Tropical Journal of Pharmaceutical Research July 2023; 22 (7): 1451-1456
ISSN: 1596-5996 (print); 1596-9827 (electronic)

Available online at http://www.tjpr.org
http://dx.doi.org/10.4314/tjpr.v22i7.13

Original Research Article

Clinical effect of platelet-rich fibrin in combination with narrow-band ultraviolet B treatment in patients with small area deep burn wounds

Jianhua Yang[1], Xue Li[2], Hao Liu[3], Xiaodan Zhao[1]*
[1]Imaging Center, Shandong Provincial Third Hospital, Shandong University, [2]Department of Cosmetic Surgery, Jinan Airong Plastic and Cosmetic Hospital, [3]Department of Burn Reconstructive Surgery, The 960th Hospital of the PLA, Jinan, 250000 Shandong, China

For correspondence: **Email: feixie11118383927@163.com*

Sent for review: 1 December 2022 *Revised accepted: 26 June 2023*

Abstract

Purpose: *To investigate the influence of the combined use of platelet-rich fibrin and narrow-band UV B (NB-UVB) treatment on small-area deep burn wounds in patients.*
Methods: *A total of 86 patients with small area deep burn wounds were assigned to control and study groups (n = 43/group). The control patients received routine drugs in combination with NB-UVB, while the study group was administered a combination of platelet-rich fibrin and NB-UVB therapy. Clinical efficacy indices were.*
Results: *In the study group, the pre and post-treatment serum levels of TNF-α were 222.75 ± 4.86 and 65.42 ± 5.33 ng/L, while those in control group were 221.45 ± 6.84 and 114.68 ± 2.53 ng/L, respectively. The study group serum concentrations of IL-8 at pre- and post-treatment were 120.75 ± 4.53 ng/L and 45.39 ± 8.26 ng/L, while the control group values were 122.38 ± 2.65 and 79.52 ± 2.34 ng/L, respectively. After treatment, the serum levels of TNF-α and IL-8 were significantly down-regulated in both groups, relative to pre-treatment values, with lower levels in the study group ($p < 0.001$). Wound healing time and frequency of dressing change in the study group were 20.6 ± 3.6 days and 7.1 ± 2.5 times, respectively, which were significantly lower than the corresponding control group values of 40.3 ± 10.7 days and 20.5 ± 5.6 times ($p < 0.001$). There was a significantly higher incidence of scars in the control group than in study group ($p < 0.05$).*
Conclusion: *Combined use of platelet-rich fibrin and NB-UVB in the treatment of small area deep burn wounds lowers the serum levels of inflammatory factors. However, the combined therapy should be subjected to further clinical trials prior to application in clinical practice.*

Keywords: *Small-area deep burn wounds, Platelet-rich fibrin, Narrow-band ultraviolet B (NB-UVB)*

Tropical Journal of Pharmaceutical Research is indexed by Science Citation Index (SciSearch), Scopus, Web of Science, Chemical Abstracts, Embase, Index Copernicus, EBSCO, African Index Medicus, JournalSeek, Journal Citation Reports/Science Edition, Directory of Open Access Journals (DOAJ), African Journal Online, Bioline International, Open-J-Gate and Pharmacy Abstracts

INTRODUCTION

In clinical research, deep burns which comprise deep 2nd-degree and 3rd-degree burns, refer to necrosis range reaching the deep dermis or deeper tissue. Generally, deep second-degree burn heals through changing of dressing, and it leaves obvious scars and pigmentation at later

stages, whereas patients with severe conditions suffer from dysfunctions. However, patients with deep second-degree burn in some special areas are treated with surgical methods. Patients with third-degree burns have difficulties in healing through change of dressing. Thus, surgery is needed for these patients to recover from the wounds, usually in the late stage [1-3]. Deep burns bring painful physical trauma to patients, and damaged full-thickness skin leads to a long healing time, and in severe cases, it is difficult for the wound to heal. The quality of wound healing has crucial impact on patients. Therefore, the choice of therapy is very important to patients.

Platelet-rich fibrin is a platelet preparation that contains a large number of growth factors with the potential of promoting wound healing, and its unique trimolecular stereo-reticular structure provides a framework for the rapid growth of granulation tissues [4-7]. Narrow-band ultraviolet B (NB-UVB), a phototherapy method that employs ultraviolet radiation at a wavelength of 311-312 nm, is an important treatment for dermatoses [9-11]. Not much is known about the use of platelet-rich fibrin in combination with NB-UVB for treating deep burns. In this study, a total of 86 patients with small-area deep burn wounds admitted to Shandong Provincial Third Hospital were selected for an in-depth investigation on the clinical effect of the use of platelet-rich fibrin in combination with NB-UVB in treating small-area deep burn wounds.

