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Relationship Between Serum Magnesium and Parathyroid Hormone Levels in Hemodialysis Patients

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Abstract: Objective: The aim of this study is to investigate the relationship between serum magnesium and parathyroid hormone levels in hemodialysis patients. In addition to, study the prevalence of parathyroid disorders among hemodialysis patients.

Methods: it is (Cross- Sectional) Study conducted for the period of one year (May 2019 –May 2020) at Tishreen University Hospital in Lattakia- Syria. The study included 82 patients with chronic kidney disease (CKD) undergoing hemodialysis, Laboratory analysis of calcium; phosphorous, magnesium and parathyroid hormone were conducted for all patients before starting the dialysis session. The values of PTH were compared according to the serum magnesium, we also studied the prevalence of parathyroid disorders among hemodialysis patients.

Results: The mean age was (51.62 years), and the mean duration of dialysis was (4.09 years), and (60% males, 40% females). We found in all patients normal or high serum magnesium, (36.58 % normal, 63, 42 % high), the mean of magnesium (2.78 mg/dl), and the mean of PTH (295 Pg/ml), mean of calcium (8.64 mg/dl), mean of phosporous (5.6 mg/dl). we found statistically significant differences in PTH between the group of patients with normal magnesium and the group with hypermagnesium (Mg>2.5 mg/dl), where the mean PTH values were (339.4 ± 68 pg/ml) in the normal magnesium group, and the mean PTH was (272.3 ± 43 pg/ml) in the hypermagnesium group (P.value=0.01).We found a negative linear correlation between magnesium and PTH (r=- 0.311, p=0.03), We also found that the values of PTH were outside the acceptable range (2- 9 times the upper normal limit) in (24.4%)of patients.

Conclusions: There is a statistically significant inverse relationship between serum magnesium and PTH, and this relationship is independent of calcium and phosphorous

Keywords: chronic kidney disease, magnesium, PTH, Hemodialysis.

العلاقة بين مغنزيوم المصل ومستويات هرمون جارات الدرق عند مرضى التحال الدموي

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المستخلص: الهدف: هدفت الدراسة الى فحص العلاقة بين مغنزيوم المصل ومستويات هرمون جارات الدرق عند مرضى التحال الدموي. بالإضافة إلى دراسة شيوع اضطرابات جارات الدرق عند مرضى التحال الدموى.

طرائق البحث: كانت هذه دراسة (مقطعية- عرضانية) أجريت في مشفى تشرين الجامعي في اللاذقية- سوريا خلال الفترة الممتدة ما بين أيار 2019- أيار 2020. شملت الدراسة 82 من مرضى القصور الكلوي المزمن والموضوعين على التحال الدموي، أجريت التحاليل المخبرية لكل من الكالسيوم والفوسفور والمغنزيوم وهرمون جارات الدرق (PTH) لكل المرضى قبل البدء بجلسة التحال، تمت مقارنة قيم ال PTH بحسب تركيز مغنزيوم المصل عند المرضى، كما قمنا بدراسة شيوع اضطرابات جارات الدرق عند مرضى التحال الدموى..

النتائج: كان متوسط العمر 51 سنة و متوسط مدة التحال 4.09 سنة، (الذكور 60 %، والإناث 40 %)، وجد عند كل المرضى مغنزيوم المصل طبيعي أو مرتفع) 36.58 % طبيعي، 63.42 % مرتفع) وكان متوسط المغنزيوم (2.78ملغ/دل)،و متوسط ال iPTH (295 بيكوغرام/مل)، وكان متوسط الكالسيوم (8.64ملغ/دل) ومتوسط الفوسفور (5.6 ملغ/دل). كان هناك فروقات ذات دلالة إحصائية في قيم ال PTHبين مجموعة المرضى ذو مغنزيوم طبيعي وبين مجموعة المرضى ذو المغنزيوم العالى (Mg>2.5 mg/dl)، حيث كان متوسط قيم ال PTH (339.4 ± 68 pg/ml) في مجموعة المرضى ذو المغنزيوم الطبيعي، وكان متوسط PTH (272.3 ± 43 pg/ml) في مجموعة المرضى ذو مغنزيوم المصل العالى (P.value=0.01)، حيث وجد ارتباط خطي سلبي بين المغنزيوم وال PTH (r=- 0.311, p=0.03) كما وجد أن قيم ال PTHكانت خارج المجال المقبول (2- 9 أضعاف الحد الأعلى للمجال الطبيعي)عند (24.4%) من المرضى.

