University of Mosul
Al- Rafidain Dental Journal
https://rden.uomosul.edu.iq/

Research Article

The effect of Botox Injections on Wound Healing Before and after Surgery

Hisham Abid Ahmed*[1], Abdulhameed N. Aldabagh [2], Abdulsattar Salim Mahmood[3]

[1, 2] *Oral and Maxillofacial Surgery Department/College of Dentistry/Mosul University,* ***Iraq***

[3] *Oral Diagnosis Department/College of Dentistry/University of Mosul, Iraq*

* Corresponding author: hisham.21dep14@student.uomosul.edu.iq

Article History
Received: 5 August 2023
Revised: 5 September 2023
Accepted: 17 September 2023
Published online: 1 September 2025

How to cite: Ahmed HB., Aldabagh AN., Mahmood AS. The effect of Botox Injections on Wound Healing Before and after Surgery. Al-Rafidain Dent J. 2025;25(2):323-344.

10.33899/rdenj.2023.143361.1224

ABSTRACT: The current study aimed to examine the effects of Botox therapy on the skin's wound regeneration in patients who received the treatment before or after surgery. **Materials and Methods:** 18 male albino rats, weighing between 250 and 350 grams, were used, each receiving 1 IU of Botox and saline injected subcutaneously in the center of 1.5 cm circles with 4.5 cm between them on the dorsum of each rat. In group A, the injection was seven days before surgery, and the animals had a full-thickness skin excision; in group B, the injection was immediately after wound incision, and all were kept in separate cages. Each group was divided into three equal subgroups according to the healing period (3, 7, and 14 days), and then histological tests were undertaken on skin biopsies for all the groups post-euthanasia. **Results**: The results showed significant differences between groups A and B On day three, group A exhibited mild inflammation, whereas group B and both control groups had severe inflammation. On day 7, group A had scant granulation tissue and re-epithelialization of more than half of the lesions. Group B had greater granulation tissue and less re-epithelialization. On day 14, both groups exhibited considerable granulation tissue growth; however, group A showed increased blood vessel formation and keratinocyte proliferation, resulting in extremely good re-epithelialization and skin regeneration. **Conclusion:** Botox injections can be considered an effective alternative treatment option to accelerate wound healing, and the most suitable method to administer Botox is before surgery.

Keywords: Botox; Rat; Re-epithelialization; Wound healing.

INTRODUCTION

Skin is the body's largest organ and a physical, chemical, and biological barrier [1]. This important structure protects organs against physical damage, pathogens, sunlight, excessive heat, and cold [2,3].

Local wound care's main goal is to speed up skin physiological and anatomical continuity, which keeps wounds moist, prevents external infections, and maintains tissue homeostasis. It reduces edema and improves circulation, saving time and money, and improving living standards [4,5].

Muscle paralysis caused by botulinum toxin may last for 2-6 months. From A to F serotypes, which are produced by *Clostridium botulinum*. For almost two decades, BTX-A has successfully treated eyelid spasms, speech stuttering, and hyperactive face muscles [5,6].

Recognizing these results has boosted interest in this toxin in recent years. In 2014, scientists found that BTX-A influenced skin grafting and wound contraction. Injectable BTX-A lessens the tightening of wounds, influences inflammatory cells, boosts collagen fibers, and diminishes both fat cells and hair follicles [7,8].

Abdominal-rectal muscle transplant survival was investigated in 2014 by Park et al. in rats with midline vertical scars using BTX-A. The abdominal rectus muscle's blood supply was improved after BTX-A injection [9,10].

In another study, BTX-A was shown to prevent peripheral vasoconstriction and increase the lifespan of dermal flaps in mice. The BTX-A subgroup had better outcomes than the control group overall. The BTX-A group's blood flow was healthy and unobstructed all week long. Pretreatment with BTX-A increased flap retention as well as blood flow [11,12].

Our research looked at how wounds from car accidents and other injuries heal in locations that have gotten Botox injections before and in regions that get injections just after surgery, when BOTOX® is routinely used for therapeutic and aesthetic reasons.

The study aimed to investigate the effects of BTX-A injections on the skin's wound regeneration and to explain the best method for BTX-A injection, either before or after surgery.

MATERIALS AND METHODS

The study began on 15/12/2022, at Mosul City, at the College of Dentistry, University of Mosul, Iraq, and ended on 15/06/2023 at the Center for Research in the Oral and Maxillofacial Surgery Department. (UoM. Dent, A.74/22) is the ethical approval number given by the university's research ethics committee.

Materials for the surgical procedure:

The materials used in our study include

Botulinum toxin type A BOTOX® vial 100units made in Canada (Dermatox), ketamine hydrochloride is general an anesthetic solution made in Holland, xylazine sedative analgesic solution made in Holland, disposable Towel Turkey, adhesive tape Turkey, disposable 5cc capacity plastic syringes Qatar, disposable 1cc capacity plastic syringes Italy, disposable surgical face masks Turkey, disposable surgical gloves Turkey, povidone iodine 10% Turkey, PBT Bandage China, sterile normal saline solution 0.9% NAC Egypt, permanent marker for animal tagging China, sterile gauze swabs China, plastic disposable bags for waste disposable China, formalin 10%, electronic compact scale China.

Instruments for the surgical procedure

Stainless scalpel handle no.3 USA, sterile scalpel blade no. 15 China, tissue tweezers, Pakistan, mosquito artery forceps, Pakistan, needle holder, Pakistan, scissors, Pakistan, tissue forceps, Pakistan, kidney dish, Pakistan, flap retractors, Pakistan

Animals

A total of 18 male albino rats (4–6 months old) weighing between 250 and 350 g were split into two groups (n=9) based on the methodology and then further differentiated into three groups based on the number of days after surgery each group had been allowed to recover (3, 7, and 14). They spent their time alone in sterile cages maintained between 18 and 22 degrees Celsius. They were fed the same amount of grain, fruit, veggies, and water every day. Researchers kept vital signs. The rats were divided into two groups: A (injection of Botox before surgery) with its control AC, and B (injection of Botox after surgery) with its control BC, and each received two incisions on the dorsum, one near the head for the Botox and one near the tail for the saline.

Procedures in Group A have two stages:

First, we gave group A a Botox injection at the intended site:

The study was performed under general anesthesia and sterile conditions, the general anesthesia [13] intraperitoneal injections of ketamine® (ketamine hydrochloride) 50mg/kg general anesthetic agent and xylazine® 5mg/kg sedative and analgesic solution [14,15] Complete anesthesia was obtained within 10 minutes, keeping the animal anesthesia for about 1.5-2 hours (enough to cover the surgical procedure), then rat's hair was shaved with scissors and an electrical hair clipper, the disinfected solution was applied to the area of surgery (the dorsum area of rats was wiped with 10% povidone-iodine), then, two identical circular areas were marked and prepared

on the dorsum of each rat; the diameter of the wound was (1.5 cm), and the distance between both injuries was approximately (4.5 cm) [13], the wound near the rat's head was selected for injection of BTX-A solution (study side), and the injury near the rat's tail was chosen for injecting normal saline 0.9% solution (control side). All animals in group A received a BTX-A (1U) (the dilutions of botulinum toxins (Dermatox Canada) were done for the 100 units of Dermatox with 20 ml of normal saline (0.9%) injected in a sterile container; the volume of 1U BTX-A is 0.2 ml)[16]. Injected into the subcutaneous muscle in the center of a circle [16], which causes Muscle Relaxation by blocking the acetylcholine neurotransmitters in the neuromuscular junctions[17]. (The paralyzing effect is at its peak between one and four weeks following injection) [18]. Another circular injection of 0.2 ml of normal saline was performed.

The following stages of the wound preparation

After animal preparation, anesthesia was checked, the rats were laid down, and wounds were formed on the seventh day after injection. A Circular incision of 1.5cm diameter with a total thickness incision of skin (epidermis, dermis, and subcutaneous fat tissue) by using a scalpel handle no.3, blade no.15. and scissor was surgically removed from the midline of the rat's back unital subjacent muscle, where it had been marked before to treatment with BTX-A and normal saline (Figure 1).

Group B received the identical steps, except BTX-A and saline injections were performed (post-operatively) immediately following surgery, a total thickness incision of skin and subcutaneous tissue was excised without previous treatment by using a scalpel handle no.3, blade no.15, and scissors. Still, the deep muscle was preserved at the base of the defect in the midline of the rat's back (Figure 1).