METHODS

General patient information

A total of 86 patients with small-area deep burn wounds admitted to Shandong Provincial Third Hospital, Shandong, China from June 2017 to December 2018 were assigned to control and study groups, each with 43 patients. The male: female ratio in control group was 25:18, among whom 19 patients had hand burns, 18 patients had foot burns, 4 had lower limb burns and 2 had upper limb burns. The study group had 27 males and 16 females, 18 patients had hand burns, 17 had foot burns, 6 had lower limb burns and 2 had upper limb burns. Table 1 shows that baseline data were comparable in both groups.

Criteria for inclusion

The included patients were those who satisfied the clinical diagnostic conditions for deep burns; those with burn surface area of 3-30 cm^2, and those with complete clinical medical records.

Exclusion criteria

Patients with peripheral vascular diseases; those receiving cytostatics or immunosuppressants; those with mental and other cognitive disorders, and patients who refused to cooperate with the researchers, were not included.

Ethical approval

This research was approved by the ethics committee of Shandong Provincial Third Hospital (approval no. 20220568587), and met the criteria in the Declaration of Helsinki [12]. All subjects were briefed in detail on the study protocol, purpose, processes, and significance, and signed consent forms for treatment of patients in the study.

Treatments

Firstly, patients admitted to Shandong Provincial Third Hospital underwent routine treatments such as anti-infective therapy, nutrition adjustment, etc. The necrotic tissues of skin surface were removed using a scalpel or ultrasonic debridement machine after disinfecting the wound surface, based on patient's specific conditions. Then, the wounds were rinsed repeatedly with hydrogen peroxide solution, povidone-iodine solution as well as normal saline, and electrocoagulation was performed to stop bleeding thoroughly.

Table 1: Baseline information on both groups

Group	Control group	Study group	t/χ^2	*P*-value
Gender			0.1946	0.659
Male	25 (58.14)	27 (62.79)		
Female	18 (41.86)	16 (37.21)		
Age (years)	(18.37±10.28)	(20.19±11.20)	0.7850	0.4346
Burn surface area (cm^2)	(25.57±2.76)	(24.87±3.33)	0.0613	0.2916
Bacterial culture			0.0630	0.802
Positive	10 (23.26)	11 (25.58)		
Negative	33 (76.74)	32 (74.42)		

After debridement, 5 mL of vacuum blood collection tube without anticoagulant was used to collect venous blood from median cubital vein, and 40 - 80 mL of venous blood was collected on the basis of the required amount for centrifugation at 3000 rpm for 10 - 12 min. After centrifugation, the blood was divided into 3 layers: the top layer of pale-yellow platelet-poor plasma clarifying liquor, the bottom layer of dark red cell fragments, and the middle layer of pale-yellow platelet-rich fibrin [13]. A Cellogel strip was taken out with a sterile syringe needle, thus remaining tail section alternating with erythrocyte. If columnar platelet-rich fibrin could not be placed on patient's trauma, sterile gauze in flake shape obtained by squeezing was used to cover the wounds. In young patients or those with poor physical conditions, venous blood consistent with cross-matching from healthy immediate family members was collected.

All patients were irradiated using a topical NB-UVB treatment equipment at 1-day intervals, with first irradiation dose of 0.4 - 0.6 J/cm^2. During the treatment, the patients were required to wear special goggles to protect their eyes, and the medical staff observed whether erythema, edema, or other unwanted events occurred. Irradiation dose was increased by 10 % of the original dose, based on patients' conditions. Additional dose was not used if a patient had erythema. If erythema appeared, the irradiation was stopped. However, once erythema was reduced, the irradiation started from 50 % of the original dose, and the dose was increased gradually.

Parameters evaluated

Pre- and post-treatment fasting venous flood (3 mL) was collected from each patient for the determination of serum indicators. The blood was spun using a centrifuge (manufacturer: Jinan Bokun Science and Technology Co., Ltd.; model: TD-4X) at 3000 rpm for 10 min, and the supernatant obtained was kept in a refrigerator at -80 ℃. Serum levels of TNF-α and IL-8 were assayed with ELISA kits from Shanghai Enzyme-linked Biotechnology Co., Ltd. and Wuhan Fine Biotech Co., Ltd., respectively, with operations in line with the kit instructions. The wound healing time, the frequency of dressing changes, and the hyperplasia of scars were recorded and compared statistically between both groups.

