Use of 2-octyl-cyanoacrylate in Tissue Suture: Experimental Study in Mice

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ABSTRACT

Several researches have been aimed at the creation of a substance that allows the practical and fast suture of tissues without causing side effects. Previous works using cyanoacrylate have shown good final aesthetic results, low toxicity, easy application and successful pediatric use.

The purpose of this paper is to experimentally evaluate the effectiveness of the 2-octyl-cyanoacrylate polymer in tissue closure in mice, comparing it to the conventional thread suture (separate stitch) and to study the local reactions during the initial phases of healing by means of histopathological examinations.

We concluded that the tissue closure using 2-octyl-cyanoacrylate, when compared to the separate stitch suture, reduces inflammatory reactions, offers better arrangement of collagen tissue and, as a result, reduced fibrous reaction.

INTRODUCTION

The loss of tissue integrity in live organisms requires the approximation of the borders of the wound in order to

recover integrity, thus facilitating healing.

Suturing threads have been typically used causing tissue reactions, ranging from a granulomatous reaction of the foreign body type to a hypersensitivity response, thus changing the healing process and causing infections and suture dehiscence.

Surgical threads create a tattoo on the skin at the knot site. This tattoo may be big or small depending on the inherent local reactions of each individual and may even leave a conspicuous surgical scar.

The natural biological adhesive of superior animals is fibrin, formed from blood fibrinogen; however, the use of homologous or heterologous fibrin has disadvantages, such as the risk of diseases transmission, denaturation when in contact with antiseptics of local use such as alcohol and iodine in addition to the technical drawbacks concerning use since, once prepared, it shall be applied at the most within four hours.

Other substitutes for fibrin were then sought, including cyanoacrylates, in order to function as surgical adhesives.

Cyanoacrylate, synthesized in 1949 by Ardis [1] and described in 1959 by Coover *et al.* [2], has been widely studied since 1960. As time passed, changes have been made in its structure until the obtainment of 2-octyl-cyanoacrylate, which provides an excellent adhesive effect and low toxicity as a result of its slow degradation [1, 2].

Although there are several papers in the literature showing a better final aesthetic result and cost reduction when the surgical adhesive is used compared to the thread suture, there are not enough studies comparing the tissue suture to 2-octyl-cyanoacrylate concerning reactions observed in different healing phases. This gap encouraged this work.

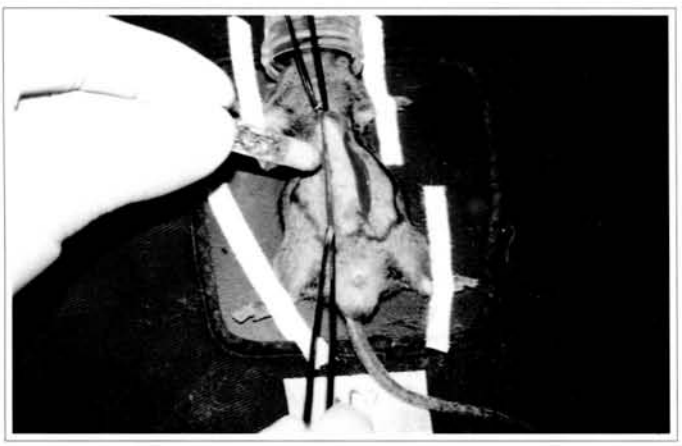

Fig. 1 – Closure of incision A with 2-octyl-cyanoacrylate.
Fig. 1 - Síntese da incisão A com 2-octil-cianoacrilato.

