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Histological comparison between histoacryl and suturing to close lung wounds in dogs

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Abstract

The study was designed to know if there is any histological difference between using suturing and histoacryl (n-2-butyl-cyanoacrylate) for closing small parenchymal lung wounds in dogs. Twelve adult dogs were used in this study. The experimental animals were divided into two equal groups of six animals each. After induction of general anesthesia, a left intercostal thoracotomy was done, and a small incision of 2cm was made on the parenchymal lung tissue. Then, in the first group, the lung wound was closed by suturing, while in the second group, the wound was sealed by applying adhesive tissue glue. The histopathological samples were collected on the 15th and 30th days postoperatively. The histopathological changes in both groups were relatively similar, manifested by formation of granulation tissue, infiltration of inflammatory cells, congestion and thinking in the wall of blood vessels, hemorrhage, edema, atelectasis, and interstitial emphysema. In conclusion, we can use histoacryl as an effective adhesive tissue glue to close small lung wounds due to the absence of any relative histopathological differences between suturing and histoacryl for closing lung wounds.

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Introduction

The pulmonary tissue is a vital respiration structure characterized by its huge size, delicacy, and air content. It is susceptible to injury. Generally, the lung tissue consists of respiratory and conducting structures. The respiratory parts act for gas exchange and oxygenation of the blood, while the conducting parts help to transport air from outside to inside (1,2). Acute lung injury is a clinical syndrome characterized by improper gas exchange or disturbance in the mechanical function of the lung that causes hypoxemia and increases breathing. Therefore, rapid intervention should be done to prevent the occurrence of respiratory failure and to decrease the high morbidity rates. Although several research studies on mechanisms of lung injury were presented, such as changes in the inflammatory response and remolding of extracellular matrix, tile now, no effective treatment other than resolving the leading cause of lung injury was recorded (3,4). Pulmonary contusion may occur due to trauma by blunt or sharp objects. The severity of vascular or bronchial structure damage ranges from mild to severe, leading to blood or air leakage and respiratory distress (5,6). There are two problems during lung tissue reconstruction, the first problem is how to achieve homeostasis and pnemostasis (1), and the second is the traumatic puncture of sutures and the difficulty stopping air or blood leakage during suturing of some vital tissues, such as liver and lung, in addition to the not easy task of performing proper accuracy of tissue positioning (7). Air leakage is one of the main sever complications following a lung surgical operation to close the defect. Therefore, several methods should be used to reduce air leaks, such as electrocautery, stapling, or glues (1,8-11). Adhesive tissue glue provides a suitable method for rapidly closing wounds without pain. The most common adhesive tissue glues are 2-octyl-cyanoacrylate (Dermabond, Surgical) and n-2-butyl-cyanoacrylate (Histoacryl Blue, Periacryl). Adhesive tissue glues are liquid monomers that change into a polymer when they react with

tissues to form a strong bond for closing the wound edges (12-15). Histoacryl is monomeric n-butyl-2-cyanoacrylate that binds rapidly with tissue fluid and becomes polymerized. It is cheap, simple, and fast, and can be used in vascular and urological anastomosis and other surgical procedures (16-18). Therefore, the aim and the importance of this study are to show the ability of histoacryl glue to close lung wounds within a shorter period and to compare its histopathological influence on the healing process of lung wounds with traditional suturing techniques.

Materials and Methods

Experimental animals

In this article, twelve adult dogs from both sexes were used. The animals were divided into two groups, each consisting of six. The animals were examined clinically to ensure their fitness and safety from any diseases. All animals were kept in specific cages in the animal house at the college of veterinary medicine, university of Mosul.

Ethical approve

The research was approved by the Ethics Committee of the Faculty of the College of Veterinary Medicine, University of Mosul. No. UM. VET. 2022. 024.

Anesthesia

The surgical operations were performed under general anesthesia using a mixture of 10% ketamine HCL and 2% xylazine (19) at dose 10 mg/kg and 2 mg/kg, BW, respectively given in a single syringe intramuscularly in the thigh muscles with atropine sulfate as a premedication at a dose of 0.05 mg/kg subcutaneously. Frequent doses of the anesthetic mixture were given when needed. All animals were connected to the positive pressure ventilation machine to maintain respiration during the thoracotomy.

