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A Comparative Study Between the Therapeutic Role of Bone Marrow-Derived Mesenchymal Stem Cells Versus Platelet Rich Plasma in Skin Burn Healing in Albino Rats

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ABSTRACT

Background and Objective: Mesenchymal stem cells (MSCs) and platelet-rich plasma (PRP) accelerate wound healing. This study aimed to comparing the therapeutic role of BMSCs & PRP in skin burn healing.

Material and Methods: The study included forty albino rats, five rats were used to supply PRP and five rats were considered as a control group. The other thirty rats were exposed to thermal injury to induce 2nd degree skin burn then divided into three groups of ten rats each; the skin burned group including rats that received no further treatment, BMSCs-treated group and PRP-treated group. Each group was subdivided into two equal subgroups and examined on days 7 & 21 after the burn. Skin specimens of all groups were handled, processed to be stained with H&E, Masson's trichrome for histological examination and by VEGF, CD105 for immunohistochemical examination.

Results: Injection the burned skin with BMSCs or PRP caused re-epithelization of the epidermis, reduction of inflammation, increased collagen fibers deposition and acceleration of angiogenesis. Visible epidermis and dermis regeneration were more evident compared to the burned group. However, the improvement of histological findings was remarkable in the BMSCs-treated group than in PRP treated one. Moreover, the main area percentage of collagen fibers deposition and VEGF immunostaining were significantly increased in the BMSCs treated group in comparison to PRP treated group.

Conclusion: BMSCs displayed better healing effect than PRP as evidenced by collagen fibers deposition and angiogenesis and returning the normal histological structure of the skin.

Keywords: Skin burn, MSCs, PRP, VEGF

INTRODUCTION

Burns are serious skin injuries that are classified according to severity into, first degree, which only affects the epidermis, the epidermis and dermis are affected by the 2nd degree. The 3rd degree of burn involves the entire layers of the skin and the muscles beneath it [1,2].

Stem cells have both anti-inflammatory and angiogenic role, that enhances wound repair through cell differentiation [3]. The immune system is stimulated by mesenchymal stem cells MSCs to release cytokines and chemokines. [4] BMSCs enhanced the wound healing and skin regeneration by supplying new cells as fibroblasts and keratinocytes [5].

PRP is a component of the plasma portion of autologous blood having a great level of platelets, clotting & growth factors [6]. The main function of PRP is starting wound healing by releasing locally active growth factors through the process of α-granules degranulation [7].

PRP is a favorable treatment for different types of wounds despite their location or causes, as it is safe and without any side effects [8].

It inhibits the production of cytokines and reduce inflammation by activation of macrophages to enhance tissue repair and regeneration, encourage the creation of new capillaries, and quickening the epithelialization process in chronic wounds [9].

This study aimed to compare the beneficial role of BM-MSCs versus PRP in skin burn management.

MATERIALS AND METHODS

Rats

Forty adult male albino rats were handled in this study, there weight about 180–220 g. Five rats were assigned as donors for supplying PRP. The other rats remained at the animal house of the Benha Faculty of Medicine, Benha University. The animals were lived in a 25℃ temperature & allowed free contact with water and food. The rats acclimatized for ten days before the start of the experiment.

Burn creation

The rats were anesthetized by chloroform; second-degree skin burn was induced by using heated brass probes. Rats' dorsal skin was shaved, and a 2.5 cm wide brass disc was heated at 85 to 90℃ and applied for twenty seconds devoid of any outside pressure on the skin. The rats were resuscitated directly with 2 ml/100 g lactated Ringer's solution injected intraperitoneally, they were given analgesics and dressing of the burned wound every day [10].

BM-MSCs preparation

The bone marrow stem cells were separated from the tibia of a 6-week-old male albino rat. In the stem cell research unit at the Biochemistry department of the faculty of medicine, Cairo University. Dulbecco's Modified Eagle Medium and 10% bovine fetal serum had been used to flush long bones. In conical sterile tubes, the bone marrow was slowly added to Ficoll-Hypaque. Mononuclear cells were aspirated from the

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opaque surface and suspended and cultured in 1% penicillin-streptomycin. Then incubated at 37℃ in 5% humidified CO2 for 14 days. After that the cultures were washed with phosphate-buffered saline PBS and the cells were released with 0.25% trypsin for five minutes at 37℃. Then centrifugation (at 2400 rpm for 20 minutes), all the cells were suspended in serum-supplemented medium. isolated BMSCs were identified by their adhesiveness and fusiform shape [(11)].

PRP preparation

Five rats were anesthetized with chloroform, and blood samples were obtained from the inferior vena cava, then spun into tubes containing 0.3% sodium heparin. Centrifugation was used to separate the plasma (300 g, 10 min). Another centrifugation (300 g, 20 min) was used to concentrate the platelets in the plasma. About 2-3 mL of PRP could be produced from 10 mL of whole blood [(12)].