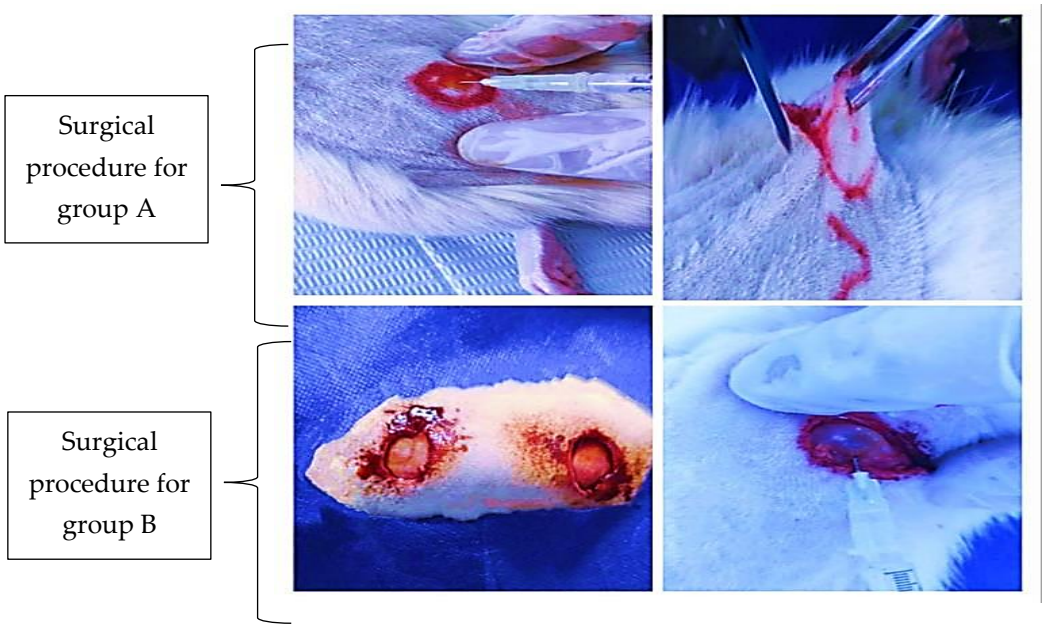

Figure (1): Surgical procedure steps for both groups

After the incision was cleaned with normal saline and wiped off with 10% povidone-iodine, the compression and waterproof bandage were applied to the wound to aid in preventing contamination with pathogens, dust, and sand for 5-7 days following the operation. Separate cages housed each of the tested animals.

The biopsies were performed immediately upon rat euthanasia, with the incision site wholly included in the tissue sample, then tissue samples at room temperature were preserved in 10% formalin for 48-72 hours then analysis of wounds by histology at 3, 7, and 14 days after injury.

Histopathological examination

Wound samples were collected from animals that had been euthanized by general anaesthesia by ether (rats to be placed in a closed container containing ether in high concentration (100%)[19], on days 3, 7, and 14. Hematoxylin and eosin were used to stain the tissue after it was fixed and processed.

Histopathology Evaluation Criteria

1. Inflammatory response criteria parameter (scoring):[20,21]

Score 1: Nil. No inflammatory cells were seen in the field of operation (X10).

Score 2: Mild. When inflammatory cells are present in few numbers, less than ½ of the field (X10).

Score 3: Moderate. Inflammatory cells could be seen in more than ½ of the field (X10).

Score 4: Severe or abundant when inflammatory cells are present in huge numbers, more than ¾ of the field (X10).

2. Granulation tissue formation Criteria (Scoring): [20,22]

Score 1: Absence of granulation tissue formation in the wound.

Score 2: Quantity of granulation tissue formation in the wound gap is scanty.

Score 3: Amount of granulation tissue formation is moderate in tissues.

Score 4: The total amount of granulation tissue formation in the wound is profound.

3. Re-epithelization parameters Criteria (Scoring): [23]

Score 0: Re-epithelialization at the edge of the wound.

Score 1: Re-epithelialization covering less than half of the wound.

Score 2: Re-epithelialization covering more than half of the wound.

Score3: Re-epithelialization covering the entire wound, irregular thickness.

Score 4: Re-epithelialization covering the entire wound, normal thickness.

RESULTS

Histological finding

A. Day Three:

Group A had less than ½ of the wound area with mild inflammatory cells, whereas groups B, AC, and BC had severe inflammatory cells, exceeding ¾ of the wound field. Both treatment groups showed moderate granulation tissue, while both control groups exhibited scant granulation tissue.

Re-epithelialization occurred on fewer than half of Group A lesions; in contrast, the AC, B, and BC wounds showed edges that were re-epithelialized. See (Figures 2-10) and Table 1.

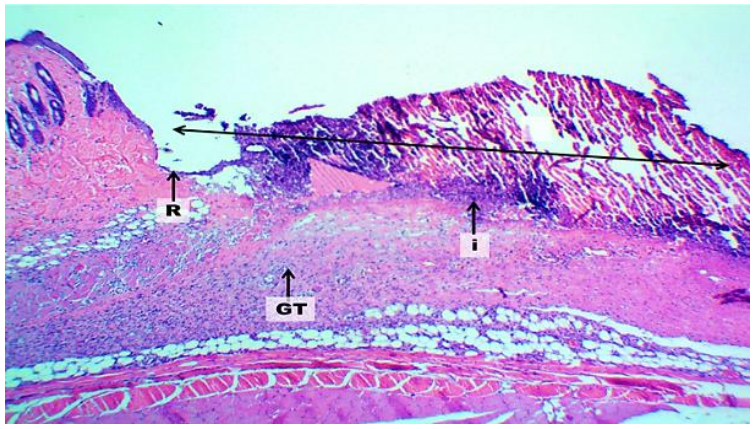

Figure (2): Histological section of rat skin of pre-surgery control group (after 3 days) showing wide wound site (↔) with severe inflammatory cell infiltration (i), destruction of the epithelium layer of skin with re-epithelialization at the edge of the wound (R), and scanty granulation tissue (GT). H&E stain, 40X magnification.

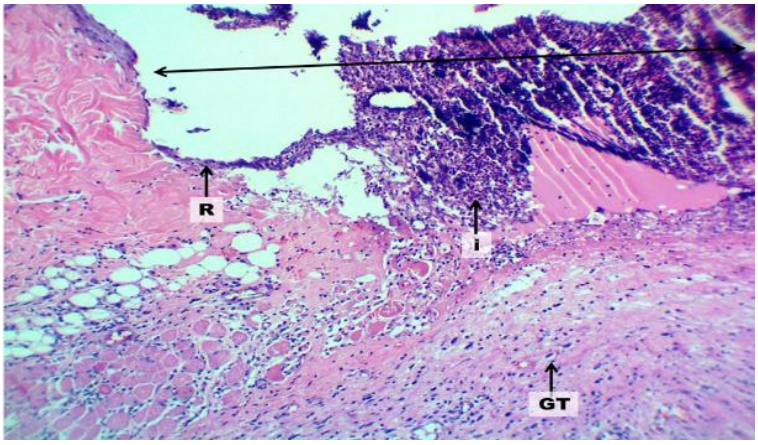

Figure (3): Histological section of rat skin of pre-surgery control group (after 3 days) showing wide wound site (↔) with severe inflammatory cells infiltration (i), destruction of epithelium layer of skin with re-epithelialization at the edge of the wound (R), scanty granulation tissue (GT) and newly formed blood vessels (angiogenesis) (B) with fibroblast cells(E). H&E stain, 100X magnification.

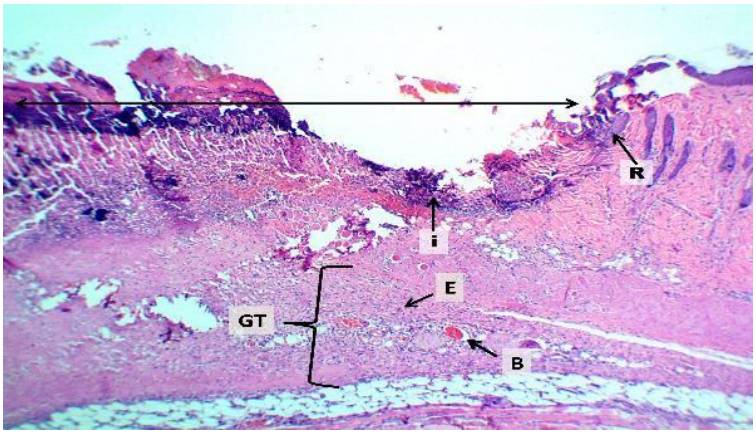

Figure (4): Histological section of rat skin of pre-surgery treatment group (after 3 days) showing wide wound site (↔) with mild inflammatory cells infiltration (i), destruction of epithelium layer of skin with slight re-epithelialization (R) moderate granulation tissue (GT) and newly formed blood vessels (angiogenesis) (B) fibroblast cells (E). H&E stain, 40X magnification.