Surgical technique

The surgical approach to reach each animal's lung tissue was intercostal thoracotomy. The left aspect of the chest was prepared for aseptic surgery. A surgical incision was established between the 6^{th} and 7^{th} intercostal space through the skin, thoracic muscles, and pleura until reaching the thoracic cavity. In all animals, a small incision about 2cm was made in the parenchyma of the lung tissue after the application of non-crushing forceps to prevent air leakage (Figure 1). In the first group, the surgical incision of lung tissue was closed by a simple continuous suture technique using vicryl suture size (2/0) as absorbable suture material (Figure 2), while in second group, an n-2-butyl-cyanoacrylate glue was used to seal or close lung wounds (Figure 3). In both groups, following the closing of the pulmonary tissue, the incision site of the lung was checked for postoperative leakage or bleeding. The intraoperative evaluation of the air leak was through a submersion test in which the wound closure site was submerged with saline, and the operated lung was ventilated. The intercostal surgical incision was closed routinely with the application of a chest tube.

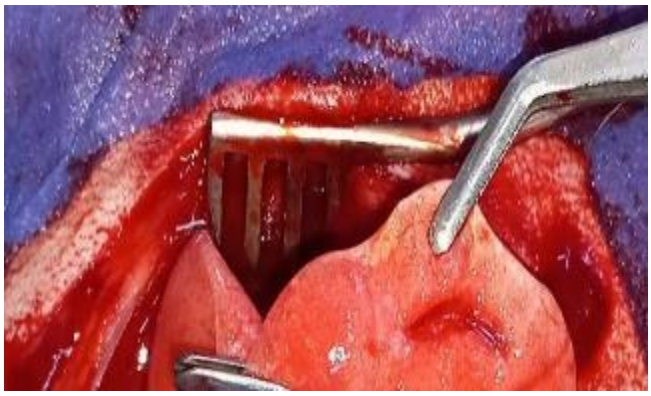

Figure 1: shows induced lung wounds.

Figure 2: shows suturing lung wounds.

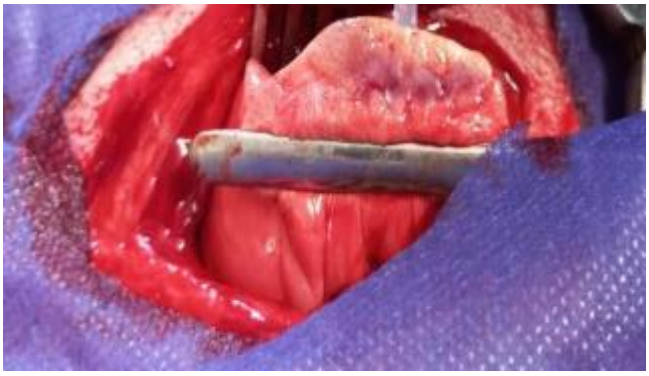

Figure 3: shows closed lung wounds by glue.

Postoperative care

The experimental animals are injected with penicillin-streptomycin as a systemic antibiotic at a dose of 1 ml /10 kg. with analgesic using metalgen at a dose of 1ml/ day for

five days postoperatively by intramuscular route injection with the daily dressing of the wound.

Assessment of wound healing

The pulmonary wound healing assessment for both groups was carried out by collecting specimens from the site of pulmonary closure to study the histopathological changes on the 15th and 30th postoperative days.

Results

In group one (suture group), the histopathological changes of the site of suturing at day 15 postoperative were characterized by new granulation tissue formation, which was represented by the proliferation of fibroblast, collagen fibers with new blood vessel formation. Hemorrhage, edema, and atelectasis with infiltration of inflammatory cells were also noticed. Besides, some sections revealed the presence of emphysema, vasculitis, and thickening in the wall of blood vessels (Figures 4-7). While at day 30 following surgery, there was an infiltration of inflammatory cells with atelectasis and interstitial emphysema with the maturation of connective tissue. Generally, the lung tissue was disorientated with fibrosis around the suture line (Figures 8-11).

