

# Histopathological Effects of Histoacryl on Oral Secondary Wound Healing: A Comparative Experimental Study

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## الخلاصة

**الأهداف:** يهدف البحث إلى تقييم المقاطع النسيجية لمراحل الالتئام للجروح الثانوية في لسان الأرنب المغطاة بوساطة السيانواكريليت (Histoacryl) اللاصق. **المواد وطرائق العمل:** لغرض إجراء الدراسة تم استخدام عشرين أرنباً محلياً من الذكور. وقد تم إجراء عييين جراحيين على كل نصف من اللسان، كل منهما ٥ ملم وبشكل بيضوي، العيب من جهة اليمين ترك بدون أن يغطي بأي شيء. والعيب من جهة اليسار غُطي بطبقة خفيفة من المستوكريل. على حسب أيام التضحية وقد قسمت الأرانب إلى أربع مجاميع في كل مجموعة خمس أرانب (٣، ٧، ١٤، ٣٠) يوماً. بعد ذلك جمعت عينات اللسان بعد التضحية فوراً، وقسمت إلى نصفين، النصف الأيمن هو السيطرة والنصف الأيسر هو للدراسة مما يعطي لكل مجموعة مجموعتين ثانويتين اضافيتين. بعد ذلك وضعت العينات في الفورمالين وأرسلت لغرض الدراسة النسيجية المختبرية. **النتائج:** أظهرت نتائج التقييم النسيجي فرقاً معنوياً عند مدة (٣، ٧، ٣٠) يوماً في لسان الأرنب لقياس الالتئام بقيمة  $p\text{-value} < 0.05$ ، بينما لم يكن هناك فرق معنوي في مجموعة أل ١٤ يوم. للالتئام في لسان الأرنب كان هناك فرق معنوي في ٣ أيام بقيمة  $p\text{-value} < 0.05$ . ولم يكن هناك فرق ل (٧، ١٤، ٣٠) يوماً. **الاستنتاجات:** يمكن الاستنتاج من هذه الدراسة، بأن مادة المستوكريل اللاصقة للجروح، سرّعت من عملية الالتئام بتقليل الالتئام وتخفيف الالتئام لكل من الجروح الفموية الثانوية.

## ABSTRACT

**Aims:** The aim of this study is to evaluate the histopathological findings of healing phases in secondary wound defect on rabbit's tongue, dressed with N-butyl -2- Cyanoacrylate (Histoacryl) tissue adhesive. **Materials and Methods:** Twenty domestic male rabbits had been selected. Two defects were done on each half of the tongue, 5mm oval shape, the right one left without covering, the left one covered by a thin layer of Histoacryl. Animals could be divided into four groups, each group contain five rabbits, according to sacrificing date into 3 days, 7 days, 14 days, and 30 days. Tongue specimen were collected after sacrificing the rabbit immediately, then divided into two halves, the right half was control one and the left half was the study one, giving off further two subdivisions for each group. The specimen were placed in formaldehyde and sent for histopathological examination regarding inflammatory and reepithelialization scoring. **Results:** The histopathological findings of this study revealed that there was a significant difference of inflammation between the two groups at 3 days, one week, one month, of tongue at  $p\text{-value} < 0.05$ , while there was no significant difference at two weeks period. In reepithelialization of the tongue a significant difference at 3 days at  $p\text{-value} < 0.05$ , and no significance at one week, two week, and one month. **Conclusion:** This study concluded that histoacryl tissue adhesive accelerate healing by decreasing inflammation, and inducing reepithelialization of mucosal secondary wound defects.

