

Significance of parathyroid scintigraphy and correlation of findings with parathyroid hormone values in patients undergoing hemodialysis

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ABSTRACT

Aim To compare finding of thyroid gland scintigraphy with serum concentration of parathyroid hormone in patients undergoing hemodialysis.

Methods This retrospective-prospective study included 50 patients undergoing hemodialysis with established hyperparathyroidism who were treated at Cantonal Hospital Zenica in the period 2009 – 2014. Besides anthropological data, concentration of parathyroid hormone in serum of patients was monitored too. Scintigraphy was performed at the Department of Nuclear Medicine using two-headed gamma camera Prism 2000xp.

Results Of the total number of 50 patients, 24 (48%) were males and 26 (52%) were females. The average age was 49.34±11.82 years. A total of 17 (34%) patients had normal findings of scintigraphy, 11 (22%) had mildly pronounced uptake of radiopharmaceuticals (score of 1), 14 (28%) had moderately pronounced uptake (score of 2), and eight (16%) had intensive uptake of radiopharmaceuticals (score of 3). A statistically significant difference was established in the length of hemodialysis treatment and scintigraphy finding ($p=0.041$).

Conclusion Scintigraphy of parathyroid glands in patients undergoing hemodialysis allows us to select them for parathyroidectomy. Scintigraphy of parathyroid glands and a value of parathormone in serum should be incorporated into the test algorithm for patients with secondary hyperparathyroidism caused by chronic kidney disease.

Key words: chronic kidney disease, hyperparathyroidism, parathyroidectomy

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INTRODUCTION

The term “chronic kidney insufficiency” is used to denote terminal (fifth) stage of chronic kidney disease (1). With progression of kidney damage, chronic kidney weakness is developed and leads to progressive disruption of homeostasis in bone mineral turnover, which is manifested by an abnormal concentration of phosphorus and calcium in serum and tissues, as well as changes in concentrations of individual circulating hormones, parathyroid hormone (PTH) (2,3). Due to reduced phosphorus excretion by kidneys, hyperfunction of parathyroid glands occurs (4). Secondary hyperparathyroidism is developed and it influences the metabolism of calcium and balance of bone degradation and formation (5).

Parathyroid glands constantly stimulate creation of PTH and with time they acquire an increasing volume (6).

Hypercalcemia occurs as elevated levels of parathyroid hormone concentration in serum, which results in increased mobilization of calcium from bones mediated by osteoclasts, increased reabsorption of calcium in kidney glomeruli, increased gastrointestinal reabsorption of calcium and 1,25 dihydroxyvitamin D and increased secretion of phosphate in urine, hence hypophosphatemia appears in serum (7-9).

Secondary hyperparathyroidism represents one of the leading complications in patients undergoing hemodialysis, which occurs due to disorder of level regulation of serum phosphorus (PO₄), calcium (Ca), PTH and (tissue) vitamin D. The disease is characterized by disorder of parathyroid glands, which are responsible for secretion of parathyroid hormone. Long-lasting secondary hyperparathyroidism is associated with cardiovascular complications and kidney osteodystrophy (10).

When the function of parathyroid glands is increased, it cannot be reduced in any way, and the disease that causes it has advanced, it is recommended to undergo an operation which implies extracting glands (11-13).

Parathyroid gland scintigraphy is an imaging method that shows, by means of radiopharmaceutical Tc-99 MIBI, abnormal tissue of parathyroid glands (14). Successful parathyroidectomy depends on recognition and surgical removal of

all hyperfunctional parathyroid glands. Screening is not used to establish the diagnosis (15). Increased Ca in plasma and PTH are sufficient. Scintigraphy does not identify normal parathyroid glands which are small to be seen (20-50mg). Scintigraphy detects abnormal parathyroid glands, it determines size and precisely defines a relation with the thyroid gland. Also, scintigraphy detects ectopic glands (16).

With PTH concentration in patient's serum, scintigraphy is used as a screening method for the assessment of functional status of parathyroid glands and as an important diagnostic procedure in preoperative evaluation of patients with hyperparathyroidism (17-21).

The control of parathyroid glands has not been automatic so far, therefore, the patient and his/her doctor have to get actively involved into solving the problem that has arisen.

