

EFFECT OF N- BUTYL-2-CYANOACRYLATE (HISTOACRYL BLUE®) ON BONE HEALING (A HISTOLOGIC STUDY ON GUINEA PIGS)



Walid A Abdullah*,
Hesham Khalil**,
Manal A. AlSheddi***

BDS, MSc, PhD
BDS, MSc, OMF Prosth Certi, MFDSRCS, PhD
BDS, MSc, DMSc, ABOMP Diplomat

OBJECTIVE: the aim of this study was to evaluate the effect of n butyl-2-cyanoacrylate on bone healing.

METHODOLOGY: Thirty adult male guinea pigs with an average weight of 400-500 grams were used in this study. Animals were divided into two groups (A&B). Group (A) included 21 animals, and Group (B) was a control group which included 9 animals. Each animal of both groups was subjected to a unilateral (left side) mandibular body surgically created (1) mm width bony defect, the inferior border of the mandible was left intact, the surgically created defects of Group (A) were filled with Butyl-2-cyanoacrylate. While, the surgically created defects of Group (B) were left to heal spontaneously without any materials added.

RESULTS: Clinical results and observations showed no infection or foreign body reaction in any of the animals either the control or the study group. Histological results: by the end of the second week the histoacryl group showed less granulation tissue and mild inflammation compared to the control sites. At the end of the third week, the control showed more pronounced granulation tissue regression and decreased inflammation compared to the study sites, and by the end of the fourth week, both the control and study sites exhibited similar histology with absence of inflammation and granulation tissue.

CONCLUSION: The application of cyanoacrylate tissue adhesive to bone defects shows absence of foreign body reactions, infection, and no disturbance of bone healing, with an anti-inflammatory effect, yet it should be used with caution to decrease the amount of the glue introduced inside the gap as a residue of the glue was seen histologically in the first two weeks after the application.

KEY WORDS: Bone healing mandibular, histoacryl blue, guinea pigs, n-butyl-2-cyanoacrylate, surgical defect.
J Pak Dent Assoc.2009; 18(4): 146 - 150.

INTRODUCTION

Tissue adhesives represent a group of compounds that can be applied locally for a variety of indications, including hemostasis, wound closure, and fistula repair.¹ The main types of tissue adhesives used currently in gastrointestinal endoscopy include

cyanoacrylates, fibrin glues, and thrombin.^{1,2}

The cyanoacrylate tissue adhesives are liquid monomers that polymerize on contact with tissue surfaces in an exothermic reaction creating a strong yet flexible film that bonds the apposed wound edges.^{3,4}

Different studies have shown through biomechanical assessment that adhesion provided by the glue is comparable with that provided by conventional plate-and-screw fixation methods, harmful side effects of breakdown products on adjacent tissues, including the incited inflammatory response, are not present. Recent literature demonstrated that butyl-2-cyanoacrylate glue, or longer chain cyanoacrylate compounds, provide a reasonable alternative to conventional rigid fixation techniques.^{5,8}

The aim of this study was to evaluate the effect of n butyl-2-cyanoacrylate on bone healing of guinea pigs.

* Assistant Professor of Oral and Maxillofacial Surgery, Maxillofacial Surgery Dept., College of Dentistry, King Saud University, KSA. & Lecturer of Oral and Maxillofacial Surgery, Oral and Maxillofacial Surgery Dept., College of Dentistry, Mansoura university, Egypt.

** Assistant Professor of Oral and Maxillofacial Surgery, Maxillofacial Surgery Dept., College of Dentistry, King Saud University- AlKharj, KSA.

***Assistant Professor Oral Pathology/Biology and Microbiology Division College of Dentistry, King Saud University, Saudi Arabia

Correspondence: "Dr Walid Ahmed Abdullah" <waa007@a@gmail.com>

METHODOLOGY

Thirty adult male guinea pigs with an average weight of 400-500 grams were used in this study. Animals were divided into two groups (A&B). Group A included 21 animals and group B with 9 animals was considered as control.