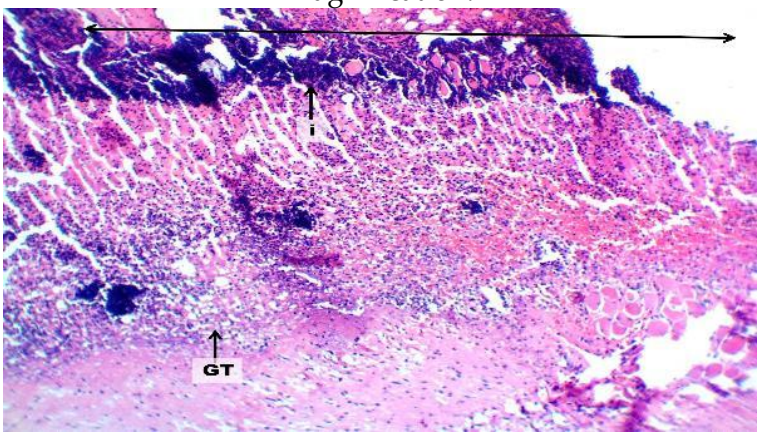

Figure (5): Histological section of rat skin of pre-surgery treatment (after 3 days) showing a wide wound site (↔) with mild inflammatory cell infiltration (i), and moderate granulation tissue (GT). H&E stain, 100X magnification.

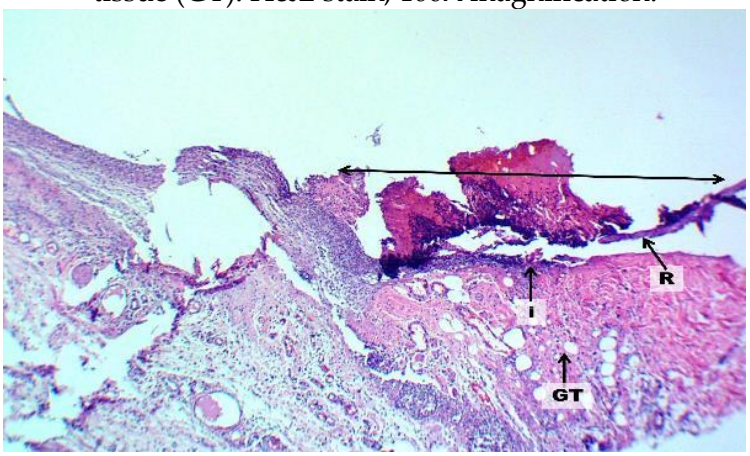

Figure (6): Histological section of rat skin of post-surgery control group (after 3 days) showing wide wound site (↔) with severe inflammatory cell infiltration (i), destruction of the epithelium layer of skin with re-epithelialization at the edge (R), and scanty granulation tissue (GT). H&E stain, 40X magnification.

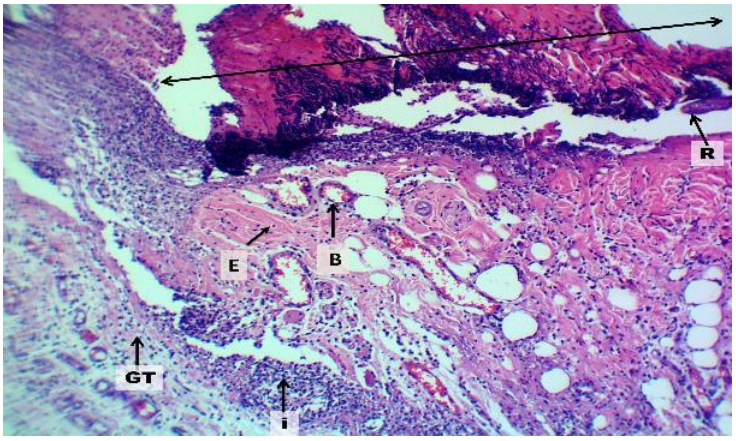

Figure (7): Histological section of rat skin of post-surgery control group (after 3 days) showing wide wound site (↔) with severe inflammatory cells infiltration (i), destruction of epithelium layer of skin with re-epithelialization at the edge (R) scanty granulation tissue (GT), newly formed blood vessels (angiogenesis) (B) and fibroblast cells (E) H&E stain, 100X magnification.

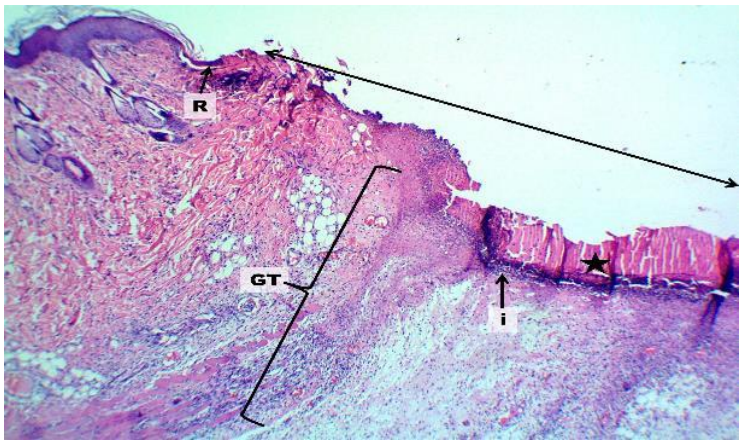

Figure (8): Histological section of rat skin of post-surgery treatment group (after 3 days) showing wide wound site (↔) with severe inflammatory cells infiltration (i), destruction of epithelium layer of skin with re-epithelialization at the edge (R), moderate granulation tissue (GT), and newly formed blood vessels (angiogenesis) (B) fibroblast cells (E). H&E stain, 40X magnification.

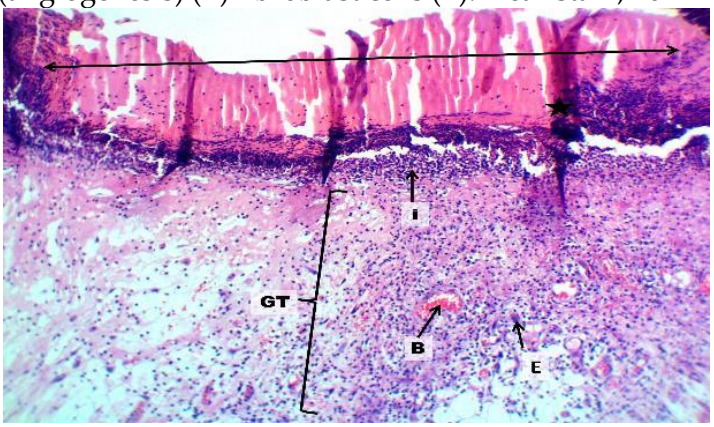

Figure (9): Histological section of rat skin of post-surgery treatment group (after 3 days) showing wide wound site (↔) with severe inflammatory cells infiltration (i), destruction of epithelium layer of skin with re-epithelialization at the edge (R), moderate granulation tissue (GT), and newly formed blood vessels (angiogenesis) (B) with fibroblast cells (E). H&E stain, 100X magnification.

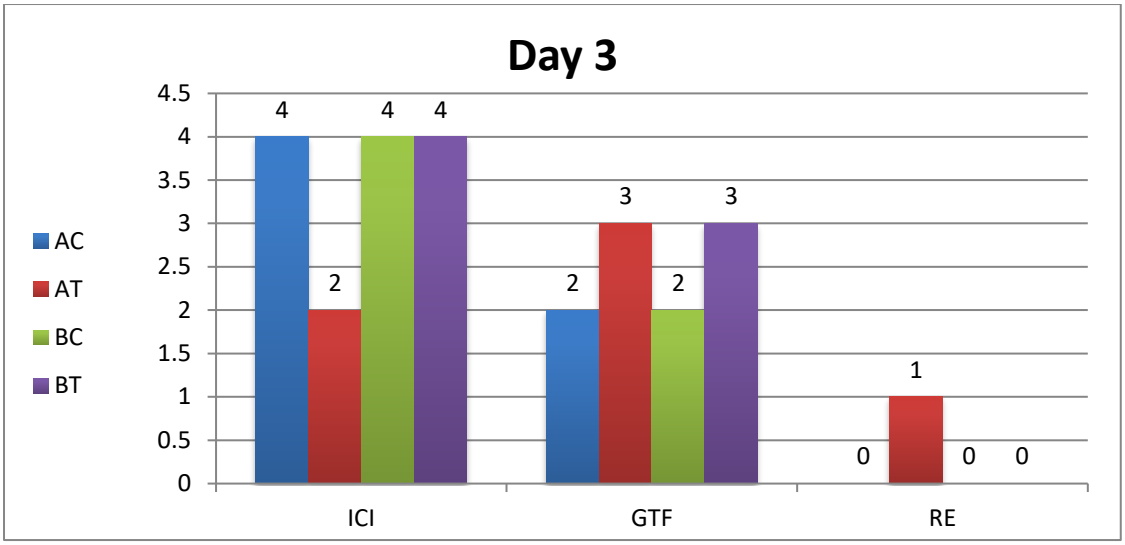

Figure (10): The histopathological descriptive Scores of the inflammatory cell infiltration ICI, granulation tissue formation GTF, and re-epithelialization RE of the control and treatment groups of the **pre- and post-surgery groups** at **day 3** of the study period

Table (1): The histopathological Scores of the inflammatory cell infiltration ICI, granulation tissue formation GTF, and re-epithelialization RE for the control and treatment groups of the pre-and post-surgery groups, as the Median of the scores.

