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Carpal Tunnel Syndrome: a Major Complication in Hemodialysis Patients

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In order to assess the prevalence of the carpal tunnel syndrome (CTS) suggestive of β2 microglobulin amyloid deposit in patients undergoing hemodialysis with cuprophan and acetate membrane, we studied 30 patients who had been receiving hemodialysis for varying lengths of time. Besides a standard physical and rheumatological examination, nerve conduction velocity studies were done in median and ulnar motor-sensory nerves. 12 patients had normal findings, 12 had CTS (9 pure CTS, 3 with neuropathy), and 9 had peripheral neuropathy. Nerve dysfunction was independent of the disease underlying renal failure, the side of the dialysis access shunt and factors such as age and sex. We suggest that hemodialysis patients need frequent EMG analysis to identify CTS early and to avoid irreversible nerve damage.

Key words: hemodialysis, carpal tunnel syndrome, β2 microglobulin

Various muscoloskeletal disorders have been described in patients with chronic renal failure by periodical hemodialysis and peritoneal dialysis (1). In additon to renal osteodystrophy, these disorders include joint infections, acute articular and paraarticular inflammnatory episodes, recurrent hemarthrosis and peripheral nerve entrapment syndromes. Destructive arthropathies have been observed in some patients treated by maintenance hemodialysis for very long periods of time. The development of a carpal tunnel syndrome (CTS) has become an increasingly recognized problem in these patients with an incidence range from 2% to 31% (2–4). CTS in patients undergoing hemodialysis can be caused by primary edema of the flexor retinaculum without venous hypertension of inflammation, destruction of the valves in the superficial veins distal to the fistula, or compression of the median nerve by deposition of amyloid (5–6). According to Kessler, this syndrome differs in certain aspects from idiopathic CTS. Males and females are equally affected. It is often bilateral and readily recurs after surgical decompression (3).

The aim of this study was to assess the prevalence of CTS suggestive of beta 2 microglobulin (β2m) amyloid deposit in a series of patients undergoing long-term hemodialysis with cuprophan and acetate membrane.

Material and Methods

Thirty patients from Hacettepe University, Hemodialysis Center, who had been treated with hemodialysis were included in this study. There were eleven females and nineteen males with a mean age of 41.3±11.6 years (range: 21–66 years). The cause of renal failure included polycystic kidney in 2 patients (6.6%), glomerulonephritis in 6 (20%), amyloidosis due to Familial Mediteranean Fever in 2 (6.6%), obstructive nephropathy in 5 (17%), diabetic nephropathy in 1 (3.3%), vesico uretheral reflux in 1 (3.3%), toxic in 1 (3.3%), pyelonephritis in 1 (3.3%) and unknown in 11 (37%) patients. Two (6.6%) of the patients had clinical and pathological findings of amyloid nephropathy. The average duration of dialysis at the time of the study was 4.5±3.0 years (range: 1–15 years). Only one of the patients had undergone subtotal parathyroidectomies. The dialysis strateghy was taken into account if it was not unchanged for more than 90% of the duration of treatment. The frequency was three sessions per week. Cuprophane and acetate membranes were used throughout the study. Besides the EMG analysis, all patients were given a standard rheumatological examination. Criteria for the diagnosis of CTS were prolonged median distal latency (DL) with normal motor conduction velocity (CV), prolonged median sensory DL with normal proximal sensory CV and prolonged sensory DL with normal ulnar sensory DL (8). Nerve conduction studies were performed with a Toennies (Product group of Erich Joeger GmbH & Co. KG) electrophysiological measuring unit. Twenty age and sex matched healthy volunteers were used as a control group. Mean age of the control group was 37.7±5.0 years. Comparison between the hemodialysis and control groups was determined by the student's t-test with $p < 0.05$ chosen as the limit of significance. For DL, 2

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Table I. The EMG findings of hemodialysis patients

	Number of patients	%
Normal	12	40
Pure CTS	9	30
CTS with neuropathy	3	10
Neuropathy	9	30
Total	30	100

standard deviation more than the mean of the controls was taken as the higher limit; for NCV, 2 standard deviation leas than the mean of the controls was taken as the lower limit.

