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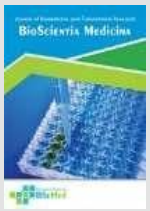

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Relationship of Parathyroid Hormone Levels with Uremic Neuropathy in Chronic Kidney Disease Patients

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A B S T R A C T

Background: Parathyroid hormone is known as one of the main uremic toxicants, which, if the amount increases in plasma, will affect motor conduction in patients with chronic kidney disease. This study aims to determine the relationship between Parathyroid hormone levels with uremic neuropathy in patients with chronic kidney disease. **Methods:** This study was an analytic observational study with a cross-sectional approach, where as many as 42 subjects participated in this study. Data analysis was performed using SPSS using univariate and bivariate, with $p<0.05$. **Results:** There was a difference in the average thyroid hormone levels in neuropathy and without neuropathy, but statistically, it was not different $p>0.05$. **Conclusion:** There is no relationship between parathyroid hormone and uremic neuropathy in patients with chronic kidney disease.

1. Introduction

Peripheral neuropathy is a problem of the nerves outside the brain or spinal cord that causes numbness, numbness, swelling, or weakness in several parts of the body. Problems can arise from various conditions, one of which arises due to chronic kidney disease, whose neuropathy is also known as uremic neuropathy. Uremic neuropathy is a distal polyneuropathy of the sensorimotor type that usually affects the lower limbs symmetrically and is caused by length-dependent axonal degradation and secondary loss of focal myelin sheaths. The incidence of uremic neuropathy ranges from 50-100% in patients with chronic kidney disease. Of the number of patients with chronic kidney disease undergoing hemodialysis, 60-100% have uremic neuropathy. The high rate of uremic neuropathy, even in people who have already had hemodialysis, is possible because the medium-sized neurotoxic molecules are not properly dialyzed by the hemodialysis membrane.[1-5]

Prolonged exposure of peripheral nerves to calcium produced due to increased parathyroid hormone can result in the accumulation of calcium in the nerves and can cause peripheral neuropathy. Several studies suggest that the parathyroid hormone is believed to play a role in the initiation of peripheral neuropathy. Increased levels of parathyroid hormone in the body can result in disturbances in nerve conduction parameter values. Nerve conduction parameters reflect the conduction of the fastest nerve fibers, which generally originate from motor nerve fibers.

Parathyroid hormone is known as one of the main toxic uremic, which, if the amount increases in plasma, will affect motor conduction in patients with chronic kidney disease.[6-10] This study aims to determine the relationship between Parathyroid hormone levels with uremic neuropathy in patients with chronic kidney disease.

2. Methods

This study was an analytic observational study with a cross-sectional approach. A total of 42 research subjects were included in this study. The study subjects met the inclusion criteria: patients diagnosed with chronic kidney disease and patients who had undergone routine hemodialysis and were willing to be included in this study. This study was approved by the medical and health research ethics committee at Dr. M. Djamil General Hospital, Padang, Indonesia (No. 608/UN.16.2/KEP-FK/2022).

Chronic kidney disease is defined as kidney damage or a glomerular filtration rate (GFR) <60 ml/minute/1.73 m^2 for 3 months or more regardless of the cause, where the diagnosis is made by a specialist in internal medicine, a hypertension kidney consultant. Parathyroid hormone was assessed using the Enzyme-linked Immunosorbent Assay (ELISA) method, according to the instructions and the ELISA kit manufacturer's manual (Cloud Clone®). Normal thyroid hormone values: 10-65 pg/nl, and thyroid hormone levels increase when ≥ 66 pg/nl. The nerve conduction parameters assessed in this study are distal latency (ms) which is the time required for an impulse to travel from the stimulation point to the electrode; amplitude (mv) is a reflection of the variation in diameter and degree of myelination of all the axons that make up a nerve; Velocity(m/s) is the ratio of the distance between the two electrodes to the time it takes for the nerve impulse to pass through them. Data analysis was carried out with the help of SPSS 25. Univariate analysis was carried out to present the distribution of the variable frequency of the test data. Bivariate analysis was carried out to determine the relationship between the test variables, with $p < 0.05$.

3. Results

Table 1 shows the basic characteristics of the research subjects. It was found that 32 out of 42 respondents with chronic kidney disease had peripheral neuropathy/uremic disorders. The mean level of parathyroid hormone was found to be higher in patients with chronic kidney disease without peripheral neuropathy. The picture of nerve conduction also shows that nerve conduction is decreased in peripheral neuropathy conditions. Table 2 shows the relationship between parathyroid hormone and neuropathy. There was a difference in the average thyroid hormone levels in neuropathy and without neuropathy, but statistically, it was not different, $p>0.05$.

4. Discussion

This study shows that there is no relationship between parathyroid hormone levels and peripheral neuropathy. Parathyroid hormone levels were also found to be higher in the group without neuropathy, namely 172 (74.6-488.1) mg/dl. There was no significant difference in each of these groups with a $p>0.05$. This is in line with studies that found that the values of each electroneurographic parameter did not show any correlation with parathyroid hormone levels and concluded that parathyroid hormone does not appear to always play a role in the etiology of uremic neuropathy.[11,12] It is suspected that there are still many uremic toxins that can affect the occurrence of peripheral neuropathy. In another study regarding the relationship between electrophysiological parameters of uremic polyneuropathy and uremic toxins in patients with chronic kidney disease, it was found that the average value of parathyroid hormone levels in patients with chronic kidney disease who were included in the study was 169.12 ± 172.85 pg/mL.[13,14]

Table 1. Characteristics of research subjects.