The world prevalence of chronic kidney disease (CKD) from the third to fifth stage is 5% or 50,000 (cases) per one million inhabitants, while the prevalence of the end-stage of kidney insufficiencies is 0.1%, or more than 100 new dialysis patients per one million of the population annually (18). Due to unregulated value of phosphorus in hemodialysis patients, kidney osteodystrophy occurs (18). In this research we wish to highlight the importance of regular monitoring of calcium, phosphorus and parathyroid hormone and to compare it with scintigraphic finding, which facilitates access to the surgeons and saves their time, especially in detecting ectopic parathyroid glands.

The aim of this study was to compare findings of parathyroid gland scintigraphy with the serum concentration of parathyroid hormone, calcium and phosphorus in patients undergoing hemodialysis.

PATIENTS AND METHODS

Patients and study design

The retrospective-prospective study included all patients undergoing hemodialysis with established hyperparathyroidism who were treated at Cantonal Hospital Zenica (covering 12 municipalities with a total of 400,000 inhabitants), Bosnia and Herzegovina (B&H), in the period 2009 – 2014 (retrospectively from 2009 to 2012, and prospectively from 2012 to 2014). A total of 50 patients was included. Besides anthropological

data (age, gender), concentration of parathyroid hormone in serum of patients as well as of calcium and phosphorus was monitored.

The research was approved by the Ethics Committee of the Cantonal Hospital Zenica.

Methods

A concentration of PTH in plasma of patients was determined by chemiluminescent enzyme immunoassay test (intact PTH) (Immulite 2000 immunoassay analyzer, Berlin/Germany Siemens). Reference value for parathormone of 9.25-7.5 pg/m was used. Serum levels of calcium and phosphorus were routinely determined in the clinical laboratory with automated equipment by using colorimetric method and quality control of standard. Reference values for calcium were 2.14-2.65 mmol/L and for phosphorus 0.87-1.45 mmol/L.

Scintigraphy was performed at the Department of Nuclear Medicine of the Cantonal Hospital Zenica by using two-headed gamma camera Prism 2000xp, according to the standard protocol with the application of 99m Tc-MIBI. Model PRISM 2000 XP is gamma camera, with computer console Philips and software version Odyssey (Cleveland, U.S.A., 1997). A degree of scintigraphy was determined as per intensity of radiopharmaceuticals accumulation (22): normal (score 1), moderately pronounced (score 2), intensive accumulation of radiopharmaceuticals (score 3).

Statistical analysis

For the description of the sample depending on nature of data, adequate methods of classical descriptive statistics were used: arithmetic mean (AM), standard deviation (SD), median (Med.), interquartile range (25.perc. and 75.perc.), absolute frequency (N) and relative frequency (%). The level of significance was <0.05.

RESULTS

Of the total number of 50 patients included in this research 24 (48%) were males and 26 (52%) were females.

The age of males was 48.25±11.62 and 50.34±12.14 (p=0.537) of females.

The average length of hemodialysis treatment was 8.45±3.94 years in males and 9.00±5.16 years in females (p=0.537).

Of the total number of 50 patients 17 (34%) had normal finding of scintigraphy, 11 (22%) had mildly pronounced accumulation of radiopharmaceuticals (score 1) (average age of 46.45 years), 14 (28%) had moderately pronounced accumulation of radiopharmaceuticals (score 2) (average age of 47.71 years), while eight (16%) patients had intensive accumulation of radiopharmaceuticals (score 3) (53.00 years). No statistically significant difference was established in gender and age of patients in relation to degree of scintigraphic finding (p=0.595) (Table 1).

A statistically significant difference was established in the duration of hemodialysis treatment and scintigraphy finding: patients who had longer hemodialysis treatment had worse scintigraphy finding (p=0.016).