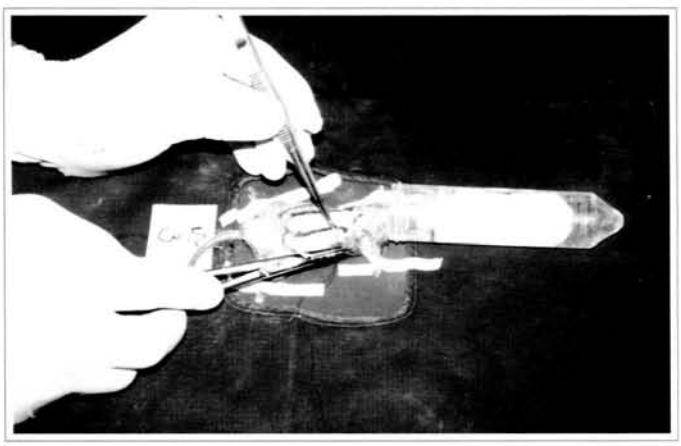

Fig. 2 – Suture of incision B with single 5-0 nylon stitches.
Fig. 2 - Síntese da incisão B com pontos simples de náilon 5-0.

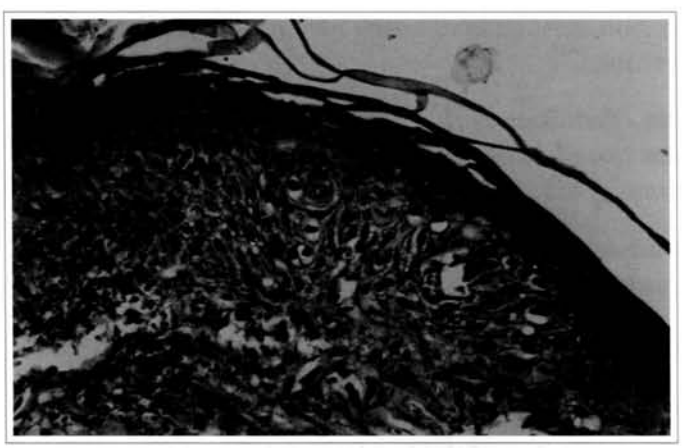

Fig. 3 – Slide of group SA (24 hours – glue) 400x.
Fig. 3 - Lâmina do grupo SA (24 horas – cola) 400x.

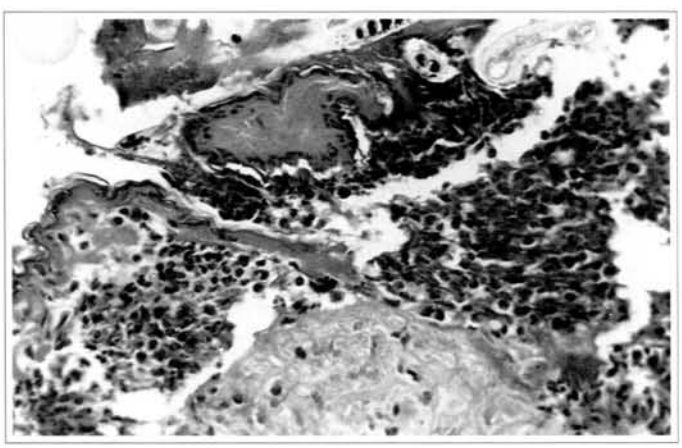

Fig. 4 – Slide of group SB (24 hours – suture) 400x.
Fig. 4 - Lâmina do grupo SB (24 horas - sutura) 400x.

METHOD

Seventeen male adult mice of the CBA strain were used. The mice were subjected to inhalatory general anesthetic containing 70% ethyl ether, followed by trichotomy, asepsis and antisepsis in the ventral region.

Two parallel incisions of 2.5 cm, 1.5 cm apart from each other, were performed until the peritoneal membrane was reached, the left wound closure (A) was carried out with 2-octyl-cyanoacrylate and the right one (B) with seven separate stitches using 5-0 nylon (Figures 1 and 2). Glue was applied after the perfect overlapping of the wound borders on its surface without the penetration in the bloody area.

Incisions A and B were divided into 3 regions, upper (U), medium (M) and lower (L), measuring 0.83 cm each. Biopsies were made following the same criteria of anesthesia, asepsis and antisepsis at days 1, 3 and 7 after the incisions on the upper, medium and lower regions, respectively, using a number 4 punch-biopsy, always by the same surgeon.

Material was packaged separately in formaldehyde and the animals were killed after the 3rd biopsy at the seventh postoperative day.

Four mice died, 1 in the first 24 hours after the incisions, 2 after the 1st biopsy and one 24 hours after the 2nd biopsy.

