

Why does Carpal Tunnel Syndrome Still Occur in our Chronic Hemodialysis Patients?

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Abstract

Despite the numerous advances in hemodialysis practice, cases of CTS are still observed in our patients. The aim of this study was to assess the prevalence of CTS and factors associated to its occurrence in our chronic HD patients.

Methods: We performed a cross-sectional study in December 2017, including consenting chronic hemodialysis patients, with a dialysis vintage of at least three months, in a reference state center in Oujda- Eastern Morocco. Diagnosis was based on signs and symptoms reported by the patient, and manoeuvres of Tinel and Phalen. Symptomatic patients underwent electromyography (EMG) on non-dialysis days, by the same neurologist in the same conditions.

Results: Our study included 112 chronic HD patients, who met the inclusion criteria. CTS was diagnosed and verified using nerve conduction examination in 8.04% of the patients. Diabetic nephropathy was the most observed initial nephropathy in CTS patients in 36.3% of the cases. Patients with CTS were older (mean age: 52.99 ± 11.32 vs. 48.4 ± 12.6 ; $p=0.002$), mainly males (63.6% vs. 55.4%; $p=0.03$), active smokers in 18.5% of the cases. They also had a longer HD duration (95.8 ± 15.75 vs. 82.11 ± 17.22 months; $P<0.001$). Moreover, CTS patients had higher diabetes mellitus prevalence (36.3% vs. 13.8%; $p<0.001$), higher HCV prevalence (18.18% vs. 2.97%; $p=0.02$), and were less likely to have a urine output >100 ml/day (27.2% vs. 3.98%; $P=0.003$). Multivariate logistic regression showed that HCV (OR: 1.45, 95% confidence interval (CI): 1.17-1.87, $p=0.034$), HD vintage [OR: 1.95, 95% CI: 1.89-3.65, $P<0.001$] and urin output <100 ml/day (OR:1.72, 95% CI: 1.03-2.57, $P=0.01$) were positively associated with CTS.

Conclusion: In this cross-sectional study, we observed that a long dialysis vintage, positive HCV and loss of residual renal function were associated with CTS in chronic HD patients. However, additional studies are required for further clarification of the pathogenesis of CTS in chronic HD patients.

Keywords: Carpal Tunnel syndrome; Hemodialysis; Renal disease; Kidney disease

Introduction

Carpal tunnel syndrome (CTS) is a well-known manifestation of dialysis related amyloidosis, mainly caused by the deposition of β_2 -microglobulin in the carpal tunnel. It is considered as the most common mononeuropathy in endstage renal disease (ESRD) patients [1,2]. A long duration of hemodialysis (HD) as well as increased plasma beta-2-microglobulin (BMG) are believed to play an important role in its development in HD patients [3]. Nevertheless, the exact causes leading to CTS occurrence remain unclear. Diagnosis is based on both clinical signs and nerve conduction findings. Dialysis improvement and renal transplantation represent the best prevention while surgery remains the most performed curative treatment [4]. Although our hemodialysis practice has witnessed big advances with the use of high efficiency biocompatible membranes and a high water quality, cases of CTS are still observed in our patients.

The aim of this study was to assess the prevalence of CTS and factors associated to its occurrence in our chronic HD patients.

Patients and Methods

We performed a cross-sectional study in December 2017, including consenting chronic hemodialysis patients, with a dialysis vintage of at least three months, in a reference state center in Oujda Eastern Morocco.

Diagnosis was based on signs and symptoms reported by the patient such as paresthesia and pain in the median nerve territory.

Manoeuvres of Tinel and Phalen were used on both hands and were considered positive if they reproduced spontaneous pain or paresthesia in the thumb, forefinger and middle finger, which represent the territory of the median nerve. A sensory deficit in the median nerve territory as well as amyotrophy of external thenars were noted.

Demographic and biology data were collected from patients medical records. The latter included-reactive protein (CRP), intact parathyroid hormone (PTH 1-84).

Symptomatic patients underwent electromyography (EMG) on non-dialysis days, by the same neurologist in the same conditions.

Definitions

Tinel's sign: The examiner taps over the median nerve as it passes through the carpal tunnel in the wrist. A sensation of tingling in the distribution of the median nerve over the hand is considered as a positive response [5].

Phalen's maneuver: The patient allows wrist to fall freely into maximum flexion and maintains the position for 60 seconds or more. A sensation of tingling in the distribution of the median nerve over the hand is considered as a positive response [5].