Period	Group	Median of **ICI**	Median of **GTF**	Median of **RE**
3rd day	AC	4	2	0
	A	2	3	1
	BC	4	2	0
	B	4	3	0
7th day	AC	3	3	1
	A	2	2	2
	BC	3	3	0
	B	3	4	1
14th day	AC	2	4	2
	A	1	2	4
	BC	2	3	2
	B	1	2	3

Data expressed as the Median of the scores.

B. Day Seven:

In group A, mild inflammatory cells entered less than half the wounds. One sample had no infiltrating inflammatory cells.

AC, B, and BC had moderate wound inflammation.

Group A specimens had angiogenesis, fibroblasts, and scant granulation tissue.

Group B specimens have profound wound granulation

We found moderate wound granulation tissue in all AC and BC cases.

More than half of the group A lesions were re-epithelialized .

Less than half of groups B and AC wounds were re-epithelialized.

Re-epithelialization of wound edges was seen in BC specimens.

See (Figures 11-19) and Table 1.

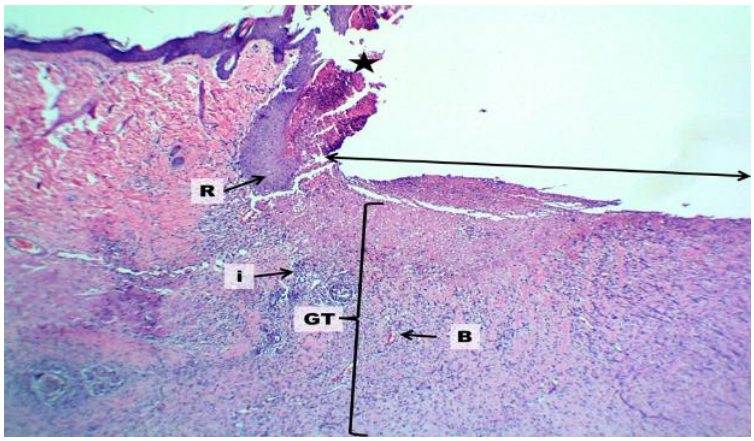

Figure (11): Histological section of rat skin of pre-surgery control group (after 7 days) showing wide wound site (↔) with moderate inflammatory cells infiltration (i), destruction of epithelium layer of skin with re-epithelialization less than half field (R), moderate granulation tissue (GT), and newly formed blood vessels with (angiogenesis) (B) H&E stain, 40X magnification.

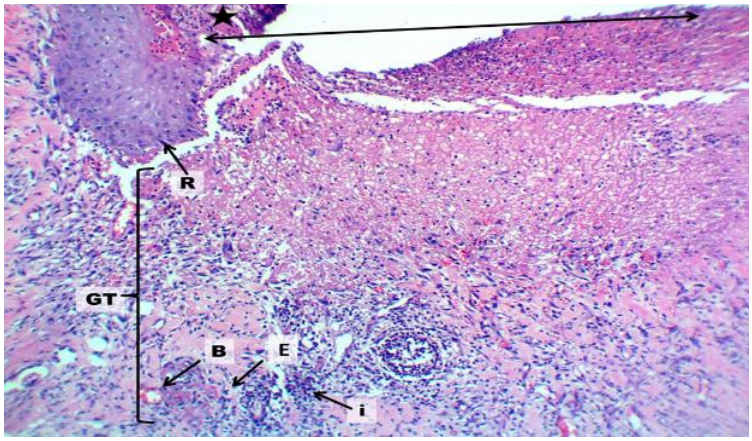

Figure (12): Histological section of rat skin of pre-surgery control group (after 7 days) showing wide wound site (↔) with moderate inflammatory cells infiltration (i), destruction of epithelium layer of skin with re-epithelialization less than half field (R) moderate granulation tissue (GT), newly formed blood vessels (angiogenesis) (B) and fibroblast cells (E) H&E stain, 100X magnification.

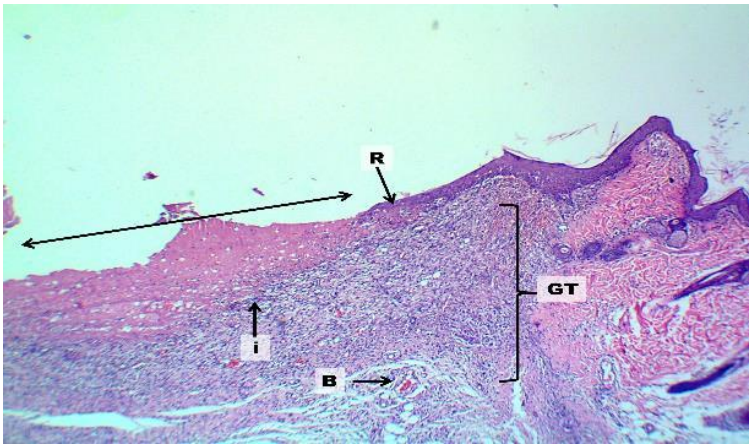

Figure (13): Histological section of rat skin of pre-surgery treatment group (after 7 days) showing wide wound site (↔) with mild inflammatory cells infiltration (i), re-epithelialization more than half field (R), scanty granulation tissue (GT), and newly formed blood vessels (angiogenesis) (B). H&E stain, 40X magnification.

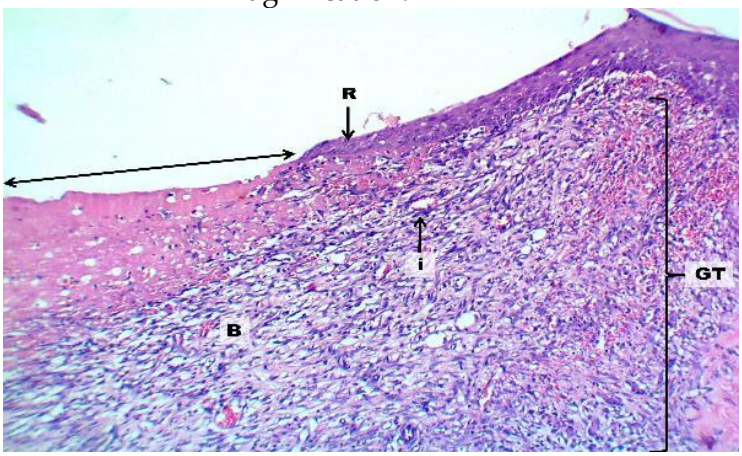

Figure (14): Histological section of rat skin of pre-surgery treatment group (after 7 days) showing wide wound site (↔) with mild inflammatory cell infiltration (i), re-epithelialization more than half field (R), scanty granulation tissue (GT), and newly formed blood vessels (angiogenesis) (B). H&E stain, 100X magnification.

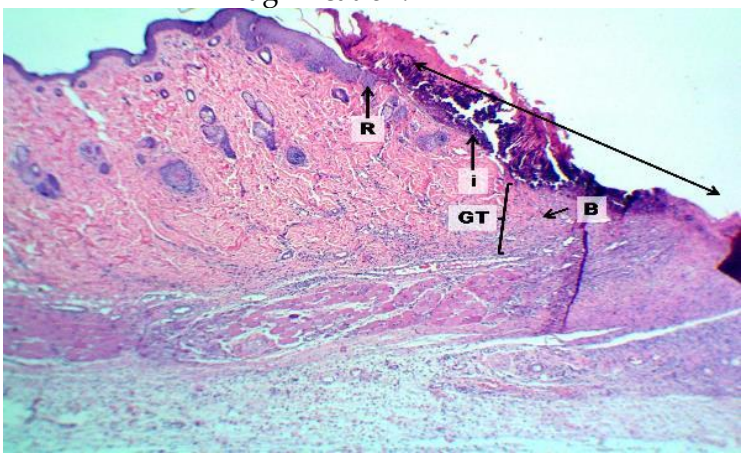

Figure (15): Histological section of rat skin of post-surgery control group (after 7 days) showing wide wound site (↔) with moderate inflammatory cells infiltration (i), destruction of epithelium layer of skin with re-epithelialization at the edge of the wounds (R) moderate granulation tissue (GT) and newly formed blood vessels (angiogenesis) (B). H&E stain, 40X magnification.