Skin segments subjected to biopsy were fixed in 10% formaldehyde and then processed with imbibition and blocking in histological paraffin. 5 mm sections, obtained with a microtome and placed on slides, were stained with Hematoxylin and Eosin (H&E).

RESULTS

Surgical parts were divided in groups according to

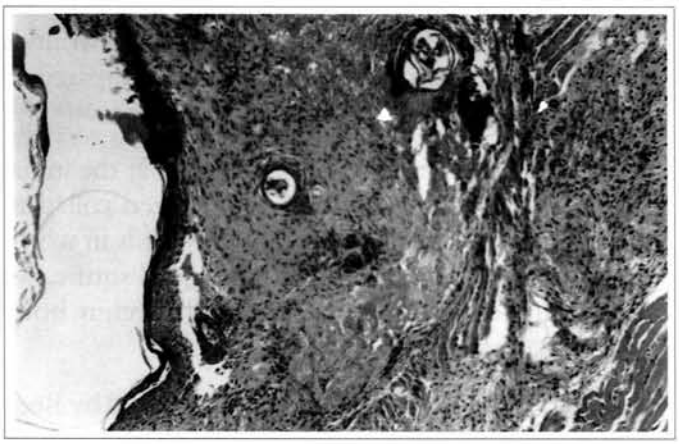

Fig. 5 – Slide of group MA (72 hours – glue) 100x.
Fig. 5 - Lâmina do grupo MA (72 horas - cola) 100x.

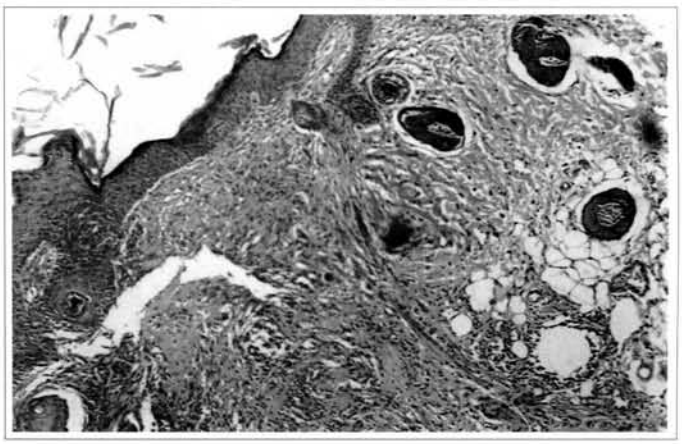

Fig. 6 – Slide of group MB (72 hours – suture) 100x.
Fig. 6 - Lâmina do grupo MB (72 horas - sutura) 100x.

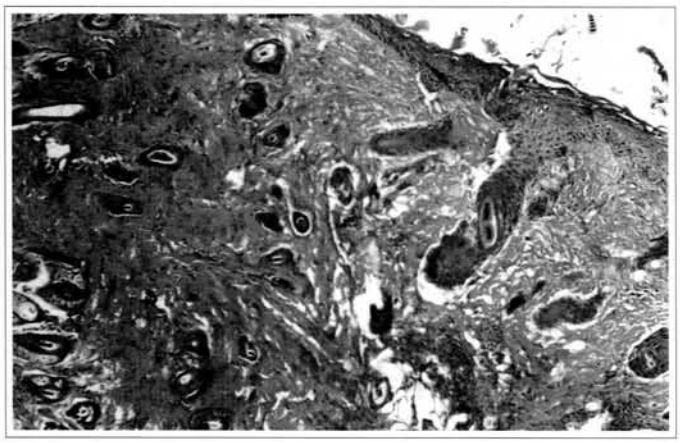

Fig. 7 – Slide of group IA (7 days – glue) 100x.
Fig. 7 - Lâmina do grupo IA (7 dias - cola) 100x.

