Acta Medica Ruha E-ISSN: 2980-1184

International Journal of Medicine and Health Sciences

Original Research Article Volume:1 Issue:2 Year:2023 DOI: 10.5281/zenodo.7850981

Effect Of Epidermal Growth Factor & Platelet-Rich Plasma In Experimental Rat Burn Model

Deneysel Sıçan Yanık Modelinde Epidermal Growth Faktör (EGF) Ve Plateletten Zengin Plazmanın Etkisi

Abdülkadir Calavul[1]

1 Şanlıurfa Metrolife Hastanesi, https://orcid.org/0000-0002-6790-128X

Abstract

Introduction: Today, drugs are being tried with various methods for the early healing of burn wounds. However, no drug still shows the desired effect in burn healing.
Objective: This experimental study investigated the effects of platelet-rich plasma (PRP) and epidermal growth factor(EGF) on burn wounds.
Method: In this study, 48 Spraque-Dawley male rats aged 12 to 16 weeks weighing 350 – 450 g were used under general anesthesia. The rats in Group 1 were in the control group, and no application was made. Only EGF was applied to the burn area created on the backs of the rats in the 2nd group, EGF + PRP was applied to the burn area created on the backs of the rats in the 3rd group, and only PRP was applied to the burn area created on the backs of the rats in the 4th group.
Results: In terms of epidermis regeneration, there was a statistically significant difference between days 7, 14, and 21 of Groups 1, 3, and 4. Regarding granulation, there was a statistically significant difference between days 7, 14, and 21 of Groups 1, 2, and 3. Regarding inflammation, Groups 1, 2, and 4 are investigated seventh, 14th, and 21st days. There was a statistically significant difference between his days. In terms of hair follicle regeneration, there was a statistically significant difference between days 7, 14, and 21 of Groups 2, 3, and 4.
Conclusion: It was concluded that platelet-rich plasma and epidermal growth factor applied by intralesional and perilesional injection methods positively affected wound healing and accelerated wound healing in rats with third-degree burns.

Keywords: Burn, Platelet Rich Plasma, Epidermal Growth Factor.

Özet

Giriş: Günümüzde yanık yarasının erken iyileşmesi için çeşitli yöntemlerle ilaçlar denenmektedir. Ancak yanık iyileşmesinde halen istenen etkiyi gösteren ilaç bulunmamaktadır.
Amaç: Bu deneysel çalışma plateletten zengin plazma(PRP) ve epidermal büyüme faktörünün (EGF) yanık yarası üzerine olan etkilerini araştırmak amacıyla yapılmıştır.
Yöntem: Bu çalışmada, genel anestezi altında 350 – 450 gr ağırlığında 12 – 16 haftalık 48 adet Spraque-Dawley erkek rat kullanıldı. PRPelde etmek için 8 adet rat kullanıldı. Kalan 40 rat randomizasyon listesine göre her grupta 10 rat olmak üzere4 grup oluşturulduktan sonra sırtlarında 2 cm boyutunda 4 adet dişi olan tarak şeklindeki metal plaka ile tam kat yanık oluşturuldu. 1. grupta yer alan ratlar kontrol grubu olup her hangi bir uygulama yapılmadı. 2. grupta yer alan ratların sırtlarında oluşturulan yanık alanına sadece EGF uygulaması, 3. grupta yer alan ratların sırtlarında oluşturulan yanık alanına EGF + PRP, 4. grupta yer alan ratların sırtlarında oluşturulan yanık alanına ise sadece PRP uygulandı. Gruplardan elde edilen preparatlar histopatolojik olarak incelendikten sonra istatistiki verilerle yorumlanıp karşılaştırıldı.
Bulgular: Epidermis rejenerasyonu açısından Grup 1,3 ve4'ün 7. 14. ve 21. günleri arasında istatiksel olarak anlamlı fark çıkmıştır. Granülasyon açısından Grup 1,2 ve 3'ün 7. 14. ve 21. günleri arasında istatiksel olarak anlamlı fark çıkmıştır. İnflamasyon açısından Grup 1,2 ve 4'ün 7. 14. ve 21. Günleri arasında istatiksel olarak

