

TREATMENT OF LEG ULCERS WITH AUTOLOGOUS HEPARINIZED BLOOD

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ABSTRACT

Background. Human blood contains growth factors, which take part in wound healing.

Objective. To test the hypothesis that topical application of human blood would improve ulcer healing, we have treated 26 leg ulcers of different etiology with repeated topical applications of human blood.

Methods. Twenty-six ulcers were treated with autologous heparinized blood under the occlusive dressing every other day. Fifteen control ulcers were treated with antiseptic ointment. The duration of follow up for each patient was 3 weeks. The surface of the ulcers was measured by planimetry. The study was performed in patients at the Department of Dermatology, Rijeka.

Results. The average surface reduction was 52.5% in ulcers treated by autologous heparinized blood. On the contrary, in control ulcers the average surface reduction was 18.2%. Complete closure of the ulcer was obtained in 3 cases (11.5%). Ulcer surface was significantly reduced in ulcers treated autologous blood ($p=0.001$), compared to controls ($p=0.62$).

Conclusion. Our results suggest that autologous heparinized blood stimulates cleansing and healing of the ulcers. It is well tolerated and an inexpensive method in the treatment of leg ulcers.

KEY WORDS

lower leg, ulcers, autologous blood, heparin, topical treatment

INTRODUCTION

Leg ulcers are mostly caused by chronic venous or arterious insufficiency that leads to inadequate tissue oxygenation and consequently worse healing (1). Numbers of methods are used in the treatment of leg ulcers with different success. One method is

topical application of autologous heparinized blood (AHB) (2). It is well known that human blood contains growth factors, which take part in wound healing (3). These factors can chemotactically attract and activate inflammatory cells and initiate new expression of quiescent genes (4-6).

In this paper we present 22 patients with chronic

Table 1. Results of topical treatment of leg ulcers with autologous heparinized blood (haemotherapy)

Ulcer No.	Ulcer etiology	No. of treatments	Ulcer surface before haemotherapy (cm ²)	Ulcer surface after haemotherapy (cm ²)	Surface reduction %
1	venous	9	13.73	5.31	61.33
2	venous	7	13.95	0.00	100.00
3	venous	10	6.64	4.87	26.66
4	venous	9	14.17	7.75	45.31
5	venous	9	18.82	13.95	25.88
6	venous	9	9.08	4.87	46.37
7	venous	9	9.74	7.01	28.03
8	venous	8	4.43	0.66	85.10
9	venous	7	4.87	0.44	90.97
10	venous	3	2.88	0.00	100.00
11	venous	8	4.65	0.00	100.00
12	venous	9	4.21	4.21	0.00
13	arterious	9	9.97	4.65	53.36
14	arterious	9	3.54	3.54	0.00
15	diabetic	9	3.76	2.88	23.40
16	venous	8	20.82	3.54	83.00
17	venous	8	19.49	2.88	85.22
18	venous	9	10.41	1.32	87.32
19	venous	8	3.10	1.55	50.00
20	arterious	9	16.39	14.39	12.20
21	venous	8	6.87	5.53	19.51
22	diabetic	10	19.04	11.95	37.24
23	arterious	9	3.76	3.76	0.00
24	venous	8	12.40	7.75	37.50
25	venous	9	3.99	2.21	44.61
26	venous	9	2.44	0.66	72.95
X			9.35	4.45	52.50

leg ulcers of different etiology that were treated with repeated applications of AHB. We assumed that human blood applied on ulcer surface would improve its healing.

PATIENTS AND METHODS

We have treated 41 leg ulcers in 22 patients (13 females, 9 males; mean age 73, range: 50-91) at the Department of Dermatology. These ulcers included 31 venous (75.61%), 7 arterious (17.07%), and 3 diabetic (7.32%) ulcers. Inclusion criteria were patients with ulcers caused by venous or arterial diseases, while exclusion criteria were ulcers associated with haematological diseases, neurologic diseases, signs of acute inflammation and patients undergoing immunosuppressive therapy. The diagnosis was based on clinical examination, supported by Doppler's ultrasound test and in some cases also by plethysmography.

Twenty-six ulcers (63.41%): 20 venous, 4 arterious, 2 diabetic, were treated with AHB under the occlusive dressing. In 15 patients (36.59%) with two ulcers (11 venous, 3 arterious and 1 diabetic) one was treated with AHB, while the other one with antiseptic

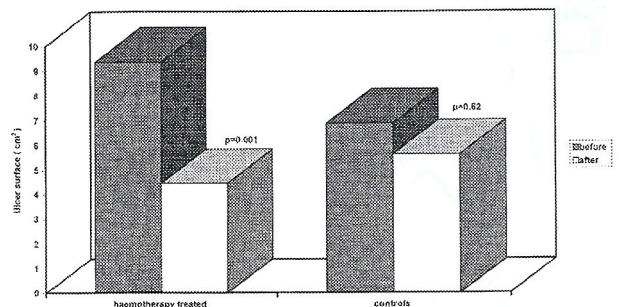


Figure 1. Surface reduction in autologous heparinized blood therapy treated ulcers and controls (mean values)