**Keywords:** Histoacryl, secondary defect, tongue of rabbit.

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## INTRODUCTION

Wound healing is essential for survival; The goal of wound management is to close the wound as soon as possible; Improperly managed wounds can be life threatening, functionally disabling, and cosmetically devastating.<sup>(1)</sup>

Wound healing is a complex and dynamic process with the wound environment changing with the changing health status of the individual.<sup>(2)</sup>

There are three types of wound healing, primary, secondary, and tertiary intention.<sup>(3)</sup>

Primary wound healing is the way most surgical wounds heal, The wound edges are approximated directly using sutures, tissue glue, tapes or a mechanical device.<sup>(1)</sup>

Secondary intention healing is characterized by filling of the defect with granulation tissue, reepithelialization, and sub-

sequent wound contraction.<sup>(4-6)</sup>

While tertiary healing occurs when approximation of the wound edges is intentionally delayed by three or more days after surgery or injury.<sup>(1,4)</sup>

Tongue is the largest structure in the oral cavity; Its extreme mobility is due to the large intertwined mass of skeletal muscle fibers that compose its bulk.<sup>(7)</sup>

Cyanoacrylates (CA) were first synthesized by Ardis in 1949; CA derivatives are one of the series of homologous compounds known as alkyl cyanoacrylates.<sup>(8)</sup>

CA have a variety of medical, dental, and commercial applications as adhesives; these adhesives have been extensively used for closure of cutaneous wounds and in a wide variety of surgical procedures; over the last three decades, surgeons have actively searched for a liquid substance with adhesive properties, which can be applied to the wound edges, holding them in proximity with minimal interference in the healing process.<sup>(9)</sup>

The possibility of using an adhesive substance that can make the closure of different tissues simpler, faster and more efficient is an appealing idea that has drawn the attention of surgeons.<sup>(10)</sup>

The application of CA is used as an alternative to the traditional ways of closing wounds after surgery; this method has its advantages because no special instruments are needed, it does not involve anesthesia and there are no stitches to remove.<sup>(11)</sup>

N-Butyl-2-CA was approved for clinical use at the beginning of 1996 and is becoming an increasingly popular method for closure of superficial lacerations under low tension; the use of the adhesive reduces treatment time and is a pain-free method of closure, allowing good cosmetic results to the facial injuries.<sup>(9, 12)</sup>

In recent years, cyanoacrylate application has gained increasing interest in a variety of surgical cases, as well as head and neck surgical procedures.<sup>(13)</sup>

### MATERIALS AND METHODS

This study was performed in the Oral and Maxillofacial Surgery Department, from 28/2/2012 to 21/6/2012 at Dental College, University of Mosul. Twenty domestic looks healthy male rabbits had been selected, the average weight of these rabbits were  $1155 \pm 500$  gm. These rabbits bred in the animal house prepared for the experimental studies in the Collage of Dentistry University of Mosul. The feeding of these rabbits done 3 times daily with normal diet (lettuce and grass) and water. They all have good health throughout the period of the study.

For achieving general anesthesia each rabbit gave 40 mg/kg ketamine injection<sup>(14)</sup> intramuscularly in the thigh muscle of the rabbit, mixed with xylazine 4 mg/kg (as a muscle relaxant) of rabbit weight,<sup>(15)</sup> as shown in Figure (1).



Figure (1): Preoperative procedure, Anesthesia given to rabbit.

After achieving anesthesia each animal laid down on its side after toweling and open the mouth, then tongue was pulled out and stitched by black silk suture (3.0,

China) from the tip to maintain the tongue out of the mouth during the surgical procedure. On each half of the tongue 5mm × 4mm oval shape defect was created, depth

about 3mm, the right one left without covering, the left side covered by a thin

layer of Histoacryl after haemostasis, which dry after 3-5 seconds Figure (2).