Corresponding Author: Abdülkadir Calavul, e-mail: calavul@hotmail.com
Received: 13.04.2023; Accepted:30.04.2023; Published Online:30.06.2023
Cite: Calavul A. Effect Of Epidermal Growth Factor & Platelet-Rich Plasma In Experimental Rat Burn Model. Acta Medica Ruha. 2023;1(2):41-51. https://doi.org/10.5281/zenodo.7850981

anlamlı fark çıkmıştır. Kıl folikül rejenerasyonu açısından Grup 2, 3 ve 4'ün 7. 14. ve 21. günleri arasında istatiksel olarak anlamlı fark çıkmıştır.
Sonuç: Üçüncü derece yanık oluşturulan ratlarda intralezyonel ve perilezyonel enjeksiyon yöntemiyle uygulana plateletten zengin plazma ve epidermal büyüme faktörünün yara iyileşmesi üzerine olumlu etkilerinin olduğu ve yara iyileşmesini hızlandırdığı sonucuna varılmıştır.

Anahtar Kelimeler: Yanık, Plateletten Zengin Plazma, Epidermal Büyüme Faktörü.

INTRODUCTION

A burn is one of the most severe traumas every individual can face. Morbidity and mortality are very high due to the long duration of treatment and secondary infections added to it. Successful results are obtained with treatments such as early debridement and grafting of the burned area. However, different treatments are used in cases where early grafting cannot be performed for various reasons, such as the operation cannot be performed due to the poor general condition of the patient and the lack of good healthy skin to obtain a graft. Especially in patients with extensive burns, using various products for earlier wound healing can affect the patient's survival and reduce infectious complications (1). Wound care materials and artificial skins are produced and used for this purpose. Studies in this area are promising, and new solutions are being explored. However, no drug still shows the desired effect in burn healing. For this purpose, platelet-rich plasma and growth factors are used in all areas of medicine due to their properties that increase and regenerate wound healing (2).

Epidermal Growth Factor is a mitogenic polypeptide consisting of 53 amino acids found in different tissues and body fluids of many mammalian species. When injected subcutaneously, it transforms into a 48-amino acid shape and becomes active. EGF has a proliferative effect on cells of both mesodermal and ectodermal origin, especially keratinocytes and fibroblasts. EGF granulation tissue increases the level of collagen and glycosaminoglycans; as a result, epithelialization accelerates, and wound tensile strength increases. Submandibular salivary gland extracts, in which EGF is abundant, have an accelerating effect on wound healing. The most important known effect of EGF is that it accelerates wound healing. It is known to accelerate wound healing by stimulating the production of proteins and the migration of epithelial cells. The effect of EGF on wound healing goes through three processes: the inflammatory phase, the fibroblastic phase, and the remodeling phase. EGF, a mitogenic polypeptide, begins to act on wound healing at the end of the inflammatory phase and is known to induce the fibroblastic formation and stimulate the formation and epithelialization of granulation tissue (3).

Platelet-rich plasma (PRP) is a natural fibrin-derived biomaterial used in all areas of medicine due to its wound-healing enhancing and regenerating properties. It provides micro vascularization and epithelium cell migration in the area where it is placed. In this way, it accelerates wound healing in open wounds. Platelet-rich plasma (PRP) forms a matrix for endothelial cells and fibroblasts with its tetra molecular structure. It accelerates angiogenesis and provides easy remodeling of fibrin. PRP is not only a simple fibrin structure but also a matrix that contains all molecules and cellular elements that provide healing (4).

This experimental study aimed to investigate the effects of platelet-rich plasma (PRP) and epidermal growth factor (EGF) on burn wounds.

METHOD

Experimental animals were procured from Dicle University Prof. Dr. Sabahattin PAYZIN Health Sciences Research and Application Center (DÜSAM) for the study. Rats were housed

in standard mass cages. Their feeding will be given in standard pellets. Room temperature was kept constant at approximately 21°C. Laboratory lighting was provided with 12 hours of daytime and 12 hours of the night, controlling the circadian rhythm. The humidity of the room is set to remain at 45±10%. A single surgeon performed all procedures.

Surgical procedures include 50 mg/kg Ketamine sodium (Ketalar® vial; Pfizer Ltd Şti, İstanbul, Turkey) and Xylazine hydrochloride (Rompun® vial, Bayer Inc, Germany) 10mg/kg mixture was administered intraperitoneally and performed under general anesthesia. Cefazolin sodium 0.25 gr/kg (Cefazol® vial, Mustafa Nevzat İlaç Sanayi, İstanbul, Turkey) was administered intramuscularly in the form of divided doses 1 hour before the operation and for three days after the operation. The working area on the backs of the rats was shaved and disinfected with a 10% povidone-iodine solution (Batticon®, Adeka İlaç Ltd Şti, Samsun, Turkey).