Group (A) included 21 animals, each animal was subjected to a unilateral (left side) mandibular body surgically created (1 mm width bony defect under general anesthesia using (intramuscular injection of ketamine 50 mg/kg), the inferior border of the mandible was left intact (Figure 1,2), the surgically created defects of group (A) were filled with Butyl-2-cyanoacrylate (Figure 3,4). The surgical wound was sutured using 3/0 silk sutures (Figure 5).

Group (B) was a control group which included 9 animals, each animal was subjected to a unilateral (left side) mandibular body surgically created (1 mm width bony defect under general anesthesia using (intramuscular injection of ketamine 50 mg/kg), the inferior border of the mandible was left intact (Figure 1,2), the surgically created defects were left to heal spontaneously without any materials added.

Amoxicillin (50 mg/kg) intramuscular (IM) q 8h was given parenterally to the animals in both groups for 5 days. No anti-inflammatory drugs were given to any of the

animals during the study period.

The animals were sacrificed to obtain the required



Figure 2. A photograph showing the surgically created bone cut in the left side of the mandible of the guinea pig through an extra-oral incision.



Figure 1. A photograph showing the preparation of the sub-mandibular and sub-mental area of the guinea pig for the surgery (shaving, and painting with iodine disinfecting solution).

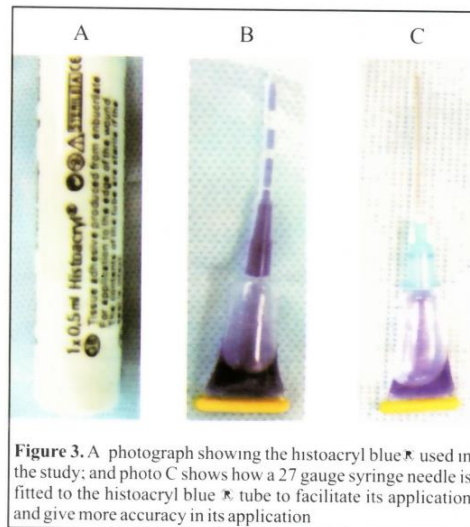


Figure 3. A photograph showing the histoacryl blue used in the study; and photo C shows how a 27 gauge syringe needle is fitted to the histoacryl blue tube to facilitate its application and give more accuracy in its application.



Figure 4. A photograph showing the application of histoacryl blue to the surgically created bone defect.



Figure 5. A photograph showing the application of histoacryl blue to the surgically created bone defect. photograph showing closure of the incision using 3/0 black silk sutures.

bony specimens at the predetermined time intervals: one week, two weeks, three weeks and four weeks postoperatively. These samples were fixed in 10% buffered formalin, decalcified, and embedded in paraffin. Histological sections stained with hematoxylin and eosin stain were examined under the light microscope.

RESULTS

Clinical results and observations;

During the surgery the application of histoacryl blue showed a mild difficulty as it required complete dryness of bone surface before its application. Yet after its application it showed enough stability to the bony defects. No infection, or foreign body reaction was recorded in any of the animals in both the control or the study group.

Histological results;

The gross examination of the specimens prior to processing showed that Butyl-2-cyanoacrylate was identifiable in the bone defect sites up to the second week, and was not evident afterward.

At the end of the first week, microscopic examination revealed mild acute inflammation and minimal granulation tissue in both the study and control sites. However, in the study site there was incomplete dissolution of Butyl-2-cyanoacrylate during processing and some residues were evident in the bone defect (Figure 6).

Such residues were also identifiable in the study site by the end of the second week with less granulation tissue and mild inflammation compared to the control sites (Figure 7). There were no signs of necrosis or foreign body reactions.

At the end of the third week, the control showed more pronounced granulation tissue regression and decreased inflammation compared to the study sites, and by the end of the fourth week, both the control and study sites exhibited similar histology with absence of inflammation and granulation tissue. There were increased collagen production and new bone formation, although the bone defects were not completely filled with bone (Figure 8).