In group two (glue group), the histological changes within the wound closure site were relatively similar to group one. On day 15 post-surgery, granulation tissue formed with infiltration of inflammatory cells. Some areas were characterized by the formation of foreign body granuloma surrounded by granulation tissue and atelectasis. Hemorrhage, edema, and interstitial emphysema were also noticed (Figures 12-14). On the 30th postoperative day, there was an area of atelectasis, interstitial emphysema, vasculitis with infiltration of inflammatory cells, granulation tissue maturation, and lung tissue rearrangement (Figures 15-19).

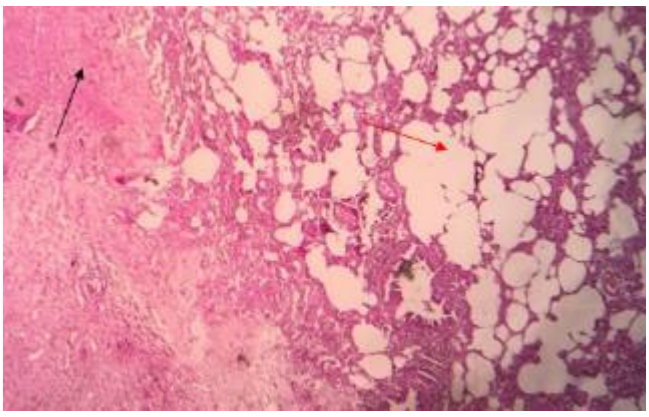

Figure 4: Micrograph showing granulation tissue formation (black arrow) and emphysema (red arrow) at the 15th postoperative days in G1. (H&E, 40X).

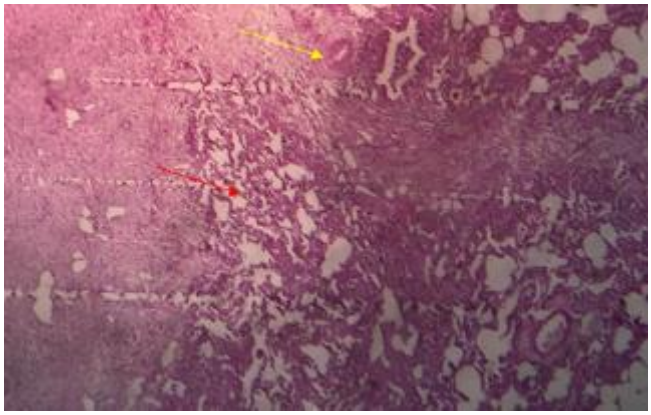

Figure 5: Micrograph showing atelectasis (red arrow) and Congestion of blood vessels (yellow arrow) at 15th Postoperative days in G1. (H&E, 40X).

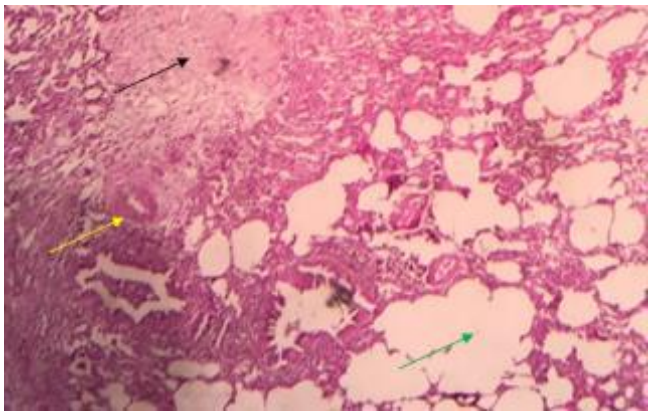

Figure 6: Micrograph showing granulation tissue formation (black arrow),congestion of blood vessels (yellow arrow) and emphysema (green arrow) at 15th postoperative days in G1. (H&E, 40X).