4-8 cc of blood was taken intracardially from rats (8 units) to obtain PRP under 60 mg/kg intraperitoneal pentobarbital (PentothalSodium®, Abbott Pharmaceuticals, Istanbul, Turkey) anesthesia. Electro-Mag branded centrifuge device in the Department of Biochemistry, Faculty of Medicine, the laboratory was used to obtain PRP. After the blood was placed in the centrifuge device, it could be centrifuged for 10 minutes at a speed of 1200 rpm. At the end of the centrifuge, the platelet-poor plasma (PPP; platelet-poor plasma) and platelet-rich plasma (PRP; platelet-rich plasma) layer in the upper part of the tube were separated from the erythrocyte and leukocyte supernatant in the lower part and then centrifuged again at 10 min 3600 rpm. The concentrate obtained at the end of the centrifuge was prepared by counting the cells of PRP and preparing it to be approximately 1.000.000 platelets/µl. The PRP obtained was mixed with 0.25cc 10% calcium chloride solution and 0.125cc 300 IU pig thrombin solution (Fibriquick® Thrombin, BioMerieuxInc, Durham, NC, USA) before surgical application, and PRP was activated and then applied.

The comb-shaped metal plate with four females 2 cm in size was left on the flame for 30 seconds and then contacted the back area of the rats for 20 seconds to create a 3rd-degree burn. According to the Parkland formula, approximately 2 ml of ringer lactate was administered intraperitoneally for resuscitation after the burn. Daily analgesia and anti-biotherapy were provided after the procedure.

In our study, 48 Sprague Dawley male rats were used. Eight rats were used to obtain PRP. The remaining 40 rats were divided into four groups, with ten rats in each group according to the randomization list.

Group 1: The control group is the only burn created. In addition, no application was made.Group 2: Only EGF was applied to the burn area created on the backs of rats. On days 0, 3, 7, and 14, EGF was administered with intralesional and perilesional regeneration of 75 µg/day.Group 3: EGF + PRP was applied to the burn area created on the backs of rats. 0, 3, 7 andOn day 14, EGF was administered by intralesional and perilesional injections of 75 µg/day and PRP of approximately 1,000,000 platelets/µl.Group 4: Only PRP was applied to the burn area created on the backs of rats. On days 0, 3, 7, and 14, PRP was administered by intralesional and perilesional injection with approximately 1,000,000 platelets/µl.

After four weeks under ketamine anesthesia, the rats were sacrificed and transferred to formalin solution after taking samples from the treated burn sites. Transverse and longitudinal sections were taken from the tissues taken for histopathological examination. The findings were compared by scoring (0: None, 1: Less, 2: Medium, 3: Good, 4: Very good).

Statistical Analysis

The data were analyzed in IBM SPSS Statistics15.0 statistical package program. As a statistical analysis, categorical variables in the descriptive findings section are presented with numbers, percentages, and median. The Kolmogorov-Smirnov test investigated whether the distribution of continuous variables was close to normal. The significance of the difference in terms of the distribution of histopathological scores between the groups was investigated by Kruskal Wallis tests. The conditions that caused the difference were determined using the Mann-Whitney test in the binary comparison of the groups. Wilcoxon Signal test was used to determine the follow-up time(s) that caused the difference if the Friedman test statistic result was significant and to compare the significance of the difference in terms of histopathologic score distribution between any two follow-up times within the groups. In all analyses, the statistically significant level was taken as $p<0.05$.

RESULTS

Multiple simultaneous comparisons of the histopathological scores of each group on days 7, 14, and 21 are presented in Table 1. In terms of epidermis regeneration, there was a statistically significant difference between days 7, 14, and 21 of Groups 1, 3, and 4. ($p=0.013$, $p=0.014$, and $p=0.028$). In terms of granulation, there was a statistically significant difference between days 7, 14, and 21 of Group 1, 2, and 3. ($p=0.039$, $p=0.008$, and $p=0.003$) There was a statistically significant difference between days 7, 14, and 21 of Group 1, 2 and 4 in terms of inflammation. ($p=0.001$, $p=0.005$, and $p=0.045$) In terms of hair follicle regeneration, there was a statistically significant difference between days 7, 14, and 21 of Group 2, 3, and 4. ($p=0.005$, $p=0.032$, and $p=0.006$)