Statistical analysis

Results were processed with SPSS version 20.0 software, while GraphPad Prism 7 was applied for graphics. Counted data were analyzed with χ^2 test and normality test, while measured data were analyzed with *t*-test. Values of $p < 0.05$ indicated statistically significant differences.

RESULTS

Serum levels of TNF-α and IL-8

Pre- and post-treatment serum concentrations of TNF-α were 222.75 ± 4.86 and 65.42 ± 5.33 ng/L, respectively, in study group, while the control group values were 221.45 ± 6.84 ng/L and 114.68 ± 2.53 ng/L, respectively. The post-treatment serum TNF-α concentrations were significantly reduced, relative to pre-treatment concentrations, but serum TNF-α after treatment was significantly lower in study group (Figure 1).

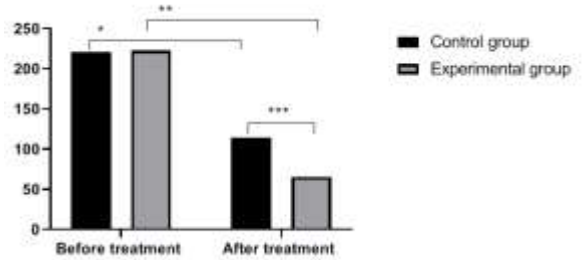

Figure 1: Comparison of the pre- and post-treatment serum TNF-α levels between both groups (n = 43). *$P < 0.001$, *$p < 0.001$, ***$p < 0.001$

Before and after treatment, the serum IL-8 levels of the study group were 120.75 ± 4.53 and 45.39 ± 8.26 ng/L, respectively, while those in the control group were 122.38 ± 2.65 and 79.52 ± 2.34 ng/L, respectively. After treatment, serum IL-8 levels in both groups were significantly reduced, but serum IL-8 level was lower in the study group (Figure 2).

Wound healing time and frequency of dressing changes

The wound healing time and frequency of dressing changes were significantly lower in study group ($p < 0.001$; Table 1).

Table 1: Comparison of wound healing time and frequency of dressing changes between the two groups (n = 43)

Group	Wound healing time (days)	Frequency of dressing change (times)
Study group	20.6±3.6	7.1±2.5
Control group	40.3±10.7	20.5±5.6
t	11.443	14.3281
P-value	<0.001	<0.001

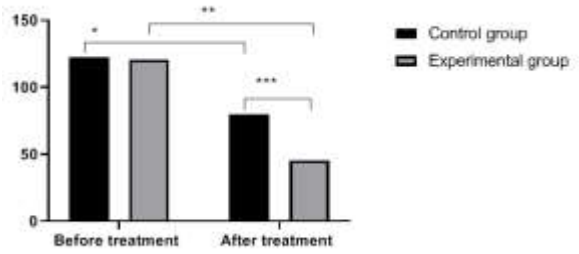

Figure 2: Pre- and post-treatment levels of IL-8 (n = 43). *, ***$P < 0.001$

Incidence of hyperplasia of scars after treatment

The incidence of the hyperplasia of scars was higher in control group than in study group, and there was statistically significant difference between both groups ($p < 0.05$; Table 2).

Table 2: Frequencies of hyperplasia of scars after treatment (n = 43)

Group	Occurrence of hyperplasia of scars	Non-occurrence
Control	37 (86.05)	6 (13.95)
Study	5 (11.63)	38 (88.37)
χ^2	47.6537	
P-value	0.000	

DISCUSSION

Platelet-rich fibrin, an autologous platelet concentrate, is rich in cytokines and growth factors. It effectively promotes the healing of multiple pathological wounds and has significant efficacy in clinics. Thus, it takes advantage of regulatory effect of cytokines, immunomodulatory effects of leukocytes, and support effect of fibrin, thereby achieving wound healing [15-18]. Growth factors contained in platelet-rich fibrin regulate the expressions of proteins and promote the proliferation of fibrocytes, thereby healing wounds and repairing damaged tissues.

Furthermore, platelet-rich fibrin gel's organizational structure is similar to human natural tissues. Characterized by a large gap and good elasticity, it plays the role of cell scaffold in cytothesis and provides a good transport pathway of oxygen and nutrients for cell proliferation. At the same time, platelet-rich fibrin entraps a large number of leukocytes that were activated during centrifugation; it constantly releases immunoregulation-related cytokines during the degradation of platelet-rich fibrin and plays a good anti-infective role in the wounds [19-22]. The present study has demonstrated significantly lower serum concentrations of inflammatory factors in the two groups after treatment than in pre-treatment, with significantly lower levels in study group. This suggests that activated leukocytes in platelet-rich fibrin exerted a better anti-infective effect and greatly reduced the levels of inflammatory factors in the wounds.