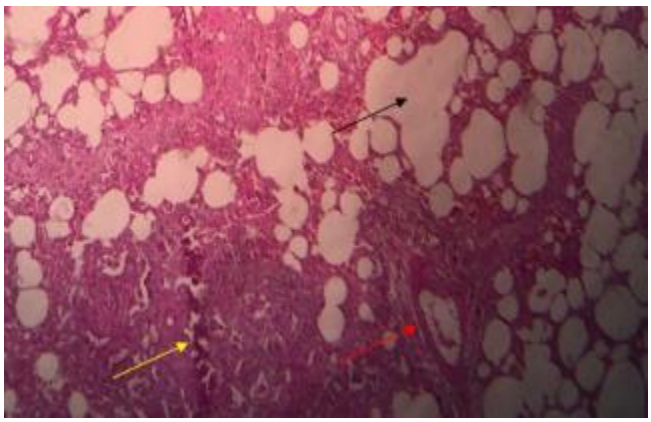

Figure 7: Micrograph showing interstitial emphysema (black arrow), vasculitis (red arrow) and hemorrhage (yellow arrow) at 15th postoperative days in G1. (H&E, 40X).

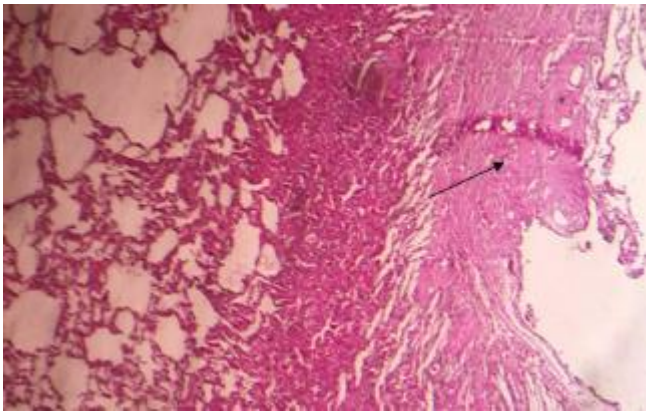

Figure 8: Micrograph showing fibrosis or maturation of connective tissue (black arrow) at 30th postoperative days in G1. (H&E, 40X).

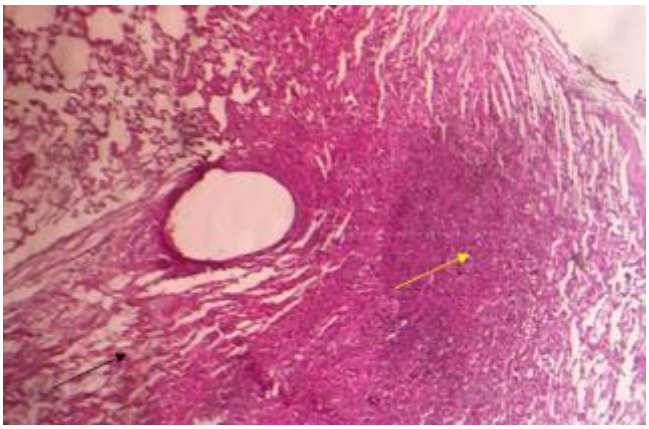

Figure 9: Micrograph showing atelectasis (black arrow) and infiltration of inflammatory cells (yellow arrow) at 30th postoperative days in G1. (H&E, 40X).

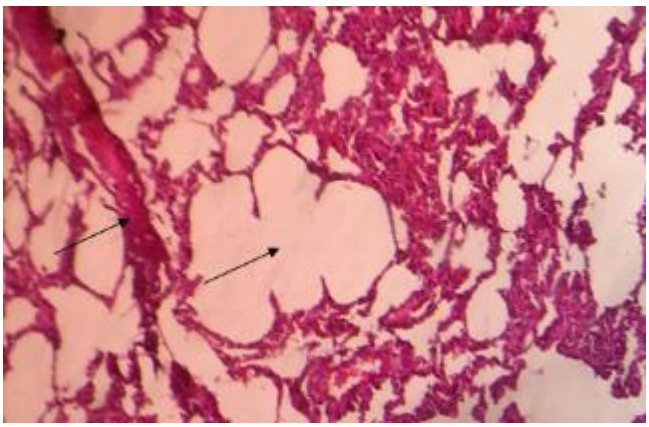

Figure 10: Micrograph showing interstitial emphysema (black arrow) at 30th postoperative days in G1. (H&E, 100X).