Experimental groups

- **Group I:** control group of five rats not subjected to thermal burn, they didn't receive any medications and were sacrificed after 21 days.
- **Group** II: Skin burn group including ten rats subjected to thermal burn they were left without medications and then divided into two subgroups each containing five animals
- Subgroup IIa: the rats were sacrificed on the 7th day after skin burn
- Subgroup IIb: the rats were sacrificed 21day post burn
- **Group III**: BMSCs-treated group including ten rats subjected to thermal burn, then given a single intradermal injection of BM-MSCs (2×10^6 in 0.5 ml of PBS) [(10)] at the edge of the burn wound then divided into two subgroups (IIIa & IIIb) each containing five animals and sacrificed as in G II.
- **Group IV**: PRP- treated group including ten rats subjected to thermal burn, then received a single intradermal injection with 1 ml PRP [(13)] at the edge of burn wound then divided into two subgroups (IVa & IVb) each containing five animals and sacrificed as in G II.

Histological Examination

Rats were sacrificed after 7 days and 21 days by inhalation of ether then burned skin specimens were collected. All specimens were directly fixed in neutral- formalin and prepared for Hematoxylin and eosin (H&E) stain to evaluate the histological structure of skin tissue and Masson's trichrome stain for detection the arrangement of collagen fibers in skin sections [(14)].

Immunohistochemical examination

VEGF immunostaining

Skin sections were de-waxed and dipped in a citrate buffer solution (pH 6.8), then treated with H2O2 (0.3%) and protein block. Then incubated with polyclonal rabbit VEGF primary antibody for 20 min. All sections were washed up with PBS and incubated with a goat anti-rabbit secondary antibody for half an hour. The peroxidase substrate 3,3-diaminobenzidine DAB was applied. Finally, the slides were stained with Mayer's hematoxylin as a counterstain [(15)].

CD105 immunostaining

For detection of BMSCs homing in skin tissue in group IV, the anti-CD105 antibody was used (rabbit, polyclonal primary antibody; Sigma Aldrich, USA; SAB1306487) [(16)].

Morphometric study

Main area % of collagen fibers deposition and VEGF immune-positive reaction was evaluated by using the software program image analysis (Image j. 1.46version) for all skin sections at X 400 magnification.

Ethical approval:

All aspects of the study were approved by the Ethical Committee of Faculty of medicine, Benha University number (RC- 15-11-2022).

Statistical study

The data was represented as mean ± SD standard deviation (SD), by using one-way (ANOVA) and post hoc LSD test with SPSS 19.0 software (IBM SPSS Statistics for Windows, Armonk, NY, USA).

RESULTS

Hematoxylin & Eosin stain:

Skin section from the control rats of (G I) presented the skin with epidermal and dermal layers. The epidermis has a keratinized stratified squamous epithelium, the dermal layer formed of the superficial papillary and deep reticular layer that contained hair follicles & sebaceous gland and the subcutaneous tissue the hypodermis (Figure 1a).

Skin section from skin burned subgroup IIa, 7 days after skin burn showed, loss of epidermal layer in burned area that was covered with a scab. Degenerated dermis with marked inflammatory cell infiltration (Figure 1b). However, the skin section from subgroup IIb 21 days after the skin burn showed a complete absence of the scab, and there was a regenerated thin epidermis. The dermal layer appeared regenerated but there were spaces in the reticular layer with the appearance of regenerated hair follicles & sebaceous glands (Figure 1c).

Skin section from stem cell treated group subgroup IIIa, 7 days after skin burn showed re-epithelization with the appearance of thin epidermis under the scab. The dermis is regenerated with less inflammatory cell infiltration and regenerated hair follicle (Figure 2a). On the other hand, skin section from subgroup IIIb 21 days after the skin burn showed a normal epidermis. The dermis appeared normal with

normal hair follicles and sebaceous glands (Figure 2b).

H&E stained section from the PRP treated group subgroup IVa, 7 days after the skin burn showed a scab covering the burned area with re-epithelization of the epidermis and a thin epidermal layer appearing beneath it. The dermis appeared degenerated with some inflammatory cell infiltration (Figure 2c). But the skin section from subgroup IVb 21 days after the skin burn showed, keratinized normal epidermis. The dermis appeared with a normal papillary layer but there were spaces in the reticular layer of the dermis and regenerated hair follicle (Figure 2d).

Masson's trichrome stain

Skin section from the control rats presented the collagen fibers in the papillary layer have fine interlocking fibers and the reticular layer has thick, wavy irregular bundles (Figure 3a). While in the skin burned subgroup IIa, on 7th-day post-burn showed few dispersed collagen fibers with green color in the degenerated dermis were detected (Figure 3b). However, subgroup IIb, 21 days after the skin burn showed irregular few fine fibers in the papillary layer and some thin regularly arranged collagen fibers in the reticular layer there were areas lacking collagen deposition (Figure 3c).

Section from stem cell treated subgroup IIIa, 7 days after skin burn showed collagen fibers in the papillary layer and the reticular layer of the dermis with large areas devoid of collagen fibers (Figure 3d). Moreover, in subgroup IIIb, 21 days after the skin burn, the arrangement of collagen fibers in the papillary layer and reticular layer showed similar pattern to that of the control group (Figure 3e).

M.T stained section from PRP treated subgroup IVa, 7 days after skin burn showed irregularly dispersed deeply stained collagen fibers in the degenerated dermis (Figure 3f). But from subgroup IVb, 21 days after skin burn showed an increase in the fine fibers in the papillary layer and the reticular layer showed thin wavy irregular collagen fibers with some empty spaces (Figure 3g).