The results of multiple comparisons in histopathological scores between follow-up times within each group are given in Table 1. Regarding epidermis regeneration, when the groups were compared according to their follow-up times, a statistically significant difference was found between the 7th and 21st days of Group 1 and Group 3 and between the 7th and 14th days of Group 4 in terms of histopathological scores. ($p<0.05$). When the groups were compared in terms of granulation according to their follow-up times, a statistically significant difference was found in terms of histopathological scores between the 7-14th and 7-21st days of Group 1 and Group 2, between the 7-14th days of Group 3, and between the 7-21st days of Group 4 ($p<0.05$).

Multiple comparisons of groups at days 7, 14, and 21 in terms of epidermis regeneration are presented in Table 1. In terms of epidermis regeneration, there was a statistically significant difference between the groups in terms of median histopathological score levels on day 7, and there was a statistically significant difference in the histopathological score of Group 1 compared to Group 2, 3, and 4. ($p<0.001$; $p<0.001$ and $p=0.008$). In addition, there was a statistically significant difference in the histopathological score of Group 4 compared to Groups 2 and 3. ($p<0.001$ and $p=0.006$). No statistically significant difference existed between groups 2 and 3 ($p=0.067$). In terms of epidermis regeneration, there was a statistically significant difference between the groups in terms of median histopathological score levels within day 14, and there was a statistically significant difference in the histopathological score of Group 1 compared to Group 2, 3, and 4. ($p<0.001$; $p<0.001$ and $p=0.005$). In addition, there was a statistically significant difference in the histopathological score of Group 2 compared to Group 4. ($p=0.042$). There was no statistically significant difference between Groups 2 and 3 and Groups 3 and 4. ($p=0.654$ and $p=0.125$).

Table 1. Multiple Comparison Of Groups On Days 7, 14 And 21 İn Terms Of Epidermis Regeneration

Epidermis Regeneration		Control Group 1 (n=10)		EGF Group2 (n=10)		EGF+PRP Group 3 (n=10)		PRP Group4 (n=10)		P-value
		n	(%)*	n	(%)*	n	(%)*	n	(%)*	
Day 7	None	8	80	-	-	-	-	2	20	**<0,001**
	Mild	2	20	1	10	3	30	7	70	
	Moderate		-	6	60	7	70	1	10	
	Good		-	3	30	-	-	-	-	
	Median	0		2		2		1		
	(Min-Max)	(0-1)		(1-3)		(1-2)		(0-2)		
Day 14	None	3	30	-	-	-	-	-	-	**<0,001**
	Mild	7	70	1	10	2	20	5	50	
	Moderate	-	-	8	80	7	70	5	50	
	Good	-	-	1	10	1	10	-	-	
	Median	Median		2		2		1,5		
	(Min-Max)	(0-1)		(1-3)		(1-3)		(1-2)		
Day 21	None	2	20	1	10	-	-	-	-	**<0,001**
	Mild	7	70	1	10	-	-	6	60	
	Moderate	1	10	5	50	5	50	4	40	
	Good	-	-	3	30	5	50	-	-	
	Median	1		2		2,5		1		
	(Min-Max)	(0-2)		(0-3)		(2-3)		(1-2)		

(%)*: Colonpercentage **: Kruskal Wallis Test wasused.

Multiple comparisons of groups on days 7, 14, and 21 in terms of granulation are presented in Table 2. There was a statistically significant difference in median histopathological score levels between the groups within the seventh day in granulation. Bilateral comparisons showed a statistically significant difference in the histopathological score of Groups 2 and 3. (p=0.007). There was no statistically significant difference in the binary comparison of the other groups. (p>0.05) In terms of granulation, there was a statistically significant difference between the groups regarding median histopathological score levels within day 14, and there was a statistically significant difference in the histopathological score of Group 1 compared to Group 2 and 3 in bilateral comparisons. (p=0.044 and p=0.001). In addition, there was a statistically significant difference in the histopathological score of Group 2 and Group 4 compared to Group 3. (p=0.019 and p=0.001). There was no statistically significant difference between groups 1 and 4 and 2 and 4. (p=0.661 and p=0.089). There was no statistically significant difference in median histopathological score levels between the groups within the 21st day regarding granulation. (p=0,134) ; There was a statistically significant difference in

the histopathological score of Group 3 and Group 1 in the bilateral comparisons. (p=0.021). There is no statistically significant difference in the binary comparison of the other groups. (p>0.05)

