Comparison between N-butyl cyanoacrylate tissue adhesive and Ethilon nylon sutures in extraoral maxillofacial incisions: A randomized prospective study

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ABSTRACT

Objectives: Wound closure is a part of any surgical procedure. Wound care and healing process are concepts, which are usually reliant upon sutures. The suture and non-suture repair of the tissues has been a major concern to surgeons for over four thousand years. The objective of this study is to compare the rates of infection, wound dehiscence, necrosis and time required by N-butyl cyanoacrylate tissue adhesive and nylon sutures in extraoral maxillofacial wound closer.

Materials and methods: 24 patients requiring external wound closing were included in this study. Patients were divided in two groups, in one group wound closer was done by N-butyl cyanoacrylate tissue adhesive and by conventional nylon suture in the other group. The software STATA[®] of StataCorp was used in statistical analysis if this study.

Results: Wound infection, dehiscence, necrosis of tissue edges, time taken for closure was much less in case of tissue adhesive than conventional sutures.

Conclusion: Advantages of tissue adhesives over conventional wound closure techniques include easy to use, excellent bacteriostatic property, decreased repair time, elimination of recall visits and comparable short and long-term cosmetic outcome. Though tissue adhesives have many advantages over conventional wound closure techniques, they can be used as an alternative to sutures only in superficial small and tension free skin incisions or lacerations.

1. Introduction

“Never judge the surgeon until you have seen him closing the wound” - Lord Moynihan.

Injury to any of the tissues of the body, especially that caused by physical means and with interruption of continuity is defined as a wound.¹ Wound healing is a natural and spontaneous phenomenon. When tissue has been disrupted so severely that it cannot heal naturally without complications or possible disfigurement of dead tissue and foreign bodies must be removed, infection treated, and the tissue must be held in apposition until the healing process provides the wound with sufficient strength to withstand stress without mechanical support. A wound may be approximated with sutures, staples, clips, skin closure strips, or topical adhesives.² Advantages of tissue adhesives over

conventional sutures include easy to use, excellent bacteriostatic activity decreased repair time and good cosmetic outcome.³ Currently available surgical tissue adhesives can be categorized as either fibrin tissue adhesives or cyanoacrylates.

Although fibrin tissue adhesives and cyanoacrylates are often discussed under the general topic of surgical tissue adhesives, these two substances have different indications and mechanisms of action.⁴

This study was aimed to evaluate the rates of associated infection, wound dehiscence, necrosis of tissue wound, time required by N-butyl cyanoacrylate tissue adhesive when compared to nylon sutures in extraoral maxillofacial wound closer.

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Fig. 1. Box plot for age distribution of patients for each group.

2. Materials and methods

This randomized prospective study involves twenty-four patients who attended our department from February 2016 till November 2017 for various surgical procedures like open reduction internal fixation, distraction osteogenesis, incision on facial skin. Twelve cases were placed in each group of case and control (Fig. 1).

The sample size was selected from the patient pool, reporting to our department, who satisfied the inclusion and exclusion criteria. Though, the sample size was rather small its was enough to show and compare the two methods of wound closure.

The software STATA® of StataCorp was used in statistical analysis if this study.

Procedures requiring extra-oral incisions less than 6 cm were included on a two-group basis. Case group received the wound closure with N-butyl cyanoacrylate (REKSEAL®) while the control group wound was closed using ETHILON® Nylon non-absorbable Suture (ETHICON).

2.1. Inclusion criteria

- Patients age group was selected between 18 and 70 years.
- Facial incision should be within 2–6 cm limit.
- Both sexes were included in the study.
- Patients who agreed to turn up for post-operative evaluation.

2.2. Exclusion criteria

- Any patient not fulfilling inclusion criteria was excluded.
- Surgical incisions which required to be closed under tension.
- Wounds from animal or human bites.
- Decubitus ulcers & crush wounds
- Known allergy to cyanoacrylate
- Patients with diabetes mellitus.
- Known personal or family history of keloid formation or scar hypertrophy.

2.3. Materials used

In our study we used two materials for skin closure, one being used in case and the other in control group.

2.4. Case group

N-butyl cyanoacrylate (REKSEAL®) from the company REKVINA PHARMACEUTICALS.