VEGF Immunohistochemical stain

The control group showed VEGF positive reaction in the superficial layer of keratinocytes of the epidermis, hair follicle and the cytoplasm of dermal fibroblasts (Figure 4a). Skin-burned subgroup IIa showed few VEGF-positive reactions in the wall of blood vessels and the cytoplasm of dermal fibroblasts of the granulation tissue (Figure 4b). While, subgroup IIb showed an increase in VEGF positive reaction in the endothelium of blood vessels, hair follicles and the cytoplasm of dermal fibroblasts (Figure 4c).

The BMSCs-treated subgroup IIIa showed numerous VEGF-positive reactions in the cytoplasm of dermal fibroblasts and hair follicles (Figure 4d). But, Subgroup IIIb showed few VEGF-positive reactions in keratinocytes of the epidermis, hair follicle and the cytoplasm of dermal fibroblasts (Figure 4e).

PRP-treated subgroup IVa showed increased VEGF-positive reaction in the endothelium of blood vessels, the cytoplasm of dermal fibroblasts and hair follicles (Figure 4f), however, subgroup IVb showed few VEGF positive reactions in keratinocytes of the epidermis, hair follicle and the cytoplasm of dermal fibroblasts (Figure 4g).

CD 105 immunostaining

Control rats presented weak positive immunoreaction for CD105 immunostaining in the cytoplasm of hair follicles & sebaceous gland (Figure 5a). BMSCs treated group showed strong positive immunoreactions for CD105 immunostaining in several sites of the epidermis & the dermis in the hair follicles, sebaceous gland & blood vessels (Figure 5b).

Morphometric analysis

On the day 7 after induction of skin burn the statistical analysis revealed a significant elevation P value ≤ 0.05 in the mean area % of collagen fibers deposition in subgroups IIIa and IVa in comparison with subgroup IIa. In addition, there was a significant elevation P value ≤ 0.05 in subgroup IIIa in comparison with subgroup IVa. Furthermore, the mean area percent of collagen fibers on day 21 after the burn induction stated a significant elevation P value ≤ 0.05 in subgroup IIIb and subgroup IVb when compared with subgroups IIb, although there was a significant elevation P value ≤ 0.05 in subgroup IIIb in comparison with subgroup IVb **(table 1& Fig 3 h)**.

On the day 7 after induction of the burn there was a significant elevation P value ≤ 0.05 in the mean area % of VEGF immune positive reaction in subgroups IIIa and IVa in comparison with that in subgroup IIa, adding a significant elevation in subgroup IIIa in comparison with subgroup IVa. On the day 21after induction of burn the statistical analysis represented a significant reduction P value ≤ 0.05 in the mean area % of VEGF immune positive cells in subgroups IIIb and IVb in comparison with subgroup IIb. Moreover, there was a significant decrease in subgroup IIIb in comparison with that in subgroup IVb **(table 2 & Fig 4 h)**

