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Neuropathy

Sequential electrodiagnostic evaluation of diabetic neuropathy after combined pancreatic and renal transplantation

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Summary. To asses the long-term evolution of diabetic polyneuropathy after a combined kidney-pancreas transplant, an electrophysiological study was performed in 20 diabetic patients before transplant, and 1 (n=18), 2 (n=16), 3 (n=10) and 4 years (n=5) at a later date. Motor and sensory scores were calculated for conduction velocity and amplitude to determine the physiopathological process. During evolution the scores were not found to be decreasing. Motor and sensory velocity scores were significantly improved ($p<0.05$) 1 and 2 years after the graft, when score values tended to stabilize. Motor and sensory amplitude scores, which are more sensitive for axonal loss assessment were slightly but not significantly improved.

Key words: Diabetic polyneuropathy - Pancreas and kidney transplantation - Electrophysiological survey

Introduction

Progressive advances in surgical techniques and results from combined transplants allow long-term studies of the outcome of diabetic complications. Polyneuropathy is the most common neurological complication of Type 1 (insulin-dependent) diabetes mellitus, and is considered to be an indicator of renal function and of glucide metabolism control. The purpose of our study was to assess the eventual short-term improvement of neuropathy in recipients, and whether it would persist during the evolution. We report a prospective sequential electrophysiological follow-up of neuropathy in 20 diabetic patients after a successful simultaneous kidney-pancreas grafting. Follow-up examinations extended on a 4-year period for a small group of patients.

Subjects and methods

Patients. Twenty patients (11 men and 9 women), mean age 40.2 years (range 25-52 years) with long-standing juvenile Type 1 diabetes and terminal diabetic nephropathy, underwent combined renal and pancreatic grafting. The mean duration of diabetes was 25 years (SD = 7). 16 patients had hemodialysis before transplantation (mean value = 21 months; SD = 16 months). The period of transplantation was 1984 (2 patients), 1985 (1 patient), 1986 (7 patients), 1987 (4 patients) and 1988 (6 patients). During the same period 122 combined renal and pancreas transplantations had been performed in our institution, with a functional success for 50 of them. Only a group of 20 patients has been regularly studied in our laboratory, the others checking with laboratories closer to their home. No patient required hemodialysis or exogenous insulin during the period of the study. 14 patients received a segmental duct obstructed pancreas transplant and 7 patients received a total pancreas transplant with bladder drainage.

Recording procedures. Electrophysiological evaluation was perfomed before transplantation then at yearly intervals : in year 1 (n=18), in year 2 (n=16), in year 3 (n=10) and in year 4 (n=5). Motor nerve conductions were measured in median, ulnar, peroneal and tibial nerves on one side only, and sensory nerve conduction velocities in median and sural ones on that same side. The amplitudes of the motor and sensory nerve action potentials were calculated distally in each nerve. When no motor or sensory responses were obtained after nerve stimulation, the amplitude was considered as zero and the conduction velocity as missing value. Care was taken to make all recordings at normal skin temperature.

Statistical analysis. Following the San Antonio recommendations for diabetic neuropathy (1988), each parameter of the motor and sensory values was expressed as a percentage of our laboratory reference mean value in a normal population group. Motor and sensory scores were calculated for velocity (MVS and SVS) and amplitude (MAS and SAS) for each patient and at each stage of the study. The expected gain was expressed as the intraindividual variation between the before-transplant reference value and the values calculated at each period of electrophysiological control. The statistical study was performed with a two-tailed t-test.

Results

Before transplantation all the patients presented classical clinical and electrophysiological evidence of polyneuropathy with classical criteria (Dyck 1988). Motor and sensory nerve conduction velocities were

reduced (MVS = 68.8 %; SVS = 67.8 %). Motor and sensory amplitudes were decreased (MAS = 49.6 %; SAS = 12.6 %). Figure 1 shows the development of the different scores during the follow-up study.

Motor velocity scores showed a clear and significant gain. The maximal gain concerned the group of 5 patients studied after 4 years (MVS gain = 12.3 %; $p<0.02$) and the group of 16 patients studied after 2 years (MVS gain = 7.7 %; $p<0.002$). Detailed and separate analysis for each nerve showed no significant improvement 1 year after the transplant, except for median nerve. The level of significance decreased after 4 years, but the group of patients under study was small. The scores evolution analysis showed that the gain was no longer significant at year 3 and 4 when the gain at year 2 was taken as a reference. Before grafting, MVS and SVS had close values. At each stage of the study a small gain for SVS was calculated, but was significant only for the group of 17 patients studied after 1 year (SVS gain = 4.9 %; $p<0.05$) and after 2 years (SVS gain = 7.1 %; $p<0.05$). After 1 year this improvement was observed in the sural ($p<0.02$) and the median ($p<0.01$) nerves, while later on, only the latter was concerned (year 2, $p<0.02$; year 3, $p<0.03$; year 4, $p<0.05$). Motor amplitudes were decreased before grafting (MAS = 49.6%) with a slight but not significant increase for the group of 16 patients studied after 2 years (MAS gain = 4.2 %; $p = 0.07$). An abrupt improvement recorded after 4 years probably expressed a technical bias due to a modification of distal blocking in a small sample (n = 4). There was a clear decrease of sensory amplitude scores, especially in the sural nerves. During evolution the slight improvement only became significant for the group of 16 patients after 2 years (SAS gain = 8.1 %; $p<0.05$).