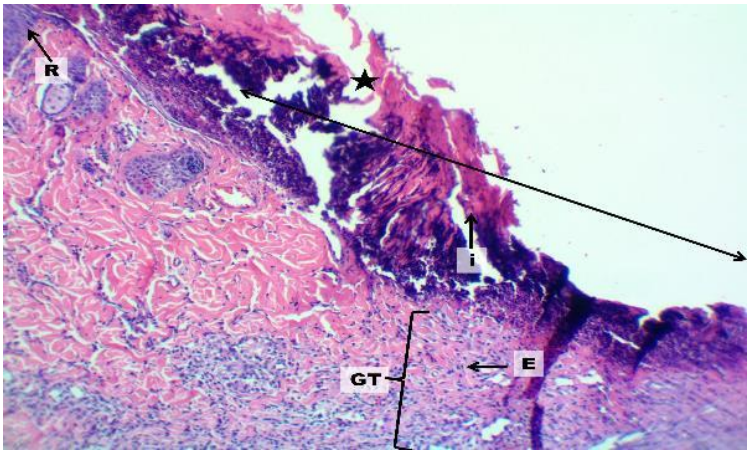

Figure (16): Histological section of rat skin of post-surgery control group (after 7 days) showing wide wound site (↔) with moderate inflammatory cells infiltration (i), destruction of epithelium layer of skin with re-epithelialization epithelialization at the edge of the wounds (R), moderate granulation tissue (GT) and fibroblast cells (E) H&E stain, 100X magnification.

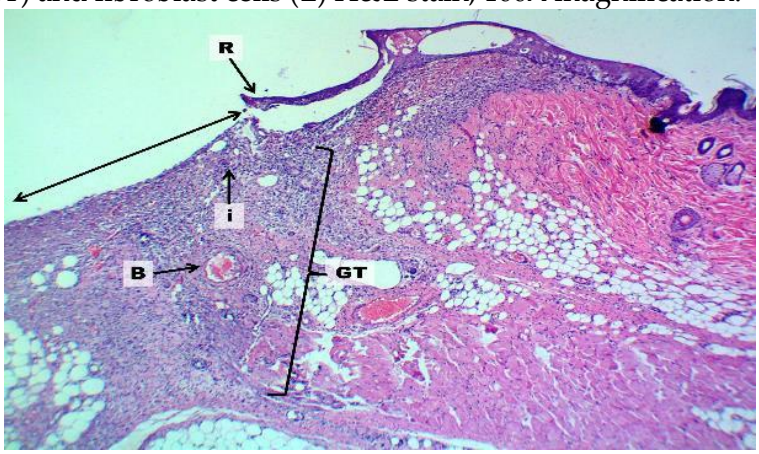

Figure (17): Histological section of rat skin of post-surgery treatment group (after 7 days) showing wide wound site (↔) with moderate inflammatory cells infiltration (i), destruction of epithelium layer of skin with re-epithelialization less than half wounds (R), profound granulation tissue (GT) and newly formed blood vessels (angiogenesis) (B). H&E stain, 40X magnification.

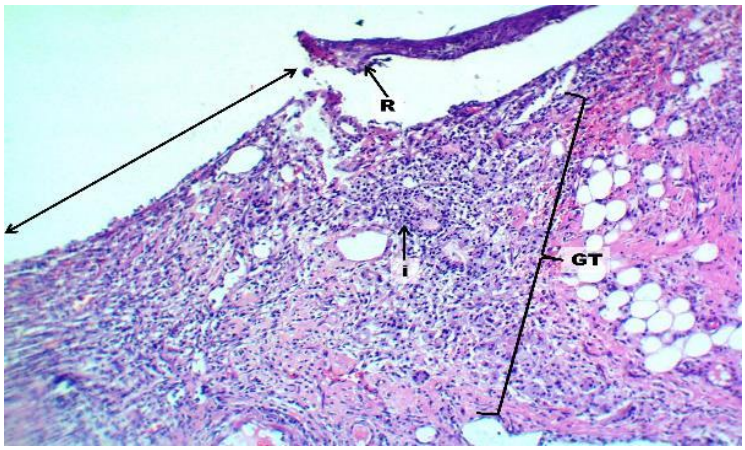

Figure (18): Histological section of rat skin of post-surgery treatment group (after 7 days) showing wide wound site (↔) with moderate inflammatory cell infiltration (i), destruction of the epithelium layer of skin with re-epithelialization less than half the wounds (R), and profound granulation tissue (GT). H&E stain, 100X magnification

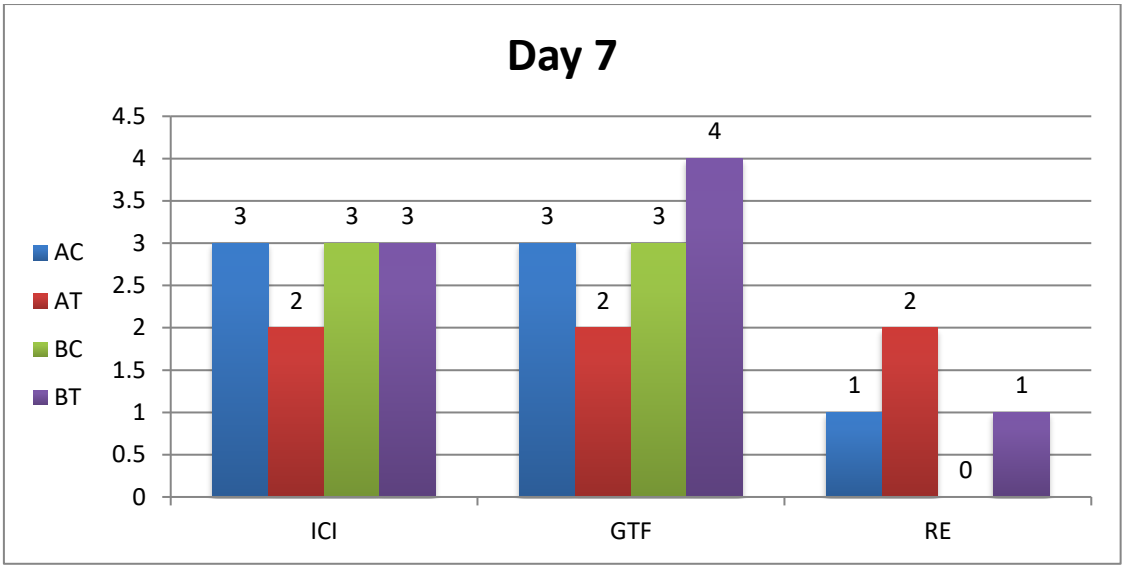

Figure (19): The histopathological descriptive Scores of the inflammatory cell's infiltration ICI, granulation tissue formation GTF, and re-epithelialization RE of the control and treatment groups of the pre- and post-surgery groups at day 7 of the study period

C. Day fourteen:

Inflammatory cells were absent in groups A and B. Less than half of the wounds had mild wounds of inflammatory cell infiltration, including one specimen.

Less than half of the wounds with mild inflammatory cell infiltration in groups AC and BC.

All groups A and B wounds had scant granulation tissue, angiogenesis, and fibroblast cells.

Group AC specimens exhibit profound wound granulation.

Group BC wounds developed moderate granulation tissue.

Full-field re-epithelialization occurred in Group A.

Group B specimens have irregular wound re-epithelialization.

Over 50% of AC and BC wounds were re-epithelialized. See (Figures 20-28) and Table 1.

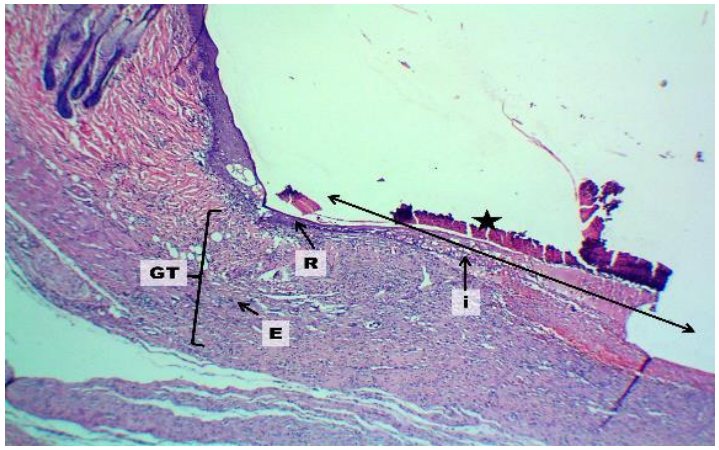

Figure (20): Histological section of rat skin of pre-surgery control group (after 14 days) showing a wide wound site (↔) with mild inflammatory cells infiltration (i), destruction of the epithelium layer of skin with re-epithelialization covering more than half of the wounds (R), profound granulation tissue (GT), and fibroblast cells (E). H&E stain, 40X.