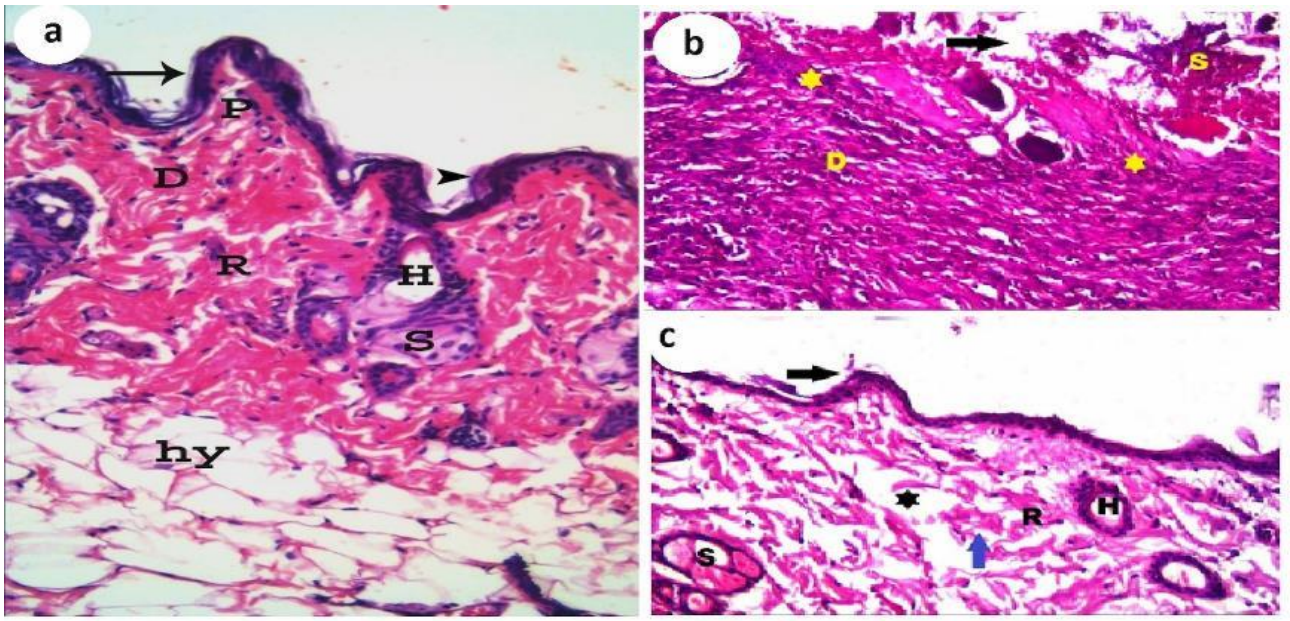

Fig (1): Photomicrographs of skin sections **(a)** from the control group presenting epidermal layer of keratinized stratified squamous epithelium (arrow), keratin (arrow head). The dermal layer (D) consisted of superficial papillary layer (P) & deep reticular layer (R) that contained hair follicles (H) & sebaceous gland (S) and the subcutaneous tissue the hypodermis (hy). **(b)** from subgroup IIa, at the 7th days post burn presenting loss of epidermal layer (arrow), the burn area covered with a scab (S) and granulation tissue in the dermis (D) with marked inflammatory cell infeltration (star). **(c)** from subgroup IIb, 21 days after skin burn showing complete absence of the scab, appereance of regenerated thin epidermis (arrow), regenerated dermal layer (blue arrow) but there are spaces in the reticular layer of dermis (star) in the reticular layer (R) with appearance of regenerated hair follicles (H) and sebecous gland (S) **(H&E, X :200).**

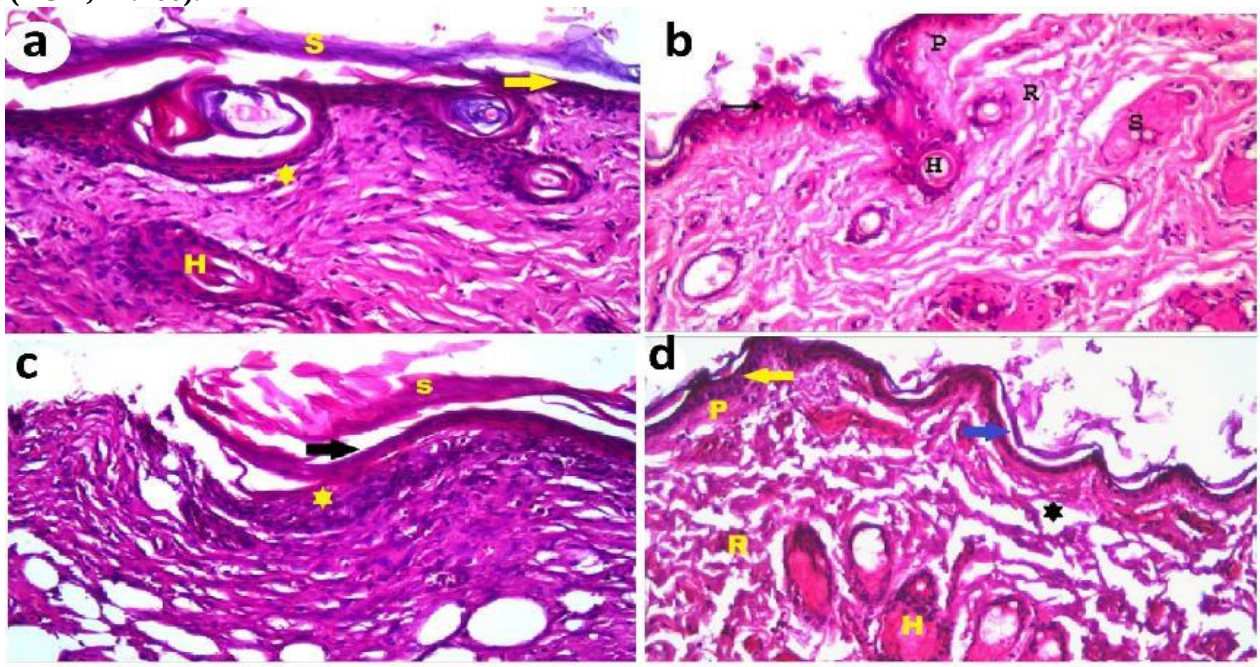

Fig (2): Photomicrographs of skin sections**(a)** from subgroup IIIa, 7 days after skin burn showing re-epithelization with appearance of thin epidermis (yellow arrow) under the scab (S) and the granulation tissue in dermis with less inflammatory cell infiltration (star) and regenerated hair follicle (H). **(b)** from subgroup IIIb, 21 days after skin burn showing normal keratinized epidermis (arrow), the dermis appeard with normal papillary layer (P) & reticular layer (R) with hair follicle (H) & sebasous gland (S). **(c)** from subgroup IVa 7 days after skin burn showing a scab (S) covering the burn area with re-epithelization of epidermis and a thin epidermal layer appear beneath it (black arrow), the granulation tissue in dermis appear with some inflammatory cell infiltration (star). **(d)** from subgroup IVb, 21 days after skin burn showing keratinized (blue arrow) normal epidermis (yellow arrow), the dermis appeared with normal papillary layer (P) but there are spaces (star) in the reticular layer of dermis (R) and regenerated hair follicle (H). **(H&E, X:200)**