Electrodiagnosis: A prolonged sensory and/or motor latency from the wrist to digits innervated by the median nerve was the electrophysiological diagnostic criterion of CTS [3].

- CRP >5 mg/l was considered positive.
- Hyperparathyroidism was defined, according to the KDIGO guidelines, by PTH 1-84 >9 times the upper normal limit of the laboratory.

Statistical analysis

Data were analyzed using SPSS version 20.0 for Windows. Patients were divided into two groups according to the presence or absence of

CTS. Categorical variables were expressed as percentages and Continuous variables as mean \pm standard deviation. Chi-square or Fisher exact tests were used for analyzing the correlation among categorical variables. Comparisons between 2 groups were performed using the Mann-Whitney U test and Student t test. Univariate and multivariate logistic regression analyses were performed to evaluate variables related to CTS, The level of significance was set at $P < 0.05$.

Results

Our study included 112 chronic HD patients, who met the inclusion criteria. Carpal tunnel syndrome was diagnosed and verified using nerve conduction examination in 11 patients, which represents 8.04% of our patients. Diabetic nephropathy was the most observed initial nephropathy in CTS patients with 36.3% of the cases, followed by polycystic kidney disease in 27.2% of the cases, chronic vascular nephropathy in 18.1% of the cases, whereas 27.2% of the cases were of undetermined origin.

The mean age of patients with CTS was 52.99 ± 11.32 years, whereas the unaffected patient group had a mean age of 48.4 ± 12.6 years. Dialysis vintage in the CTS group ranged from 47-118 months, with a mean duration of 95.8 ± 5.75 months (Table 1). Patients with CTS, had a sex ratio M/F: 1.75 (7 males, 4 females), a mean BMI of 25.13 ± 3.2 kg/m². Active smoking was reported in 22.2% of them while no history of wrist trauma was found.

Parameters	Total (n=112) Mean \pm SD/Median
Demographics	
Age (years)	49.9 \pm 17.32
Male gender	63
Body mass index (Kg/m ²)	23.4 \pm 2.04
Smoking (yes)	10.70%
Co-morbidities	
Diabetes mellitus	16.90%
Hypertension	62.70%
Previous CVD	15.10%
HBV	1.78%
HCV	5.35%
CTS dialysis related data	
HD vintage (months)	86.2 \pm 18.2
Erythropoietin U/Kg/week	66.6 \pm 36.7
Arterio-venous fistula	75.89%
Kt/v urea (Daugirdas)	1.39 \pm 0.25
Residual daily urine	>100 ml 37.5%
Biological data	
Hemoglobin (g/dl)	10.27 \pm 1.22

Serum albumin (g/dl)	40.2 ± 1.24
Creatinin (mg/dl)	89.21 ± 29.4
Cholesterol (mg/dl)	1.75 ± 0.56
LDL (mg/dl)	0.98 ± 0.48
Triglyceride (mg/dl)	1.69 ± 0.81
Ferritin (ug/l)	347.12 ± 268
Corrected-calcium (mg/dl)	89 ± 8.21
Phosphate (mg/dl)	49.2 ± 11.52
Intact parathyroid hormone (pg/ml)	356.9 ± 317.84
CRP (mg/l)	5.41 ± 4.79

Table 1: Baseline characteristics of chronic hemodialysis patients.

All patients underwent maintenance hemodialysis, nine hours (two sessions) a week in 31.25% of the cases and twelve hours a week (three sessions) in 68.75% of the cases, with the same type of High efficiency low permeability polysulfone membrane. 75.84% of the patients had arteriovenous fistula, which was located on the non-dominant side in 88.2% of them. 36.6% of the patients developed CTS in the AV fistula wrist, while in 45.4% of the patients it was located on the opposite side, and it was bilateral in 17.8% of the patients. All patients with CTS reported tingling, numbness, and pain in the first 3 radial digits. They also complained of muscle weakness and paresthesia. The latter was exacerbated at night. Moreover, all these functional signs increased during dialysis. Besides, the diagnosis of CTS was supported by positive Tinel and Phalen Tests in 63.6% and 54.5% respectively. Nerve conduction studies revealed prolonged distal sensory and motor latencies from the wrist to digits, innervated by the median nerve.

All patients with CTS underwent surgical release procedure. Histological examination of biopsy specimens collected at the time of CTS surgery showed signs of amyloid deposits in 72.7% of the patients.

Two to three days after surgical release procedure, we observed clinical improvement with the disappearance of pain and paresthesia in all patients. Nonetheless, regression of sensory and motor deficiencies was slower to achieve and took 5-6 months.