Table 2. Comparison Of Granulation, Multiple Groups İn 7, 14 And 21 Days

Granulation		Control Group 1 (n=10)		EGF Group2 (n=10)		EGF+PRP Group 3 (n=10)		PRP Group4 (n=10)		P-value
		n	(%)*	n	(%)*	n	(%)*	n	(%)*	
Day 7	None	4	40	4	40	-	-	1	10	**0,010**
	Mild	5	50	5	50	4	40	7	70	
	Moderate	1	10	1	10	6	60	2	20	
	Good		1		1		2		1	
	(Min-Max)		(0-2)		(0-2)		(1-2)		(0-2)	
Day 14	None	6	60	2	20	-	-	5	50	**<0,001**
	Mild	4	40	6	60	3	30	5	50	
	Moderate	-	-	2	20	7	70	-	-	
	Good		1		2		3		1,5	
	(Min-Max)		(1-2)		(1-3)		(2-3)		(1-2)	
Day 21	None	5	50	3	30	1	10	3	30	**0,134**
	Mild	5	50	6	60	6	60	4	40	
	Moderate	-	-	1	10	3	30	3	30	
	Good		1,5		2		2		2	
	(Min-Max)		(1-2)		(1-3)		(1-3)		(1-3)	

(%)*: Colonpercentage **: Kruskal Wallis Test wasused.

When the groups were compared in terms of inflammation (Table 3) according to their follow-up times, a statistically significant difference was found between the 7-14th and 7-21st days of Group 1 and Group 2 and between the 7-14th days of Group 4 in terms of histopathological scores. (p<0.05). In terms of hair follicle regeneration, when the groups were compared according to their follow-up times, there was a statistically significant difference in terms of histopathological scores between days 7-14 of Group 1, between days 7-14 and 7-21 of Group 2, between days 7-21 of Group 3, and between days 7-14 and 7-21 of Group 4. (p<0.05).

Table 3. Comparison Of Inflammation, Multiple Groups In 7, 14 And 21 Days

Inflammation		Control Group 1 (n=10)		EGF Group2 (n=10)		EGF+PRP Group 3 (n=10)		PRP Group4 (n=10)		P-value
		n	(%)*	n	(%)*	n	(%)*	n	(%)*	
Day 7	None	1	10	1	10	5	50	3	30	0,002
	Mild	3	30	3	30	5	50	7	70	
	Moderate	6	60	6	60	-	-	-	-	
	Good		4		4		2,5		3	
	Min		(2-		(2-4)		(2-3)		(2-3)	
	Max		4)							
Day 14	Mild	-	-	3	30	2	20	1	10	**0,606**
	Moderate	7	70	5	50	5	50	7	70	
	Good	3	30	2	20	3	30	2	20	
	Median		2		2		2		2	
	Min		(2-		(1-3)		(1-3)		(1-3)	
	Max		3)							
Day 21	Mild	2	20	-	-	1	10	2	20	**0,738**
	Moderate	5	50	7	70	8	80	5	50	
	Good	3	30	3	30	1	10	3	30	
	Median		2		2		2		2	
	Min-Max)		(1-3)		(2-3)		(1-3)		(1-3)	

(%)*: Colonpercentage **: Kruskal Wallis Test wasused.

DISCUSSION

Burn is one of the most severe traumas faced by the human body. Mortality is still high due to long-term treatment and secondary infections that are often added to it. Today, drugs are being tried with various methods for the early healing of the burn wound. However, no drug still shows the desired effect in burn healing. Bone marrow is suppressed due to silver sulfadiazine use and sepsis, especially after significant burns (5). This is an essential factor that suppresses wound healing in burns.

Platelet-rich plasma (PRP) is a natural fibrin-derived biomaterial used in all areas of medicine due to its wound-healing enhancing and regenerating properties. It provides micro vascularization and epithelium cell migration in the area where it is placed. In this way, it accelerates the healing of open wounds (6). Platelet-rich plasma (PRP) forms a matrix for endothelial cells and fibroblasts with its tetra molecular structure. It accelerates angiogenesis and provides easy remodeling of fibrin. Platelet-rich plasma is a simple fibrin structure and a matrix containing all the molecules and cellular elements that promote healing (7).