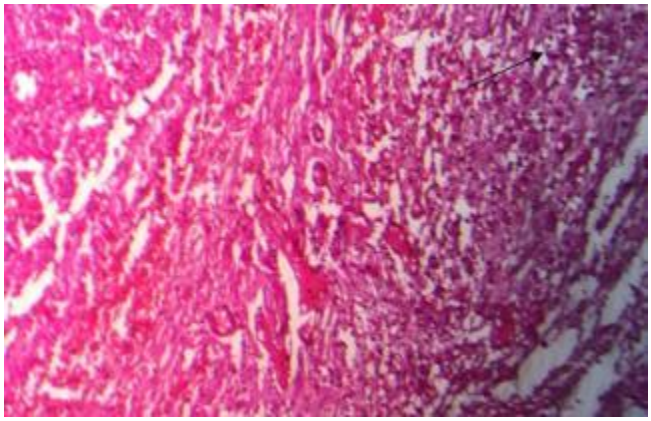

Figure 11: Micrograph showing infiltration of inflammatory cells (black arrow) at 30th postoperative days in G1. (H&E, 100X).

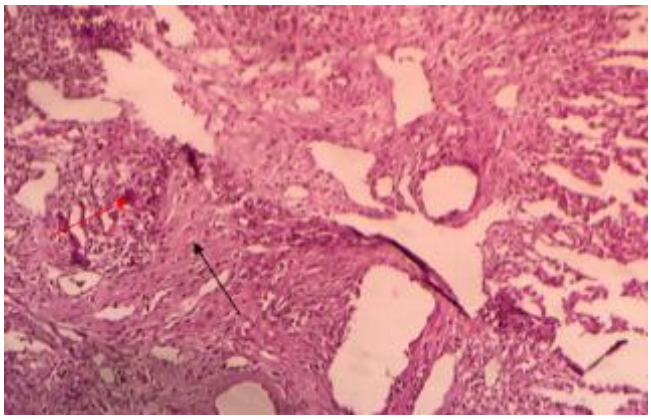

Figure 12: Micrograph showing granulation tissue formation (black arrow), surrounded foreign body granuloma (red arrow) at 15th postoperative days in G2. (H&E, 40X).

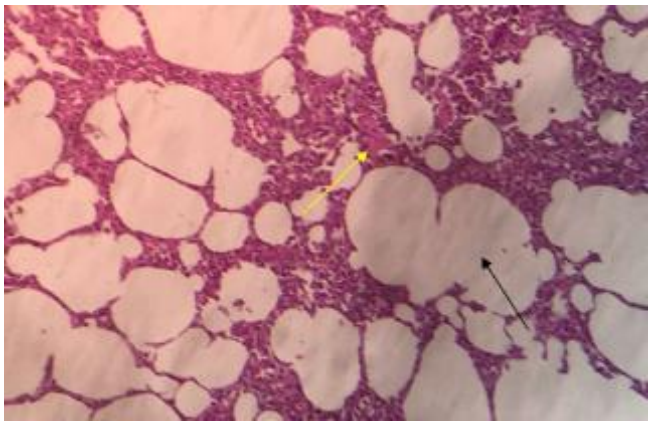

Figure 13: Micrograph showing interstitial emphysema (black arrow) and hemorrhage(yellow arrow) on the 15th postoperative days in G2. (H&E, 100X).