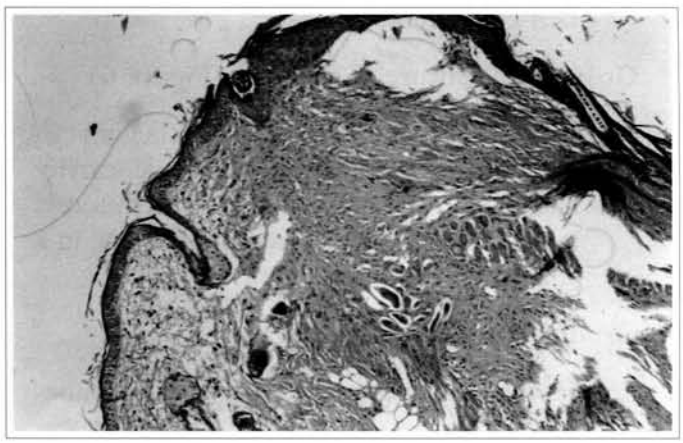

Fig. 8 – Slide of group IB (7 days – suture) 100x.
Fig. 8 - Lâmina do grupo IB (7 dias - sutura) 100x.

the type of suture – using 2-octyl-cyanoacrylate (A) or suturing threads (B) – and biopsy period – 1 (U), 3 (M) or 7 (L) days after the incisions. The histological study has shown:

Group SA (glue, 24 hours) (Figure 3)

Most of the animals have no crust. Epithelium is almost nearly regenerated, showing small blood capillaries. On dermis, the inflammatory process is discrete, however a great mobilization of fibroblasts as well as endothelial cells is noticed. It can be already noticed that the healing lesion has a good contour and is not very thick. In two animals, small subcorneal and intradermal vesicles can be seen, even in areas beside the incision site.

Group SB (suture, 24 hours) (Figure 4)

In this group, an often profuse crust can be always seen. The acute-type inflammatory process, with the predominance of polymorphonuclear neutrophils, as well as macrophages, is continuous. Even those animals in which the borders are very close and the regeneration process is developed, the inflammatory process and the fibrous tissue is accentuated.

Group MA (glue, 72 hours) (Figure 5)

A well developed healing process is seen, with no inflammatory cells, with new collagenic tissue, endothelial cells and swollen fibroblasts. The general view of the healing area shows a new and clearer collagen and a thicker, keratinized, pavemental and stratified epithelium.

Group MB (suture, 72 hours) (Figure 6)

Complete regeneration of the epithelium can be seen, however great fibroblastic activity and mononuclear-type inflammatory process are still present with macrophages and, in a smaller amount, lymphocytes.

Group IA (glue, 7 days) (Figure 7)

Healing process completed, with the epithelial and fibrous tissues being completely stabilized; it is only noticed that collagen is slightly clearer in the healing area.

Group IB (suture, 7 days) (Figure 8)

Very visible scar, with thicker collagen; the granulomatous reaction is more deeply seen, with giant cells phagocytizing foreign body (in this case, the suturing thread).

DISCUSSION

The use of cyanoacrylate in tissues closure has already been studied in several aspects. In 1974, Welker and Neupert[5] showed its low absorption and biocompatibility. Lehman *et al.*[6] in 1967, Matsumoto[7] in 1967, Heiss[8] in 1970 and Williams[9] in 1976 showed that the substance was not carcinogenic. Its adhesive power was improved by changes in the chemical structure until 2-octyl-cyanoacrylate was obtained; it has long chain rings and good flexibility and strength[2].

Its aesthetic advantage related to the thread suture was demonstrated by Keng *et al.*[10] in 1987 and by Toriumi *et al.*[11] in 1998.

2-Octyl-cyanoacrylate used in the closure of wounds seems to be easy and time-saving when compared to the thread suture.

Slides have shown reduced inflammation at the initial phase and deposition of a more organized collagen, with reduced fibrous reaction at the wounds in which glue was applied; in the case of the thread suture, we noticed increased inflammation and foreign body granuloma, including giant cells.

Such results are comparable to those obtained by Been *et al.*[2] in 1999, who also evaluated the use of methylacrylate with 2-octyl-cyanoacrylate and the suture with nylon threads; however a small sample with only 1 control for each healing phase was used.

Conclusions are more significant once this paper has 17 samples of each type of suture in 3 different periods.

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