Study on the pathogenesis of diabetic neuropathy using aldose reductase inhibitor

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Summary: The effect of a newly developed oral agent, prostaglandin E₁ (PGE₁), on diabetic neuropathy was studied by giving it 6 weeks to streptozotocin-induced diabetic rats that had been diabetic for 3 months and was compared with the effects of aldose reductase inhibitor (ARI). Although both compounds improved decreased motor nerve conduction velocity, the effect of PGE₁ continued during the 6 weeks of treatment, whereas that of ARI became weaker from weeks 4. The abnormality in sciatic nerve sorbitol and myo-inositol levels was reversed with ARI, whereas it was unchanged with PGE₁. Experiment: Twenty-three of 30 rats were made diabetic. At 12 weeks, PGE₁ treatment was initiated in 6 rats and ARI treatment in 8 rats. Another 8 rats were given saline (untreated group). The remaining 8 animals had not received STZ and were treated with saline (control group). At week 18, the rats were anesthetized with pentobarbital sodium, and the left side of the sciatic nerve was removed and fixed in 2.5% glutaraldehyde in 0.025 M cacodylate buffer, pH 7.38, at 4°C for 24 h. Tissue blocks were additional fixed in osmium tetroxide in buffer at 4°C and embedded in epoxy. Transverse semithin sections (1 μm) were stained with toluidine blue. Morphometric analyses were performed by means of a computer-assisted digitizer. The number of myelinated nerve fibers per fascicle and the myelinated nerve fiber density were determined on the screen of the digitizer. More than 30 % of the fascicular area for each nerve was used for analysis. All nerves were photographed at two magnifications and enlarged on prints to final magnifications of x240 and x950. From these prints, the number of capillaries per fascicle and the capillary density (number/μm²) were calculated with the digitizer.