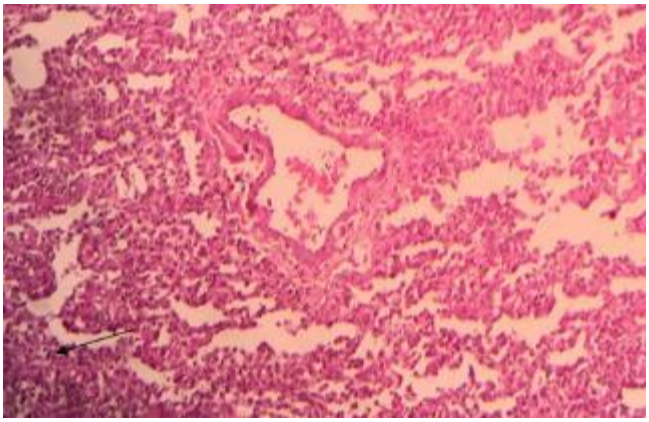

Figure 14: Micrograph showing infiltration of inflammatory cells (black arrow) at 15th postoperative days in G2. (H&E, 100X).

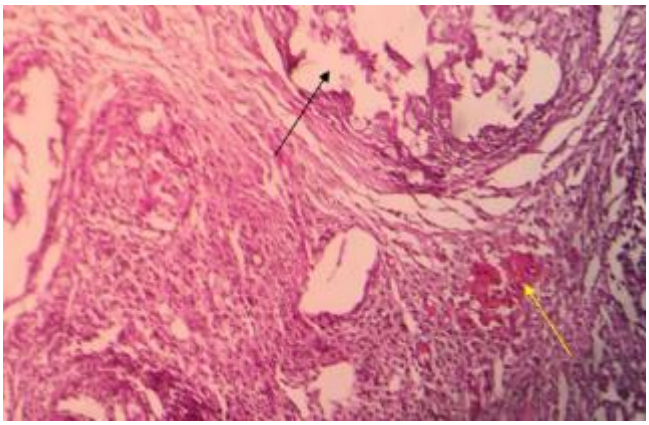

Figure 15: Micrograph showing interstitial emphysema (black arrow) and hemmorage (yellow arrow) at 30th postoperative days in G2. (H&E, 40X).

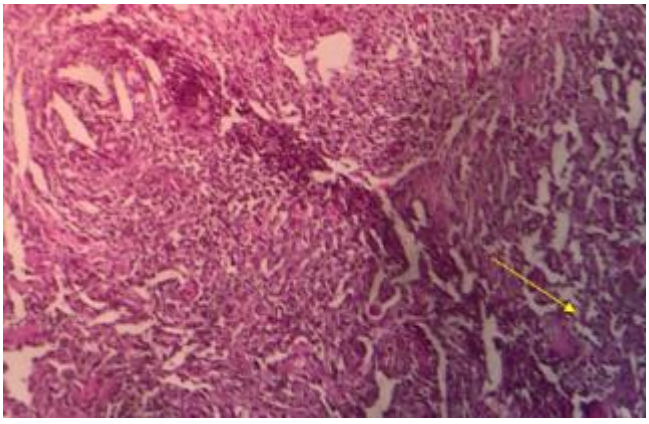

Figure 16: Micrograph showing infiltration of inflammatory cells (yellow arrow) at 30th postoperative days in G2. (H&E, 40X).

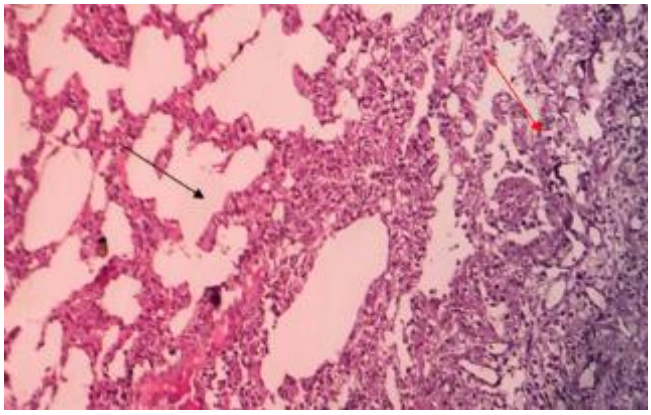

Figure 17: Micrograph showing interstitial emphysema (black arrow) and infiltration of inflammatory cells (red arrow) at 30th postoperative days in G2. (H&E, 40X).