Discussion

The fate of diabetic polyneuropahty after grafting is a much debated question (Solders et al.1987; Landgraf et al. 1989; Kennedy et al.1990). Van der Vliet et al.(1988) in a long-term study of polyneuropathy in diabetic recipients after a kidney graft, showed the stability of motor nerve conduction velocity and the decrease of amplitude values, and the authors concluded that correction of uraemia did not prevent axonal loss, which is probably due to diabetes. This axonal degeneration may leave motor axons with a close to normal velocity conduction. Therefore an electrophysiological study restricted to the nerve conduction velocity measurement is not sufficient. The use of scores allows the joint study of conduction velocities from different nerves, increasing the number values and reducing the influence of entrapment (i.e. carpal tunnel syndrome). These scores are of interest for determining the severity of the neuropathy and the physiopathological process concerning segmentary demyelination or axonal loss. Electromyographic examinations with concentric needle electrode or single-fiber electromyography (Shields 1987) are sensitive methods to assess axonal

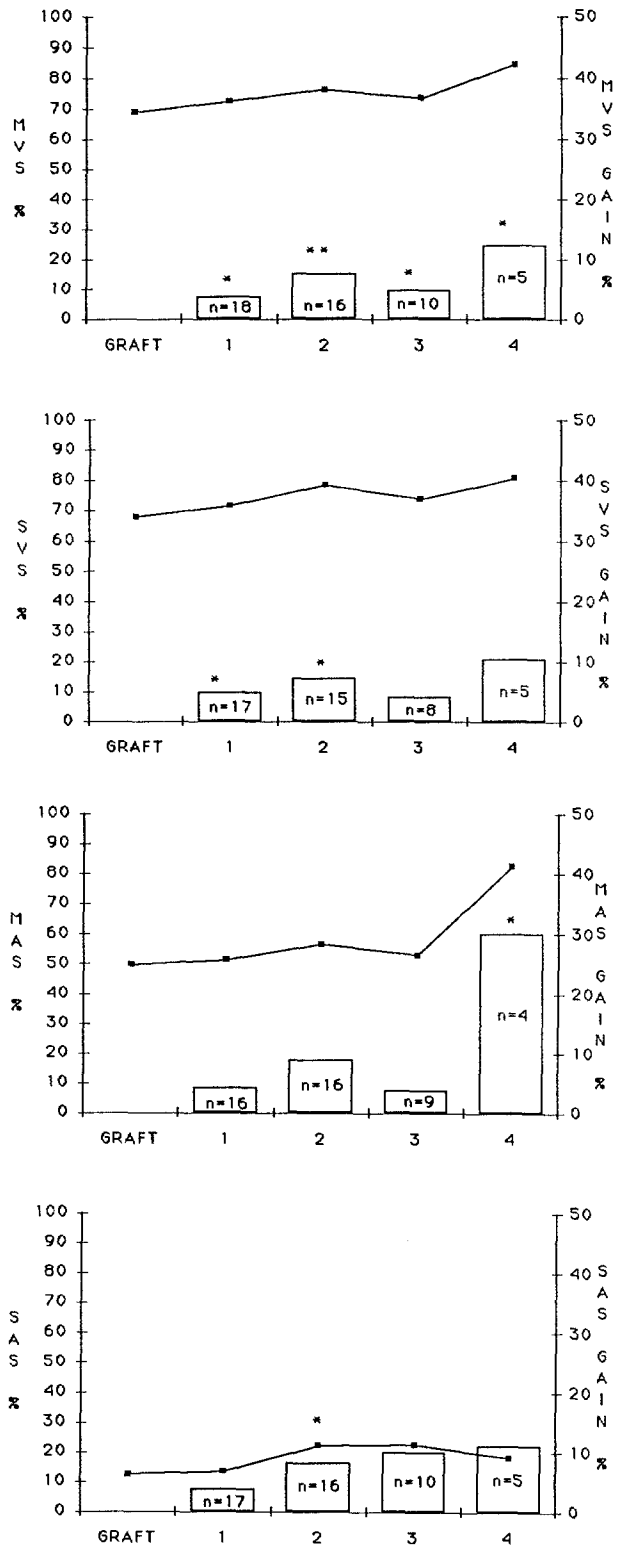

Fig.1. Electrophysiological scores (left side scale) before the graft and after 1, 2, 3 and 4 years of follow-up (MVS= motor velocity score ; SVS=sensory velocity score ; MAS=motor amplitude score ; SAS=sensory amplitude score)
Histogram represents the gain (right side scale) wich is the intraindividual scores variation within the group between the values before and after graft. The asterisks indicate a significant gain (* = $p<0.05$; ** = $p<0.01$) .

degeneration with reinnervation, but they are occasionally painful and fairly often time-consuming.

Our study confirms the improvement of some electrophysiological values in diabetic pancreas and kidney combined transplant recipients. Motor and sensory conduction velocities (for determination of the demyelinating process) were significantly improved, but sensory amplitudes modifications (for axonal process) were only slightly improved. The maximal gain takes place after 2 years, and stabilizes then. But the small number of studied recipients after 4 years does not allow anticipatation of the long-term issue of these modifications. The maximal improvement delay excludes metabolic or toxic changes induced by the grafting as the sole explanation. The long duration of diabetes and thus of polyneuropathy, may explain the fact that diabetic patients have a limited potential for reinnervation. This time factor could prompt a comparative study with the result of transplantation at an earlier stage of the disease.

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