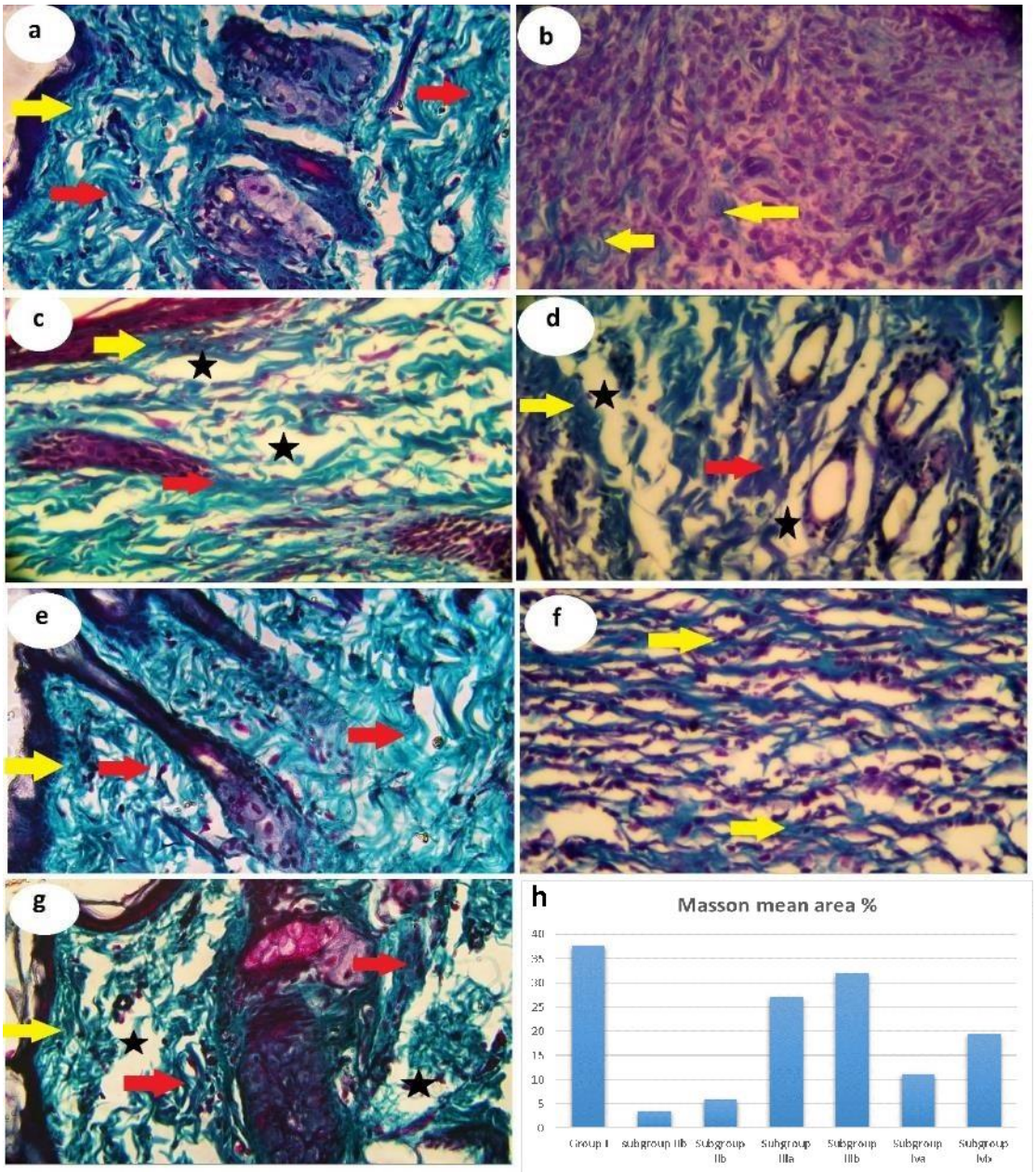

Fig (3): Photomicrographs of a skin sections with Masson trichrome stain **(a)** the control group presenting the collagen fibers in the papillary layer has fine interlocking fibers (yellow arrow) and the reticular layer has thick, wavy irregular bundles (red arrow) **(b)** from subgroup IIa at the 7th day post burn presenting few dispersed collagen fibers in the granulation tissue of dermis (yellow arrow). **(c)** from subgroup IIb, after 21 days' post burn presenting the papillary layer with few irregular fine collagen fibers (yellow arrow) and some thin irregularly arranged collagen fibers in the reticular layer (red arrow), there are area lacking of collagen deposition (star). **(d)** from subgroup IIIa, 7 days after skin burn showing collagen fibers in the papillary layer (yellow arrow) and in the reticular layer of dermis (red arrow) with large areas devoid of collagen fibers (star). **(e)** from subgroup IIIb, 21 days after skin burn showing the arrangement of collagen fibers in the papillary layer (yellow arrow) & the reticular layer (red arrow) similar to the control group**(f)** from subgroup IVa, 7 days after skin burn showing irregularly dispersed deeply stained collagen fibers in the granulation tissue of dermis (yellow arrow). **(g)** from subgroup IVb, after 21 days' post burn presenting the papillary layer with increase in the fine collagen fibers (yellow arrow) & the reticular layer with thick wavy irregular fibers (red arrow) with some empty spaces (star). **(MT, X:400), (h)** A graph illustrating the average main area % of collagen fibers deposition for all groups