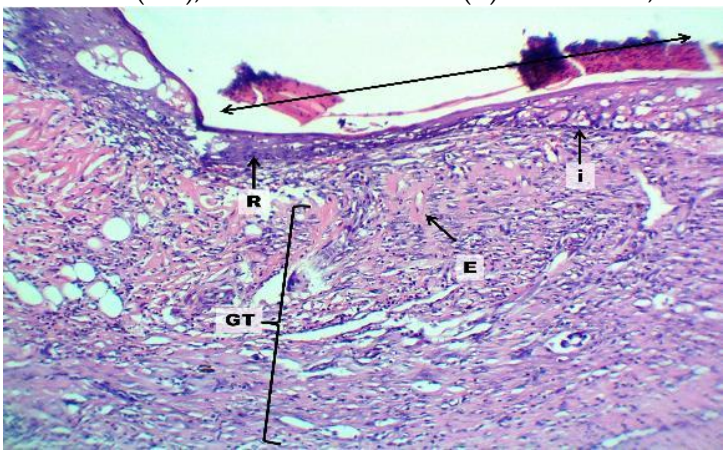

Figure (21): Histological section of rat skin of pre-surgery control group (after 14 days) showing a wide wound site (↔) with mild inflammatory cells infiltration (i), destruction of the epithelium layer of skin with re-epithelialization covering more than half of the wounds (R), profound granulation tissue (GT), and fibroblast cells (E). H&E stain, 100X.

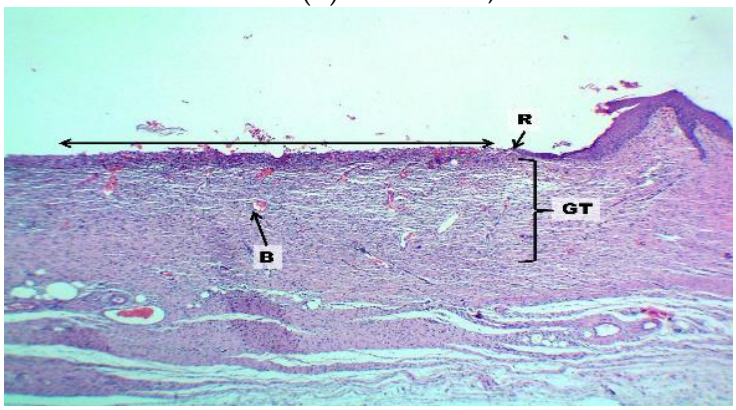

Figure (22): Histological section of rat skin of pre-surgery treatment group (after 14 days) showing narrow wound site (↔) with mild inflammatory cells infiltration (i), destruction of epithelium layer of skin with re-epithelialization covering the entire wound with normal thickness (R) scanty granulation tissue (GT), good newly formed blood vessels (angiogenesis) (B), and fibroblast cells (E). H&E stain, 40X.

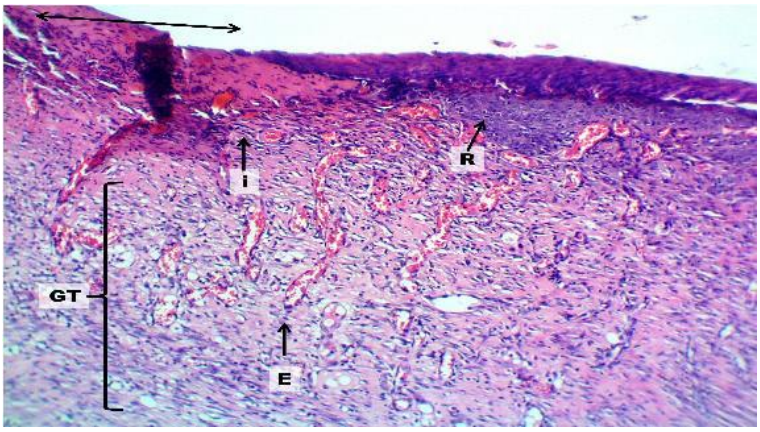

Figure (23): Histological section of rat skin of pre-surgery treatment group (after 14 days) showing narrow wound site (↔) with mild inflammatory cells infiltration (i), destruction of epithelium layer of skin with re-epithelialization covering the entire wound with normal thickness (R), scanty granulation tissue (GT) and good newly formed blood vessels (angiogenesis) (B). H&E stain, 100X.

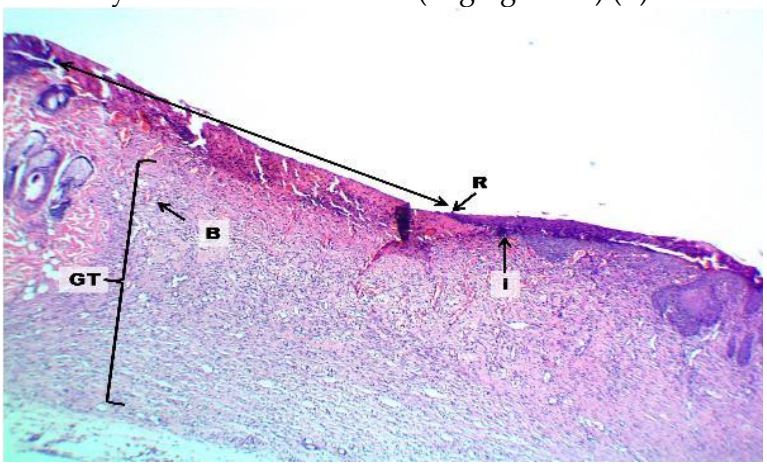

Figure (24): Histological section of rat skin of post-surgery control group (after 14 days) showing wide wound site (↔) with mild inflammatory cells infiltration (i), destruction of epithelium layer of skin with re-epithelialization covering more than half of the wounds (R), moderate granulation tissue (GT) and newly formed blood vessels (angiogenesis) (B). H&E stain, 40X.

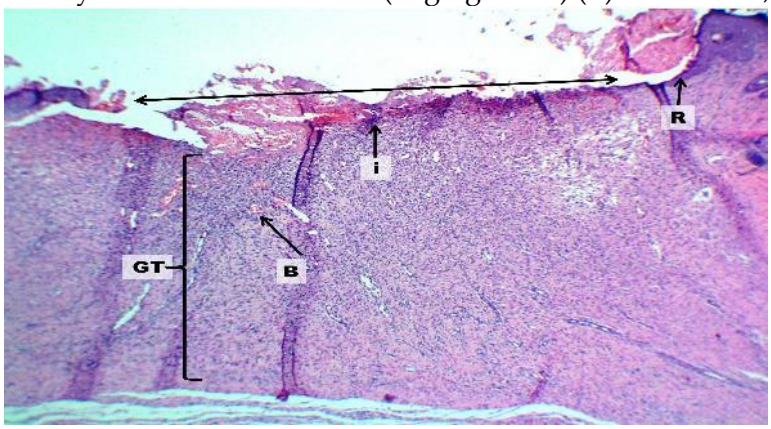

Figure (25): Histological section of rat skin of post-surgery control group (after 14 days) showing wide wound site (↔) with mild inflammatory cells infiltration (i), destruction of epithelium layer of skin with re-epithelialization covering more than half of the wounds (R), moderate granulation tissue (GT) and fibroblast cells (E). H&E stain, 100X.

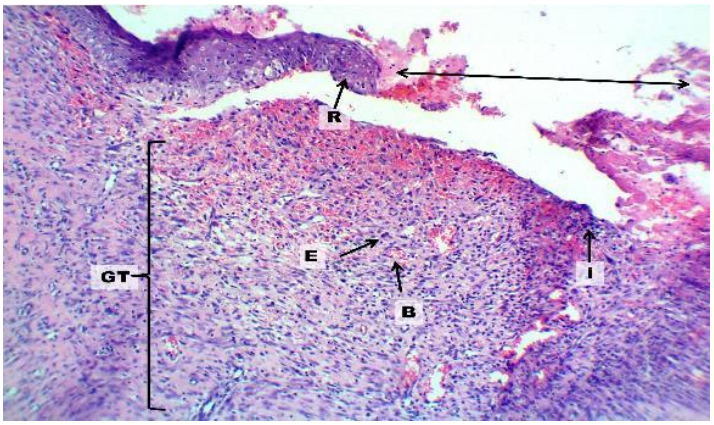

Figure (26): Histological section of rat skin of post-surgery treatment group (after 14 days) showing wound site (↔) with mild inflammatory cells infiltration (i), destruction of epithelium layer of skin with re-epithelialization covering the entire wounds with irregular thickness (R), scanty granulation tissue (GT) and good newly formed blood vessels (angiogenesis) (B). H&E stain, 40X.