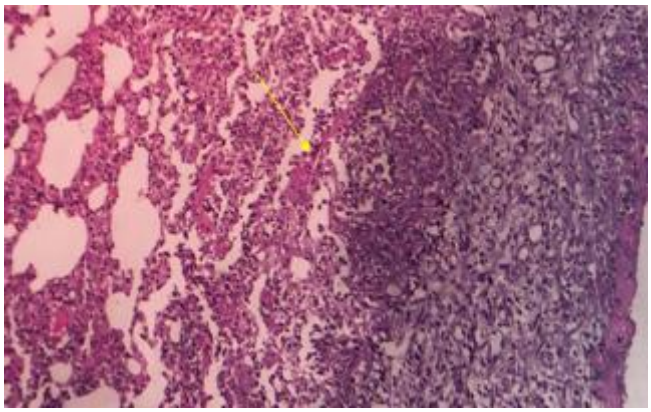

Figure 18: Micrograph showing vasculitis (yellow arrow) at 30th postoperative days in G2. (H&E, 40X).

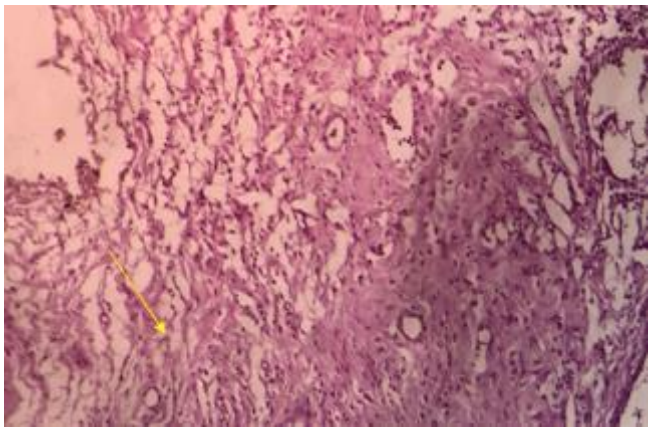

Figure 19: Micrograph showing atelectasis (yellow arrow) at 30th Postoperative days in G2. (H&E, 40X).