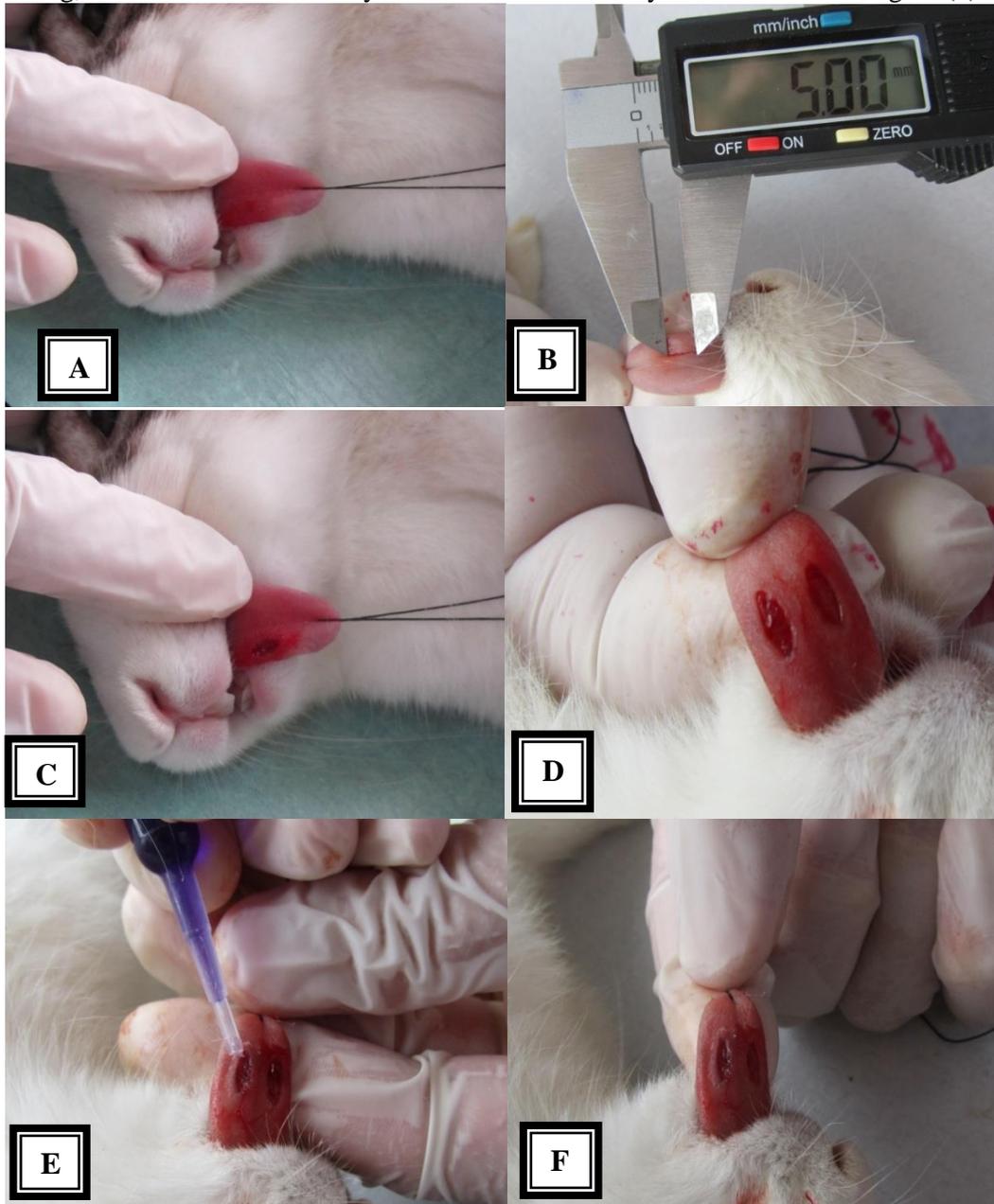


Figure (2):Surgical Procedure for Tongue.

- A. Tongue stitch for retraction.
- B. 5mm ulcer was made.
- C. Oval shape defect was created by cutting the edges of incision.
- D. Similar defect was made in the other side of tongue.
- E. Histoacryl applied to the defect in the left side of tongue.
- F. Tongue after Histoacryl application.

The specimens of tongue were collected after sacrificing the rabbit, the tongue was sectioned by blade as whole from the base which is about 2 cm in length, then

divided into two halves longitudinally, these two halves preserved in 10% formaldehyde for 48 hours Figure (3).