Table 2. Results of the therapy in control ulcers

Ulcer No.	Ulcer etiology	No. of treatments	Ulcer surface before therapy (cm ²)	Ulcer surface after therapy (cm ²)	Surface reduction %
1	venous	9	4.43	3.99	9.93
2	venous	9	22.15	19.93	10.02
3	venous	9	21.48	20.59	4.14
4	venous	9	2.44	0.89	63.52
5	venous	9	4.65	0.33	92.90
6	venous	9	3.10	0.66	78.71
7	venous	9	1.77	1.77	0.00
8	arterious	9	2.88	2.88	0.00
9	diabetic	9	1.11	1.11	0.00
10	venous	8	3.99	3.99	0.00
11	venous	9	2.43	0.67	72.42
12	arterious	9	1.99	1.99	0.00
13	arterious	9	6.64	5.54	16.56
14	venous	8	11.29	8.86	21.52
15	venous	8	12.84	11.29	12.07
X			6.88	6.64	18.20

ointment (Betaisadona ointment - 10% Polyvinyl-iodine complex, Mundipharma) every other day.

Before starting the therapy all ulcers were disinfected with 3% hydrogen peroxide and mechanically cleaned with curette. Every other day the fresh AHB was applied to the ulcers and immediately covered with occlusive absorbent dressing (Metoder[®]). The mixture of 1 ml venous blood and 0.1 ml heparin (Solopak[®], 25,000 IU, Smith & Nephew, USA) was applied per every 4 cm² of the ulcer's surface.

The mean duration of ulcers was 15 months (range: 1-84); the average surface of haemotherapy treated ulcers was 9.35 cm² (range: 2.44-20.82), while the average surface of the control ulcers was 6.88 cm² (range: 1.11-22.15). At the beginning of the therapy there was no significant difference in ulcer's surface between AHB treated group and controls ($p=0.42$). The average duration of AHB treatment was 16 days (8 treatments). The surface of the ulcers was measured by planimetry. Statistics were done by Student's t-test. The nature and purpose of the study were explained to the patients and a verbal informed consent was obtained from them.

RESULTS

Table 1. presents the results of AHB treatment in individual patients. Complete healing and closure of the ulcer was obtained in 3 (11.5%) cases of

venous ulcers. There was no reduction of ulcer's surface in 3 (11.5%) cases, one venous, and one arterious ulcer.

The average surface reduction of AHB treated ulcers was 52.5%. In control ulcers the average surface reduction was 18.2% (Table 2). Figure 1. shows surface reduction in AHB treated ulcers and controls after the therapy. As seen the ulcer's surface was significantly reduced after haemotherapy ($p=0.001$). At the same time in controls, after ointment therapy, the surface reduction was not statistically significant ($p=0.62$). After each treatment we noticed the diminution of fibronectic material and a rapid formation of new granulation tissue. At the same time in control ulcers the formation of granulation tissue was slower and the fibronectic material was more adherent. However, the difference between these two methods was not significant ($p>0.05$).

In 2 patients we noticed after a few applications an erythema and papular exanthema surrounding the ulcers on the treated leg. The other patients showed no local or systemic side effects.

DISCUSSION AND CONCLUSIONS

In this study we report on topical application of autologous human blood in the treatment of chronic leg ulcers measured by surface reduction. We observed that AHB improved healing in the majority of ulcers

compared to controls by stimulating the formation of granulation tissue and increasing epithelization.

The best results were obtained in venous ulcers. However, slight or no changes at all, were observed in ulcers caused by arterious insufficiency and diabetes, factors generally considered to be of bad prognostic significance.

Ulcer's surface reduction after accomplished AHB was statistically significant. At the same time in control ulcers the surface was not significantly reduced. These results show that haemotherapy gives better results than classic treatment with ointments. The results between these two treatment methods were not significantly different ($p>0.05$).

We also noticed rapid formation of granulation tissue and fast reduction of fibronectin material in comparison to controls. This is in agreement with the results of Triquet et al. (2) in which the quantity of new-formed granulation tissue on the ulcer surface

was measured during the topical haemotherapy treatment. According to our experience AHB is a successful method in preparing the ulcers for skin grafting.

In 3 cases in which total closure was obtained, a progressive epithelization, starting from small islands of keratinocytes in the centre of the ulcer was observed. Usually the epithelization starts from the wound edge what we noticed in 80% of our cases. (7)

Our results suggest that AHB therapy stimulate healing and cleansing of the ulcers. This method involves synergistic activity of growth factors, occlusive dressing, and heparin. These initial results suggest that these factors promote and stimulate wound healing. (8) Heparin, at low concentrations stimulates the growth of myocytes and fibroblasts, but is inhibitory at higher concentrations. (9,10) Further research will be necessary to explain the exact role of heparin and occlusive dressing during the haemotherapy.

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