الاستنتاج: أظهرت الدراسة أن هناك علاقة عكسية هامة إحصائيا بين مغنزيوم المصل وهرمون جارات الدرق عند مرضى التحال الدموي المزمن. وهذه العلاقة لا تعتمد على الكالسيوم والفسفور.

الكلمات المفتاحية: هرمون جارات الدرق، الداء الكلوي المزمن، المغنزيوم، التحال الدموى.

Introduction.

Hyperparathyroidism is a common complication in patients with chronic kidney disease, and is characterized by an imbalance of calcium, phosphorous and vitamin D [1] which is associated with increased cardiovascular morbidity and mortality [2] [3] and is an economic problem in CKD patients [4]

Secondary hyperparathyroidism occurs in response to calcium and calcitriol deficiency and phosphorous retention caused by deteriorating renal function [5], and therefore, studies have focused on the role of calcium and phosphorous balance in controlling secondary hyperparathyroidism [6] [7],

Currently, many studies have shown that magnesium plays an important role in the pathophysiology of cardiovascular morbidity and mortality in patients with Chronic Kidney Disease– Mineral and Bone Disorde (CKD- MBD) [8] [9]. Several studies have also shown the association between magnesium deficiency, increased vascular calcifications, and cardiovascular mortality in patients with end- stage renal disease [10] [11]. In addition, treatment with magnesium- containing preparations contributed to a decrease in PTH secretion [12].

The studies also showed the correlation between serum and dialysate magnesium in patients with Hemodialysis (HD). When the dialysate magnesium concentration was changed from 1.8 mg/dL to 0.5 mg/dL, the mean serum magnesium concentration decreased from 2.7 mg/dL to 2.2 mg/dL, and a rise in Their PTH levels was observed [13 [14]

Therefore, interest has increased in studying the relationship between serum magnesium and parathyroid hormone, as it is believed that magnesium has a similar role to calcium in regulating PTH secretion. [15].

Studies showed that the role of hypermagnesium in inhibiting PTH secretion is greatest in the case of moderate calcium deficiency, while this inhibition was not significant in the case of hypercalcemia or severe hypocalcemia [16].

Also, severe magnesium deficiency (less than 0.5 mm/dl) has an inhibitory effect on PTH secretion, as the inhibition of intracellular protein signaling Gai/q occurs, which leads to structural activation of calcium- sensing receptor (CaSR), and this effect is constant regardless of the change in serum calcium values [17] [18].

Therefore, we aimed to study the relationship between serum magnesium concentration and parathyroid hormone levels in hemodialysis patients.

Patients and methods.

This is a cross- sectional, descriptive observational study conducted on chronic hemodialysis patients who started hemodialysis at least 3 months ago in Tishreen University Hospital between 2019-2020, The exclusion criteria were: patients who underwent partial or total parathyroidectomy, and patients taking magnesium- containing preparations.

This study included 82 patients with end- stage renal disease treated with hemodialysis, they undergo two HD sessions per week using a high- flux polysulfone dialyzer, on the Fresenius 4008S device, with a blood flow rate of 200- 250 ml/ minute, and the flow of dialysate was 500 ml/min, and the concentration of magnesium in the dialysate was 0.5 mm/l.

Laboratory tests were conducted before starting the dialysis session for Magnesium, PTH, Calciume, Phosphorous, Alkaline phosphatase, Hemoglobin, Albumine, Creatinin, Urea.

