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Comparison of Diltiazem Ointment and Safflower Oil in Reducing the Necrosis of Accidental Flap of Rat

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Abstract

Background: This study aimed to compare diltiazem-ointment and safflower oil in reducing the necrosis of accidental rat flaps.

Method: We divide 40 mice into four groups. We created a 10 × 3 random flap on the back of rats after washing with ketamine intraperitoneal. The flap was used for these four groups of ointments from two days before surgery to five days after surgery. We used diltiazem ointment in the first group, safflower essential oil in the second group and vaseline in the third group. The fourth group was for control

Results: The mean necrosis of the flap was observed in 49% of the vaseline group, 52% of the diltiazem group, 53% safflower essential oil group, and 47% of the control group. The P-value with the independent groups' test was more than 0.05 and confirmed no significant difference between Wistar rat groups. Vaseline, diltiazem, and safflower essential oil did not increase blood flow to the random flap in mice.

Conclusions: Diltiazem and safflower did not improve blood flow to the flap. Since this drug has not been used for flaps, it is suggested that further studies be conducted in this field.

Keywords: Diltiazem, Safflower Necrosis, Accidental Flap

1. Background

The accidental skin flap is one of the most common procedures in plastic and reconstructive surgery. Compared to other repair methods, the harmony of these flaps in terms of color, consistency, and thickness with the original texture has added to the importance of these flaps. Necrosis of the flap is still one of the most critical complications in reconstructive surgery (1). Different modifications and refinements can be applied to make it easier to use different flaps and increase their usability. Skin random flaps also have various limitations, including limiting the length to-width ratio, limiting the amount of rotation, the proximity of the flap to the wound or defect, and placing the flap in the zone of injury (2). Unfortunately, necrosis of the distal flap is one of the events that cannot always be prevented with proper flap design. Several drugs, such as topical drugs, have been studied to prevent ischemic flap, including sympatholytics, vasodilators, calcium channel blockers, prostaglandin inhibitors, the release of anticoagulants, and glucocorticoids (3, 4).

Ischemic pathogenesis is not well understood, but some mechanisms include vasospasm, blood flow in the arterial-venous shunt, vascular endothelial cell damage, thrombosis within the microcirculatory vessels, and tissue damage due to ischemia (5). Early ischemia is not significant enough to cause necrosis due to flap lifting. Past studies have shown that most tissues can survive with 10% of their average blood flow. Necrosis in the flap causes significant morbidity, repeated surgery, and longer patient stays in the hospital. Different methods have been used to increase the survival of flaps using different drugs (6). The random flap is one of the types of flaps used in plastic surgery treatments. Random flaps are used on all parts of the body. The allowable length and width of the random flap in different body parts have been determined during extensive research. The flap becomes accustomed to ischemia, and the vascularization of the flap improves. Of course, the delay also has its side effects, which include the need for additional surgery, the possibility of damage

to the flap pedicle, and the development of scars (7, 8).

2. Objectives

This study was conducted to compare diltiazem ointment and safflower oil in reducing the necrosis of accidental rat flaps.

3. Methods

In this interventional study, 40 Wistar rats weighing 250 to 300 g were blocked and randomly assigned to three intervention groups and one control group. The first group used diltiazem ointment; the second group received safflower oil, and the third group utilized vaseline ointment from two days before surgery to five days after surgery in the flap area. The flap was designed by McFarlane's method (9) on the back of the mice (10 × 3 cm flap). The ointment was applied three times a day. Drugs in all groups were applied by an animal laboratory expert who was unaware of the content of the ointments. Then, after a week, the Wistar rats were photographed with a digital camera next to the ruler, and then the necrotic area was calculated by an expert person who was unaware of the groups with an accuracy of 0.1 mm. This way, the coordinates of all corners of the necrotic area were recorded and painted in paint software. After calculating the area the Wistar rats were sacrificed with chloroform.

The safflower plant is cultivated in field conditions and was prepared in Khuzestan province. After scientific approval, it was used by Arak University Medicinal Plants Research Center. The plant was rinsed twice with ordinary water and dried in a dark place at a temperature of 23 ± 2°C. After the drying process, it was pulverized by the crushing machine, and the resulting powder was distilled twice with distilled water and sterilized by the cloning generator. Then, 2.5 kg of the plant with 5,000 cc of distilled water was placed in the device, and the device's flame was adjusted so that 4 cc of essential oil was obtained per minute. The oil, with an oily shape and high volatility was separated from the device in containers for storing essential oil and kept at a completely sterile condition at 4°C until use. In the end, the data were entered into SPSS software and statistically analyzed.