Discussion

The exposure of lung tissue for different injurious causes some biochemical responses. Therefore, there are several pathways can be activated (20). In the lung, the epithelial layer lining lungs and the respiratory system are susceptible to damage by different causes such as infection, irritations, and toxins. These lining layers are ready to regenerate after superficial damage. The acute damage of the lung epithelium can stimulate a pronounced regenerative response driven by proliferative responses from another healthy nearest epithelium (21,22). Air leak after lung surgery is regarded as the most sever complication because of the delicate nature of lung tissue. However, in both groups, the careful closure of lung tissue by suturing or glue has led to prevent air leaks, and this is agreed with Patwa and Shaha (1), Macchiarini *et al.* (8), Ayed and Raghunathan (9), Anegg *et al.* (10), who mentioned that lung wounds could be closed using several methods to reduce air leaks such as electrocautery, stapling or glues. In this experimental research, the closure of a lung wound with histoacryl was characterized by its speed, easiness, and prevention of air leakage beside the good wound edges binding that was in accordance with Reece *et al.* (23), Kamer and Joseph (24), who generally planned to use the adhesive tissue glue to connect wound edges until completion the process of wound healing and to provide a mechanical support to wound. In addition to the ability of tissue glue for wound sealing, it acts as a barrier to prevent leaks of tissue fluids such as blood, urine, and air. Additionally, Detweiler *et al.* (25) mentioned that tissue adhesives glue had many advantages, including less time consuming, less experience needed, and preventing leakage and ischemia when compared with suturing of some hollow organs such as blood vessels, bile ducts, and esophagus. Good results for closing lung wounds by histoacryl were also mentioned (26,27), who concluded that the surgical use of cyanoacrylate exhibited good healing results while reinforcing the site of bronchial and ureter anastomosis. The inflammatory response is very important to restore normal respiratory function. Therefore, like other tissue, the synthesis or formation of collagen appears as part of the normal healing process. Collagen is extracellular matrix and plays an important role in the regulation of the wound healing stages (28). Collagen formation is necessary to attach the cell and keep the alveolar structure. The excessive deposition of collagen may interfere with the lung ventilation mechanism and exchange of gases. However, excessive collagens remove enzymes called matrix metalloproteinases in the inflammatory cells (29). Histopathological sections revealed the infiltration of inflammatory cells in both groups due to the presence of forging materials, including suture material and glue. These findings were in accordance with Koh and Dipietro (30), Al-Hyani (31), Ushe *et al.* (32), who found that the infiltration of inflammatory cells appeared due to tissue injury, the exitance of suture materials or because of pulmonary infection after performing thoracic surgery. In addition, within the injured tissue, the inflammatory cells would attract to the injury site due to releasing cytokines (33,34). Hemorrhage or edema was also noticed. Hemorrhage appears due to cutting the lung tissue, while edema formation is noticed due to lung tissue injury (35) or as a result of anesthesia and intubation of the trachea (36,37). The Herrero *et al.* (38) mentioned that the alveolar epithelium damage is considered a main role to increase pulmonary permeability and subsequent formation of edema. In both groups, atelectasis was developed, and this may be due to the formation of pneumothorax following thoracotomy when the air enters the thoracic cavity and causes pressure on the lung tissue (39). In addition, atelectasis was occurred after anesthesia and lung injury (40,41). In the histoacryl group, the histopathological findings also revealed granuloma formation. This is similar to Pelissier *et al.* (42), who stated that adhesive tissue glue might cause a mild acute inflammatory reaction that could be relatively resorbed after 2 months when put on vascularized tissue. Generally, in this research, the histopathological data showed no difference between the effect of histoacryl or suturing on the lung tissue. This agrees with Dowson *et al.* (43), who found that there were no variances in the quality of skin healing between using of suturing and application of cyanoacrylate tissue glue, although the fact that several types of glues are presented commercially with different physical properties according to their molecular weights. Furthermore, many studies mentioned that applying tissue glue to close some tissue defects did not cause inhibition or delay of the healing process (42).

Conclusion

It is concluded that histoacryl could be used successfully for closing minor pulmonary wounds and careful suturing despite the lack of histopathological difference between these techniques.

Acknowledgments

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Conflict of interest

The authors declare that there is no conflict of interest.

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مقارنة نسيجية بين الهستوكريل والخياطة لغلق الجروح الرئوية في الكلاب

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الخلاصة

صممت هذه الدراسة من اجل معرفة إذا ما كان هناك أي فرق نسيجي بين استخدام الصمغ النسيجي والخياطة في غلق الجروح الرئوية الصغيرة في الكلاب. أثني عشر كلبا بالغا تم استخدامها في هذه الدراسة. قسمت حيوانات التجربة الى مجموعتين، ضمت كل مجموعة منها ست حيوانات. بعد إحداث التخدير العام تم إخضاع الحيوانات لعملية فتح القفص الصدري ما بين الأضلاع من جهة اليسار وعمل جرح صغير بقدار ٢ سم في متن نسيج الرئة. في المجموعة الأولى تم غلق جرح نسيج الرئة باستخدام الخياطة في حين تم غلق الجرح في المجموعة الثانية عن طريق وضع الصمغ اللاصق للأنسجة. تم فحص التغيرات النسيجية في ١٥و٣٠ يوم بعد إجراء العملية من خلال اخذ عينة صغيرة من منطقة غلق الجرح. أظهرت التغيرات النسيجية وجود تشابه نسبي في كلتا المجموعتين والتي تمثلت بتكون نسيج حبيبي، ارتشاح للخلايا الالتهابية، احتقان وتثخن في جدار الأوعية الدموية، نزف، وذمة، انكماش وانتفاخ رئوي. بالاستنتاج وجد بالإمكان استخدام الصمغ اللاصق للأنسجة لغلق الجروح الرئوية الصغيرة مع عدم وجود فرق ما بين الخياطة والصمغ النسيجي لغلق الجروح الرئوية نسيجيا.