Bone marrow-derived mononuclear cell therapy improves ischemia parameters and enhances wound healing in patients with diabetic foot ulcers

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Background

Therapeutic vasculogenesis by autologous stem cell therapy (ACT) is a new treatment method for patients with critical limb ischemia (CLI) and diabetic foot ulcers (DFU). Standard treatment – percutaneous transluminal angioplasty (PTA) or by-pass are not eligible for all patients mainly due to high risk of the procedure angiographic finding - lack of outlaw or long stenoses.

Aim

The aim of our study was to compare changes of transcutaneous oxygen pressure ($TcPO_2$) and healing of DFU in patients treated by cell therapy and conservatively.

Methods

- Forty-five diabetic patients with no-option CLI ($TcPO_2$<30 mm Hg), ulcer size between 0.5 and 7 cm^2 with Texas classification 1C-3D treated by cell therapy in our foot clinic over 5 years were included into the study (ACT group)
- Forty-two patients with the same inclusion criteria treated conservatively during the same period were included into the control group
- Both groups did not significantly differ in mean age, gender, glycated hemoglobin and mean diabetes duration (Table 1)
- Change of $TcPO_2$ and number of healed patients were assessed after 6, 12, 24 and 36 months.

Table 1. Characteristics of patients

Therapeutic method	ACT	Conservative	p
Number of patients	**n = 45**	**n = 42**	
Age *(years)*	64 ± 11	68 ± 8.8	NS
Gender *(% of men)*	80	73.9	NS
Mean diabetes duration *(years)*	24.2 ± 13.6	20.9 ± 10.8	NS
Glycated hemoglobin *(mmol/mol)*	59.6 ± 13.8	62 ± 15.2	NS
Hypertension *(%)*	91.1	92.9	NS
End stage kidney disease *(%)*	20	11.9	NS
Immunosuppressive therapy *(%)*	17.8	7.1	NS
Ischemic heart disease *(%)*	64.4	45.2	**0.07**

Results

- There was no significant difference in mean size, depth or TEXAS stage of the ulcers and $TcPO_2$ (17.7±10.3 vs. 16.5±9.8 mm Hg) between ACT and control groups at baseline. We observed a significant increase of $TcPO_2$ in all measured intervals from 6 months up to 3 years (change of $TcPO_2$ 22 mm Hg; p<0.001) after cell therapy, but no significant increase in control group (change of $TcPO_2$ 4 mm Hg; Figure 1)
- The number of healed patients were significantly higher in ACT group compared to controls after 6 months (34.8 vs. 13.5%, p=0.021), 12 months (43.2 vs. 21.4%, p=0.025) and 24 months (67.5 vs 38.1%, p=0.009). Number of healed patients in 36 months was without a significant difference (Figure 2).