Platelet-rich plasma not only contains a large number of platelets but also contains all clotting factors. Many cytokines and growth factors secreted from activated platelets affect various stages of wound healing. Platelets begin secreting these factors approximately 10 minutes after clotting, and over 95% of the growth factors are secreted within an hour. After preparation, PRP remains stable for about 8 hours (8).

Platelet-rich plasma effectively combines soft and hard tissue reconstruction in oral and maxillofacial surgery. Many studies show that PRP increases wound healing in chronic wounds that do not heal (9). Again, in acute traumas and incisional wounds, PRP has been shown to positively affect wound healing up to twice as much (7). Platelet-rich plasma increases epithelial differentiation and allows collagen to be organized into tightly packed bundles of fibers more dense and parallel to the epidermis (10). It has been shown that wounds treated with platelet-rich plasma do not have prolonged inflammation leading to scar growth and bacterial infections and that the inflammation phase is shortened (7).

In our study, when the histopathological findings were examined one by one, In terms of epidermis regeneration, there was a statistically significant difference between days 7, 14, and 21 of Group 1, 3, and 4. ($p=0.013$, $p=0.014$, and $p=0.028$) In terms of granulation, there was a statistically significant difference between days 7, 14 and 21 of Group 1, 2 and 3. ($p=0.039$, $p=0.008$ and $p=0.003$) There was a statistically significant difference between days 7, 14 and 21 of Group 1, 2 and 4 in terms of inflammation. ($p=0.001$, $p=0.005$and $p=0.045$).

Şençimen et al. (11) performed autogenous bone graft and PRP membrane for the treatment of alveolar defect and closure of the oro-nasal opening in a 21-year-old male patient with unilateral cleft lip and palate who did not improve despite two previous operations and reconstructed the alveolar defect by taking an autogenous bone graft from the anterior iliac crest under general anesthesia. Approximately 6 ml of PRP membrane was obtained by centrifugation of 80 ml of blood intravenously. In the clinical and radiographic examination performed in the second postoperative month, it was observed that the oronasal opening was closed, and bone healing was achieved in which graft survival occurred.

EGF is a mitogenic polypeptide consisting of 53 amino acids found in different tissues and body fluids of many mammalian species. When injected subcutaneously, it transforms into a 48-amino acid shape and becomes active. EGF receptors described in many cell culture media may be of nonepidermal origin. It performs its effect on the cell by binding to its receptors. Receptors have been shown in fibroblasts, cornea, lens, small intestine epithelium, glia, and epithelial carcinoma cells. It combines with EGF receptors outside the cell. Triphosphate binds to activate adelilatcyclase and tyrosine kinases, after which cell proliferation accelerates (12). EGF is most commonly secreted by mesodermal cells. EGF is endogenously secreted from the human submandibular salivary gland. EGF plays a significant role in embryogenesis, angiogenesis, and repair of tissues and vascular systems. EGF has been experimentally shown to accelerate wound healing in many studies (13). Studies on systemic administration of EGF have shown that EGF accelerates wound healing by adhering to epithelization, granulation tissue formation, and new vessel formation (14-19).

Türkyılmaz et al. (20) and Memişoğlu et al. (21) concluded that topical application of EGF accelerates wound healing. As a result of the studies conducted by Babül et al. (22), they reported that EGF accelerated wound healing. In his research on wound healing of different forms of EGF, Şimşek (23) reported that EGF applied topically with bioadhesive gels accelerates wound healing compared to systemic and solution-form applications.

Erbaş et al. (24) reported that EGF increased serum zinc levels in their studies showing the accelerating effects of EGF in wound healing, while Türken et al. (25) reported that EGF increased liver prostaglandin E2 levels but had no effect on brain prostaglandin E2 levels. Aral (14) stated that the effect of EGF on skin allografts did not prevent the rejection of skin allografts in the study he investigated.

In the study by Özçetin et al. (26), seven child patients treated in the burn unit used gel material containing EGF, one of the current treatment alternatives, during dressings. The contributions of EGF applied in this way on wound healing have been shown in different studies (27-28). Similarly, we observed the positive effects of EGF application on burn wound healing.