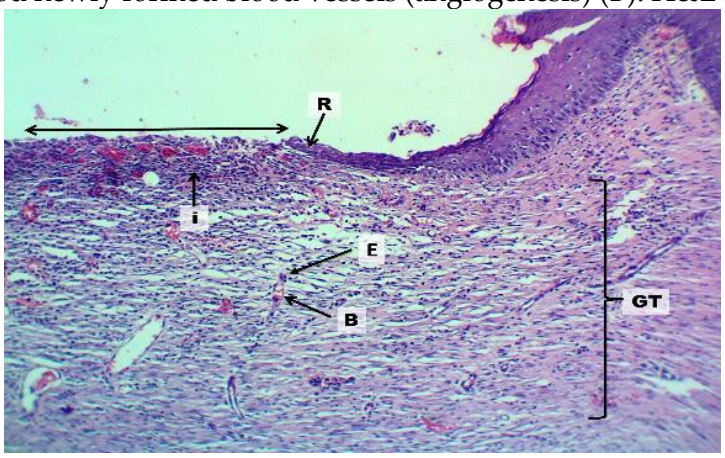

Figure (27): Histological section of rat skin of post-surgery treatment group (after 14 days) showing wound site (↔) with mild inflammatory cells infiltration (i), destruction of epithelium layer of skin with re-epithelialization covering the entire wounds with irregular thickness (R), scanty granulation tissue (GT), good newly formed blood vessels (angiogenesis) (B), and fibroblast cells (E) H&E stain, 100X.

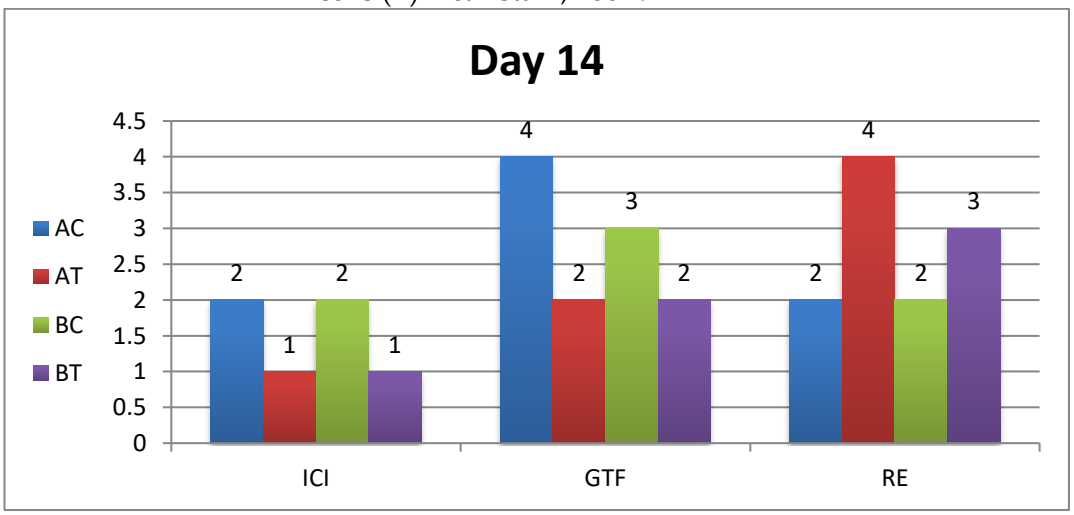

Figure (28): The histopathological descriptive Scores of the inflammatory cell infiltration ICI, granulation tissue formation GTF, and re-epithelialization RE of the control and treatment groups of the pre- and post-surgery groups at day 14 of the study period

DISCUSSION

Surgeons now face one of their greatest challenges when treating wounds that are too large to be sutured [24]. The tension at the wound's margins has to be released to lessen the severity of this condition.

Wound healing and scarring are both impacted by tension. Reduced blood flow and an increased fibroblastic response may be avoided by avoiding severe tissue tension during wound therapy [25,26]. Healing cutaneous wounds may be aided by a novel approach of reducing muscle contracture. Type A botulinum toxin is a potent neurotoxin that may paralyze striated muscle for 2-6 months. It's been used for over 20 years in therapeutic settings without any reported adverse effects in people [27].

The observation periods were chosen according to phases of wound healing, the initial phase of inflammation on day three, the phase of angiogenesis and proliferation on day seven, and the final phase of re-epithelialization and remodeling on day fourteen. [28].

In the histological analysis using H. & E. stain, the inflammatory cell infiltration of the third day period showed a significant lowering in group A than group AC, B, and BC, as shown in Tables 1,2,4. The reasons were Botox affects the inflammatory response by Botox injection of the underlying muscle minimizes microtrauma result in the short duration of inflammation and reduced inflammatory response in addition to the Botox prevents the production of prostaglandin, bradykinin, and serotonin this agreed with [29], and [30], and proximity of the group B Botox action because the maximal efficacy of Botox injection between (1-4) weeks, as suggested by [18].

Granulation tissue formation of groups A and B was similar on the 3rd day period see Table 4.

Group A had a statistically significant improvement in wound healing and re-epithelialization than Group B because the last one was still at the beginning of treatment effectiveness, this supported by [18] see (Table 4).

On the 7th day period, there was a significant decrease in group A than group B in granulation tissue formation because Botox decreases cytokines such as platelet growth factor PGF, transforming growth factor TGF, epidermal growth factor EGF, fibroblast growth factor FGF, and insulin-like growth factor ILF during this stage, supported by [24] see (Table 4).

On day 14, as is typical during the wound-healing process, the number of inflammatory cells had decreased in all groups, which agreed with [24] see (Table 1).

Both re-epithelialization and skin regeneration were shown to be statistically significantly different between groups A and B. The cause of this difference was inhibiting sympathetic nor-epinephrine production with an intradermal injection of

Botox before skin surgery improves wound healing by improving circulation [31] see (Table 4).

When comparing treatment with control Groups, we discovered a statistically significant difference in re-epithelialization and skin regeneration. This is because Botox injection at a low dose 1 IU influenced the migration and proliferation of keratinocytes and endothelial cells, leading to better sprouting blood vessels, re-epithelialization, and remodeling in the wound site. Also, the Botox denervating the underlying muscles decreases stress on the wound borders, leading to a better quality scar, which agrees with [31,32] see (Table 2,3,4).

In addition to the many studies that have shown that injecting Botox into the skin before surgery may reduce the sympathetic nervous system's release of nor-epinephrine, leading to vasodilation and thus increasing the circulatory perfusion, which may improve wound healing and re-epithelialization, this justifies the significant increase of group A over group B in our study [31].

CONCLUSIONS

Within the limitations of the current study, as concluded that Botox injections should be considered as an effective alternative adjuvant option to accelerate wound Both methods improved secondary intention wounds and accelerated skin regeneration and re-epithelization. We suggest Botox injections for wound healing before surgical intervention is desirable.

Acknowledgment: The authors would like to thank members of the oral and maxillofacial surgery department, College of Dentistry, and the animal house/Faculty of Veterinary Medicine, University of Mosul, Iraq.

Authors' Contribution

Ahmed HB., Aldabagh AN., Mahmood AS. contributed to conceptualization, validation, and writing the original draft. Ahmed HB was responsible for formal analysis, methodology, and project administration. Aldabagh, AN, and Mahmood AS for supervision, review & editing of the manuscript. Ahmed HB contributed to the investigation, software development, validation, and visualization. Aldabagh, AN, and Mahmood AS were involved in data curation, resources, and review & editing. All authors have read and approved the final manuscript.

Funding: This study is self-funded

Ethical statement: The study was conducted at the College of Dentistry, University of Mosul, at the Center for Research in the Oral and Maxillofacial Surgery Department. (UoM. Dent, A.74/22) is the ethical approval number given by the university's research ethics committee.

Conflict of interest

The authors declare that there are no conflicts of interest regarding the publication of this manuscript

Availability of data and materials: The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Declaration of Generative AI and AI-assisted technologies

No artificial intelligence tools were used. The authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

REFERENCES

1. Darwin E, Tomic-Canic M. Healing chronic wounds: current challenges and potential solutions. *Current dermatology reports.* 2018;7:296-302.
2. Rodrigues M, Kosaric N, Bonham CA, Gurtner GC. Wound healing: a cellular perspective. *Physiological reviews.* 2019;99(1):665-706.
3. Lephart ED. Equol's anti-aging effects protect against environmental assaults by increasing skin antioxidant defense and ECM proteins while decreasing oxidative stress and inflammation. *Cosmetics.* 2018;5(1):16.
4. Khunger N. Accelerated wound healing: Harnessing the power of platelets, biomaterials, stem cells and gene therapy. *Journal of cutaneous and aesthetic surgery.* 2017;10(1):1.
5. Sharma S, Rai VK, Narang RK, Markandeywar TS. Collagen-based formulations for wound healing: A literature review. *Life sciences.* 2022;290:120096.
6. Sherris DA, Gassner HG. Botulinum toxin to minimize facial scarring. *Facial plastic surgery.* 2002;18(01):035-040.
7. Kucukkaya D, Irkoren S, Ozkan S, Sivrioglu N. The effects of botulinum toxin A on the wound and skin graft contraction. *Journal of Craniofacial Surgery.* 2014;25(5):1908-1911.
8. Zhang S, Li K, Yu Z, et al. Dramatic effect of botulinum toxin type A on hypertrophic scar: A promising therapeutic drug and its mechanism through the SP-NK1R pathway in cutaneous neurogenic inflammation. *Frontiers in Medicine.* 2022;9:520.