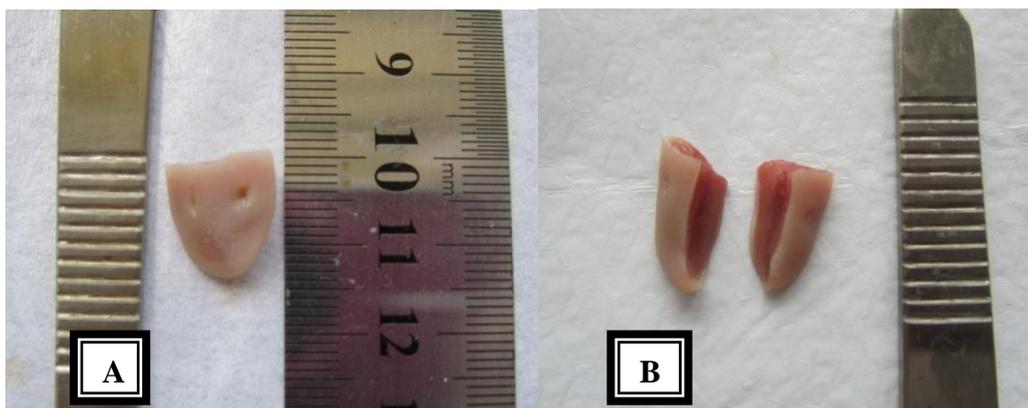


Figure (3): Specimen Collection. A. Tongue after sacrificing the rabbit. B. Two halves of tongue after sectioned longitudinally

According to sacrificing date, animals could be divided into four groups<sup>(16)</sup>:

- G1: Animals sacrificed after 3 days.
- G2: Animals sacrificed after 1 week.
- G3: Animals sacrificed after 2 weeks.
- G4: Animals sacrificed after 1 month.

Each one of these groups include two sub groups which is:

Subgroup C: Which included the control group of the tongue.

Subgroup H: Which included the study group of the tongue.

Histopathological Examination used to assess the slides, this system include histopathological scoring for both inflammatory and reepithelialization<sup>(16-20)</sup>. Inflammatory scoring include the following:

Score 1: Predominance of acute inflammation.

Score 2: Predominance of granulation tissue.

Score 3: Predominance of chronic inflammation (fibroblasts beginning to proliferate).

Score 4: Resolution and cicatrization (reduction or disappearance of chronic inflammation).

While reepithelialization scoring include the following:

Score 0: Reepithelialization at the edge of the wound.

Score 1: Reepithelialization covering less than half of the wound.

Score 2: Reepithelialization covering more than half of the wound.

Score 3: Reepithelialization covering the entire wound, irregular thickness.

Score 4: Reepithelialization covering the entire wound, normal thickness.

Statistical analysis was made by using spss 19 computer soft ware program. Data were analyzed by using Mann - Whitney NPar Test was used to compare means between groups as shown in Figure (8, 9). Kruskal -Wallis NPar Test was used to compare means within groups as shown in Figure (10, 11).

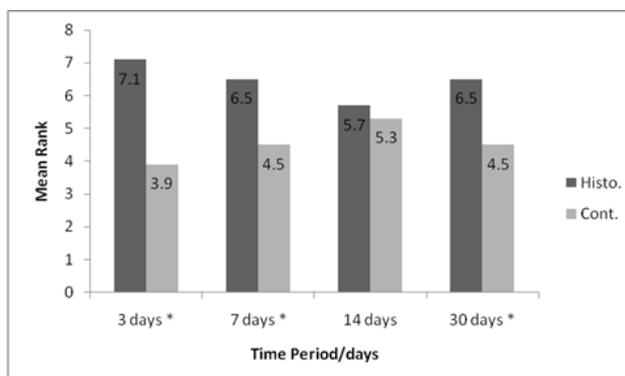


Figure (8): Mean Ranks for Comparison between control and Histoacryl of inflammation score of tongue.

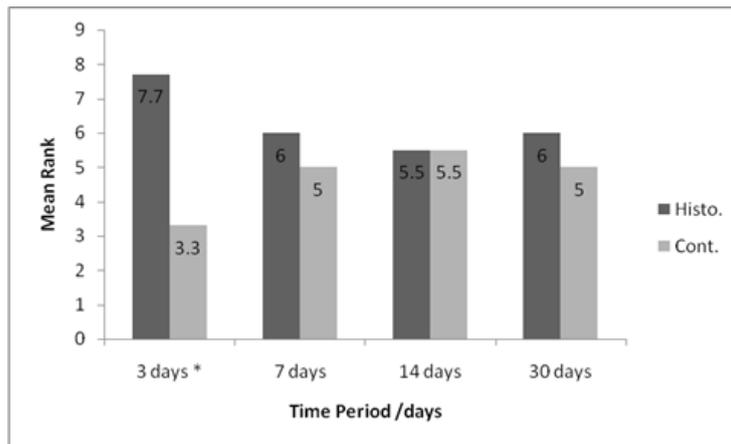


Figure (9): Mean Ranks for Comparison between control and Histoacryl of reepithelialization score of tongue.