Considering all the results of our study, a very consistent relationship is exhibited between the groups regarding all the evaluation criteria used. In our study, when the groups were compared regarding epidermis regeneration according to their follow-up times, a statistically significant difference was found between the 7-21st days of Group 1 and Group 3 and between the 7-14th days of Group 4 terms of histopathological scores ($p<0.05$). In terms of granulation, when the groups were compared between the groups according to their follow-up times, there was a statistically significant difference in terms of histopathological scores between the 7-14th and 7-21st days of Group 1 and Group 2, between the 7-14th days of Group 3, and between the 7-21st days of Group 4 ($p<0.05$). There was a statistically significant difference in histopathological scores between days 7 and 14 of Group 4 ($p<0.05$).

CONCLUSION

In our experimental model, platelet-rich plasma and epidermal growth factors applied by intralesional and perilesional injection methods positively affect wound healing in rats with third-degree burns. Based on these results, Epidermal growth factor and platelet-rich plasma can be used clinically in burns. Especially in patients who do not have the opportunity to graft and have a large burn surface, epidermal growth factor, and platelet-rich plasma may be an alternative for these patients since the rapid healing of the burn areas will reduce complications and increase survival.

Funding: There is no specific funding related to this research.

Competing interests: The authors declare that they have no competing interests.

Abbreviations

ATP: Adenosine triphosphate

EGF: Epidermal growth factor

FGF: Fibroblast growth factor

HE: Hematoxylin-eosin

IGF: Insulin-like Growth Factor

IL-1:Interleukin-1

NO: Nitric oxide

PDGF: Platelet-derived growth factor

PMNL: Polymorphonuclear leukocyte

PRP: Platelet rich plasma

PTZ: Prothrombin time

TFP: Platelet poor plasma

TGF-α:Transformative growth factor-α

TGF-β:Transformative growth factor-β

VEGF: Vascular endothelial growth factor

REFERENCES

1. Palackic A, Jay JW, Duggan RP, Branski LK, Wolf SE, Ansari N, El Ayadi A. The rapeutic Strategiesto Reduce Burn Wound Conversion. Medicina (Kaunas). 2022 Jul 11;58(7):922. doi:10.3390/medicina58070922.

2. Surowiecka A, Chrapusta A, Klimeczek-Chrapusta M, Korzeniowski T, Drukała J, Strużyna J. MesenchymalStemCells in BurnWound Management. Int J Mol Sci. 2022 Dec 5;23(23):15339. doi:10.3390/ijms232315339.

3. Shakhakarmi K, Seo JE, Lamichhane S, Thapa C, Lee S. EGF, a veteran of woundhealing: highlights on itsmode of action, clinicalapplicationswithfocus on woundtreatment, andrecentdrugdeliverystrategies. ArchPharmRes. 2023 Mar 16. doi:10.1007/s12272-023-01444-3.

4. Verma R, Kumar S, Garg P, Verma YK. Platelet-richplasma: a comparative and economica ltherapy for wound healing and tissue regeneration. Cell Tissue Bank. 2022 Oct 12:1–22. doi:10.1007/s10561-022-10039-z.

5. Monstrey S, Assesment of burn dept hand wound healing potential. Burns. 2008;34: 761-769.

6. Sonnleitner D, A simplified technique for producing platelet-rich plasma and platelet concentrate for intraoral bone grafting techniques: a technicalnote. Int J Oral Maxillofac Implants. 2000;15: 879-604

7. Carter CA, Platelet-richplasma gel promotes differentiation and regeneration during equine wound healing. Experimental and Molecular Pathology, 2003;74: 244- 255.

8. Tekin A, Effects of platelet richplasma on colonic anastomosi s. Journal of Surgical Research, 2007;146:190-194.

9. Ganio C, The treatment of nonhealing wound susingautologous platelet-derivedgrowthfactors. J Foot Ankle Surg. 1993;32: 263-8.

10. Kaps C, Human platelet supernatant promotes proliferation but not differantiation of auricularchondrocytes. Med Biol Eng Comput. 2002;40: 485-90.

11. Şençimen M, Gülses A, Özkaynak Ö, Varol A, Okçu KM, Doğan N. Trombositten zengin fibrin membran kaplıotojen kemik grefti ile tek taraflı alveol yarığı onarımı. Hacettepe Diş Hekimliği Dergisi 2009, 37-42.

