surgery, tympanoplasties, ossiculoplasties, ophthalmology.
As a method of skin closure it has theoretical advantages such as ease of application, no need for dressings (as it is a sterile wound sealant) and requires no subsequent removal. It provides potential savings in cost and time. It is therefore important to establish whether it is a safe and efficient method of skin closure in clinical practice. The aim of this study was to assess its value in skin closure of minor surgical wounds by comparing it with subcuticular Dexon in a controlled clinical trial.

Patients and methods
Forty three consecutive patients who had minor operations at Burton General Hospital, Burton-on-Trent, England (during the period from May to November 1986) involving a groin incision and performed by either of the authors (MKT and TEB) were included in the study.

Informed consent was obtained preoperatively in this approved study. The patients were randomised just prior to skin closure into two groups. Even numbers were closed with Dexon subcuticular suture (Dexon group) and odd numbers were closed with Histoacryl-Blue tissue adhesive (Histoacryl group). When the patients had bilateral operations, the left side was closed with Histoacryl and the right side with Dexon.

The operative technique for closing the deeper layers was the same whichever method of skin closure was used. The subcutaneous fat was closed using Dexon 3–0 sutures before skin closure. No antibiotics or antiseptics were used on the wound. Patients in the Dexon group had subcuticular skin closure using Dexon 30 on a straight needle with an anchoring knot at both ends of the wound. Patients in the Histoacryl group had a thin layer of tissue adhesive (Histoacryl) applied sparingly over the wound. The Histoacryl comes in a small plastic vial with a thin nozzle which enables small regulated quantities of glue to be expressed (see Fig. 1). The wound closure was done in short segments at a time using two pairs of forceps to carefully appose the skin edges and allow the glue to polymerise before proceeding further along the wound. The glue hardens by exothermic polymerisation on contact with tissue moisture and is usually sufficiently hardened within 20 seconds to hold skin edges together.

The length of the incision and the time taken to complete closure of skin using the two different methods were carefully recorded. The patients and wounds were assessed at one week and one month postoperatively in the surgical outpatients clinic. A simple scheme was used to assess the wound for:

1. Comfort
2. Inflammation
3. Haematoma
4. Infection (defined as the presence of pus or opened wound)

Cosmesis was assessed by an independent observer (the experienced clinic sister) on a scale of one to five where one equals poor and five equals excellent.

Results
Forty six wounds in 43 patients (35 men and eight women) were included in the study. Three
patients were lost to follow-up (one from the Dexon group and two from the Histoacryl group). Their age range was six to 80 years. The age distribution was similar in the two groups (Dexon group mean age was 49.7 years, Histoacryl group mean age was 53.4 years). The sex distribution was similar in the two groups.

The operations consisted of 26 inguinal hernia repairs, two femoral hernia repairs. Ten sapheno femoral ligations, six testicular operations and two groin explorations for lymph node biopsies.

Table I shows the mean incision lengths in both groups as well as the speed of skin closure using the two different methods. The speed of skin closure was faster using Histoacryl. This difference was statistically significant using the Student’s test (P < 0.1).

<table>
<thead>
<tr>
<th></th>
<th>Mean incision lengths</th>
<th>Time taken to close each incision (mean)</th>
<th>Speed of wound closure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dexon (n=23)</td>
<td>7.7(+) 1.51cm</td>
<td>149.2 sec.</td>
<td>19.28 s/cm</td>
</tr>
<tr>
<td>Histoacryl (n=23)</td>
<td>8.3(+) 1.84cm</td>
<td>116.5 sec.</td>
<td>14.11 s/cm</td>
</tr>
</tbody>
</table>

SE diff. = 1.66
p < 0.01 using t test

Wound Assessment: The results of the wound assessment at one week and four weeks were satisfactory in both groups. None of the wounds were exceptionally uncomfortable. There were two small superficial haematomas which resolved spontaneously in the Dexon group. There were no infections or excessive inflammation in any of the wounds assessed.

The mean score for the Dexon group was 3.91 at one week and 4.0 at four weeks. The Histoacryl group had a mean score of 4.62 at one week and 4.71 at four weeks. The differences in the scores using a 2 x 5 contingency table and Chi squared analysis were statistically significant at both one week and four weeks with P value of <0.05 (Table II).