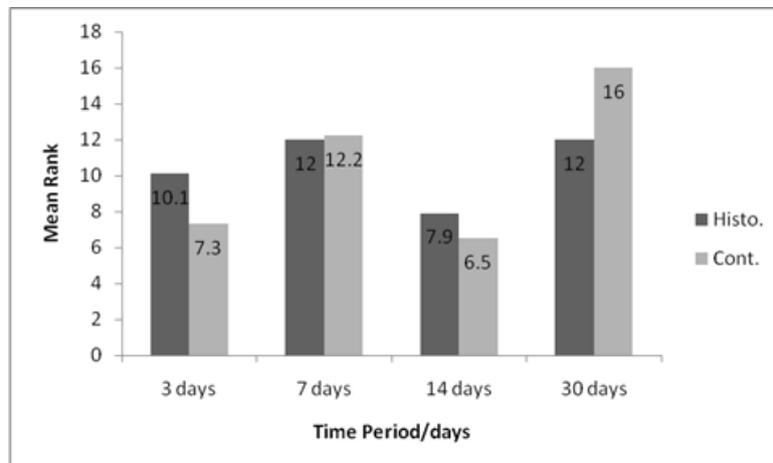


Figure (10): Mean Ranks for comparison within groups of control and histoacryl of inflammation score of tongue.

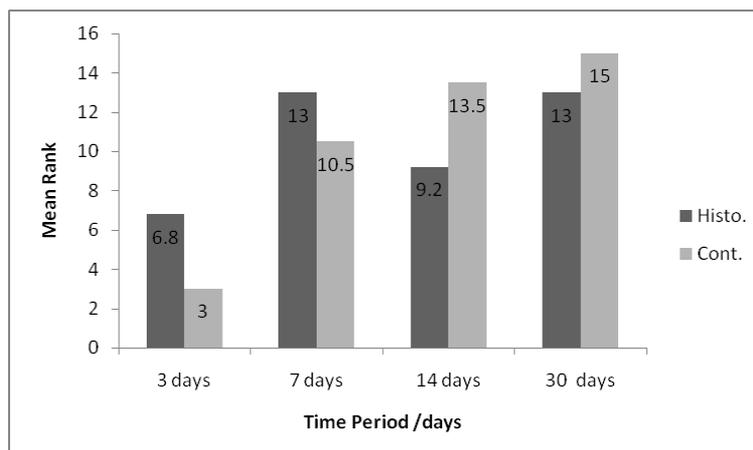


Figure (11): Mean Ranks for comparison within groups of control and histoacryl of reepithelialization score of tongue.

## RESULTS AND DISCUSSION

The results include inflammatory and reepithelialization examination in the four

periods of the study as shown in Table (1).

Table (1): Mann-Whitney Statistical Test (p-value) of Histopathological Finding of Tongue Comparing Between Control and Histoacryl Groups.

Duration	Inflammation (p-value)	Reepithelialization (p-value)
3Days	0.015*	0.016*
7 Days	0.031*	0.69
14 Days	0.841	1.00
30 Days	0.031*	0.69

Significance (\*): p value  $\leq 0.05$

In the three days period, there is a predominance of polymorpho nuclear leukocytes in the control group slides with minimal reepithelialization at the wound edge,

while the Histoacryl slides showed decrease in the inflammation and complete reepithelialization with irregular thickness Figure (4).