The normal range for magnesium was considered (1.7- 2.5 mg/dl), the normal range for PTH was considered (8.7- 79 Pg/ml), and the acceptable range of PTH was considered from 2- 9 times the upper limit of the normal range according to KDIGO. Total calcium values were corrected for albumin values.

Statistical Analysis

Results are presented as mean and standard deviation (SD). Differences in categorical variables were analyzed using the chi- square test. Student's t- test was used to compare the mean of quantitative variables between groups. Possible relationships between serum levels of PTH and those of Ca, P, and Mg were evaluated by linear correlation analysis. P- value less than 0.05 is considered significant. Computations were performed with the IBM SPSS statistics (Version 22).

Ethical consideration:

All patients were provided a complete and clear informed consent after the discussion about the study. This study was performed by the Declaration of Helsinki.

Results.

The demographic and clinical parameters of the 82 patients included in the study were as shown in Table (1). The mean age was (51.62 ± 15.13 y).), (49 males, 33 females). the mean of PTH was (295 ± 131.52 pg/ml), and mean of magnesium was (2.78 ± 0.49 mg/dl), 65 patients were received vitamin D, and 67 patients were received calcium carbonate as phosphate binder.

Table (1) Demographic and Clinical parameters characteristics of the study population

Age (year)	51.62 ± 15.13
Sex (female/male) (n)	33/ 49
Time on dialysis (year)	4.09 ± 2.14
Receive Vitamin D (n)	65
Receive Calcium carbonate (n)	67
Magnesium (mg/dl)	2.78 ± 0.49
iPTH (pg/ml)	295 ± 131.52
Creatinin (mg/dl)	8.75 ± 2.75
Urea (mg/dl)	125.7 ± 31.2
Hemoglobin (g/dl)	8.7± 1.59
Albumine (mg/dl)	3.95 ± 0.32
Alkaline phosphatase (mg/dl)	140.5 ± 65
Calciume (mg/dl)	8.64 ± 1.2
Phosphorous (mg/dl)	5.6 ±1.4

The etiology of end- stage renal disease (ESRD) was nephrosclerosis (35.3%), diabetic nephropathy (31.7%), chronic glomerulonephritis (6%), polycystic kidney disease (4.8%), others (drugs, congenital, ...) (8.5%), and unknown (13%), fig (1).

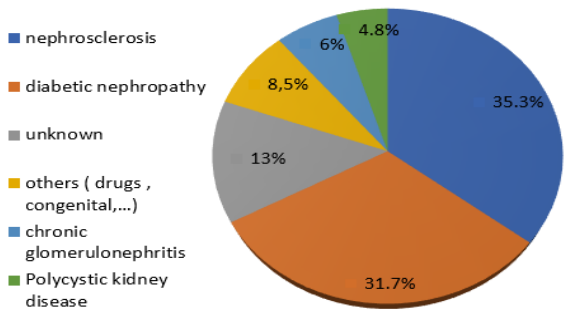

Fig (1) –etiology of end- stage renal disease (ESRD) in 82 hemodialysis patients

We classified the patients into two groups according to their serum Mg levels, 30 patients with normal Mg (mg ≤ 2.5 mg/dL) and 52 patients with high Mg (mg > 2.5 mg/dl).serum P and serum Mg level were different between the two groups (Table 2). Age, diabetes, creatinin, alkaline phosphatase (ALP), hemoglobin, albumine, calcium, and administration of vitamine D were not different between the groups. There was a significant difference between the groups for iPTH level and phosphorous.

Serum intact PTH levels showed significant inverse correlation with serum Mg level (r = –0.311; P = 0. 01), Fig (2).