12. Klegerman M. E, Plotnikoff N. R, Proteins as BiologicalResponseModifiers, in Klegerman. M. E, Grovers, M. J, (EDS), Pharmaceutıcal Biotechnology, Interpharm Press, USA, (1992).

13. Cohen S. The Epidermal Growth Factor (EGF), Cancer, 51 1787-1791 (1983).

14. Aral İ. L, Epidermal Büyüme Faktörü (EGF)'nin Deri Allogreftleri üzerine olan Etkilerinin Histopatolojik Olarak araştırılması. Doktora Tezi, Gazi Üniv. Sağlık Bilimleri Enstitüsü, Ağız, Diş, Çene Hastalıklarıve Cerrahisi Anabilimdalı, Ankara, (1993).

15. Aral İ. L, Güngör N, Oygür T,Cinel L, Epidermal Büyüme Faktörü (EGF)"nin Deri Allogrefleri Üzerine Olan Etkilerinin Histo patolojik Olarak Araştırılması. G.Ü. Diş. Hek. Fak. Der. 1995;12(1):47-53.

16. Bhora F. Y, Dunkin B. J, Batzri S, Aly H. M, Bass B. L, Sıdawy A. N, Harmon J. W, Effect of GrowthFactors on Celi ProliferationandEpithelization in Human Skin,J. Res. Surg. 1995;59 (2):236-244.

17. Guglietta A, Sullivan P. B, Clinical Applications of Epider mal GrowthFactor, Eur. J. Gastroenterol. Hepatol. 1995;7(10) pp. 945-950.

18. Steenfos H. H, Growth Factorsand Wound Healing, Scand. J. Recons. Surg. HandSurg. 1994;28(2) pp 95-105.

19. Wingren U, Franzen L, Larson G. M, Malcherek P, Schultz G.S, Epidermal Growth Factor Accelerates Connective Tissue Wound Healing in the Perforaled Rat Mesentary, J. Surg. Res. 53(l)p48-54(1992).

20. Türyılmaz A, Çelebi N, Gönül B, Epidermal Büyüme Faktörü (EGF)nün Yara İyileşmesindeki Rolü. FABAD J. Pharm. Sci. 1996; 21,61-69.

21. Memişoğlu E, Öner F, Ayhan A, Başaran L, Kaş HS, Hıncal A. Wound Healing Effectiveness of Chitosan Gel Preparations Withand Without EGF in Rabbit Model. Proceed. 8™ inler. Pharm. Technol. Symp. (IPTS). Sept. 9-i 1, 1996, Ankara-Turkey.

22. Babül A, Gönül B, Özoğul C, Dinçer S, Erdoğan D, Pınar L, Çelebi N, EGF Accelerates Mice Skin Wound Healing, Proceed. 8th inler. Pharm. Technol. Symp. (IPTS-96), Sept. 9-1 1, 1996, Ankara-Turkey.

23. Şimşek MB, Farklı oranlardaki Epidermal Büyüme Faktörünün Yara İyileşmesi Üzerine Etkisinin Histopatolojik Olarak Araştırılması, Doktora Tezi, G.Ü. Sağlık Bilimleri Enstitüsü, Ağız. Diş, Çene Hastalıkları ve Cerrahisi Anabilim Dalı, 1998.

24. Erbas D, Oygur T, Anıl A. Submandibular bez ekstresinin yara iyileşmesine olan etkisi. G.Ü. Dishek. Fak. Der. 1988;5 (2):139-147.

25. Türken M, Erbaş D, Yılmaz D, SMG Ekstresinin Submandıbuler Bezi ve Kan PG Seviyelerine Etkileri, G.Ü. Tıp. Fak. Dergisi. 1989;5(1) pp 109-115.

26. Özçetin B, Altıntaş M, Sarıkaya S, et al. Çocuk yanıklarında epidermal büyüme faktörlü tedavi deneyimimiz. I. Ulusal Çocuk Yanıkları Kongresi. 2011. Poster sunumu.

27. Jahovic N, Güzel E, Arbak S, et al. Thehealing-promotingeffect of saliva on skin burn is mediatedby epidermal growthfactor (EGF): role of theneutrophils. Burns. 2004; 30: 531-538.

28. Değim Z, Çelebi N, Alemdaroğlu C, et al. Evaluation of chitosan gel containingliposome-loaded epidermal growth factor on burnwound healing. International WoundJ ournal. 2011; 8: 343-354.