2.5. Control group

4.0 ETHILON® Nylon Sutures, ETHILON JOHNSON & JOHNSON.

2.6. Armamentarium

Case group (cyanoacrylate):

1. Disposable hypodermic syringes.
2. N-butyl cyanoacrylate (REKSEAL®) vial.
3. 3.0 vicryl absorbable suture.
4. Surgical scalpel.
5. Tweezers.
6. Cotton roll.
7. Addison's tissue forceps.
8. Mosquito forceps.
9. Dry gauze.
10. Straight probe.
11. Skin hooks.
12. Mayo suture cutting scissors.
13. Needle holding forceps.

Control group (suture):

1. 4.0 ETHILON® Nylon sutures.
2. Surgical scalpel.
3. 3.0 vicryl absorbable suture.
4. Tweezers.
5. Cotton roll.
6. Addison's tissue forceps.
7. Mosquito forceps.
8. Dry gauze.
9. Straight probe.
10. Skin hooks.
11. Mayo suture cutting scissors.
12. Needle holding forceps.

2.7. Our protocol

1. Informed consent is taken for all the patients that include both the groups in the study.
2. Short case history for each case has been maintained and skin sensitivity test is done for case group patients prior to surgery.
3. Intraoperative timing of skin closure was maintained in both groups via a stopwatch.
4. On 1st, 3rd and 7th postoperative day patient was observed for any dehiscence, necrosis and infection.

3. Follow up of patients was done to assess any future complications

3.1. Surgical procedure

All procedures were done under general anesthesia, twelve patients were selected for case group (cyanoacrylate), and twelve patients were selected for control group (suture).

Extraoral incisions were made in the desired maxillofacial region for various surgical procedures as per inclusion criteria.

Incision lengths in the range of 2–6 cm were closed in both groups by sutures and cyanoacrylates.

In case group (Fig. 2), the wound was closed in layers. The deeper tissues and muscles were closed with 3.0 vicryl sutures. The skin edges were cleaned and dried. The skin edges were approximated, everted and maintained in position with tissue forceps, skin hooks, N butyl cyanoacrylate was applied sparingly along the edges of the wound with the help of applicators or disposable hypodermic needle. The approximated skin edges were maintained in the respective position to dry, after which wet gauze dressing was placed intermittently for the first

Fig. 2. Application of N-butyl cyanoacrylate in incision closure.

24 h later it was kept open.

In control group (Fig. 3), 3.0 vicryl was used to approximate the underlying muscles and tissues. The skin was closed with 4.0 nylon sutures with simple interrupted suture technique. An antiseptic dressing (povidone-iodine) was applied immediately after closure of the wounds and changed intermittently for the first 24 h only.

Skin closure timing was monitored in both groups using a stopwatch.

Any signs of inflammation, dehiscence, pus discharge, wound gaping or any blackening of skin with tissue necrosis was noted on an evaluation sheet during the 1st, 3rd and 7th postoperative day for on both groups.

4. Result

The study included both male and female patients of ages 18 to 70. The z value of probability for timing and age being 0.33 does not signify the variation of time taken for closure with the age (*Two sample Mann Whitney test*).

Fig. 3. Closure of incision by using suture.

4.1. Wound infection

None of the cases showed wound infection in the first 2 days. Only three cases showed wound infection on 3rd and 7th postoperative days at sites closed with sutures. P value being 0.064 (Fig. 4).

4.2. Wound dehiscence

Wound dehiscence was not seen in any of the cases in the first postoperative day. Only two cases of N-butyl cyanoacrylate site showed wound dehiscence (16.67%). Whereas suture site showed wound dehiscence in three cases (25%). P value being 0.615 (Fig. 5).

4.3. Necrosis of tissue edges

No case had tissue necrosis. There was no difference in the incidence of necrosis of tissue edges the incisions closed with N-butyl-2-cyanoacrylate and sutures.

4.4. Time taken for closure

Comparatively the time taken for closure of skin was faster in application of cyanoacrylates than application of sutures. The average time for closure of incisions using cyanoacrylate was 78 ± 1.17 s and that of sutures is 222 ± 1.17 s (Figs. 6 and 7).

