Evidence for Hypoxic Hypothesis of Diabetic Neuropathy

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We propounded the hypoxic hypothesis of diabetic neuropathy to reconcile morphologic descriptions of microangiopathy and descriptions of diffuse metabolic abnormalities in human (HDN) and experimental diabetic neuropathy (EDN). We have provided the following evidence for endoneurial hypoxia. 1) Indirect evidence of endoneurial hypoxia (reduced creatine phosphate; increased lactate) in acute and chronic experimental diabetic neuropathy. 2) Reduced nerve blood flow in chronic EDN. 3) Direct evidence of endoneurial hypoxia based on microelectrode recordings of endoneurial oxygen tensions in chronic EDN. Sixty percent of oxygen tension values fell below the critical oxygen tension. 4) Oxygen supplementation partially prevented both the electrophysiological and biochemical abnormalities in experimental diabetic neuropathy. 5) To examine the role of sugar alcohol accumulation, PnO2 measurements were made in chronic experimental galactose neuropathy. PnO2 reduction occurred in proportion to the increase in intercapillary distance. 6) To examine the role of hypoxia alone, rats were reared in a hypoxic (10% oxygen) environment for up to ten weeks. These animals developed nerve conduction slowing and RICB in the absence of sugar alcohol accumulation or myoinositol reduction. 7) Computer simulation studies are in good agreement with experimental data.

References

2) Tuck RR, Schmelzer JD, Low PA. Brain 107: 935-950, 1984