Influence of glucoregulation with continuous subcutaneous insulin infusion on nerve conduction velocity and beat to beat variation in diabetics


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ABSTRACT. Limited and contrasting data are available on the relationship between metabolic control and diabetic neuropathy. In eight type I diabetics peripheral and autonomic neuropathy were studied, first in conditions of poor metabolic control and then after one and three months during which an improved control of glycemic levels had been obtained by continuous subcutaneous insulin infusion. Autonomic neuropathy was investigated by evaluating beat to beat variation during deep breathing; peripheral neuropathy by measuring maximum motor conduction velocity of peroneal and median nerves and sensory conduction velocity of median nerve. Our data showed significant improvement of motor conduction velocity in both nerves studied, whilst sensory conduction velocity did not show any significant variation. The changes observed in beat to beat variation in five subjects with initially abnormal scores might reflect an improvement in autonomic nervous function, even if long-term studies are needed.

INTRODUCTION
The pathogenesis of diabetic neuropathy is probably multifactorial and a direct influence of metabolic control is likely to be the most important factor in systemic and autonomic polineuropathy (1).
Various mechanisms have been proposed as a basis for the structural and functional impairment of nerve in diabetes. A reduced myoinositol availability and concentration in the nerve is thought to interfere with the regeneration of phosphoinositides and with nerve conduction (2, 3). An increased formation and retention of sorbitol within the nerve has been suspected of leading to damage to the axon (4).
More recently disturbances of axonal transport have been observed early in the course of experimental diabetes (5).
These mechanisms are readily activated by hyperglycemia and appear to be reversible with normalization of blood glucose (6, 7).
The evidence for influence of good glycemic control in delaying the onset and reducing the severity of diabetic neuropathy in man is somewhat controversial (8-10).
The difficulty in relating the metabolic abnormalities of diabetes to the neurological complications of this disease derives in part from the fact that conventional treatment often fails to restore body fuel metabolism to normal even under optimum conditions.
Recently Pickup et al. developed the technique of low-volume, continuous, subcutaneous insulin infusion (CSII) to achieve, as confirmed by several reports, long-term strict diabetic control (11, 12).
More recently Pietri et al. (13) reported improvement in motor nerve conduction velocity after six weeks of CSII delivered with a portable insulin pump.
Brunetti et al. (14) showed improved motor nerve conduction velocity after three days of treatment with an artificial beta cell.
All these studies, conducted for relatively short periods, are focused on peripheral nerves, whilst autonomic neuropathy has received less attention.
An extensive longitudinal study by Watkins et al. on the behavior of beat to beat variation under deep breathing in diabetic patients under conventional treatment showed a tendency to gradual deterioration over the years (15). A short term treatment with continuous intravenous insulin infusion was reported to improve Valsalva ratio and beat to beat variation under deep breathing in patients with short term diabetes but not in those with longer duration of the disease (16).
The aim of the present work was to verify if peripheral and autonomic neuropathy could be modified after short and medium term glyco-metabolic control obtained with CSII.

MATERIALS AND METHODS

Eight type I diabetics, 4 males and 4 females, mean age 36.6 years (range 24-54), mean duration of diabetes 14.3 years (range 6-33), were studied. Six (4 M, 2 F) out of eight patients had mild signs and symptoms of diabetic neuropathy (reduction of ankle jerks and at least one of sensory functions with painful paresthesia of the feet; moreover two out of the six patients complained of a progressive reduction of libido and ejaculate). These clinical findings did not change during the observation period. The other two subjects had neither signs nor symptoms of diabetic neuropathy.

All patients were hospitalized for at least two weeks. In the first four days conventional insulin therapy was maintained with no attempt to achieve optimum control; during this period initial baseline studies were performed. These studies included a 24 h glucose profile (obtained at hourly intervals from 08.00 to 20.00 and at 2 h intervals from 20.00 to 08.00), measurement of glycosylated hemoglobin (two determinations) and evaluation of peripheral and autonomic neuropathy.

After this control period all subjects received continuous subcutaneous insulin infusion with a Microjet pump model MC2. In the subsequent week (occasionally 2 weeks) optimal control was obtained (complete absence of glycosuria, mean daily blood glucose \( \leq 130 \text{ mg/dl} \)) and patients instructed in the use of the apparatus; they were then followed in the outpatients clinic and recalled after one and three months to repeat all studies (24 h plasma glucose profile, glycosylated hemoglobin and neurophysiologic parameters).

Blood glucose control by reactive strips (Haemogluco-test 20-800 - Boeringher Mannheim®) was performed 4 times daily twice a week; control of glycosuria was performed 5 times daily. Every two weeks 6 blood glucose determinations were performed by a Miles-