5. Discussion

5.1. Summary of key findings

Primary outcome measures include wound infection, wound dehiscence and tissue necrosis. Firstly, three cases closed with sutures showed wound infection on 3rd and 7th postoperative days and no cases closed with cyanoacrylate. Which was supported by a study done by Kumar MS et al.,⁷ in which he found that on the 3rd and 7th postoperative days epithelialization was better on the sides treated with n-butyl-2-cyanoacrylate but significant inflammation and scar formation in the sites closed with black silk suture. Similar data was found by Vishakha N. et al.⁸ in a study done on pediatric lacerations. Vaaka PH et al.,⁹ in their study found higher incidence of wound infection and wound dehiscence in wounds treated with silk sutures, when compared to n-butyl-2-cyanoacrylate tissue adhesive.

Secondly, only two (16.67%) sites closed by of N-butyl cyanoacrylate showed wound dehiscence but three (25%) cases closed by sutures showed wound dehiscence. Higher incidence of wound dehiscence was observed in wounds treated with silk sutures than cyanoacrylate in study done by Vaaka PH et al.⁹ However, Kim et al.¹⁰ and Soni A et al.,¹¹ when comparing conventional sutures and cyanoacrylate tissue adhesive, found no wound dehiscence, allergic reactions, or any other significant wound closure complications occurred with either technique.

Thirdly, no case had tissue necrosis. There was no difference in the incidence of necrosis of tissue edges the incisions closed with N-butyl-2-cyanoacrylate and sutures. Similarly, Kumar MS et al.⁷ found no evidence of necrosis in any of the treated cases.

Secondary outcome measure of our study includes time taken for wound closure, which was almost three times faster in case of cyanoacrylates than sutures. In a study done by Soni A et al.¹¹ in total forty incisions, mean time of closure was significantly faster with cyanoacrylates at 69.50 ± 33.39 s compared with 379.00 ± 75.39 s in the suture group.¹¹ Vishakha N. et al.⁸ and Vaaka PH et al.⁹ found the mean time taken for skin closure is much faster and time-saving in case of cyanoacrylates.

Fig. 4. Infection rate in suture and cyanoacrylate.

Fig. 5. Wound dehiscence in suture and cyanoacrylate groups.

5.2. Strengths and limitations of the study

In this randomized prospective study, we compared the rate of wound infection, dehiscence, necrosis of tissue edges and time taken for closure by N-butyl cyanoacrylate tissue adhesive and Ethilon nylon sutures in extraoral maxillofacial incisions. Twenty-four patients reporting to our department from February 2016 to November 2017 for various surgical procedures like open reduction internal fixation, distraction osteogenesis, were included which required incision on facial skin as per inclusion criteria of this study. The 24 cases were equally and randomly distributed in two groups one to be treated with (case group) and another with Ethilon nylon sutures (control group), each having 12 cases. However, in this study we did not compare the

cosmetic outcome of cyanoacrylates and traditional sutures, which may be cited as the limitation of our study. Although, Jonathan G. Martin et al. found in their study that scar cosmesis and patient outcomes did not significantly vary between skin adhesive versus subcuticular suture.¹² No differences were observed after 6 months in collagen expression, in the study done by Gemma Pascual et al., except slightly reduced collagen I deposition in Glubran/Ifabond and collagen III deposition in the suture group.¹³

5.3. Interpretation and implications

Cyanoacrylate has a plethora of advantages over conventional sutures as they do not demand any specialized armamentarium or skill.

Fig. 6. Histogram of frequency in time taken for closure by both groups.

Fig. 7. Box plot for time taken for closer by sex of patients.

Moreover, there is no need of removal as conventional sutures. N-butyl cyanoacrylate is being used by the developed countries as an alternative to conventional sutures. But in developing countries like India its usage is very limited, which is mostly because of lack of awareness and availability. In our country where there is an alarming paucity of doctors, especially in the government sectors, semi-skilled persons can use cyanoacrylate tissue glue to yield satisfactory results in emergency wound closure in tension-free areas in tertiary health care centers.

5.4. Controversies raised by this study

No controversies were raised by this study because the results of this study correlates with the existing studies.

