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## **INVESTIGATING HYPOGLYCEMIC AWARENESS IN TYPE 2 DIABETES**

**Introduction.** Hypoglycemia is the rate-limiting factor that often prevents patients with diabetes from safely and effectively achieving their glycemic goals [1, 2]. Hypoglycemic events can have serious implications for patient health, psychological well being, and adherence to treatment regimens, can impact the health economics of the patient, their employer [4]. It is primarily associated with treatment with insulin and insulin secretagogues, equally common for both types of diabetes [3, 5, 8].

While severe hypoglycemic events are undoubtedly dangerous to patients, equally important are nonsevere hypoglycemic events, which are frequently and incorrectly dismissed as unimportant because they can be asymptomatic [6]. In fact, nonsevere hypoglycemic events are actually much more common than severe hypoglycemic events, yet, nonsevere ones may go unrecognized. Even if they are recognized, they may not be significant enough to be remembered by the patient and to be mentioned to the primary care physician and are therefore also significantly under-reported [6]. Recurrent episodes of untreated hypoglycemia can lead to hypoglycemia-associated autonomic failure, an impaired ability of the body to counter-regulate subsequent and more serious events, which leads to unawareness of hypoglycemia [8]. Hypoglycemia also commonly goes undetected when it occurs during the night. Nocturnal hypoglycemia can lead to serious clinical consequences, including sudden death during sleep, thought to be a result of cardiac rate and rhythm disturbances in response to prolonged nocturnal hypoglycemia [6].

Considering that, the **purpose** of this study was to discuss the importance of all hypoglycemic events in the successful management of patients with diabetes, emphasizing data regarding the incidence of hypoglycemia in type 2 diabetes patients taking insulin and/or oral hypoglycemic agents to estimate the prevalence of hypoglycemia and try to prevent it from happening.

**Materials and methodology.** To accomplish this, 15 patients with diabetes mellitus type 2 (47% men and 53% women, mean age –  $60,9 \pm 1,44$  years), hospitalized to Chernivtsi Regional Endocrinological Center, participated in the study.

The verification of the diagnosis and disease severity was based on the acting national and international regulating documents. All patients underwent standard general clinical and laboratory-instrumental examination. Glucose blood concentration was determined by glucose oxidase method before and 2 hours after meal (pre- and postprandial glycemia) to assess carbohydrate metabolism. Detection of glycated haemoglobin (HbA<sub>1C</sub>) was used as informative criterion of continuous glycemetic control (by colorimetric method).

In 40% of participating patients the duration of diabetes was less than 5 years, in 20% – 6-10 years, in 40% of patients had diabetes longer than 10 years. Among all examined patients 40% were treated by oral hypoglycemic agents, 60% were on combined hypoglycemic therapy.

Except standard clinical patients' examination findings and information from medical records, self-report 10-item Hypoglycemia questionnaire, provided by the Hypoglycemic Health Association of Australia, was used in order to reveal unrecognized hypoglycemic episodes and to identify the probability of hypoglycemic events in the examined patients [7]. Individual's risk profile was calculated according to scoring scheme by the assessment of hypoglycemia signs as «rarely», «occasionally», and «usually», being assigned a certain number of points. If total score was less than 8 points, hypoglycemia was considered as «unlikely», between 8 to 15 points – as «possible», in case of total score above 15 – as «present». Despite this questionnaire is easy to fill in, the researcher accompanied the patients while they completed the questionnaires to aid quality control during data collection.

**Results and discussion.** The analysis of carbohydrate metabolism parameters evidenced a poor compensation of the disease in patients of the examined cohort.

According to the obtained findings, the probability of hypoglycemia development was assessed as «possible» only in 20% of the enrolled patients; all of them were on combined hypoglycemic therapy. In the majority of cases (80%) the «present» hypoglycemia was defined in the patients treated by various types of hypoglycemic therapy. Our analysis demonstrated, that the gradient for risk according to the age and duration of diabetes as well as to the level of its compensation was noticeable.

Thus, the frequency of hypoglycemia in people with type 2 diabetes, mostly middle aged or elderly, is usually underestimated and much higher than documented. Impaired awareness of hypoglycemia, more prevalent in type 2 diabetes than is appreciated, is associated with increased risk of a variety of adverse clinical outcomes, including microvascular events (nephropathy, retinopathy, neuropathy), macrovascular events (heart failure, peripheral vascular disease, myocardial events, stroke), and death. Accompanied by such factors, as age, a past history of vascular disease, interactions with other drugs, alongside with treatment either by sulfonylureas or insulin, hypoglycemia poses particular problems and the mortality may be unrecognized.

Though the risk of therapy-induced hypoglycemia is highest among patients treated with insulin, there are risks associated with other treatments. Sulfonylurea therapy, which increases insulin output from the pancreas, is one of the key contributors to hypoglycemia in patients with type 2 diabetes who are early in the progression of the disease. The risk of hypoglycemia with oral antidiabetes drugs is variable and, as with sulfonylureas, depends upon their respective pharmacokinetic and pharmacodynamic profiles. It is important to remember that if insulin or insulin secretagogues, such as a sulfonylurea, are added into the treatment regimen as the disease progresses, the risk of hypoglycemia will increase.

The incidence of type 2 diabetes is projected to increase in coming years, while the average age of patients with type 2 diabetes is decreasing; therefore, the number of patients with advanced type 2 diabetes, for whom sulfonylureas and oral antidiabetes drugs will not provide sufficient glycemic control, and who will require the addition of insulin to their treatment regimen, is also likely to increase dramatically. Combined with increasingly tighter glycemic targets, this may contribute to an increasing prevalence of hypoglycemia in the future.

**Conclusion.** A recent inquiry emphasised the benefits of using charts or scores for hypoglycaemia risk assessment in getting treatment decisions made alongside realistic estimates of patient susceptibility to hypoglycemia as the rate-limiting factor for the achievement of glycemic treatment goals. Such approach to the individual patient has daily practice implications, as it provides a useful tool for primary care physicians, who are responsible for guiding therapy to achieve euglycemic control in patients with diabetes. It helps to recognize asymptomatic hypoglycemia and to optimize management and outcomes in patients who are initially categorized as at hypoglycemia risk.

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