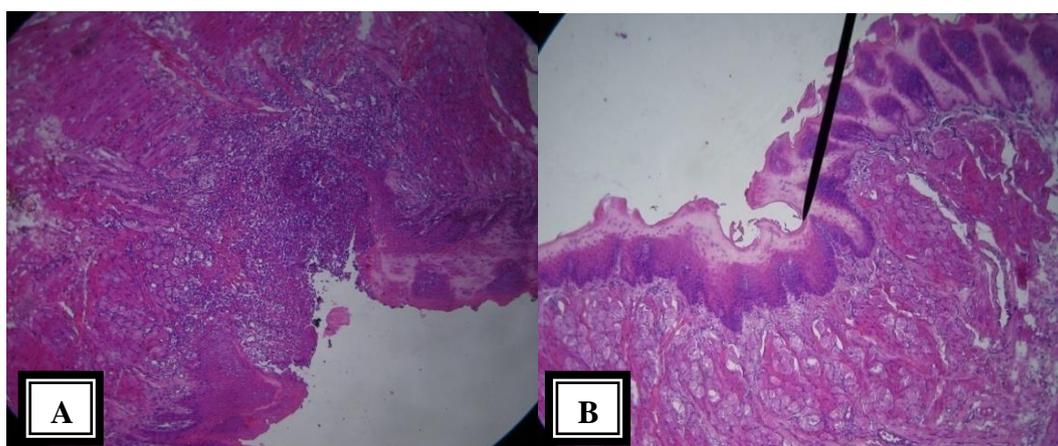


Figure (4): Three Days periods. A: for control group. B: for Histoacryl group (Magnification power  $\times 100$ ).

Singer et al found that tissue adhesive function as microbial barrier and as an occlusive dressing. <sup>(21)</sup> Wounds treated with 2-octyl cyanoacrylate reepithelialized more rapidly than those treated with a hydrocolloid dressing, a standard bandage, or dry air exposure. <sup>(22)</sup>

In one week period, the control group slides showed decrease of inflammation and reepithelialization with irregular thickness, while the Histoacryl group slides showed resolution of inflammation and complete reepithelialization (Figure 5)

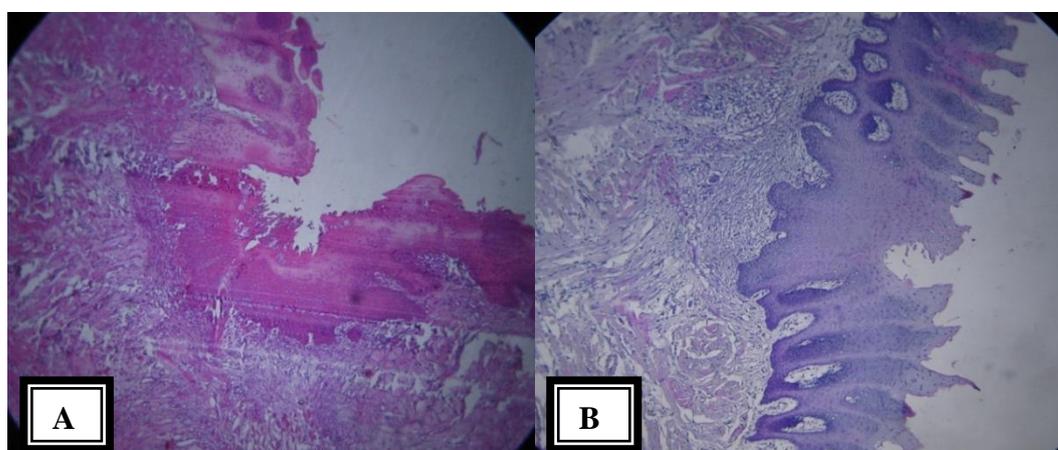


Figure (5): One Week Period. A: for control group. B: for Histoacryl (Magnification power  $\times 100$ ).

Alonso et al found that at day 7 the specimens showing greater resolution of

the acute inflammatory response were those belonging to scalpel + Histoacryl, as was observed in other comparative studies.<sup>(16)</sup> While Ashoka found that both groups of incision closed by suture and adhesive (2 Octyl cyanoacrylate) had the same suc-

cess rate in preventing infection at 7 days.<sup>(23)</sup>

In the two weeks period, both control and Histoacryl groups showed resolution of inflammation and approximately complete reepithelialization (Figure 6).