Results

Of the thirty patients receiving long term hemodialysis treatment for chronic renal failure, 12 (40%) had normal electroneurophysiological findings. Ten of the 30 patients (33.3%) had also renal osteodystrophy diagnosed by radiological evidence of destructive arthropathy, predominantly in the shoulders, wrists, hips and knees, and spondyloarthropathy (3). A total of 12 patients (40%) were found to have CTS; 4 (13.3%) being bilateral. Nine (30%) of these 12 patients had pure CTS, while 3 (10%) were with neuropathy. These results are summarised in Table I.

All of the patients with CTS verified by EMG criteria had typical paresthesias of the fingers and the region of the hand supplied by the median nerve. The diagnoses of sensory disturbance was supported in 5 (16.6%) cases by positive Tinel's sign and/or positive Phalen test.

The median motor and sensory DL, amplitudes and NCVs were compared between thw two limbs of the hemodialysis patients in order to find out the effect of the site of the fistula, but no significant correlation was found ($p > 0.05$). In fact, the affected limb in unilateral cases was more often contralateral than ipsilateral to the side of the shunt.

We found significant difference between the DLs of the ulnar and median nerve (in both limbs, with or without shunt) in dialysis patients ($p < 0.001$). There were also significant differences between the CVs of these two nerves ($p < 0.001$) (Table II). Subclinical median mononeuropathy has not been described as a diagnostic entity in dialysis patients, but it is worth noting as a possible precursor to clinically significant CTS since it was very often evident in these patients.

When we compared the electrophysiological results of the hemodialysis patients and controls, significant correlation was found in all parameters including median motor and sensory DL, amplitude and NCV, ulnar DL, amplitude and NCV (Table III). These results confirm the findings that peripheral nerve dysfunction often complicates chronic renal failure and dialysis.

Table II. Comparison of the ulnar-median motor distal latency and nerve conduction velocities between the shunt(+) and shunt(–) limbs of the hemodialysis patients

	Mean	St. Dev.	P.
mm-DL (shunt+)	3.7467	0.7276	<0.001
mm-DL	3.2125	0.4588	
mm-DL (shunt–)	3.6933	0.4748	<0.001
mm-DL	3.2125	0.4588	
mm-NCV (shunt+)	49.5556	5.2794	<0.001
mm-NCV	54.3750	4.2876	
mm-NCV (shunt–)	49.7241	4.3334	<0.001
mm-NCV	54.3750	4.2876	
ms-DL (shunt+)	3.6055	0.8023	<0.01
us-DL	3.2010	0.4025	
ms-DL (shunt–)	3.5034	0.3599	<0.01
us-DL	3.2010	0.4025	
ms-NCV (shunt+)	51.2609	6.4612	>0.05
us-NCV	54.4613	8.7651	
ms-NCV (shunt–)	49.6769	10.0865	>0.05
us-NCV	52.4613	8.7651	

mm: median motor; um: ulnar motor; ms: median sensory; us: ulnar sensory

The serum β2m levels were measured by enzyme-linked immunosorbent assay and found elevated in all cases (mean: 12.53±0.99 mg/dl, min: 10.63, max: 14.03, normal <0.3 mg/dl). There was no correlation between serum β2m levels and the EMG findings of the patients. Neither could we find any correlation between the presence of CTS and/or neuropathy and factors such as age, sex, duration of the dialysis, and site of the vascular access.

Table III. The comparison of the electrophysiological results of the hemodialysis patients and the controls

	Patients mean ± Std. Dev.	Controls mean ± Std. Dev.	P
mmDL	3.75±0.73	3.41±0.37	<0.05
mm-am,p	9.31±4.03	7.01±2.35	<0.05
mm-NCV	49.55±5.28	56.60±4.90	<0.05
ms-DL	3.60±0.80	3.29±0.28	<0.05
ms-amp	21.27±8.33	30.24±12.17	<0.05
ms-NCV	51.26±6.46	59.35±4.61	<0.05
um-DL	3.21±0.45	2.97±0.35	<0.05
um-amp	10.46±3.59	8.41±1.34	<0.05
um-NCV	54.37±4.29	60.95±5.42	<0.05

mm: median motor; ms: median sensory; um: ulnar motor
DL: msec; Amp: μvolt; NCV: m/sec

Discussion

The development of CTS has become an increasingly recognized problem in patients who are treated by long-term hemodialysis, and the incidence in large groups of dialysis patients has been reported to range from 2 to 31 per cent (2, 4). Also, long term hemodialysis patients have been reported to have an incidence of peripheral neuropathy as high as 25%, and this correlation may render the nerves more sensitive to physical or vascular damage (2).