Table (2) Characteristics of the 82 Patients Classified According to Serum magnesium Level

	Magnesium > 2.5 (mg/dl)	Magnesium ≤ 2.5 (mg/dl)	P.value	Test
number of patients	52	30		
Age (year)	52.6 ±15.1	49.8 ±15.1	0.2	T student
Time on dialysis (year)	4.2 ± 2.1	3.8 ± 2.3	0.25	T student
Sex (male) (n)	30	19	0.61	chi
Diabetes (n)	18	8	0.45	chi
Receive Vitamin D (n)	36	29	0.13	chi
Receive Calcium carbonate (n)	45	22	0.13	chi
iPTH (pg/ml)	272.3 ± 43	339.4 ± 68	0.01	T student
Hemoglobin (g/dl)	8.8 ± 1.7	8.6 ± 1.3	0.27	T student
Alkaline phosphatase (mg/dl)	130.0 ± 21	158.7 ±34	0.08	T student
Calciume (mg/dl)	8.8 ± 1.3	8.2 ± 0.8	0.11	T student
Phosphorous (mg/dl)	5.2 ± 1.3	6.6 ± 1.1	0.045	T student

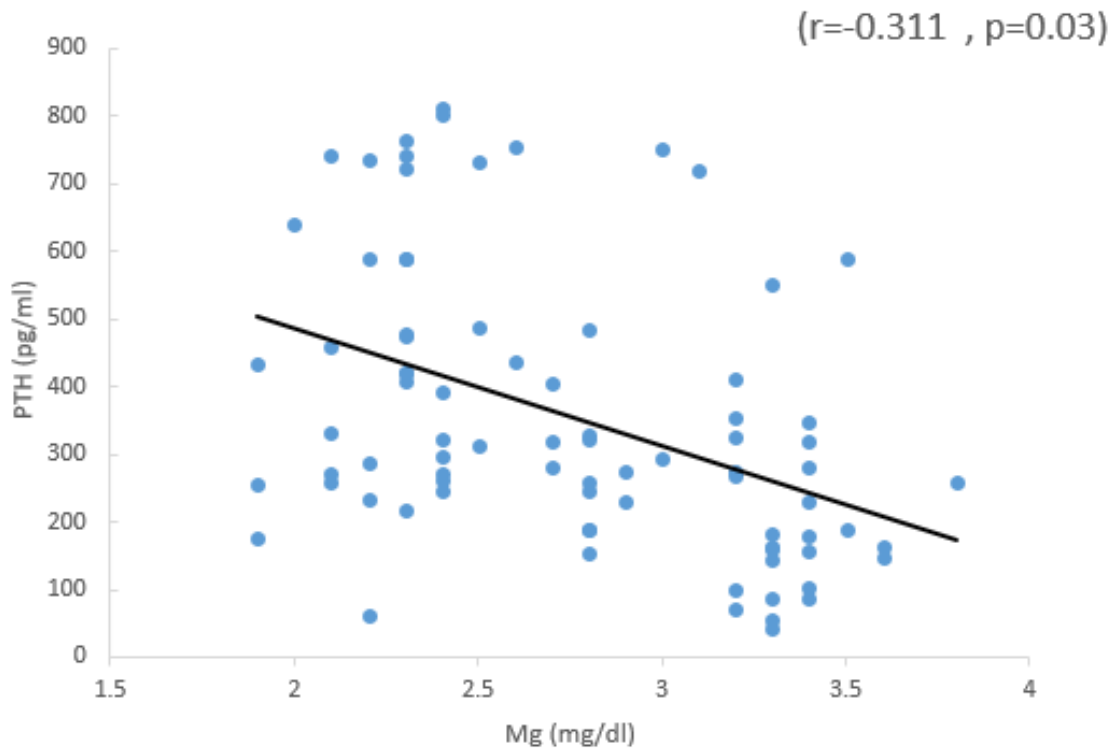

Fig (2) Relationship between serum magnesium concentration and PTH levels in 82 hemodialysis

The mean value of iPTH was 295 pg/mL.we divided patients into two groups according to iPTH level being lower or higher than the mean value. magnesium, calcium, Phosphorous, and Alkaline phosphatase level were different between the two groups (Table 2).

The serum Mg level was significantly higher in patients with low PTH levels (3.10 vs 2.69, *P*< 01).