Subgroup analysis for CTS patients and unaffected ones is presented in Table 2. The patients with CTS were older (mean age: 52.99 ± 11.32 vs. 48.4 ± 12.6; p=0.002), mainly males (63.6% vs. 55.4%; p=0.03), active smokers in 18.5% of the cases vs. 8.9% of unaffected patients (p=0.02). They also had a longer HD duration (95.8 ± 15.75 vs. 82.11 ± 17.22 months; P<0.001). Moreover, CTS patients had higher diabetes mellitus prevalence (36.3% vs. 13.8%; p<0.001), higher HBV prevalence (9.09% vs. 0.99%; p<0.001), higher HCV prevalence (18.18% vs. 2.97%; p=0.02), higher PTH1-84 level (455.09 ± 117.29 vs. 358.03 ± 212.45 pg/mL; P<0.001), and less patients with urine output >100 ml/day (27.2% vs. 3.98%; P=0.003).

Parameters	Patients with CTS (n: 11; 9.8%)	Patients without CTS (n: 101; 90.17%)	p
Age (years)	52.99 ± 11.32	48.4 ± 12.6	0.061
Male sex (%)	63.60%	55.40%	0.03
Body mass index (kg/m ²)	25.13 ± 3.2	23.02 ± 4.14	0.65
Smoking	18.10%	8.90%	0.02
Diabetes mellitus	36.30%	13.80%	<0.001
Hypertension	54.50%	49.50%	0.16
Previous CVD	36.30%	20.70%	0.07
HBV (%)	9.09%	0.99%	<0.001
HCV (%)	18.18%	2.97%	0.02
Hemodialysis vintage (months)	95.8 ± 15.75	82.11 ± 17.22	<0.001
Arteriovenous fistula (%)	81.80%	74.20%	0.06

Erythropoietin, U/kg/wk	62.21 ± 31.9	67.2 ± 34.2	0.19
Kt/V Daugirdas	1.41 ± 0.27	1.38 ± 0.39	0.06
Urine output >100 cc/d	27.20%	39.60%	0.03
Hemoglobin, g/dL	10.28 ± 1.19	10.21 ± 1.52	0.2
Albumin, g/dL	40.01 ± 1.13	40.31 ± 1.05	0.46
Creatinine, mg/dL	88.9 ± 21.17	90.07 ± 27.15	0.09
Ferritin, mg/L	217.09 ± 187.04	349.2 ± 147.02	0.42
Corrected calcium, mg/dL	86.22 ± 9.23	91.07 ± 10.19	0.81
Phosphate, mg/dL	52.5 ± 14.26	49.57 ± 12.42	0.09
Intact parathyroid hormone, pg/mL	455.09 ± 117.29	358.03 ± 212.45	<0.001
CRP, mg/L	7.42 ± 6.81	5.68 ± 3.71	0.07
Cholesterol, mg/dL	1.62 ± 0.22	1.78 ± 0.15	0.13
Triglyceride, mg/dL	1.58 ± 0.18	1.7 ± 0.08	0.21
LDL, mg/dL	0.99 ± 0.26	0.95 ± 0.13	0.07

Table 2: Subgroup analysis for CTS patients and patients without CTS.

Predictors of CTS by univariate logistic regression (Table 3)

Univariate logistic regression analyses showed that male sex, smoking, HBV, HCV, HD vintage, urine output <100 ml/day, and log iPTH were positively associated with CTS.

Parameters	Univariate logistic regression	
	Odds ratio (OR), 95% confidence interval (CI)	p
Age (years)	1.07 (0.83, 1.12)	0.082
Male sex	3.19 (1.54, 4.2)	0.03
Body mass index (kg/m ²)	1.07 (0.79, 1.02)	0.6
Smoking (yes)	2.71 (1.52, 5.2)	0.021
Diabetes mellitus (yes)	1.31 (1.06, 1.34)	<0.001
Hypertension (yes)	1.81 (0.61, 3.79)	0.24
Previous CVD (yes)	0.92 (0.61, 3.28)	0.313
HBV (yes)	2.04 (1.69, 4.27)	<0.001
HCV (yes)	1.459 (1.53, 1.96)	0.02
Hemodialysis vintage (months)	1.25 (1.03, 1.73)	<0.001
Arteriovenous fistula (yes)	1.04 (0.85, 1.94)	0.07
Kt/v urea	1.46 (0.81, 2.9)	0.08
Urine output >100ml/day	0.31 (0.14, 0.67)	0.028
Hemoglobin (g/dl)	1.65 (0.79, 4.01)	0.27

