

Modification of foot risk factors in the treatment of diabetic neuro-ischemic foot of risk

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Evidence has emerged to suggest that ischemia and hypoxia play a paramount role in the pathogenesis of diabetic foot. Reduced tissue blood flow in experimental diabetic complications may be prevented and corrected by several disease-modifying drugs. Actovegin is a deproteinised hemoderivative produced from calf blood by ultrafiltration. Actovegin stimulates oxygen absorption, oxygen utilization, and cellular energy metabolism. We conducted a pilot open labelled randomized 6 week study to evaluate the efficacy of treatment using i.v. infusions of Actovegin (2000 mg/day) qd for 2 weeks followed by oral administration (1200 mg/day) for 6 weeks. Sulodexide (content of heparinoid and dermatansulfate fractions) was chosen as comparator drug. **Materials and Methods.** 38 DMt1 and DMt2 patients aged $64,5 \pm 2,1$ years ($HbA1c = 7,6 \pm 1,2\%$) with intermittent claudication and sensori-motor neuropathy ($NDS 14,5 \pm 1,2$) without foot ulcers were enrolled in the study. Patients were randomized for the actovegin or sulodexid treatment group. Treadmil test (Gardner protocol) has been performed for evaluation of peak walking time (PWT) before, after infusion period and at the end of the study. Blood tests were performed, with the determination of fibrinogen, antitrombotic activity, factors of oxidation and antioxidation. **Results.** Both kind of treatment brought about a progressive increase in the maximum walking time during tredmil test (Tab. 1) but absolute difference of PWT did not differ between two treatment groups. Relative difference of PWT Actovegin 0-6weeks differed versus PWT Sulodexid ($95,1\%$ vs $38,1\%$, $p < 0,05$). NDS decreased at the study termination in the both groups of treatment. Mean $TcpO_2$ level was $45,0 \pm 4,3$ mm Hg before and it did not increase after the treatment. Both fibrinogen/coagulation parameters and oxidation/antioxidation markers did not change in both treatment groups. **In conclusion:** Both actovegin and sulodexide 6 weeks treatment course was followed with statistical significant elevation of maximum walking time and improvement of neuropathic deficit score in groups of patients with neuropathy and ischemia. Efficacy of the treatment was more pronounced for patients treated by Actovegin. Different underlying mechanism of drug influence can be further investigated. Possible treatment efficacy can be augmented with increasing of treatment duration. Table 1. PWT during the treatment ($M \pm SEM$)

	0 week	2 weeks	6 weeks
PWT Actovegin, sec	$275,8 \pm 42,7$	$354,1 \pm 48,9, p < 0,05$ vs 0week	$435,9 \pm 53,2 p < 0,01$ vs 0week
PWT Sulodexide, sec	$281,3 \pm 34,1$	$337,5 \pm 39,5$	$378,2 \pm 43,8 p < 0,05$ vs 0week