Bicknell et al. (1) studied median, ulnar and peroneal NCVs in 46 patients who had been on chronic peritoneal or hemodialysis for varying lengths of time. Only 6 patients had normal findings, thirtyseven (80%) had peripheral polyneuropathy, sixteen (35%) had subclinical median mononeuropathy and 9 (20%) had overt CTS. They found that nerve dysfunction was independent of the disease underlying the renal failure, the side of the dialysis access shunt, and the presence or absence of osteodystrophy. Gilbert et al. (2) evaluated 485 patients who were receiving long-term renal hemodialysis, and in 46 (9%) of these, found CTS in at least one hand. Their study also revealed that there was no correlation between the time of onset of CTS and such factors as the patient's age, sex, or race, the cause of renal failure, the site of vascular access for hemodialysis, or parathyroidectomy history. Schwarz et al. (9) examined 145 patients on hemodialysis for periods of 1 month to 16 years for CTS, and detected typical symptoms and clinical manifestations of CTS, either unilaterally or in both hands, in 21 (15%) of these patients. They established a highly significant correlation between the incidence of CTS and the duration of dialysis. They also reported immediate relief of pain after carpal tunnel release in 8 of the 21 patients. Spertini (10) found 12 CTS among 100 patients treated by chronic hemodialysis, and reported dramatic improvement of pain and paresthesiae within a few hours after surgery. In his study, no relationship could be established between CTS and the type of nephropathy, the severity of polyneuritis, and the presence of vascular access. Kessler et al. (3) conducted a survey in 19 centers in France among 171 patients receiving hemodialysis for over 10 years and found 32% CTS which increased with the duration of dialysis.

In our study, we had similar results as in the literature. Among 30 patients who had been treated by hemodialysis for a mean duration of 4.5 years, nine (30%) were found to have pure CTS and 3 (10%) to have CTS with neuropathy. Of the 12 patients having CTS, four were bilateral. Also 9 (30%) patients had neuropathy verified by slower conduction velocities of the median motor and/or sensory nerves. When the differences between the means of EMG results (patients vs normal controls) were calculated, significant difference was found in all parameters studied. The serum β2m levels were elevated in all patients and there was no significant correlation between the presence of CTS and/or neuropathy and factors such as age, sex, duration of the hemodialysis, site of vascular access, and serum β2m levels.

Munoz-Gomez (11) reported CTS in 4 of the 7 patients with chronic renal failure treated by periodic hemodialysis, and showed amyloid deposits in specimens removed during CTS surgery. McClure (12) examined the excised material from decompression surgeries of the CTS in 3 patients receiving long-term hemodialysis. He reported that the excised material contained amyloid, which by immunocytochemical techniques was shown to contain β2m.

β2m is a small protein which is present in normal biological fluids. Its protein nature would allow it to undergo pleating to give the appropriate physical properties of an amyloid. It is increased in the serum of patients undergoing long term hemodialysis, presumably because it will not pass through conventional dialysis membranes (12). A report by Chanard (13) indicates that dialysis with a polyacrylonitrile An69 membrane instead of a cuprophane membrane may reduce β2m levels, amyloid deposition and median nerve dysfunction. If such membranes come into wider use, it will be interesting to see whether the incidence of overt CTS and subclinical median nerve dysfunction is reduced and whether β2m levels and periarticular manifestations of amyloidosis are likewise lessened.

The significance of subclinical median neuropathy is not certain yet. It can be a random variation in latency or a part of early polyneuropathy. In our patients with normal findings, there were differences between median and ulnar latency; the median DL being greater than the corresponding ulnar DL. Similarly in the neuropathy group, the median motor latency exceeded the ulnar. We think that subclinical median neuropathy identified by EMG may be an indicator of the subsequent overt CTS.

Taken together, the relationship of CTS to dialysis suggests that this complication is related to the dialysis procedure, favored partly by the vascular access, but mostly by yet unknown general metabolic or toxic factors. Management of the CTS has not been altogether satisfactory. The application of a splint to the wrist, particularly at night is often useful for mild symptoms. The respoonse to injection with local anesthetic agents and corticosteroids is only transient, while surgical decompression of the median nerve has been of the greatest benefit to patients with marked disability and pain from CTS. In patients who need surgical decompression for CTS, the results of treatment are best when the symptoms have been present only a short time. Once motor and sensory deficits develop, the responce is poor or nonexistent. Accordingly, nerve conduction studies should be started early and repeated regularly on all dialysis patients.

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