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Cardiometabolic Risk Factors In Patients With Hyperparathyroidism

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Abstract: Hyperparathyroidism is one of the more common endocrine diseases and is often asymptomatic. But, even if it is asymptomatic, it may increases the cardio metabolic risk. Subjects and Methods: In this retrospective study we have looked for the presence of cardio metabolic risk factors in 84 patients (72F/12M) with a mean age of 51 years presenting with hyperparathyroidism. We have also looked for the predictive factors of the occurrence of dysglycemia by comparing patients with dysglycemia (G1) to those with normoglycemia (G2). Results: 31.3% of our patients were overweight whereas 28.8% were obese. 32.5% had high blood pressure (HBP), 31% had low HDL-cholesterol level, 41.8% had high triglyceride level and 28.5% had dysglycemia (19% had diabetes and 9.5% had prediabetes). G1 patients were older than those of G2: 58 ± 11 vs. 48.6 ± 15.3 years. Familial background of HBP was found in 45.8% (G1) vs. 27% (G2). The body mass index was of 27±5 kg/m^2 (G1) vs. 26.5±5 kg/m^2 (G2). Mean serum calcium level was 11.1±2 mg/dl (G1) vs. 10.7 ±2.2 mg/dl (G2). Mean PTH level was 236 ±222 pg/ml (G1) vs. 382±479 pg/ml (G2). Mean 25(OH) vitamin D level was 11±4 ng/ml (G1) vs. 12±8 ng/ml (G2). Conclusion: Cardio metabolic risk factors are frequent in patients with hyperparathyroidism. Compared to normoglycemic patients, patients with dysglycemia are older, but there were no differences in the other parameters analyzed in this study.

Key words: hyperparathyroidism, cardio metabolic risk factors, dysglycemia

Introduction:

Hyperparathyroidism (HPT) has become one of the most common endocrine diseases, asymptomatic form is the most common form of hyperparathyroidism nowadays. Several studies have suggested that HPT confers a higher risk of high blood pressure, obesity, glucose intolerance, type 2 diabetes and insulin resistance. However, the association between HPT and these cardio metabolic risk factors still remains controversial. An increased risk of cardio metabolic anomalies may influence the decision on how to manage asymptomatic patients with hyperparathyroidism. In this study we looked for the presence of cardio metabolic risk factors in patients with HPT, thereafter we looked for predictive factors for dysglycemia in patients with HPT.

Subjects and Methods:

It is a retrospective study concerning 86 patients (74 females and 12 males) presenting HPT which was primary in 51.2% and secondary in 48.8%. The mean age of our patients was 51 years. In these patients we looked for the presence of the following cardio metabolic risk factors:

- Overweight defined by a body mass index (BMI) between 25 and 29.9 kg/m^2.
- Obesity defined by a BMI equal or greater than 30 kg/m^2.
- High blood pressure (HBP) defined by a systolic blood pressure equal or greater than 140 mm Hg and/or a diastolic blood pressure equal or greater than 90 mm Hg or on treatment patients.
- Hypertriglyceridemia defined by a triglyceride level equal or greater than 150 mg/dl.
- High-density lipoprotein (HDL) cholesterol level less than 35 mg/dl in men or less than 45 mg/dl in women.
- Type 2 diabetes defined by a fasting glucose level equal or greater than 126 mg/dl and/or glucose level two hours after an oral glucose tolerance test (OGTT) with 75 grams of glucose equal or greater than 200 mg/dl.
- Impaired fasting glucose (IFG) defined by a fasting glucose level between 100 and 125 mg/dl.
- Impaired glucose tolerance (IGT) defined by a glucose level two hours after an OGTT between 140 and 199 mg/dl.
- Dysglycemia encompasses all categories of glucose abnormalities (type 2 diabetes, IFG, IGT).

In a second time we divided the patients in two groups: group 1 (G1) include dysglycemic patients, group 2 (G2) include normoglycemic patients and we search for the presence of predictive factors for dysglycemia.

Results:

31.3% of patients were overweight, while 28.8% were obese. HBP was present in 32.5%. 31% have low HDL-cholesterol and 41.8% have high triglyceride level.

28.5% were dysglycemic, either diabetic in 19% or prediabetic (IFG and/or IGT) in 9.5%.

When we compare patients of G1 with those of G2 we found that patients of G1 were older than those of G2: 58 ± 11 years vs. 48.6 ± 15.3 years ($p<0.01$).

Diabetes in first degree relatives was present in 62.5% in G1 and 46.7% in G2. HBP was present in 45.8% in G1 and 27% in G2.

Mean BMI was 27±5 kg/m^2 in G1 and 26.5±5 kg/m^2 in G2.