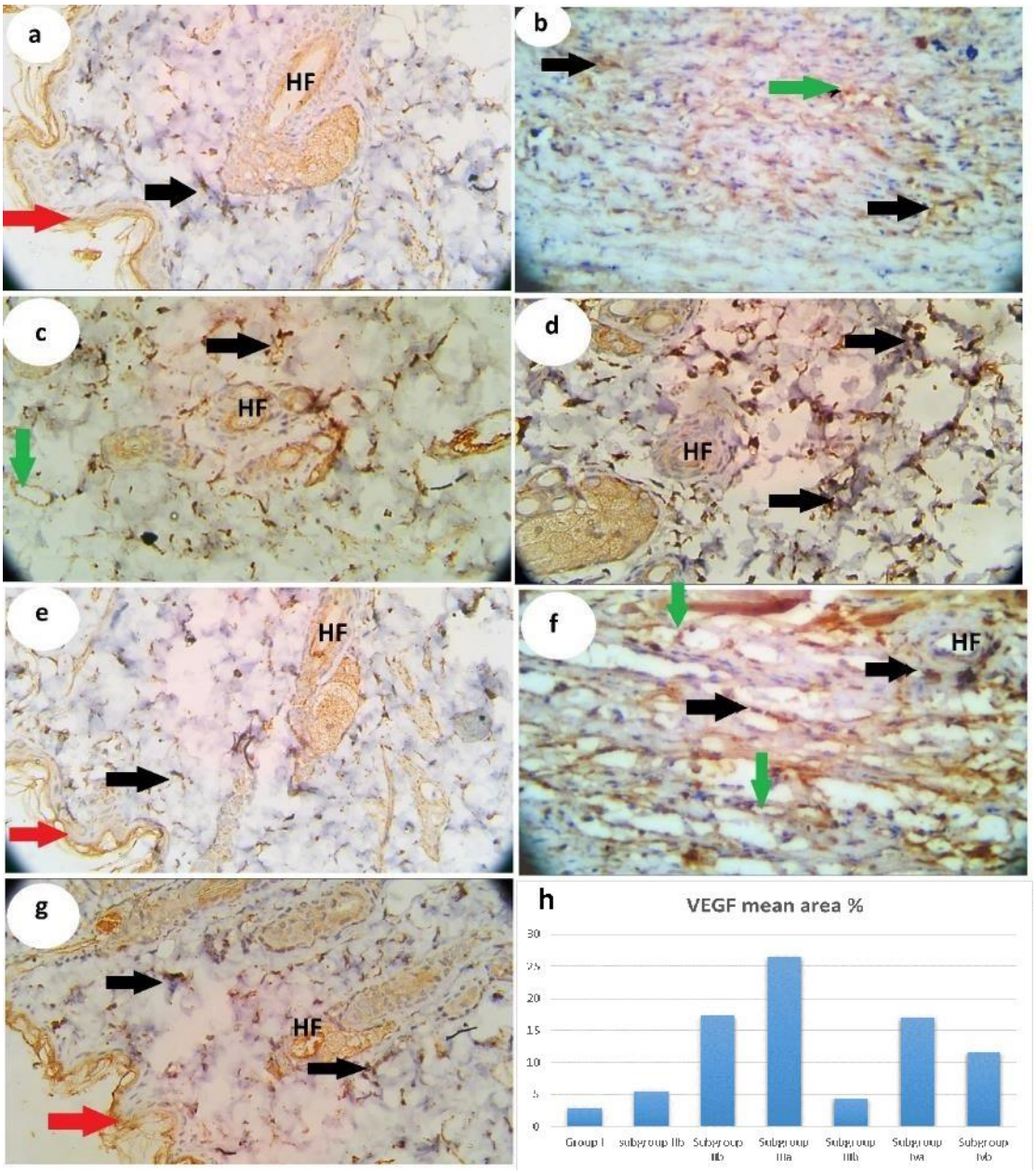

Fig (4) Photomicrographs of skin sections with VEGF immunostaining **(a)** the control group presenting VEGF positive reaction in the superficial layers of keratinocytes of epidermis (red arrow), hair follicle (HF) and the cytoplasm of fibroblasts (black arrow) **(b)** from subgroup IIa, 7 days after skin burn showing few VEGF positive reaction in the wall of blood vessels (green arrow) and the cytoplasm of fibroblasts (black arrow) of the granulation tissue **(c)** from subgroup IIb, 21 days after skin burn showing increase VEGF positive reaction in the endothelium of blood vessel (green arrow) , hair follicle (HF) and the cytoplasm of fibroblasts (black arrow) **(d)** from subgroup IIIa 7 days after skin burn showing numerous VEGF positive reaction in the cytoplasm of fibroblasts (black arrow) and hair follicle (HF) **(e)** from subgroup IIIb 21 days after skin burn showing few VEGF positive reaction in keratinocytes of epidermis (red arrow), hair follicle (HF) and the cytoplasm of fibroblasts (black arrow) **(f)** from subgroup IVa 7 days after skin burn showing increase VEGF positive reaction in the endothelium of blood vessel (green arrow), the cytoplasm of fibroblasts (black arrow) and hair follicle (HF) **(g)** from subgroup IVb 21 days after skin burn showing few VEGF positive reaction in keratinocytes of epidermis (red arrow), hair follicle (HF) and the cytoplasm of fibroblasts (black arrow) **(VEGF immunostaining, X :400) (h)** A graph illustrating the average mean area % of VEGF immunoreactivity for all groups