5.5. Future research directions

Further research in future can be done on intraoral wound closure, bone fracture healing, efficacy as hemostatic agent, dental splinting, and neurosurgical wound closer by tissue adhesives. Akcal MA et al.¹⁴

found that cyanoacrylate was rapidly and easily applied in the segmental fractures of rat tibia model but did not cause any superior radiological and clinical results compared to the control group. Sohn JJ et al.¹⁵ in 2016 proved that application of Short-chain cyanoacrylates (SCCA), such as ethyl-2-cyanoacrylate causes bone damage resulting in the loss of bone regeneration in the Calvaria of CD1 Mice. Parimala Sagar et al.¹⁶ in 2015 concluded that isoamyl cyanoacrylate can be used for intraoral wound closure, as an alternative to sutures for gluing the mucoperiosteum to bone, for example, after impaction removal, periapical surgeries, and cleft repair. Chadwick et al.¹⁷ successfully achieved local hemostasis, in a woman with a facial arteriovenous malformation, using a combination of cyanoacrylate and local hemostatic agents, which proved the hemostatic property of cyanoacrylates. Cobb AR et al.¹⁸ in 2011 proved in their study that such adhesives can be used for short-term dental splinting. Tacconi and Spinelli¹⁹ did a study on 475 cases of spinal surgery and concluded that cyanoacrylate glue can be a valid and useful alternative for spinal wound closure. Tacconi et al.,²⁰ in a recent study done on 362 patients, confirmed that cyanoacrylate glue can be a valid and useful alternative to traditional techniques for wound closure in brain surgery, carrying several advantages.

5.6. Contraindications

Contraindications of using cyanoacrylates include gangrenous, actively infected, or decubitus injuries. Use on patients with a known hypersensitivity to cyanoacrylate or formaldehyde is also an absolute contraindication.²¹ The major disadvantage is reduced tensile strength, so they should not be used in high tension areas.²² It should not be used in the wounds in high moisture or friction areas such as the axilla, hands, or feet, animal or human bites, stab or puncture wounds, vermillion surface wounds, and patients with burst stellate lacerations. Cyanoacrylates are also not recommended in patients with peripheral vascular disease, clotting disorders, insulin-dependent diabetes, or a personal or family history of keloid formation or hypertrophy.²¹

6. Conclusion

Conventional skin suturing techniques do have certain disadvantages namely undesired trauma, pushing of microorganisms in deeper tissue layers, requirement of application of local anesthesia and more time consumption. It can inflict needle stick injury to operating hand and also requires recalling the patient for suture removal. When tension upon the wound edges is too high, it produces prominent cross-hatching along the scar and a poor cosmetic appearance.²

Longer chain cyanoacrylate degrades slower than the shorter chained ones. Tissue adhesives are not indicated for wound closure over highly mobile areas such as joints and in areas of usage and friction such as hands or feet.⁵

Based on the present study N-butyl cyanoacrylate gave comparative better results and hence can be used safely and as a reliable method for closing small tension free facial incisions placed in maxillofacial regions in preference to sutures. However further studies should be conducted to compare its performance and possible side effects which might be explored in the future.

Conflicts of interest

The authors do not have any conflict of interest and financial or personal relationship with any other person or organisation that could inappropriately influence (bias) this work.