9. Park TH, Rah DK, Chong Y, Kim J-k. The effects of botulinum toxin A on survival of rat TRAM flap with vertical midline scar. *Annals of plastic surgery.* 2015;74(1):100-106.
10. Goldberg SH, Gehrman MD, Graham JH. Botulinum toxin A and B improve perfusion, increase flap survival, cause vasodilation, and prevent thrombosis: a systematic review and meta-analysis of controlled animal studies. *HAND.* 2023;18(1):22-31.
11. Kim YS, Roh TS, Lee WJ, Yoo WM, Tark KC. The effect of botulinum toxin A on skin flap survival in rats. *Wound repair and regeneration.* 2009;17(3):411-417.
12. Adler M, Pellett S, Sharma SK, Lebeda FJ, Dembek ZF, Mahan MA. Preclinical evidence for the role of botulinum neurotoxin A (BoNT/A) in the treatment of peripheral nerve injury. *microorganisms.* 2022;10(5):886.
13. Witmanowski H, Błochowiak K. The whole truth about botulinum toxin–a review. *Advances in Dermatology and Allergology/Postępy Dermatologii i Alergologii.* 2020;37(6):853-861.
14. Struck MB, Andrutis KA, Ramirez HE, Battles AH. Effect of a short-term fast on ketamine–xylazine anesthesia in rats. *Journal of the American Association for Laboratory Animal Science.* 2011;50(3):344-348.
15. Senadi GC, Dhandabani GK, Sobral MV, et al. A 9-aminoacridine derivative induces growth inhibition of Ehrlich ascites carcinoma cells and antinociceptive effect in mice. 2022.
16. Uchiyama A, Yamada K, Perera B, et al. Protective effect of botulinum toxin A after cutaneous ischemia-reperfusion injury. *Scientific Reports.* 2015;5(1):1-7.
17. Poenaru D, Sandulescu MI, Cinteza D. Pain Modulation in Chronic Musculoskeletal Disorders: Botulinum Toxin, a Descriptive Analysis. *Biomedicines.* 2023;11(7):1888.
18. Satriyasa BK. Botulinum toxin (Botox) A for reducing the appearance of facial wrinkles: a literature review of clinical use and pharmacological aspect. *Clinical, cosmetic and investigational dermatology.* 2019:223-228.
19. Afshar A, Khoradmehr A, Nowzari F, et al. Tissue Extract from Brittle Star Undergoing Arm Regeneration Promotes Wound Healing in Rat. *Marine Drugs.* 2023;21(7):381.
20. Gupta A, Kumar P. Assessment of the histological state of the healing wound. *Plastic and Aesthetic Research.* 2015;2:239-242.
21. Myrstad M, Ihle-Hansen H, Tveita AA, et al. National Early Warning Score 2 (NEWS2) on admission predicts severe disease and in-hospital mortality from Covid-19–a prospective cohort study. *Scandinavian journal of trauma, resuscitation and emergency medicine.* 2020;28:1-8.
22. Van De Vyver M, Boodhoo K, Frazier T, et al. Histology scoring system for murine cutaneous wounds. *Stem Cells and Development.* 2021;30(23):1141-1152.

23. Al-Saffar MT, Mahmood AS, Sulaiman MS. Impact of Local Anesthesia on Wound Healing. *Indian Journal of Forensic Medicine & Toxicology.* 2020;14(4):1869-1874.
24. Haghighi A, Ronagh A, Sabiza S, Rezaie A. Evaluation of secondary intention wound healing process after botulinum toxin-A injection in rat. 2020.
25. Sherris DA, Larrabee Jr WF, Murakami CS. Management of scar contractures, hypertrophic scars, and keloids. *Otolaryngologic Clinics of North America.* 1995;28(5):1057-1068.
26. Hom DB, Bernstein JD. Reducing Risks of Facial Scarring. *Facial Plastic Surgery Clinics.* 2023;31(2):195-207.
27. Persu C, Castro-Diaz DM, Jinga V, Chirca N, Ciofu I. Botulinum toxin, treatment option for neurogenic detrusor overactivity. *FARMACIA.* 2022;70(2):198-203.
28. Alhakamy NA, Caruso G, Privitera A, et al. Fluoxetine Ecofriendly Nanoemulsion Enhances Wound Healing in Diabetic Rats: In Vivo Efficacy Assessment. *Pharmaceutics.* 2022;14(6):1133.
29. Lee B-J, Jeong J-H, Wang S-G, Lee J-C, Goh E-K, Kim H-W. Effect of botulinum toxin type a on a rat surgical wound model. *Clinical and Experimental Otorhinolaryngology.* 2009;2(1):20-27.
30. Oryan A, Alemzadeh E. Comparison of botulinum toxin type A and aprotinin monotherapy with combination therapy in healing of burn wounds in an animal model. *Molecular biology reports.* 2020;47:2693-2702.
31. Al-Qattan MM, Al-Shanawani BN, Alshomer F. Botulinum toxin type A: implications in wound healing, facial cutaneous scarring, and cleft lip repair. *Annals of Saudi medicine.* 2013;33(5):482-488.
32. Gugerell A, Kober J, Schmid M, Buchberger E, Kamolz L-P, Keck M. Botulinum toxin A: dose-dependent effect on reepithelialization and angiogenesis. *Plastic and Reconstructive Surgery Global Open.* 2016;4(8).

تأثير حقن البوتكس على التئام الجروح قبل وبعد الجراحة

هشام عبد احمد [1] عبد الحميد ناطق الدباغ [2] عبد الستار سالم محمود [3]

1,2 فرع جراحة الفم والوجه والفكين، كلية طب الاسنان، جامعة الموصل، الموصل، العراق
3 فرع التشخيص الفموي، كلية طب الأسنان، جامعة الموصل، الموصل، العراق

الملخص

الأهداف: تهدف الدراســة الحالية إلى هدفت هذه الدراســة إلى فحص آثار العلاج بالبوتكس على تجدد الجلد في الجروح التي تلقت العلاج قبل الجراحة أو بعدها. **المواد وطرائق العمل**: تم حقن 18 من ذكور الجرذان البيضـــاء التي تزن ما بين (250-

350) جرام لكل منها 1 وحدة دولية من (البوتكس والمحلول الملحي) محقونة في العضل تحت الجلد في مركز دوائر 1.5 سم مع 4.5 سم بينهما، المجموعة أ؛ الحقن قبل الجراحة بسبعة أيام ثم خضعت الحيوانات لاستئصال الجلد كامل السماكة. المجموعة ب الحقن مباشرة بعد حدوث الجرح ثم تحفظ جميعها في أقفاص منفصلة. تم تقسيم كل مجموعة إلى ثلاث مجموعات فرعية متساوية وفقًا لفترة الشفاء (3 و7 و14 يومًا) ثم أجريت الاختبارات النسيجية على خزعات الجلد لجميع المجموعات بعد القتل الرحيم. **النتائج**: اظهرت النتائج ان هناك فروق ذات دلالة إحصائية بين المجموعتين (أ) و (ب) في اليوم الثالث، أظهرت المجموعة (أ) التهابًا خفيفًا، في حين أن المجموعة (ب) وكلتا المجموعتين الضابطة كانت مصابة بالتهاب شديد. في اليوم السابع، كان لدى المجموعة (أ) نسيج حبيبي ضئيل وإعادة تكوين النسيج الظهاري لأكثر من نصف الآفات. كان للمجموعة ب أنسجة حبيبية أكبر وأقل إعادة اندمال بتشكل النسيج الظهاري. في اليوم الرابع عشر، أظهرت كلتا المجموعتين نموًا كبيرًا في الأنسجة الحبيبية، لكن المجموعة أ زادت الأوعية الدموية وتكاثر الخلايا الكيراتينية، مما أدى إلى إعادة تكوين النسيج الظهاري وتجديد الجلد بشكل جيد للغاية. **الاستنتاجات**: ونستنتج مما سبق بأن تعتبر حقن البوتكس خيار علاجي بديل فعال لتسريع التئام الجروح وأنسب طريقة لإدارة البوتكس هي قبل الجراحة.

الكلمات المفتاحية: الصلابة الدقيقة، الخشونة، المركب، الفيتامينات المتعددة، أوميغا ٣.