The average value of PTH in patients who had a regular scintigraphy was 605.17pg/m, in patients with mild accumulation of radiopharmaceuticals 1068.90 pg/m, in patients with moderate accumulation of radiopharmaceuticals 1575.00pg/m, while in patients with intensive accumulation of radiopharmaceuticals it was 1830.12pg/m (p=0.001). The average value of calcium in patients who had a regular scintigraphy was 2.23 mmol/L, in patients with mild accumulation 2.12 mmol/L, in patients with moderate accumulation 2.23 mmol/L, while in patients with intensive accumulation of

Table 1. Average age of patients and duration of hemodialysis treatment in relation to scintigraphy finding

Parameter	Scintigraphy finding	No. of patients	Value	SD	SEM	95% CI	Min.	Max.
Age (years)	Normal	17	50.82	13.56	3.29	43.84-57.79	20.00	67.00
	Mild	11	46.45	11.57	3.49	38.67-54.23	31.00	64.00
	Moderate	14	47.71	10.35	2.76	41.73-53.69	25.00	66.00
	Intensive	8	53.00	11.32	4.00	43.53-62.46	41.00	74.00
p=0.595								
Duration of hemodialysis treatment (years)	Normal	17	6.45	4.65	1.12	5.07-9.86	2.00	23.00
	Mild	11	7.47	3.11	0.93	4.36-8.54	3.00	12.00
	Moderate	14	10.14	3.52	0.94	8.10-12.17	5.00	18.00
	Intensive	8	12.12	5.59	1.97	7.45-16.79	2.00	19.00
p=0.016								

SD, standard deviation; SEM, Standard Error of Mean; Min, minimum; Max, maximum;

Table 2. Average values of parathyroid hormone (PTH), calcium and phosphate in relation to scintigraphy finding

Parameter	Scintigraphy finding	No of patients	Value	SD	SEM	Min.	Max.
PTH (pg/mL)	Normal	17	605.17	342.84	83.15	79.00	1032.00
	Mild	11	1068.90	411.84	124.17	378.00	1643.00
	Moderate	14	1575.00	598.29	159.90	535.00	2473.00
	Intensive	8	1830.12	733.47	259.32	1369.00	3519.00
p=0.001							
Calcium (mmol/L)	Normal	17	2.23	0.21	0.05	1.71	2.64
	Mild	11	2.12	0.31	0.09	1.54	2.51
	Moderate	14	2.33	0.24	0.06	1.94	2.68
	Intensive	8	2.42	0.26	0.09	2.08	2.66
p=0.069							
Phosphate (mmol/L)	Normal	17	2.1224	0.59	0.14	1.00	3.25
	Mild	11	1.8427	0.96	0.29	0.59	3.04
	Moderate	14	2.0921	0.78	0.20	0.86	4.08
	Intensive	8	2.0938	0.68	0.24	0.86	2.93
p=0.788							

SD, standard deviation; SEM, Standard Error of Mean; Min, minimum; Max, maximum;

radiopharmaceuticals the average value of calcium was 2.42 mmol/L. The average value of phosphorus in patients who had a regular scintigraphy was 2.1224 mmol/L, in patients with mild accumulation of radiopharmaceuticals it was 1.8472 mmol/L, in patients with moderate accumulation 2.0921 mmol/L, and in patients with intensive accumulation of radiopharmaceuticals the average value of phosphorus was 2.0938 mmol/L (p=0.069 and p=0.788, respectively) (Table 2).

DISCUSSION

Demographic data of the patients included in this research correlate with the results of other researchers. Study released by Resić et al. (23) included 100 patients from Bosnia and Herzegovina (55 males and 45 females) who were on chronic hemodialysis program, with average age of 52.6 years, which is in accordance with our research. Hadžibulić et al. (24) noticed 59.26% males and 40.74% females with average age of 53.16 and 51.72 years, respectively, and found that length of time spent on dialysis for females was statistically significantly longer, 5.8 years on average, comparing to males, 3.4 years. It is not case in our research, where the average duration of hemodialysis treatment was 8.74 years minimum and maximum 23 years. No statistically significant difference was established in the average duration of hemodialysis treatment in relation to gender (8.45 and 9.00 years in males and females, respectively) in our research. Kudamija et al. (25) found that the average time spent on hemodialysis treatment was 8.7 years, which is in correlation with our research.

Resić et al. (23) noticed a statistically significant difference in the duration of hemodialysis, the average duration of dialysis was 6 years, and the largest number of patients (62%) was up to 5 years on hemodialysis, which is different from the results we obtained in the present research.

