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First experience with different methods of stem cell therapy in patients with ischemic diabetic foot

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Background and aims: Presently, there are ongoing studies focusing on revascularization of ischemic limbs utilizing various methods of cell therapy - mononuclear fraction of bone marrow stromal cells (BMSC) or CD34-positive fraction of mononuclear cells obtained by separation from peripheral blood after previous stimulation by granulocyte colony stimulating factor (G-CSF) - peripheral blood progenitor cells (PBPC). The aim of our pilot study was to evaluate our first experience with both of these methods in the treatment of patients with ischemic diabetic foot and assess transcutaneous oxygen (TcPO₂) measurements, ischemic pain, healing and adverse events. **Patients and methods:** The indication for stem cells therapy was ischemic diabetic foot disease after unsuccessful standard revascularisation. Exclusion criteria were any suspicion of organ cancer, haematological abnormality, and acute infection, high risk of anaesthesia, non-treated proliferative retinopathy and lower limb oedema. 7 diabetic patients (5 with foot ulcers, 4 with ischemic pain) with mean age 64.4 ± 7.4 years, mean diabetes duration 26 ± 12.5 years, were included into the study during one year. 5 patients were treated by BMSC and 2 patients by PBPC; the procedures for extraction of BMSC by trepanobiopsy of iliac bone and for separation of PBPC from peripheral blood after stimulation by G-CSF have been well standardized. The cell suspension was concentrated to volume of 40-90 ml with satisfactory CD 34+cells concentration and implanted into the muscle of the affected limb, by approximately 0.5-1 ml punctures. The clinical assessment and TcPO₂ measurements were repeated during 6 months follow-up. The Wilcoxon test was used for statistical significance. **Results:** The TcPO₂ significantly increased from the median value of 14 (2-27) mmHg before treatment to 34 (4-53) mmHg, $p = 0.047$ after 1 months, to 35 (22-49) mmHg, $p = 0.016$ after 2 months, to 42 (25-52) mmHg, $p = 0.016$ after 3 months and to 41 (41-53) mmHg, $p = 0.062$ after 6 months (where data of 5 patients are available). The local finding on the foot improved in all of 5 patients with foot ulcers, median of ulcer area reduction after 3 months was 95.8 (23; 100)%, $p < 0.1$, after 6 months 2 patients were healed and 2 patients had small superficial ulceration. One patient (after kidney and pancreas transplantation) died after 5 months due to cardiac failure. The resting pain assessed by Visual Analog Scale decreased from 5 ± 1.8 before treatment to 2.25 ± 1.8 after 3 months ($p < 0.1$) and was only between 0 - 1 in all patients after 6 months. One transient leg oedema was seen. **Conclusion:** Our first experience support the methodological feasibility and benefit of stem cells treatment of ischemic diabetic foot but long-term effect and optimal indication are apt topics for further long-term studies. Supported by grant MZO 00023001