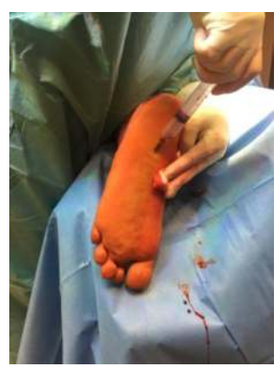


Figure 1. Changes of $TcPO_2$

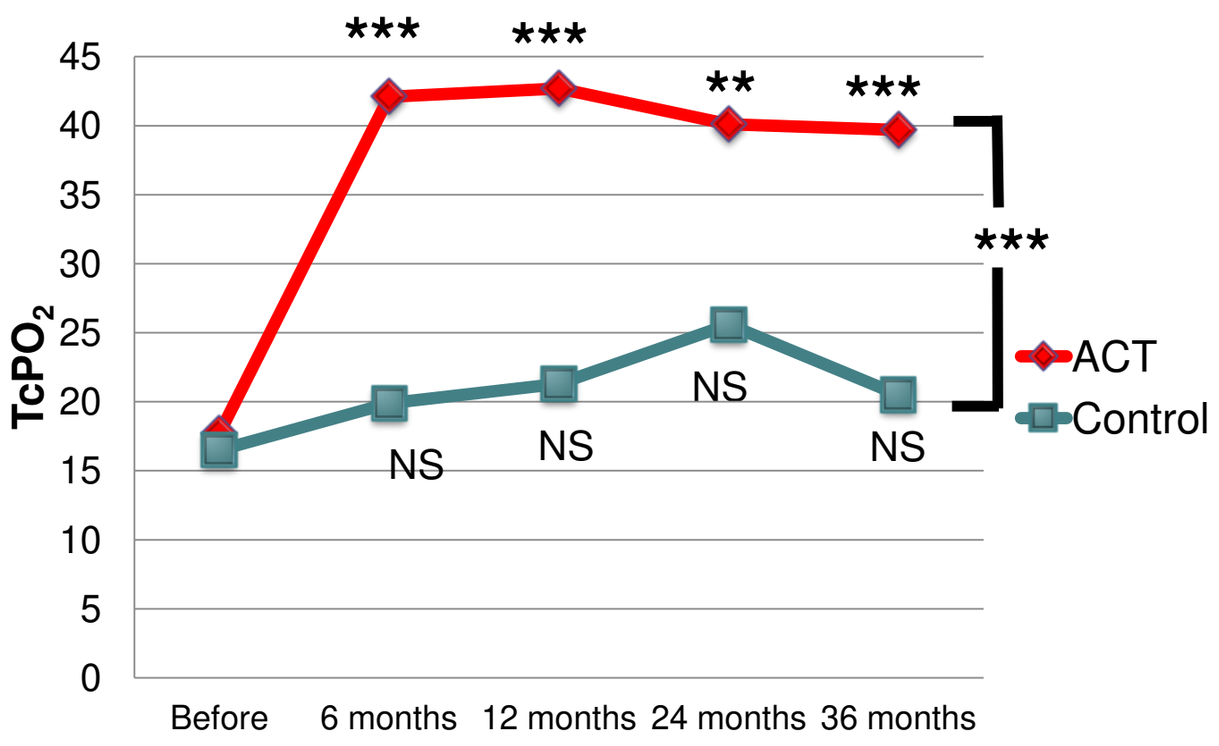
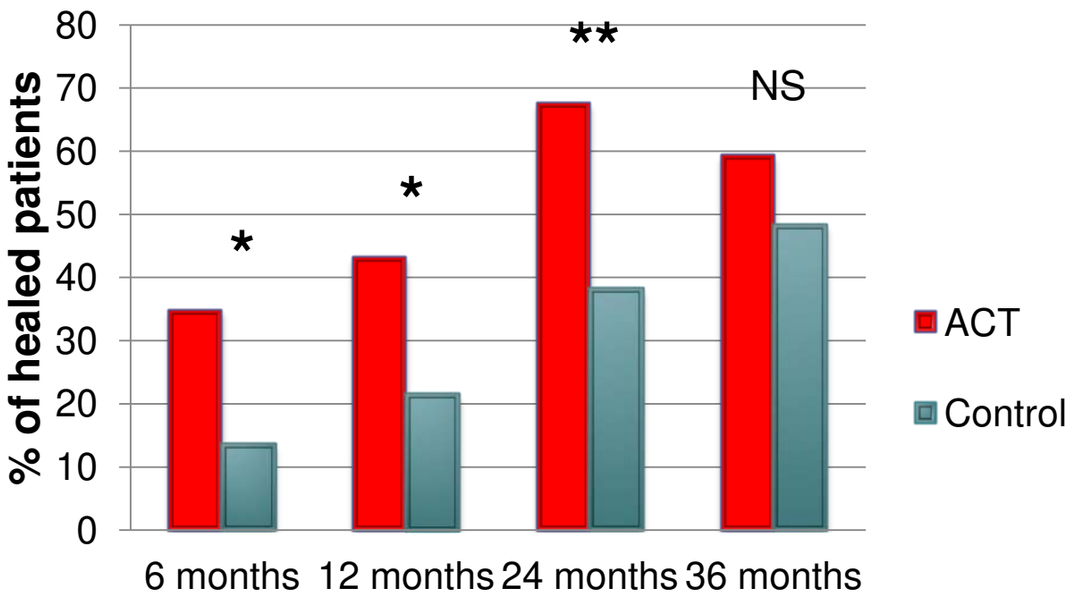


Figure 2. Wound healing



Conclusions

- Our study proved faster wound healing and a significant increase of $TcPO_2$ in diabetic patients with no-option CLI treated by cell therapy in comparison with conservative treatment
- Autologous bone marrow-derived mononuclear cell therapy seems to be a promising alternative for treatment of most severe stages of CLI.

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