With Dexon subcuticular closure, the knots at the ends frequently persist for more than four weeks and can be a source of irritation to the patients (see Fig. 3). There is also an increased scar reaction around the knotted ends. Fig. 4 shows a glued wound with good healing at one week.

Discussion
The results confirm that closing small groin wounds using Histoacryl is safe. It is also a faster method of skin closure when compared with subcuticular Dexon. The glued wounds were found to be comfortable with no clinical evidence of excessive inflammation. None of the glued wounds developed an infection or haematoma. Several papers have demonstrated the safety of tissue adhesives in clinical use. Bhaskar and colleagues showed less inflammatory reaction
Fig. 1 Shows histoacryl being applied for skin closure.

Fig. 2 Shows a patient with bilateral groin wounds at four weeks. The (R) side was glued and the (L) side closed with Dexon.
**Table II**
Comparison of the cosmesis scores between the two groups

<table>
<thead>
<tr>
<th></th>
<th>1=poor</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5=excellent</th>
<th>Mean Score</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dexon</strong> (n=22)</td>
<td>0(0)</td>
<td>1(0)</td>
<td>6(7)</td>
<td>9(8)</td>
<td>6(7)</td>
<td>3.91 (4.0)</td>
</tr>
<tr>
<td><strong>Histoacryl</strong></td>
<td>0(0)</td>
<td>0(0)</td>
<td>0(0)</td>
<td>8(6)</td>
<td>13(15)</td>
<td>4.62 (4.7)</td>
</tr>
</tbody>
</table>

Table II shows the no. of wounds for each of the five scores in both groups. The first figure is at one week and the figures in parenthesis shows the no. at four weeks. Statistical analysis of the scores using the x2 test and 2x5 contingency table gives a x2 value of 9.62 at one week and x2 of 10.18 at four weeks. The differences in the scores at both one week and four weeks are therefore statistically significant (P < 0.05).

Fig. 3 Shows a wound closed with Dexon subcuticular at four weeks with increased scar reaction around the protruding knotted ends. This wound scored a four.

in dental wounds with cyanoacrylates compared to controls wounds in rats. Ronis and Harwick\(^1\) found that histologically there was no evidence of foreign body reaction or cartilage toxicity using Histoacryl in rat ear wounds. In another histological study by Javelet and colleagues,\(^10\) foreign body giant cells were found in the wounds closed with isobutyl cyanoacrylate at one week, but by ten weeks and 20 weeks all the wounds had healed completely.
Fig. 4 Shows a glued wound with good healing at one week. This wound scored a five.

The cosmesis assessment of the wound by an independent observer show that the glue wounds had healed with consistently better appearances at both one week and four weeks. Dexon subcuticular skin closure was chosen for comparison because we have been using this method with very acceptable cosmetic results for a long time. In addition it does not require subsequent removal of sutures which is the other advantage with Histoacryl. In the trial we noticed that often, the glued wounds did not require any dressings or protective spray as the tissue adhesive forms a sterile seal over the wound. The problem with the persistent Dexon anchoring knots and related increased scar reaction is difficult to overcome except by using a different method of ‘finishing’ the subcuticular stitch. This will usually require some form of post operative trimming or removal of excess suture material.

We encountered no major problems in this study. Initially a great deal of patience was required to develop a technique for accurate and speedy skin closure using Histoacryl. We soon found that for longer wounds, opposing the wounds edges accurately using two pairs of forceps one segment at a time is the best method. The Histoacryl is then applied on that segment sparingly; and 10–20 seconds later the glue should have polymerised and be strongly adherent enough to proceed to the next segment. The skin has to be clean and dried before application of the glue. The need for excellent wound haemostasis must be emphasised, and like subcuticular Dexon skin closure a subcutaneous stitch is important in taking up some of the wound tension before skin closure. Although the cost of each vial of Histoacryl is more than a packet of skin suture each vial can be used on at least three wounds thus making the cost comparable.
There is also a place for using tissue adhesives in other types of wounds where there is minimal tension eg. traumatic skin lacerations, thyroid surgery, scrotal incisions, vasectomies. However more clinical trials are needed to assess their value in clinical practice. It may be particularly useful in paediatric surgery as removal of sutures can be a traumatic experience for children. Baron has reported good results in his series of 510 children where tissue adhesive was used in facial soft tissue wounds. In plastic surgery the use of tissue adhesive in skin grafting is well established.

References


