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Short Communication

Use of the n-butyl cyanoacrylate adhesive and the polyglactine thread suture for corneal rhaphy in rabbit (*Oryctolagus cunicullus*)

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The aim of this study was to evaluate the cicatricial repair of perforating cornea in rabbits, by using the N-butyl cyanoacrylate adhesive compared to the 910-polyglactine thread suture through macroscopic and histological assays. Corneas from 18 adult rabbits were perforated and subsequently occluded with N-butyl cyanoacrylate synthetic adhesive (right cornea) or by separated single points using the 910-polyglactine thread (left cornea). The rabbits were divided into groups containing three animals per group. Examination after 7, 15, and 30 days post-operative showed that both the synthetic adhesive and the suture were efficient in the occlusion of the surgical wounds, thus stabilizing the intra-ocular content. The N-butyl cyanoacrylate adhesive was shown to be superior to the 910-polyglactine suture thread with regards to the evolution and the organization of the healing process.

Key words: rabbit, cornea, surgery, suture, synthetic adhesive

Cornea is subjected to traumas and injury processes due to its highly exposed location. Among the corneal injuries, the abrasions, the ulcers, the lacerations and perforations [22] are the most relevant lesions. The perforations resulting of destructive, infectious or non-infectious, conditions are important factors in ophthalmology due to its high morbidity [3].

Surgical repairs of penetrating lesions of the cornea have been the matter in frequent studies. The aims of the repairs were to restore the integrity of the ocular globe, to stabilize the intra-ocular content, to preserve the vision and to prevent the glaucoma [3]. Corrections of the defects and corneal lesions can be performed using conjunctival pedicular grafts [11], contact lens [13], corneal transplant in autologous [6,21] or homologous [4,10] tissues, synthetic implants [32], biological implants [18], and synthetic adhesive [24,17].

The synthetic adhesives were used as substitutes for conventional sutures [23]. According to Schmeissner [28], the adhesion mechanism occurs by penetration of the monomeric film into the tissue, occurring electrostatic attraction through hydrogen bonding and general attraction of the masses or Van der Waal forces. The usefulness of the adhesive in surgery is determined by the physical-chemical behavior that should be adjusted to the biological parameters [28]. The cyanoacrylate adhesive is the only with physical-chemical and biological properties evaluated for medical use [16]. They can be sterilized and to promote an adequate barrier against bacterial invasion [14].

Different types of cyanoacrylate adhesive have been used in surgery and the methyl-2 cyanoacrylate has been used for repair of veins, ureteres**,** and bronchi [12], arteries [9], teeth [5] and skin [23]. The methyl-heptyl/spray has been used in hemostasis and anastomosis of liver, kidney, stomach, and intestine of dogs [20]; the butyl-2 in intestinal anastomoses of dogs [30], the isobutyl and N-butyl for skin approximation of dogs [19], the isopropyl in hemostasis of stomach in dogs [25], the isobutyl for the synthesis of mammal glands in bovine [1], and the N-butyl in skin of dogs [26] and cornea of cats [8].

The aim of this study was to evaluate the cicatricial repair of the perforating cornea of rabbits by using the N-butyl cyanoacrylate adhesive and compared to the 910-polyglactine thread suture through macroscopic and histological assays.

A total of 18 adult rabbits of both sexes, weighting from 2 to 4 kg, were divided into three groups containing 6 animals per group, for corneal rhaphy using either N-butyl cyanoacrylate adhesive or 910-polyglactine thread. The animals were observed up to 7 days post-operative (*po*) in the group I, 15 days *po* in the group II, and 30 days *po* in the group III.

After 12 h-starvation, the animals received antibiotics

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(enrofloxacin at 5.0 mg/kg, intramuscularly) and analgesics (flunixin meglumine at 1.0 mg/kg, intramuscularly). After 30 min they received pre-anesthetic (acepromazine at 0.5 mg/kg, intramuscularly) and anesthetic (ketamine at 15.0 mg/kg, intramuscularly) medications.

The eyelids were separated using blepharostato and the ocular globe was fastened with auxiliary scleral-conjunctival suture points by using the 4-0 polypropilene thread. In the central area of the right cornea, a total perforation of 4 mm in width was carried out with fixed sheet scalpel, and subsequently obliterated with a drop of the N-butyl cyanoacrylate adhesive. In the left ocular globe, the same procedures of scleral-conjunctival fixation and corneal perforation were performed, even so the wound was approached with separated single points using the 910-polyglactine thread.