Characteristics		Neuropathy (%)	No Neuropathy (%)
Gender			
Male		19 (59%)	2 (20%)
Female		13 (41%)	8 (80%)
Age (years), Median (min-max)		56 (21-71)	44 (34-60)
< 50 years		13 (40%)	7 (70%)
> 50 years		19 (60%)	3 (30%)
Hemodialysis duration			
< 28 months		19 (59%)	7 (60%)
≥ 28 Months		13 (41%)	3 (40%)
Parathyroid hormone (Mean, Min-Max)		151.20 (83.2-495.8)	172 (74.5 – 488.1)
Median nerve	Distal latency (ms)	4.5 ± 1.5	3.4 ± 0.6
	Amplitude (mV)	5.9 ± 3.3	9.8 ± 1.6
	Velocity (m/s)	45.6 ± 10 .6	50.2 ± 16.1
Ulnar nerve	Distal latency (ms)	4.6 ± 1.2	2.4 ± 0.4
	Amplitude (mV)	4.3 ± 0.9	8.6 ± 2.4
	Velocity (m/s)	46.7 ± 11	53 ± 4.1
Right peroneal nerve	Distal latency (ms)	6.7 ± 3	4 ± 0.7
	Amplitude (mV)	1.4 ± 1.7	4.1 ± 2
	Velocity (m/s)	32.4 ± 11.3	46.6 ± 6.5
Left peroneal nerve	Distal latency (ms)	7.1 ± 2.6	4.2 ± 1
	Amplitude (mV)	1.2 ± 1.1	3 .7 ± 1
	Velocity (m/s)	30 ± 11.3	45.4 ± 6
Right tibial nerve	Distal latency (ms)	5.4 ± 2.1	3.9 ± 1
	Amplitude (mV)	6.4 ± 5	16.2 ± 5
	Velocity (m/s)	35.3 ± 9.2	44.4 ± 5.4
Left tibial nerve	Distal latency (ms)	5.3 ± 2.1	4.1 ± 0.6
	Amplitude (mV)	7 ± 5.4	16.1 ± 4.9
	Velocity (m/s)	34.6 ± 7.7	46.8 ± 5.1
Median sensory nerve	Distal latency (ms)	5 ± 2	3.3 ± 0 .5
	Amplitude (μV)	18.7 ± 11.1	33.8 ± 11.2
	Velocity (m/s)	37.9 ± 14.7	55 ± 10.1
Ulnar sensory nerve	Latency (ms)	4.2 ± 1.8	2.8 ± 0.4
	Amplitude (μV)	22.3 ± 23	36.5 ± 12.1
	Velocity (m/s)	44.9 ± 16.5	70.2 ± 31
Right sural nerve	Latency (ms)	7.9 ± 2.6	2.6 ± 1
	Amplitude (μV)	2.7 ± 3.3	21.2 ± 6.4
	Velocity (m/s)	28 ± 14	64 ± 11.3
Left sural nerve	Distal latency (ms)	7.5 ± 2.8	2.5 ± 0.4
	Amplitude (μV)	3.3 ± 4.5	19.2 ± 11.6
	Velocity (m/s)	31.2 ± 19.5	69 ± 13,3

Table 2. Relationship between parathyroid hormone and neuropathy.

	Neuropathy	No Neuropathy	P
Parathyroid hormone (pg/nL)	151.20 (83.2-495.8)	172 (74.5 – 488.1)	0.637

*Mann-Whitney, p <0.05.

This study correlated serum parathyroid hormone levels of chronic kidney disease patients with nerve conduction parameters but found no significant correlation between these parameters.[15,16] This shows that even though there was a tendency to increase parathyroid hormone in the neuropathy and without neuropathy groups, the increased parathyroid hormone concentration did not significantly affect

neuropathy. It is suspected that there are other factors that can also be the cause of neuropathy in patients with chronic kidney disease. One of the factors that cause neuropathy in patients with chronic kidney disease is the presence of uremic toxins that are able to enter the endoneurial space and cause direct nerve damage, with hydroelectrolytic changes that result in shrinkage or expansion of the endoneurial space. This gives rise to motor and sensory axons in patients with uremic neuropathy who experience chronic depolarization prior to dialysis. Other studies further corroborate that there is a link between creatinine clearance and the severity of the decreased nerve conduction velocity present in uremia. It is known that neuropathy is caused by the accumulation of medium-sized molecules (300 to 12,000 Daltons), which are dialyzed more slowly than urea and creatinine.[17,18] In contrast, ultrafiltration which removes most of the medium-sized molecules, increases NCV (Nerve Conduction Velocity) and clinical parameters. The results of this study are supported by other studies which suggest that nerve dysfunction is related to the content of uremic serum toxic factor, which inhibits axon membrane function and activation of Na+/K+ATPase pumps. It can be concluded that apart from increasing parathyroid hormone, neuropathy in patients with chronic kidney disease is also caused by uremic toxins and the accumulation of other uremic toxin molecules measuring 300-12,000 Daltons.[19,20]

5. Conclusion

There is no relationship between parathyroid hormone and uremic neuropathy in patients with chronic kidney disease.

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