Mean serum calcium level was 11.1±2 mg/dl in G1 and 10.7 ± 2.2 mg/dl in G2.
Mean parathormone (PTH) level was 236 ±222 pg/ml in G1 and 382±479 pg/ml in G2.
Mean level of 25(OH) vitamin D was 11±4 ng/ml in G1 and 12±8 ng/ml in G2.

*These results are depicted in **table 1:***

Table 1: Comparison between dysglycemic and normoglycemic patients

Parameters	Group 1	Group 2	p
Age (years)	58 ± 11	48.6 ± 15.3	<0.01
First relative with diabetes %	62.5%	46.7%	NS[1]
High blood pressure %	45.8%	27%	NS
Body Mass Index (Kg/m^2)	27±5	26.5±5	NS
Serum calcium (mg/dl)	11.1±2	10.7 ±2.2	NS
Parathormone (pg/ml)	236 ±222	382±479	NS
25(OH) vitamin D (ng/ml)	11±4	12±8	NS

[1] Not significant

Discussion:

A high prevalence of overweight, obesity, type 2 diabetes mellitus, prediabetes, HBP and dyslipidemia was found in our patients presenting with hyperparathyroidism. While classically HPT is related to bone or kidney symptoms, many studies suggested that HPT may be associated with increased risk of cardio metabolic risk factors. In a retrospective observational study including 73 patients with primary HPT Garcia-Martin found a high prevalence of obesity (59.9%), type 2 diabetes mellitus (25%), high blood pressure (47.2%), and dyslipidemia (44.4%), serum calcium and PTH levels positively correlated with BMI. After comparison between patients on observation and patients who underwent surgery, there was no difference between the two study groups and no improvement in cardio metabolic risk factors had occurred one year after surgery in operated patients [1]. Luboshitzky compared 139 patients with primary HPT to 111 subjects of similar age and body weight defined as controls for cardiovascular risk factors. Hypertension, dysglycemia and dyslipidemia were documented in 57.6, 33.8 and 72.7% of the patients, compared with 27.9, 10.2 and 64.9%, respectively, in controls. HPT patients had higher percentages of metabolic syndrome (MS) and insulin resistance (IR) than control patients. Furthermore, the risk of MS and IR was positively correlated with the severity of HPT. Patients with severe primary HPT had MS in 37.5%, and IR in 38.9 % compared to 34.3% and 23.9% in mild primary HPT, and 14.4% and 14.4% in control patients respectively [2]. Cardenas has looked for the prevalence of type 2 diabetes in 609 patients with primary HPT. The prevalence rate of type 2 DM in patients with primary HPT was significantly higher than that in the general population, 15.9% versus 7.8%, respectively. However, this difference was not significant after age stratification except for the age group of 64 to 75 years. After adjustment, there was no significant difference in the prevalence of diabetes between patients with primary HPT and the control patients except in men [3]. In another study, 59 patients with primary HPT without known diabetes and 60 control patients underwent an oral glucose tolerance test. The prevalence of IGT and diabetes was higher in HPT than in control patients 40.7% and 15.3% versus 25% and 5% respectively. The indices of insulin resistances were also higher in HPT than in control patients, 2.6 versus 1.7 for the homeostasis model assessment of insulin resistance (HOMAIR) and 3.5 versus 5.1 for the insulin sensitivity index composite (ISI comp) respectively [4]. Several mechanisms have been linked to the increased prevalence of cardio metabolic factors in HPT patients, calcium levels, PTH levels and chronic inflammation are involved. Serum calcium and PTH have been related to HBP. Experimentally induced hypercalcemia by intravenous infusion of calcium increases blood pressure values, with resumption of normal blood pressure after discontinuation of calcium infusion. The same findings are observed with continuous infusion of PTH [5]. Insulin resistance may be secondary to increased intracellular calcium levels in adipocytes, increased intracellular calcium may also impede catecholamine-induced lipolysis by activating phosphodiesterase 3B [6], HPT may therefore predispose to the development of obesity. In addition, osteoblasts and adipocytes have common precursors, so, chronic PTH elevation may promote adipocytes proliferation [7]. High levels of PTH may be associated with high levels of inflammatory cytokines such as MCP-1, TNF-α, IL-6 and C-reactive protein (CRP). This low level inflammatory state is a marker of insulin resistance and a factor of cardiovascular risk [8]-[10]. Finally, recurrent episodes of pancreatitis secondary to hypercalcemia may lead to the development of diabetes [11].

Conclusion:

Our study showed that patients with hyperparathyroidism have a high prevalence of overweight, obesity, high blood pressure, dyslipidemia and dysglycemia. So, with the predominance of asymptomatic forms of hyperparathyroidism nowadays, these cardio metabolic risk factors should be kept in mind when to decide how to manage patients with asymptomatic hyperparathyroidism.

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