DISCUSSION

N-2-Butyl cyanoacrylate is a type of cyanoacrylate which is bioabsorbable and biocompatible. It is used in fixation of bony fractures, and osteotomies. Other uses of this material include as a hemostatic agent, an embolic agent, in retinal tears and in corneal ulcers.⁹

Although, Gluing is an amazing idea in the fixation of small bone fragments, no bone adhesive could be established successfully for all day clinical use,¹⁰ some authors stated that, they inhibit new bone formation, cause a foreign body reaction, and may impede fracture healing.¹¹

Our clinical results agreed with those of Ddas B¹² as

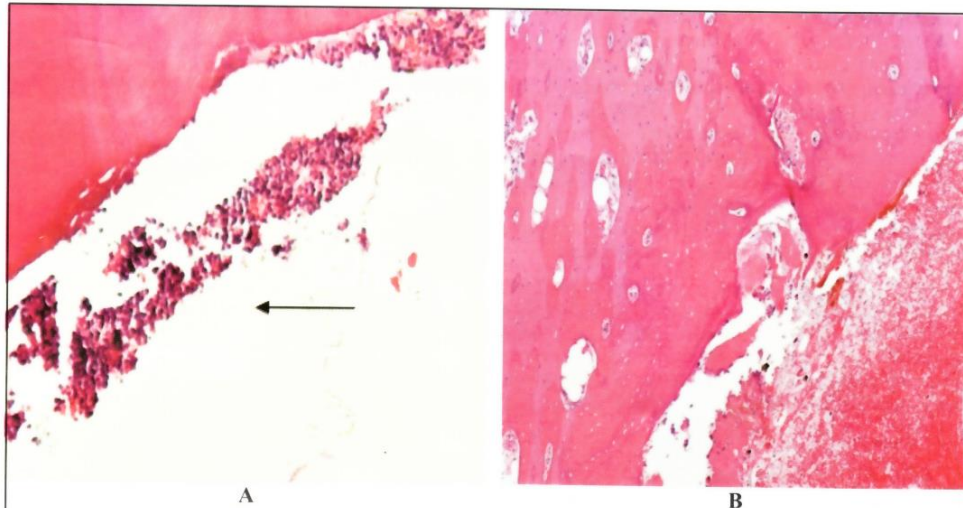


Figure 6 (A & B). Photomicrographs of the study and control sites at 1st week post surgically. (A) the study site shows, a mild acute inflammatory infiltrate and Butyl-2-cyanoacrylate residues (arrow). (B) the control site shows, mild acute inflammation and minimal granulation tissue.

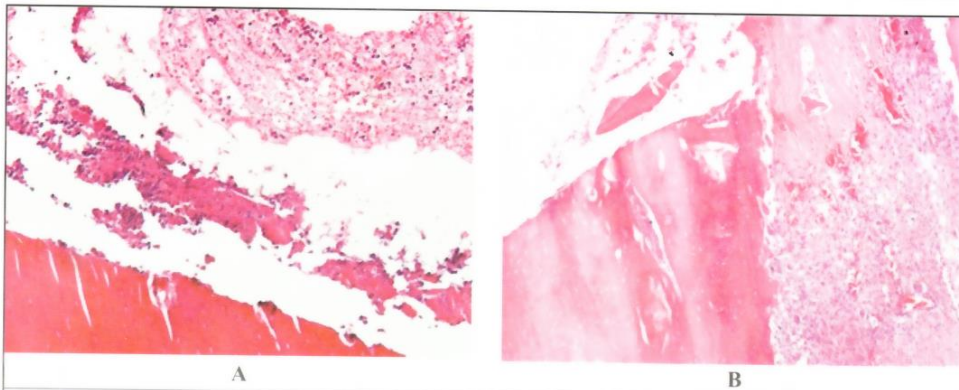


Figure 7 (A & B). Photomicrographs of the study and control sites at 2nd week post surgically. (A) showing inflammation, and less granulation tissue compared to the control site, and there is Butyl-2-cyanoacrylate residues still remaining. (B) the control site shows, more inflammatory infiltrate and more granulation tissue than the study group.

there were no serious infections, foreign body reactions, or necrosis and in contrast to that of Ekelund and Nilsson¹¹ who stated that glues cause foreign body reactions.