The results of the present study also revealed that the study group had significantly shorter wound healing time, lower frequency of dressing changes, and higher incidence of scars than the control group, with statistically significant differences. The reason for these differences may be that a variety of growth factors in platelet-rich fibrin regulate the expression of proteins and proliferation of fibrocytes, and promote wound healing and tissue repair.

NB-UVB irradiation produces immunosuppressive effects and has good efficacy, high safety, and light toxicity, without an increase in the incidence of skin cancer after irradiation. It induces apoptosis of T lymphocytes and keratinocytes, thereby producing mediators with anti-inflammatory or immunomodulatory effects in the irradiated site, down-regulating cytokines such as IL-2, IL-8, and IL-10; reducing inflammatory response, and alleviating the clinical symptoms in burn patients. It was also found that its combination with NB-UVB produced a better therapeutic effect. Yoshimura *et al* [23] reported that the platelet-rich fibrin prepared from autologous blood had high safety and unique therapeutic advantages for small-area deep burns. Compared with conventional drugs, it significantly reduced the number of dressing changes, accelerated wound healing, reduced pain during dressing changes, and improved the long-term healing quality of skin, with high clinical application value. This report further indicates that platelet-rich fibrin in combination with NB-UVB has a high clinical value in the treatment of small-area deep burns.

Limitations of this study

Limited by research conditions, this single-center study used a small sample size. At the same time, no long-term follow-up observation was performed on patients. Therefore, in the follow-up study, the sample size will be increased in multi-center research, and the clinical follow-up time will be extended to provide more evidence-based data for the treatment of patients with small-area deep burns.

CONCLUSION

The combination of platelet-rich fibrin and NB-UVB irradiation in the treatment of small-area

deep burn wounds decreases the serum levels of inflammatory factors, reduces serum levels of TNF-α and IL-8, decreases the frequency of dressing change and incidence of scars in patients. It also promotes rapid healing of deep burn wounds. Therefore, the combined therapy has a potential for use in clinical practice but validation of the findings of this study in further clinical trials is necessary.

DECLARATIONS

Acknowledgements

None provided.

Funding

None provided.

Ethical approval

This work was approved by the Ethics Committee of Shandong Provincial Third Hospital, Shandong (approval no. 20220568587).

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

We declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. Jianhua Yang and Xiaodan Zhao designed the study and drafted the manuscript. Xue Li, Hao Liu, and Xiaodan Zhao were responsible for the collection and analysis of the study data. Jianhua Yang and Xiaodan Zhao revised the manuscript critically for important intellectual content. All authors read and approved the final manuscript.

REFERENCES

1. *Yanaga H, Udoh Y, Yamauchi T, Yamamoto M, Kiyokawa K, Inoue Y, Tai Y. Cryopreserved cultured epidermal allografts achieved early closure of wounds and reduced scar formation in deep partial-thickness burn wounds (DDB) and split-thickness skin donor sites of pediatric patients. Burns 2001; 27: 689-698.*
2. *Josty IC, Narayanan V, Dickson WA. Burns in patients with epilepsy: changes in epidemiology and implications for burn treatment and prevention. Epilepsia 2000; 41: 453-456.*
3. *Pournajaf A, Rajabnia R, Razavi S, Solgi S, Ardebili A, Yaghoubi S, Khodabandeh M, Yahyapour Y, Emadi B, Irajian G. Molecular characterization of carbapenem-resistant Acinetobacter baumannii isolated from pediatric burns patients in an Iranian hospital. Trop J Pharm Res 2018; 17: 135-141.*
4. *Aravindaksha SP, Batra P, Sood V, Kumar A, Gupta G. Use of platelet-rich fibrin membrane as a palatal bandage. Clin Adv Periodontics 2014; 4: 246-250.*
5. *Eren G, Tervahartiala T, Sorsa T, Atilla G. Cytokine (interleukin-1beta) and MMP levels in gingival crevicular fluid after use of platelet-rich fibrin or connective tissue graft in the treatment of localized gingival recessions. J Periodontal Res 2016; 51: 481-488.*
6. *Padilha WSM, Soares AB, Navarro-Junior H, Joly JC, Peruzzo DC, Napimoga MH, Martinez EF. Histologic evaluation of leucocyte- and platelet-rich fibrin in the inflammatory process and repair of noncritical bone defects in the calvaria of rats. Int J Oral Maxillofac Implants 2018; 33: 1206-1212.*
7. *Dohan Ehrenfest DM, de Peppo GM, Doglioli P, Sammartino G. Slow release of growth factors and thrombospondin-1 in Choukroun's platelet-rich fibrin (PRF): a gold standard to achieve for all surgical platelet concentrates technologies. Growth Factors 2009; 27: 63-69.*
8. *Bielecki T, Dohan Ehrenfest DM. Platelet-Rich plasma (PRP) and platelet-rich Fibrin (PRF): Surgical adjuvants, preparations for in situ regenerative medicine and tools for tissue engineering. Curr Pharm Biotechnol 2012; 13: 1121-1130.*
9. *Kubanov AA, Chikin VV, Karamova AE, Monchakovskaya ES. Uzkopolosnaya srednevolnovaya ul'trafioletovaya terapiya bol'nykh atopicheskim dermatitom: effektivnost' i bezopasnost' [Narrow-band medium-wave ultraviolet therapy in patients with atopic dermatitis: efficacy and safety]. Vopr Kurortol Fizioter Lech Fiz Kult 2022; 99: 79-88.*
10. *Zumstein MA, Berger S, Schober M, Boileau P, Nyffeler RW, Horn M, Dahinden CA. Leukocyte- and platelet-rich fibrin (L-PRF) for long-term delivery of growth factor in*