Albuminemia <40 (mg/l)	1.51 (0.69, 2.51)	0.52
Serum Creatinin (mg/l)	0.94 (0.75, 1.09)	0.45
Corrected Calcium	1.11 (0.82, 1.41)	0.79
Phosphate (mg/l)	0.65 (0.52, 1.03)	0.08
Log intact parathyroid hormone	2.17 (1.85, 4.14)	<0.001
CRP >5mg/l	1.15 (0.63, 1.29)	0.06
Cholesterol (mg/l)	1.03 (0.63, 1.08)	0.09
Triglyceride (mg/l)	1.07 (0.74, 1.25)	0.19

Table 3: Univariate logistic regression analysis of CTS in our patients.

Predictors of CTS by multivariate logistic regression (Table 4)

Multivariate logistic regression including variables with P<0.05 in univariate logistic regression showed that HCV (OR: 1.45, 95%

confidence interval (CI): 1.17-1.87, p=0.034), HD vintage [OR: 1.95, 95% CI: 1.89-3.65, P<0.001] and urine output <100 ml/day (OR: 1.72, 95% CI: 1.03 -2.57, P=0.01) were positively associated with CTS.

Parameters	Odds ratio	95% confidence interval (CI)	P value
Male sex (yes)	0.82	(0.45, 2.60)	0.067
Smoking (yes)	2.06	(0.9, 3.8)	0.231
Diabetes mellitus (yes)	0.98	(0.78, 1.49)	0.09
HVB (yes)	1.58	(0.92, 2.26)	0.17
HVC (yes)	1.45	(1.17, 1.87)	0.034
Hemodialysis vintage (months)	1.95	(1.89, 3.65)	<0.001
Urine output <100 ml/day	1.72	(1.03, 2.57)	0.01

Table 4: Multivariate logistic regression analysis between CTS and clinical variables in MHD patients.

Discussion

Despite the improvement of our hemodialysis practice, CTS still occurred in 8.04% of our chronic HD patients, that were older with a mean age of 52.99 ± 11.32 and predominantly males (sex ratio M/F: 1.75). Multivariate logistic regression showed that positive HCV, long hemodialysis vintage and urine output <100 ml/day were significantly associated with CTS.

In fact, in spite of its occurrence, CTS was not frequent in our study, compared to published data that reported a prevalence of CTS of approximately 8% to 31% in HD patients [6,7].

Hemodialysis vintage is correlated with CTS prevalence. In Jadoul et al. study, increasing prevalence of histologically proven CTS with dialysis vintage was demonstrated. A study assessing long-term HD found that CTS developed in 50% of patients after a mean HD duration of 133.2 months [8,9]. In our study, the mean HD duration was 95.8 ± 5.75 months, which is shorter than what was reported in other studies; therefore, it could be an explanation of the lower CTS prevalence in our patients, which was approximately 8.04%.

Besides there's also a positive correlation between HCV infection and CTS in HD patients, that was observed in previous studies [6]. As

the longer the patients are dialyzed, the higher are their probabilities of HCV infection. In the current study, patients with HCV infection were more likely to develop CTS.

According to several authors, absence of residual renal function (RRF) is linked to CTS. In fact, β2M is cleared by glomerular filtration and subsequent proximal tubular reabsorption and catabolism; therefore, decrease in kidney function, and the consequent reduction in RRF, leads to progressive increase in the plasma levels of β2M. In our study, urine output <100ml/min was positively associated to CTS [8-10].

Other parameters as male sex, diabetes mellitus, positive HBV and intact parathormone were positively associated to CTS in univariate logistic regression analysis. Nonetheless, after using multivariate logistic regression, these associations were not observed.

Besides, Huang et al. investigated in a recent study the association between chronic inflammation, malnutrition and CTS in hemodialysis patients, and found out these parameters were positively linked to CTS [6]. In fact, the immune system is chronically stimulated in chronic kidney disease, and hemodialysis represents an additional factor in promoting inflammation [8]. Most our patients did not present neither hypoalbuminemia nor inflammation due probably to the use of

biocompatible high flux membranes and a high quality water as established by previous reports [11].

Conclusion

In this cross-sectional study, we observed that a long dialysis vintage, positive HCV and loss of residual renal function were associated with CTS in chronic HD patients. Surgical release procedure of the wrist is an effective treatment method. However, additional studies are required for further clarification of the pathogenesis of CTS in chronic HD patients.

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