During the period post-operative the animals were maintained with a protective Elizabethan collar and submitted to administration of flunixin meglumine (1.0 mg/kg, intramuscularly) for three days and ophthalmic ointment containing chloramphenicol and vitamin A, at 12 h-intervals for seven days.

After the predetermined periods of observation, the animals were sacrificed under barbiturate anesthesia and intravenous injection of KCl according to the ethics code for the use of animals in scientific research [2]. The corneas were collected, fixed in formaldehyde solution for 48 hours, embedded in historesin and stained with toluidine blue for histological assays.

The mean time to obliterate the corneal perforation was 5 seconds when using the N-butyl cyanoacrylate adhesive and 60 seconds for the suture points with the polyglactine thread. Therefore, the period of time required to occlude the perforation using the adhesive was smaller, thus allowing that the animals were maintained under anesthesia during a short period of time. Similar results were obtained by Queiroz *et al*. [26], when testing the adhesive in skin of cats.

During the period *po*, no extravasation of aqueous humor was observed in both the corneas submitted to the adhesive and the thread suture for the repair of the perforation. Such fact was due to the efficient linkage of the adhesive to the corneal tissues [28] and the approximation of the corneal wound with separated single points. Similar data were reported by Barros *et al*. [3], when applying separated single points to attach equine pericardium as penetrating graft in the repair of dog corneas. Nevertheless, in this experiment, the corneal obliteration was obtained immediately after its administration when using the adhesive, and just after the application of the last suture point when using the polyglactine thread. The rapid and efficient obliteration of the corneas with no apparent alterations was due to the fact that the cyanoacrylate adhesive presents physical-chemical and biological properties evaluated for medical use [16]. The adhesive could maintain the wound free from contaminations, promoting an adequate barrier against bacterial invasion, as already reported by Kaplan [14].

For a period of 30 days *po*, no dehiscence of both the adhesive and the suture points applied on the corneas was found. On the other hand, Queiroz *et al*. [26] when using the cyanoacrylate adhesive in skin of cats verified dehiscence in 20% of animals in the 7th day *po*. The absence of dehiscence in this experiment was likely due to the employed material and the post-operative immobilization with Elizabethan collar**,** which avoided the interference of the animals in the surgical site.

According to Barros *et al*. [3] and Laus *et al*. [18], blepharospasm is often found in the presence of suture thread or strange bodies on the cornea, thus sensitizing the eyelid conjunctive. When using equine pericardium in the repair of dog corneas, Barros *et al*. [3] noticed blepharospasm for 30 days *po* due to presence of suture thread in the cornea. In this experiment, the animals presented blepharospasm only up to the 5th day *po*, possibly due to the use of a fine layer of adhesive and the small number of suture points applied in the repair of the corneas.

On the 10th day *po*, neovascularization of the corneas submitted to synthesis with polyglactine thread was observed, agreeing with the findings of Wilkie & Wolf [32] who used synthetic material in the repair of the cornea in dogs. According to Morales *et al*. [22], the corneal vascular neoformation appears due to persistent, infected or destructive, stroma lesions in order to improve the tropism of the injured site and to carry inflammatory mediators. In the present study, the absence of neovascularization in the corneas obliterated with the adhesive suggests that a rapid organization of the corneal stroma has occurred in the absence of infection, thus without needing of inflammatory mediators.

The corneal opacity is related to edema due to water capture and disarrange of the normal pattern of collagen lamellas of the stroma [31]. In the present study, the opacity occurred with larger intensity in the cornea where the perforation was approximated with suture thread. This fact was likely due to the smallest affluence of water close to the stroma in the perforation obliterated with the adhesive, demonstrating that a better continuity of the corneal borders and stromal reorganization have occurred.

By optical microscopy, both the adhesive N-butyl cyanoacrylate and the polyglactine thread were found in the site of corneal rhaphy after 30 days *po*. The presence of the adhesive can be due to its low biodegradability, staying up to 92% in the applied site for five months [7] and being slowly removed by macrophages [27]. However, the presence of the adhesive did not cause apparent local alterations during the observed period.