References

1. Bruns Thomas B, Robinson Bryan S, Smith Ralph J, et al. A new tissue adhesive for laceration repair in children. *J Pediatr*. 1998;132:1067–1070.
2. Eaton AC. A controlled trial to evaluate and compare a suture less skin closure technique (Op-site skin closure) with conventional skin suturing and clipping in abdominal surgery. *Br J Surg*. 1980;67:857–860.
3. Ozturan Orhan, Miman Murat Cem, Aktas Davut, Oncel. SemihButylcyanoacrylate tissue adhesive for columellar incision closureThe. *J Laryngol Otol*. Jul 2001;115:7 (ProQuest).
4. Schneider GMS Current Topics in Otorhinolaryngology. *Head Neck Surg*. 2009;8 ISSN 1865-1011.
5. Elemen L, Seyidov TH, Tugay M. The advantages of cyanoacrylate wound closure in circumcision. *Pediatr Surg Int*. 2011;27:879–883.
7. Kumar MS, Natta S, Shankar G, Reddy SH, Visalakshi D, Seshiah GV. Comparison between silk sutures and cyanoacrylate adhesive in human mucosa- a clinical and histological study. *J Int Oral Health*. 2013;5(5):95–100.
8. Devrukhkar VN, Hegde RJ, Khare SS, Saraf TA. Evaluation of isoamyl 2-cyanoacrylate tissue adhesive in management of pediatric lacerations: an alternative to suturing. *Ann Maxillofac Surg*. 2015;5(1):49–54.
9. Vaaka PH, Patlolla BR, Donga SK, Ganapathi AK, Kurapati V. Cyanoacrylate: an alternative to silk sutures: a comparative clinical study. *J NTR Univ Health Sci*. 2018;7:108–114.
10. Kim J, Singh Maan H, Cool AJ, Hanlon AM, Leffell DJ. Fast absorbing gut suture versus cyanoacrylate tissue adhesive in the epidermal closure of linear repairs following mohs micrographic surgery. *J Clin Aesthet Dermatol*. 2015;8(2):24–29.
11. Soni A, Narula R, Kumar A, Parmar M, Sahore M, Chandel M. Comparing cyanoacrylate tissue adhesive and conventional subcuticular skin sutures for maxillofacial incisions—a prospective randomized trial considering closure time, wound morbidity, and cosmetic outcome. *J Oral Maxillofac Surg*. 2013 Dec;71(12):2152.e1–2152.e8.
12. Martin Jonathan G, Hollenbeck Scott T, Janas Gemini, et al. Randomized controlled trial of octyl cyanoacrylate skin adhesive versus subcuticular suture for skin closure after implantable venous port placement. *J Vasc Interv Radiol*. 2017;28(Issue 1):111–116 ISSN 1051-0443.
13. Pascual Gemma, Rodríguez Marta, Mesa-Celler Claudia, et al. Sutures versus new cyanoacrylates in prosthetic abdominal wall repair: a preclinical long-term study. *J Surg Res*. 2017;220:30–39 ISSN 0022-4804 <https://doi.org/10.1016/j.jss.2017.06.074>.
14. Akcal MA, Poyanli O, Unay K, Esenkaya I, Gokcen B, Firatligil AS. Effect of N-butyl cyanoacrylate on fracture healing in segmental rat tibia fracture model. *J Orthop Surg Res*. 2014;9:76. <https://doi.org/10.1186/s13018-014-0076-5> Published 2014 Sep. 11.
15. Sohn JJ, Gruber TM, Zahorsky-Reeves JL, Lawson GW. Comparison of 2-ethyl-cyanoacrylate and 2-butyl-cyanoacrylate for use on the Calvaria of CD1 mice. *J Am Assoc Lab Anim Sci*. 2016;55(2):199–203.
16. Sagar Parimala, Prasad Kavitha, Lalitha RM, Ranganath Krishnappa. Cyanoacrylate for intraoral wound closure: a possibility? *Int J Biomater*. 2015;6 2015 Article ID 165428 <https://doi.org/10.1155/2015/165428>.
17. Chadwick Jeffrey W, terBrugge Karel, Lam David K. Novel technique using cyanoacrylate and local hemostatic agents in the management of high-risk exodontia bleeding in a patient with a large facial arteriovenous malformation. *J Oral Maxillofac Surg*. 2016;74(Issue 8):1574–1583 ISSN 0278-2391.
18. Cobb AR, Ahmad S, Kumar M. Use of n-butyl 2-cyanoacrylate tissue adhesive to splint traumatised teeth in the emergency department. *Br J Oral Maxillofac Surg*. 2011 Sep;49(6):483–485.
19. Tacconi L, Spinelli R. Skin closure: our experience with glue in spinal surgical cases. A ten years experience. Open access 002. *J Neurol Neurosurg*. 2018;7(2):555709.
20. Tacconi Leonello, Spinelli Roberto, Signorelli Francesco. Skin glue for wounds closure in brain surgery: our updated experience. *World Neurosurgery*. 2019;121:e940–e946 ISSN 1878-8750.
21. Perera AGN, Tavarez MM. 2-Octyl cyanoacrylate. [Updated 2018 Dec 13]. *StatPearls*. Treasure Island (FL): StatPearls Publishing; 2018 Jan [Internet]. <https://www.ncbi.nlm.nih.gov/books/NBK532293/>. Available from:.
22. Singer AJ, Thode HC. A review of the literature on octylcyanoacrylate tissue adhesive. *Am J Surg*. 2004;187(2):238–248.