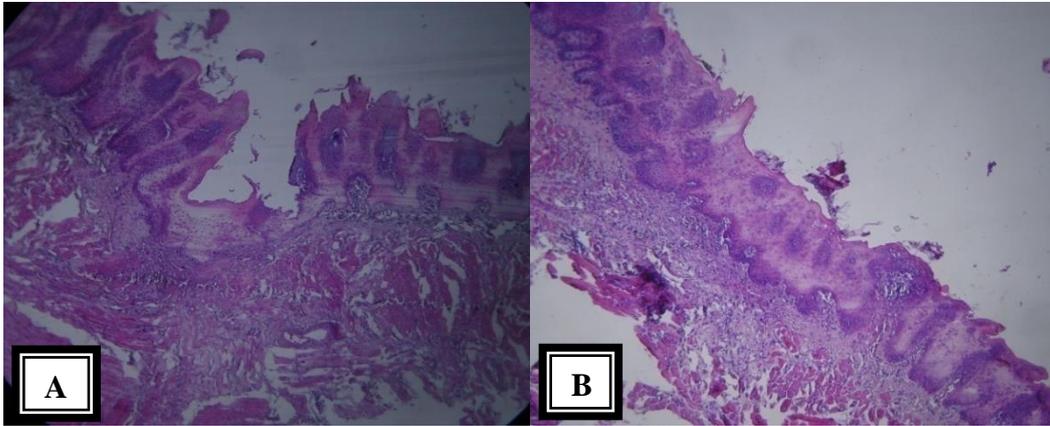


Figure (6): Two Weeks Period. A: for control group. B: for Histoacryl (Magnification power  $\times 100$ ).

Mota et al showed that at the 14th day, 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, polymorpho nuclear cells and macrophages. While, in the wound obliterated with the Histoacryl, a total epithelialization of the epithelium layers was observed with organizing stroma and absence of polymorpho nuclear and mononuclear cells.<sup>(24)</sup>

resolution of inflammation and complete reepithelialization of the wound of Histoacryl group more predominance than control group Figure (7). After 3 weeks, Labori et al found that all of the tissue glues had induced histological changes. Specially, cyanoacrylate derivatives have a satisfactory adhesive properties were observed after 3 weeks.<sup>(25)</sup>

In the one month period, the complete

All patients within the clear corneal wound were fully epithelialized (range, 3–4 weeks) by using 2-octyl cyanoacrylate.<sup>(26)</sup>

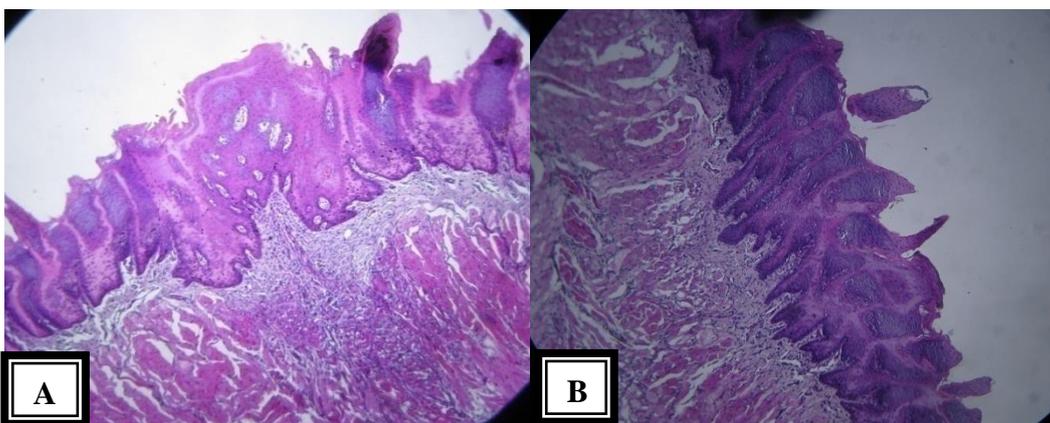


Figure (7): One Month Period. A: for control group. B: for Histoacryl (Magnification power  $\times 100$ ).

## CONCLUSION

Histoacryl reduce the inflammatory phase of the secondary defect of the tongue. Histoacryl induce faster reepithelialization in comparison to the control group in the tongue.

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