4. Results

Of 40 animals, we lost one from the control group during the study. We had nine Wistar rats in the control group and 10 in the other four groups. No infection or hematoma was observed. At the end of the study, the mean necrosis of the flap was observed in 49% of the vaseline group, 52% of the diltiazem group, 53% of the safflower essential oil group, and 47% of the control group. The P-value with the independent groups' test was more than 0.05, confirming no significant difference between the Wistar rat groups. Vaseline, diltiazem, and safflower essential oil did not increase blood flow to the random flap in Wistar rats (Table 1).

Table 1. Comparison of Necrosis Area in Groups

Groups	Flap Area	Necrosis Area	Necrosis Area Percentage
Vaseline	17,85	8.53	48%
Diltiazem	19.54	10.28	52%
Safflower	20.63	10.88	53%
Control	18.69	9.51	47%
P-value	> 0.05	> 0.05	< 0.05

5. Discussion

The accidental skin flap is one of the most common procedures in plastic and reconstructive surgery. Compared to other repair methods, the harmony of these flaps in terms of color, consistency and thickness with the original texture has added to the importance of these flaps. Necrosis of the flap is still one of the most important complications in reconstructive surgery. Hence, the study aimed to compare diltiazem ointment and safflower oil in reducing the necrosis of accidental rat flaps. Our survey observed no significant difference between the Wistar rat groups, while other studies have shown different results.

The use of random skin flaps dates back to 600 BC, which is written in Samhita Sushruta. In 1597, the use of distal arm flaps was described by Tag-Liacozzi (10). The first report on using a skin flap model in mice was published in 1965 by Mr. McFarlane et al. (9). The flap was 10 × 4 cm on a cranial base. The skin behind the mouse was raised to the level of the deep fascia of the muscle, which caused 94 - 25% necrosis in 94% of the mice.

Baser et al. conducted a study investigating the effect of the delayed-release operation on flap survival in mice. They showed that surgical delay prepares tissues to reduce ischemia and improves vasculitis in the transferred flap (11). Bahrami et al. studied the effect of delayed growth factor and flap survival and concluded that in the group, delayed action, fibroblasts, and growth factors increased and improved flap survival (12). In a similar study in 2013, Ebrahimi et al. found that laser therapy improved angiogenesis by improving flap function and its survival (13).

In addition, Ghanbari et al. conducted a study to investigate the effect of tadalafil on the survival of random skin flaps. The results showed that high and low doses of this drug were effective in increasing blood flow and ultimately increasing the survival of skin flaps (14). In a similar study, Hasani-Ranjbar et al. studied the effect of losartan drug on ischemic skin flaps and its role in improving survival. There was no significant difference in the results obtained in the study. An increase in the number of fibroblasts, neutrophils, and capillaries was observed in all groups except the losartan group. Therefore, they concluded that losartan does not improve the survival of skin flaps, but has anti proliferative properties on fibroblasts (15).

Plastic surgeons commonly use aspirin and heparin to improve blood flow to the flap. Although some studies have shown a positive effect, other researchers have not seen an improvement in blood flow; the same is true for corticosteroids. However, these three drugs are the most common drugs used in the clinic, and other drugs have not received public acclaim (16). Diltiazem ointment is usually recommended to reduce postoperative pain and defecation. Diltiazem is also a topical drug for the treatment of fissure disease, which is found in gels and ointments. This ointment does not cause any side effects and can quickly reduce the patient's pain and discomfort. It blocks the entry of calcium into the cell or the release of calcium from cellular reserves; therefore, this drug slows down the venous and sinus vestibular conduction velocity and relaxes the smooth muscles of the walls of the arteries and heart. The most important therapeutic properties of safflower essential oil include antioxidant properties, increased cellular energy production, angiogenesis, and increased circulating blood flow; also, they have rare salts that are effective in tissue repair. In addition, Mousavi-Jazi essential oil is used to treat diabetic foot ulcers by improving blood flow. Experimental studies have shown its effectiveness in treating bed sores and improving skin and wound complications in patients with scleroderma (17). Therefore, these results corroborate those observed in the present evaluation and indicate the importance of this approach in this patient group. Accordingly, most studies, have observed that these treatments can effectively improve patients' conditions.

5.1. Conclusions

In this study diltiazem and safflower did not improve blood flow to the flap. Since this drug has not been used for flaps, it is suggested that further studies be conducted in this field.

Footnotes

Authors' Contribution: All authors equally contributed to manuscript preparation and submission.

Conflict of Interests: We have no conflict of interest.

Ethical Approval: Double publication, data fabrication, and plagiarism have been observed by the authors and approved by the Ethics Committee of Arak University of Medical Sciences with code IR.ARAKMU.REC.1398.216. Link: ethics.research.ac.ir/EthicsProposalView.php?id=62566

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