The results of this study showed that parathyroid hormone values were statistically significantly higher in the patients who had worse scintigraphy finding than the patients with normal scintigraphy finding; average values of calcium and phosphate did not statistically significantly differentiate in relation to scintigraphic finding. According to the literature (17), the percentage of patients on dialysis who, according to parathyroid hormone values, have an inclination to secondary hyperparathyroidism is about 32.7%. Secondary hyperparathyroidism in chronic kidney disease is characterized by high level of parathyroid hormone which is the key link in the development of bone and cardiovascular complications (19).

Reihel et al. (26) suggested that their patients with chronic kidney disease, who had been on hemodialysis treatment, had parathyroid hormone values five times higher than referential values with the average value of 625.17 pq/mL. According to KDIGO Guidelines, targeted values of parathyroid hormone in dialysis patients are 3 to 9 times higher than referential values (27). Resić et al. (23) found average parathyroid hormone value of 493.7 pg/dL, which is three times higher than the reference values and it is in accordance with the result of our research. They also found that 60.5% of patients had hypophosphatemia and 49% had

the elevated product $\text{Ca} \times \text{P} > 4.4 \text{ mmol}^2/\text{L}^2$, which represents a risk factor of vascular and soft tissue calcifications and development of coronary and peripheral arterial diseases. Positive correlations between scintigraphy finding and increased parathyroid hormone value were reported by Akim et al. (28) in their research.

Chronic kidney disease is a worldwide public health problem with serious adverse health consequences for affected individuals. Secondary hyperparathyroidism is a frequent complication of chronic kidney disease and a leading cause of clinically significant bone disease. The consequences of insufficiently controlled secondary hyperparathyroidism and negative effects of selected therapeutic interventions lead to high rates of morbidity and mortality in patients with chronic kidney disease (29).

Parathyroid gland scintigraphy in patients on hemodialysis allows us to select the same patients

for parathyroidectomy. In our research, it was shown that parathyroid hormone values are statistically significantly higher in subjects who had worse scintigraphy finding than the patients with normal scintigraphy finding; statistically significant, positive correlation was established between the duration of hemodialysis treatment and parathyroid hormone values. In conclusion, scintigraphy of parathyroid glands and parathyroid hormone value in serum as a golden standard should be incorporated into the algorithm of tests in patients with secondary hyperparathyroidism caused by chronic kidney diseases.

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Competing interest: none to declare.

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Značaj scintigrafije paratireoidnih žlijezda i korelacija nalaza s vrijednostima paratireoidnih hormona kod pacijenata na hemodijalizi

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SAŽETAK

Cilj Komparirati nalaze scintigrafije paratireoidnih žlijezda sa serumskom koncentracijom parathormona kod pacijenata na hemodijalizi.

Metode U retrospektivno-prospektivno istraživanje, u periodu od 2009. do 2014. godine, bili su uključeni pacijenti na hemodijalizi s utvrđenim hiperparatireoidizmom koji su klinički obrađivani u Kantonalnoj bolnici Zenica. U istraživanje je uključeno ukupno 50 pacijenata. Uz antropološke podatke, praćena je koncentracija parathormona u serumu pacijenata. Scintigrafija je rađena na Odjelu za nuklearnu medicinu Kantonalne bolnice Zenica na dvoglavoju gama-kameri *Prism 2000xp*.

Rezultati Od 50 ispitanika 24 (48%) je bilo muškog, a 26 (52%) ženskog spola. Prosječna starosna dob je iznosila 49.34±11.82 godine. Od 50 ispitanika 17 (34%) je imalo uredan nalaz scintigrafije, blago naglašen unos radiofarmaka (scor 1) imalo je 11 (22%), umjereno naglašen (scor 2) 14 (28%), a intenzivan unos radiofarmaka (scor 3) 8 (16%) ispitanika. Ustanovljena je statistički značajna razlika u dužini trajanja hemodijaliznog tretmana i nalaza scintigrafije.

Zaključak Scintigrafija paratireoidnih žlijezda kod pacijenata na hemodijalizi omogućava njihovu selekciju za paratireoidektomiju. Scintigrafiju paratireoidnih žlijezda i vrijednost parathormona u serumu kao zlatni standard, treba uvrstiti u algoritam pretraga kod pacijenata sa sekundarnim hiperparatireoidizmom uzrokovanim hroničnim bubrežnim oboljenjima.

Ključne riječi: hronična bubrežna bolest, hiperparatireoidizam, paratireoidektomija