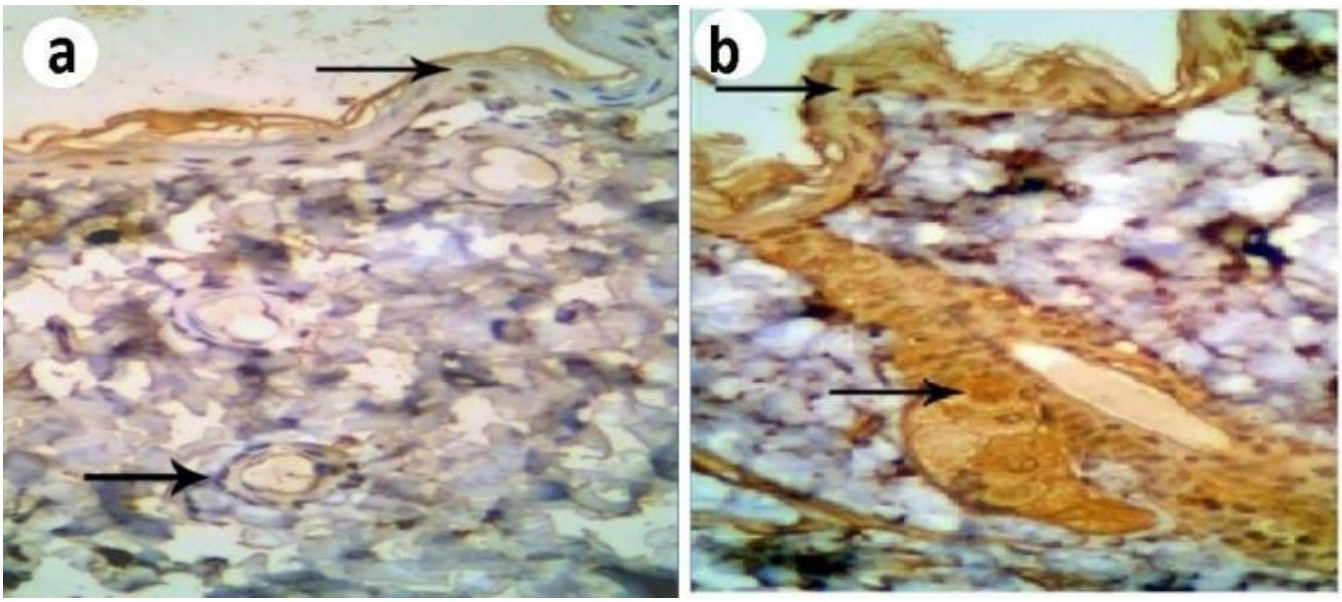

Fig (5) photomicrographs of skin sections with CD 105 immunostaining **(a)** the control group presenting negative CD 105 immunoreaction for stem cell (arrow). **(b)** BMSC treated group 21 days' post burn subgroup IVb showing positive CD 105 immunoreaction for stem cell (arrows) **(CD 105 immunostaining, X :400)**

Table (1): illustrating the averages mean area percentage of collagen fibers deposited ± SD for all groups

Mean area % ± SD	**Group I**	**subgroup IIa**	**subgroup IIb**	**subgroup IIIa**	**subgroup IIIb**	**subgroup IVa**	**subgroup IVb**
Masson%	37.72 ±9.3	3.44±1.2	5.8 ±2.7	26.97 ± 5.4	31.84 ± 9.4	11.1 ± 1.9	19.29 ± 2.9
Significance P ≤ 0.05	With sub-groups IIa, IIb& IVa.	With subgroups I , IIIa &IVa	With subgroups I IIIb & IVb	With sub-groups IIa & IVa	With sub-groups IIb & IVb	With subgroup IIa.	With sub-group IIb

Table (2): illustrating the averages mean area percentage of VEGF immunoreactivity ± SD for all groups

Mean area % ± SD	**Group I**	**subgroup IIa**	**subgroup IIb**	**subgroup IIIa**	**subgroup IIIb**	**subgroup IVa**	**subgroup IVb**
VEGF %	2.9 ±1.8	5.45±0.59	17.3 ±0.95	26.4 ± 1.2	4.4 ± 0.86	16.99 ± 1.8	11.6 ± 1.2
Significance P ≤ 0.05	With subgroups IIb, IIIa, IIIb &IVa.	With sub-groups IIIa &IVa	With subgroups I ,IIIb& IVb	With subgroups I, IIa & IVa	With sub-groups IIb& IVb	With subgroup IIa	With subgroups I & IIIb

DISCUSSION

Skin burn is a severe public health problem worldwide. Burns cause disability and psychological difficulties [17].

This study was planned to compare between the role of BMSCs and PRP in the management of skin burn.

