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„Metabolic disturbances in patients with symptoms consistent with reactive hypoglycemia. Effect of a dietary interventions on the occurrence of the neurovegetative and neuroglycopenic symptoms in nondiabetic individuals”

Streszczenie w języku angielskim

Introduction: Reactive hypoglycemia (RH) refers to neurovegetative and neuroglycopenic symptoms and low blood glucose level that occurs in non-diabetic patients in the postprandial period (no symptoms in fasting and nocturnal period). It is not uncommon that the patients who present with symptoms attributed to hypoglycemia have no glucose decline. Their symptoms may occur in the postprandial period, but the frequency of those warning signs does not have a fully interpretable pattern. It remains unclear whether reactive hypoglycemia is a disorder caused by improper insulin secretion, result of eating habits that are not nutritionally balanced or whether itis a psychosomatic disorder. Pathomechanism of hypoglycemia in non-diabetic subjects has not been widely studied, hence it is not yet fully understood. Due to this fact, there are no specific biochemical guidelines for the diagnosis. There are currently no studies that analyze eating habits of individuals without metabolic disturbance and who manifest symptoms attributed to hypoglycemia in the postprandial period. Moreover, there is no research data available that provide a realistic reflection of the effect of dietary interventions and evaluation of patient adherence from the long-term perspective.

Aim of the study: to investigate metabolic parameters in patients admitted to the hospital with suspected RH and to evaluate the impact of the dietary interventions, and their sustained outcome, on the severity of hypoglycemic-like symptoms occurring in non-diabetic patients.

Materials and Methods: The study was performed in the Central Clinical Hospital of the Ministry of Internal Affairs and Administration (MSWiA) in Warsaw between 2019 and 2022. Study group included subjects who reported symptoms attributed to hypoglycemia. Control group consisted of asymptomatic individuals without any diagnosed metabolic disorders who were hospitalized for reasons unrelated to metabolic disorders and/or RH. After obtaining written informed consent, all subjects underwent biochemical examinations:

• fasting glucose and insulin with Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) evaluation

• five-hour oral glucose tolerance test with 75g of glucose (OGTT). The blood samples were drawn to evaluate glucose and insulin at the baseline (before glucose intake) and every sixty minutes for a period of five hours after ingestion of glucose.

• profile included total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) and triglycerides (TG) measurements. TG/HDL-C ratio

Mixed Meal Tolerance Test (MMTT) was performed only for the patients from study group. Patients consumed a non-liquid meal containing 60% of carbohydrate, 25% of fat and 15% of protein prepared by the dietician. The meal included three slices (75 g) of white bread, one tablespoon (10 g) of butter, three tablespoons (75 g) of semi-fat white cheese and two tablespoons (50 g) of jam. After the ingestion, patients were observed during a period of five hours and in case of occurrence of any symptoms suggesting hypoglycemia the blood sample was taken.

RH was confirmed if the patient manifested hypoglycemic symptoms and had glucose level ≤55 mg/dL during OGTT.

Hyperinsulinemia was defined as an approximately tenfold increase of insulin level during five-hour OGTT.

The dietary interventions included two healthy diet models—Low Glycemic Index Diet (LGID) and Mediterranean diet (MD). Each subject was introduced to a particular diet via one-on-one education performed by a registered dietitian. Each patient was advised about recommended and unrecommended meal choices based on the food pyramid, charts, and detailed guidelines. Every diet had to be implemented for three months with one follow up consultation in the middle.

The final follow-up appointment took place twelve months later and that is when each patient underwent a detailed assessment of their current dietary habits and evaluation of the frequency of symptoms consistent with hypoglycemia.

Results:

1. There was no significant difference in age (37.0 ± 9.9 vs. 33.8 ±9.5; p = 0.162) and BMI (23.7 ± 3.0 kg/m2vs. 24.9±4.9 kg/m2; p = 0.198) between patients in study group (n = 40) and control group (n=35)

2. Based on the OGTT result, hypoglycemia has been found in twelve (30%) subjects from study groups. Those patients had glucose level lower than 55 mg/dl in first three hours of OGTT. Ten (25%) patients had hypoglycemic symptoms but without glucose decline during the test. Eight (23%) subjects from had biochemical hypoglycemia but without clinical manifestation.

3. There was no significant difference in HOMA-IR compared study group and control group (1.7 ± 0.8 vs. 2.1 ± 1.4). HOMA-IR was statistically significantly lower in patients with RH diagnosis compared to those who did not meet HR diagnosis (1.2 ± 0.5 vs 1.8±0.8, p = 0.029).

4. Hyperinsulinemia has been found in sixteen (40%) subjects from study group and eleven (31%) subjects in control group. There was no significant difference (p = 0.440) in hyperinsulinemia occurrence in study group and control group, as well as in patients with confirmed RH and those who did not meet the diagnostic criteria of RH (50% vs 36%, p = 0.398)

5. During MMTT, seventeen (42%) subjects from study group had manifested symptoms attributed to hypoglycemia, but non of them had glucose level below 55 mg/dl.

6. The majority of participants reported undertaking various dietary modifications in order to reduce hypoglycemic-like symptoms (without professional medical support). The Dukan diet (40%), vegetarian diet (35%), and gluten-free diet (32%) were the most frequently selected dietary patterns to reduce postprandial hypoglycemic-like symptoms.

7. The individualized dietary counselling significantly improved the patients' eating habits in comparison to those present prior to intervention in terms of healthy diet index ($p < 0.001$) and unhealthy diet index ($p < 0.001$). The patients chose whole grains, vegetables, products providing a source of valuable protein (lean meat, dairy, and legumes), and products representing a healthy source of fats (nuts, seeds, fish, and vegetable oils) more frequently compared to the pre-intervention period.

8. There was a statistically significant reduction in the severity in eight out of the ten analyzed hypoglycemic-like symptoms after the dietary interventions. The most notable change was observed

in the following symptoms: hunger, impaired concentration, hand tremor, and fatigue. The outcomes were comparable for both recommended diets, the LGID and the MD. The reduction in hypoglycemic-like symptoms continued after the twelve-month period.

Conclusions:

1. Hyperinsulinemia and insulin resistance were not responsible for symptoms suggesting hypoglycemia and for glycemic declines.

2. Hypoglycemic-like symptoms are not always associated with low glycemia (<55 mg/dl).

3. The occurrence of hypoglycemic symptoms along with lower glucose values were observed more frequently during the five-hour OGTT where glucose was obtained from liquid than during the MMTT where glucose was provided from solid food. The source of glucose may influence postprandial glycemic fluctuations and the onset of symptoms suggesting hypoglycemia.

4. Healthy modification in the dietary habits under dietary supervision reduced the severity of postprandial hypoglycemic-like symptoms.

5. Adherence to LGID and MD had significant impact in terms of symptoms reduction, which supports their effectiveness. Therefore, dietary intervention should focus on appropriate nutritional management.

6. Long-term dietary intervention focused on appropriate nutritional management should be a beneficial step towards comprehensive treatment of non-diabetic patients who present with hypoglycemic-like symptoms in the postprandial period.