On the 7th day *po*, a disorganization of the corneal layers without coalescence of the borders was noticed in the site of the suture points (Fig. 1B), while when using the adhesive

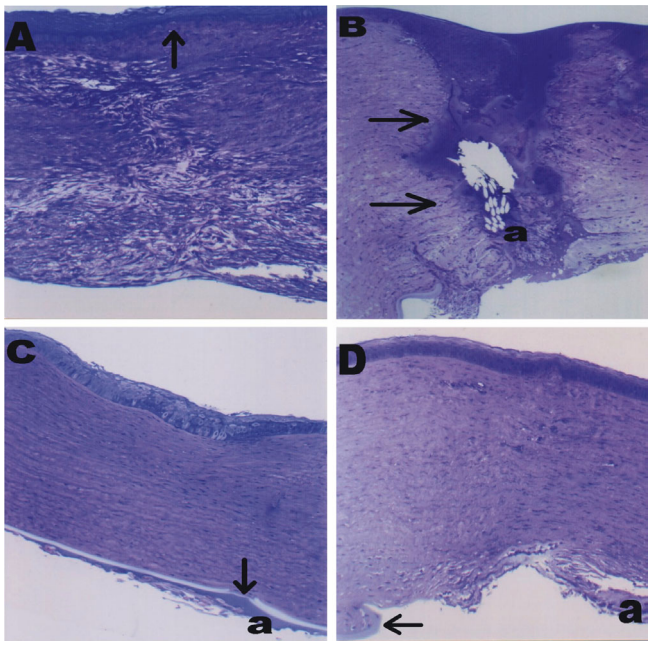

Fig. 1. Photomicrographs of perforating cornea from rabbits submitted to the repair with the synthetic adhesive (A and C) and the suture thread (B and D). In A the wound borders are coalesced and an epithelialization of one of the corneal epithelium layers (arrow) after 7 days of post-operative (*po)* can be visualized. In B a disorganization of the corneal layers (arrow) and the presence of the suture thread (a) after 7 days *po* are visualized. In C a total reorganization of the corneal layers, Descemets membrane almost totally regenerated (arrow) and presence of the adhesive (a) after 30 days *po* are visualized. In D the epithelium already is formed with incomplete organization of the stroma (a) and the Descemets membrane (arrow) after 30 days *po*.

an epithelialization of one of the epithelial layers with the coalesced borders of the wound and presence of macrophages was verified (Fig. 1A). However, Matsumoto *et al*. [20] stated that cyanoacrylate fragments between the tissues delay the healing process, because they avoid proliferation of fibroblasts and blood vessels in dogs. The results obtained in this experiment, even so, demonstrate an improvement in the healing process of corneal lesion obliterated with adhesive when compared to the lesion repaired with the suture thread.

Around the 15th day *po*, the lesion sutured with the 910 polyglactine thread showed an epithelialization of a layer of the corneal epithelium, with disorganized stroma and intense amount of vessels, polymorphonuclear cells and macrophages. However, in the wound obliterated with the adhesive, a total epithelialization of the epithelium layers was observed with organizing stroma and absence of polymorphonuclear and mononuclear cells. No evidence of polymorphonuclear and mononuclear cells in a tissue repair reflects an absence of inflammatory reaction [18]. On the other hand, Thorbeck [30] and Queiroz *et al*. [26] reported that cyanoacrylates promote inflammatory reactions and necrosis in tissues. Such fact was not observed in this experiment, although is coincident to the findings reported by Oliveira *et al*. [23] when using methyl-cyanoacrylate in the skin repair in dogs.

After 30 days *po*, a total reorganization of the corneal layers was observed in the lesion repaired with N-butyl cyanoacrylate, except for the posterior limiting lamina of the cornea, which was found almost totally regenerated (Fig. 1C). In the site of the corneal suture with polyglactine an incomplete reorganization of the stroma and the posterior limiting lamina of the cornea was observed (Fig. 1D). However, Barros *et al*. [3] reported that dog corneas obliterated with pericardium showed complete reorganization of the stroma after 70 days *po*. In this experiment, it was noticed that the corneas with the adhesive showed complete reorganization of the stroma on the 30th day *po*. Such fact was likely due to the appropriate coalescence of the corneal wound borders induced by the adhesive and as consequence a rapid epithelialization of the lesion.

The N-butyl cyanoacrylate synthetic adhesive and the suture with the 910 polyglactine thread applied in perforating corneas of rabbits stabilized the intra-ocular content without presenting dehiscence of the rhaphy. The process of corneal healing in rabbits occurs more quickly in the perforations obliterated with the N-butyl cyanoacrylate synthetic adhesive when compared to the perforations approached with the 910 polyglactine thread.

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