In this study the histological findings in skin burn sections 7 days after the burn showed loss of epidermal layer, the burned skin area was covered by a scab, the dermis was degenerated with inflammatory cell infiltration and damaged hair follicle, with few scattered collagen fibers. This was in accordance with [13] who stated that, the burned area showed granulation tissue that have newly formed blood vessels, extravagated blood with lymphocytes and macrophage infiltration. Furthermore, other authors noticed fluid escaped from the blood vessels producing edema in between the collagen fibers [18].

Moreover, after 21 days post-burn, the skin area showed partial improvement with appearance of a thin epidermis on the surface of the burned area and the dermal layer has fine irregular collagen fibers. In the same way, another team found that the scab appeared on the 7th day after induction of the burn until the 14th day then the scab was separated on the 21st day leaving soft granulation tissue [19]. Another study added that on the 21st day post-burn the new epidermis formed by the stratum basal from the closely normal no damaged epidermis [20].

In this study intra-dermal injection of BMSCs at the edge of the burn wound induced partial improvement in skin sections in subgroup IIIa on the 7th day after burn induction in comparison with that in skin burn subgroup IIa, the skin section on the 7th day after skin burn showed re-epithelization with the appearance of thin epidermis under the scab. The dermis is regenerated with less inflammatory cell infiltration and degenerated hair follicles. Statistically significant elevation in the mean area percent of collagen fibers distribution in BMSC treated subgroup IIIa in compared with skin burn subgroup IIa and PRP treated subgroup IVa. This finding indicates that intradermal injection of BMSCs was better than PRP in the management of skin burn. In the same line, another study reported that administration of BMSC to skin lead to dermal fibroblast and vessel proliferation with collagen deposition and wound repair [21]. Another study added that BM-MSCs were able to increase the synthesis of extracellular matrix through cell proliferation and differentiation [22]. MSCs produce different growth factors that have an essential role in epithelialization, cellular migration [23].

The skin sections on the 21st day post-burn after BM-MSCs injection showed, complete recovery and return of normal histological structures of skin burned area. statistically significant elevation in the mean area percent of collagen fibers distribution in stem cell treated subgroup IIIb in compared with skin burn subgroup IIb and PRP subgroup IVb. BMSCs injection intra-dermal and intra-peritoneal were efficient in the enhancement of 2nd-degree skin burn healing [10].

The healing mechanism of BMSCs was recognized by decreasing the proinflammatory cytokines and elevating the anti-inflammatory cytokines [21] MSCs have good antimicrobial properties by secretion of antimicrobial and immune modulate factors that control phagocytosis through immune cells [24].

In the current study intra-dermal injection of PRP at the edge of the burned wound induced partial improvement in skin sections in subgroup IVa on the 7th day after burn in comparison with subgroup IIa. The skin sections on the 7th day after the skin burn showed a scab covering the burned area with re-epithelization of the epidermis and a thin epidermal layer appear beneath it, the dermis appeared degenerated with some infiltration of inflammatory cells. There was a statistically significant increase in mean area % of collagen fibers distribution in PRP-treated subgroup IVa in comparison with subgroup IIa. PRP enhanced cellular proliferation and differentiation as it had a beneficial effect in releasing different growth factors [25]. Also, PRP has an advantageous role in angiogenesis and epithelialization of skin graft sites [26].

While the skin sections on the 21st day post-burn after PRP injection showed, a normal epidermis, the dermis appeared with thick collagen fibers in the reticular layer that contained hair follicles and sebaceous glands. There was a statistical significant increase in the main area percent of collagen fibers distribution in PRP treated subgroup IVb in compared with skin burn subgroup IIb. On the same line, PRP elevated the matrix metalloproteinase proteins and enhanced production of type I collagen fibers [27].

In this study on the 7th day post-burn, there was a significant elevation in the mean area percent of VEGF immune positive cells in subgroups IIIa and IVa in comparison with subgroup IIa, also there was statistically significant elevation in subgroup IIIa in comparison with subgroup IVa. This result revealed that the highest level of VEGF immunoreactivity was in stem cell-treated subgroup IIIa than PRP-treated subgroup IVa and the lowest level was in skin burn subgroup IIa. Therefore, both BM-MSCs and PRP accelerated the angiogenesis and neovascularization in the skin burned area. However, BMSCs released the VEGF earlier and at a higher level than PRP.

BM-MSCs enhanced epidermal formation and improved vascularization through increasing vascular endothelial growth factor VEGF that was the main angiogenic factor for enhancement and regulation of microvasculature, growing vascular endothelial cells. Consequently, this factor was necessary for wound healing [28].

On the 21st day after induction of the burn there was a significant reduction in the mean area % of VEGF immune positive cells in subgroups IIIb and IVb in comparison with subgroup IIb, but there was a significant decrease in subgroup IIIb in comparison with subgroup IVb. Decreasing the level of VEGF in stem cell treated subgroup IIIb indicates complete healing of skin burned area more rapidly than PRP treated subgroup IVb. In the same line [29] reported that treatment of burned skin with hematopoietic stem cell led to significant elevation in angiogenic VEGF markers, especially after 19 days. The angiogenic reaction of stem cells and PRP was important for wound healing as it is essential for increasing the oxygen and nutrient provided to keratinocytes [30].

CONCLUSION

The study concluded that both BMSCs and PRP were effective in skin burn healing but BMSCs has a dominant therapeutic effect than PRP in the treatment of skin burn wounds.

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