Table (3) Characteristics of the 82 Patients Classified According to Serum Intact PTH Level

	iPTH >295 (pg/ml)	iPTH <295 (pg/ml)	P. value	Test
number of patients	47	35		
Age (year)	50.5 ± 14.8	52 ± 15.8	0.45	T student
Time on dialysis (year)	4.3 ±2.15	3.75 ± 2.06	0.46	T student
Sex (male) (n)	31	18	0.68	Chi 2
Diabetes (n)	15	11	0.68	Chi 2
Recive Vitamin D (n)	37	28	0.13	Chi 2
Recive Calcium carbonate (n)	43	24	0.83	Chi 2
Magnesium (mg/dl)	2.69 ± 0.47	3.10 ± 0.41	< 0.01	T student
Hemoglobin (g/dl)	8.54 ± 1.51	9.52 ± 1.56	0.09	T student
Alkaline phosphatase (mg/dl)	158.26 ± 45.22	105.7 ± 23.76	< 0.01	T student
Calciume (mg/dl)	8.45 ± 1.11	9.37 ± 1.34	< 0.01	T student
Phosphorous (mg/dl)	6.05 ± 1.36	4.83 ± 1.27	< 0.01	T student

In the multivariate regression analysis of correlations with serum iPTH level, the serum Mg level independently correlated after adjustment for other factors (P=013) (Table 4).

Table (4) multivariate correlations between intact parathyroid hormone (iPTH) levels and other factors.

Model	Multivariate- β	P.value
P	0.42	0.012
ALP	0.38	0.01
Ca	- 0.29	0.025
Mg	- 0.21	0.013

Discussion.

Our observational study found that a high level of serum Mg was high among this group of Hemodialysis patients, 63.4 % of patients have Hypermagnesemia. In this study, we did not find any patient with magnesium values lower than the normal range and this is consistent with other studies that found that hypermagnesemia is predominant in hemodialysis patients, as in the study of Navarro et al [19], which found hypermagnesemia in 73% of patients, and it is also consistent with the study of Ohya et al [20] where hypermagnesemia was found in 53.9% of uremic patients. In this study, patient undergoes Two HD sessions per week, which explains the high magnesium values we have compared with other studies that use the same concentration of magnesium in the dialysate, considering that hemodialysis is the only method to excrete magnesium in patients with hemodialysis, especially with neglect of residual renal function.

Multiple abnormalities contribute to the development of secondary hyperparathyroidism in CKD patients. Serum Ca, vitamin D, fibroblast growth factor- 23, and serum P levels have a key role in regulating PTH. Ca is the dominant activator of the calcium- sensing receptor (CaSR), but Mg can also activate it, although with 2- to 3- fold less efficacy than Ca. Therefore, serum Mg may have a role in regulating the secretion of PTH. The correlation between serum Mg and PTH levels in patients undergoing HD has been investigated in previous studies (19, 21) and they found negative correlation between PTH and serum magnesium in hemodialysis patients. In this study, an inverse relationship was found between serum magnesium and parathyroid hormone concentrations (r=- 0.311, P.value = 0.03). And In the multivariate regression analysis of correlations with serum iPTH level, the serum Mg level independently correlated after adjustment for other factors (r=- 0.21, P. value =0.013), In the study of Ohya et al [20], magnesium was found to be an independent correlation factor with parathyroid hormone in patients with uremia, and the study of Navarro et al [19] showed a significant inverse relationship (r =- 0.48; P < 0.001 between magnesium and PTH, while In the study of El okely et al [22], did not find any statistically significant relationship between serum magnesium and PTH. n this study, 62 patients (75.6%) were found

to have PTH values within the required range according to KDIGO, while 13 patients (16%) had PTH values above the required range. In comparison with the study of Li Zuo [13], it was found that (39.1%) of the hemodialysis patients had PTH within the required range, and 29.7%) of the patients had a PTH higher than the required range.

In summary, our study showed that a high level of serum Mg is common in hemodialysis patients. In these patients, there was a significant inverse correlation between the serum Mg and iPTH levels.

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