rotator cuff repair: review, preliminary results and future directions. Curr Pharm Biotechnol 2012; 13: 1196-1206.

11. *Yu Q, Shen Y, Gan Y, Zheng L. Protective effect of total flavonoids from boxthorn leaf against UVB irradiation-induced skin injury. Trop J Pharm Res 2019; 18: 1943-1947.*
12. *World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. JAMA 2013; 310(20): 2191-2194.*
13. *Chadwick JK, Mills MP, Mealey BL. Clinical and radiographic evaluation of demineralized freeze-dried bone allograft versus platelet-rich fibrin for the treatment of periodontal intrabony defects in humans. J Periodontol 2016; 87: 1253-1260.*
14. *Sharma A, Pradeep AR. Treatment of 3-wall intrabony defects in patients with chronic periodontitis with autologous platelet-rich fibrin: a randomized controlled clinical trial. J Periodontol 2011; 82: 1705-1712.*
15. *Kawase T, Okuda K, Wolff LF, Yoshie H. Platelet-rich plasma-derived fibrin clot formation stimulates collagen synthesis in periodontal ligament and osteoblastic cells in vitro. J Periodontol 2003; 74: 858-864.*
16. *Samson Yashar S, Gielczyk R, Scherschun L, Lim HW. Narrow-band ultraviolet B treatment for vitiligo, pruritus, and inflammatory dermatoses. Photodermatol Photoimmunol Photomed 2003; 19: 164-168.*
17. *Ozden MG, Aydin F, Sentürk N, Bek Y, Cantürk T, Turanli AY. Narrow-band ultraviolet B as a potential alternative treatment for resistant psychogenic excoriation: an open-label study. Photodermatol Photoimmunol Photomed 2010; 26: 162-164.*
18. *Kohyama S, Morimoto Y, Nakai K, Kaji T, Tokumaru A, Nawashiro H, Shima K, Satoh Y, Takishima K, Kikuchi M, et al. Effectiveness of narrow-band ultraviolet-B phototherapy for prevention of intimal hyperplasia in a rat carotid balloon injury model. Lasers Surg Med 2007; 39: 659-666.*
19. *Serish, Srinivas CR. Minimal erythema dose (Med) to narrow band ultraviolet - B (NB-UVB) broad band ultraviolet-B (BB-UVB) - A pilot study. Indian J Dermatol Venereol Leprol 2002; 68: 63-64.*
20. *Zhang DM, Hong WS, Fu LF, Wei XD, Xu AE. A randomized controlled study of the effects of different modalities of narrow-band ultraviolet B therapy on the outcome of cultured autologous melanocytes transplantation in treating vitiligo. Dermatol Surg 2014; 40: 420-426.*
21. *Arca E, Taştan HB, Erbil AH, Sezer E, Koç E, Kurumlu Z. Narrow-band ultraviolet B as monotherapy and in combination with topical calcipotriol in the treatment of vitiligo. J Dermatol 2006; 33: 338-343.*
22. *Bilgili SG, Karadag AS, Calka O, Ozdemir S, Kosem M. A case of generalized lichen nitidus successfully treated with narrow-band ultraviolet B treatment. Photodermatol Photoimmunol Photomed 2013; 29: 215-217.*
23. *Yoshimura J, Asano Y, Takahashi T, Uwajima Y, Kagami S, Honda H, Idezuki T, Igarashi A, Sato S. A case of scleredema adultorum successfully treated with narrow-band ultraviolet B phototherapy. Mod Rheumatol 2016; 26: 302-306.*