The histological observations of the present study also disagree with Ekelund and Nilsson¹¹ who mentioned that

the application of glues to the bone fractures inhibits new bone formation and may impede the fracture healing. Although we found remnants of the glue inside the bony defects at the first two weeks of the follow up period. The application of the glue to bony defects showed no or little

effect on bone healing compared with the control group. Histoacryl blue showed an anti-inflammatory effect which was proved by the decrease in the number of inflammatory cells in the cyanoacrylate group compared to control group in the first two weeks of the follow up which is completely mismatched with the foreign body reaction effect stated by Ekelund and Nilsson,¹¹ and in agreement with Ddas¹² and Heiss et al¹⁰ as Heiss C et al¹⁰ stated that histomorphometrical analysis of his study did not reveal any significant differences in fracture healing between the glue and the control group at any time.

Our study strongly agree as with Caroli et al¹³ who stated that during his experiments to evaluate the ability of cyanoacrylate adhesive to ensure setting of small bone fragments that would otherwise be unstable, the results obtained showed good stability of the bone fragments, good bone consolidation and absence of foreign body reactions.

CONCLUSION

The application of cyanoacrylate tissue adhesive to bone defects shows absence of foreign body reactions, infection, and no impeding of bone healing, with an anti-inflammatory effect, yet it should be used in caution to decrease the amount of the glue introduced inside the gap as a residue of the glue was seen histologically in the first two weeks after application.

ACKNOWLEDGEMENT

This research was funded by College of Dentistry Research Center (CDRC), King Saud University, KSA. Project number is (F1177).

REFERENCES

- 1 Marvin Ryou, MD, Christopher C Thompson, MD Tissue Adhesives: A Review. *Tech Gastrointest Endosc*, 2006, 8: 33-37
- 2 Himel, HN, Persing, J. A. Tissue adhesives in plastic surgery. *Adv Plast Reconstr Surg* 1994; 10: 73
- 3 Vogel, A., O'Grady, K., and Toriumi, D. Surgical tissue adhesives in facial plastic and reconstructive surgery. *Facial Plast Surg* 1993; 9: 76
- 4 Singer JA, and Thode HC. A review of the literature on octylecyanoacrylate tissue adhesive. *Am J Surg* 2004; 187: 238-248
- 5 Shermak MA, Wong L, Inoue N, Chao E, Manson PN. Butyl-2-Cyanoacrylate Fixation of Mandibular Osteotomies. *Plastic reconsurg* 1998; 102: 319-324
- 6 Quinn, J, Wells, G., Sutchffle T. A randomized trial comparing octylecyanoacrylate tissue adhesive and sutures in the management of lacerations. *JAMA* 1997; 277: 1527
- 7 Trott, A. T. Cyanoacrylate tissue adhesives: An advance in wound care. *JAMA* 1997; 277: 1559
- 8 Kamer, FM, Joseph, J. H. Histoacryl: Its use in aesthetic facial plastic surgery. *Arch Otolaryngol Head Neck Surg* 1989; 115: 193
- 9 Ddas B, Alkan S, Celik M, Basak T. Treatment of tripod fracture of zygomatic bone by N-2-butyl cyanoacrylate glue fixation, and its effects on the tissues. *Eur Arch Otorhinolaryngol* 2007; 264: 539-544
- 10 Heiss C, Hahn N, Wemisch S, Alt V, Pokinskyj P, Horas U, Kilian O, and Schnettler R. The tissue response to an alkylene bis(dilactoyl)-methacrylate bone adhesive. *Biomaterials* 2005; 26: 1389-1396
- 11 Ekelund A, Nilsson OS. Tissue adhesives inhibit experimental new bone formation. *Int Orthopaed* 1991; 15: 331-334
- 12 Ddas B, Alkan S, Celik D, Coskun BU, Yalimz I, Basak T. The efficacy of N-2-butyl cyanoacrylate in the fixation of nasal septum to the anterior nasal spine in rabbits: experimental study. *Eur Arch Otorhinolaryngol* 2007; 264: 1425-1430
- 13 Caroli A, Marcuzzi A, Limontini S, Maiorana A. An experimental study of a cyanoacrylate biological adhesive in view of its use in the fixation of various fractures of the fingers. *Ann Chir Main Memb Super* 1997; 16: 138-145