

# Hypoglycemia as a medication-related harm identified in patients admitted to geriatric wards

**To the editor** The article by Bieñ<sup>1</sup> presented the results of a cross-sectional study aimed to assess the prevalence of and reasons for medication-related harm (MRH) in geriatric patients, as well as to recognize how MRH and drugs prescribed after geriatric interventions affect patients' survival.

The analysis of 301 geriatric patients admitted to the hospital for any reason combined with a 2-year survival analysis identified MRH in 35.2% of patients (hypotension [19.3%], hypoglycemia [13.3%], parkinsonism [4.3%], benzodiazepine addiction [5.7%], and other drug- or dosage-related disorders).

Following a geriatric intervention, 4 drug classes showed a positive correlation with survival: thiazides, selective serotonin reuptake inhibitors, paracetamol, and angiotensin-converting enzyme inhibitors. The author concluded that geriatric-based deprescribing and drug optimization mitigate the negative impacts of MRH on patients' survival and may reduce the rehospitalization rate and healthcare costs.

The study team collected and analyzed a large amount of data, leading to an interesting and important debate. Nevertheless, we would like to make a comment focused on hypoglycemia-related MR, which may contribute to a further and more detailed discussion of the issue.

The frequency of hypoglycemic episodes was analyzed in the whole group of patients with diabetes regardless of the type of diabetes and method of treatment (ie, sulfonylureas, metformin, or insulin, as stated by the author). It is known that the frequency of hypoglycemia is higher in patients with type 1 diabetes compared with those with type 2 diabetes treated with a similar insulin therapy.<sup>2</sup> Still, we may presume that the majority of patients in the study had type 2 diabetes. It also has been proven that the risk of hypoglycemia is much higher in insulin-treated patients with type 2 diabetes compared with those on oral antidiabetic drugs. For example, the United Kingdom Prospective Diabetes Study 73 showed that patients treated with basal insulin reported hypoglycemia (3.8% per year) more often than those

treated with diet (0.1%), sulfonylurea (1.2%), or metformin (0.3%), but less frequently than those treated with a multiple daily insulin regimen (5.3%).<sup>3</sup>

Thus, it would be interesting to inspect hypoglycemia-related MRH separately for insulin- and non-insulin-treated patients and, if possible, after excluding those with type 1 diabetes. Such an analysis could detect the real contribution of insulin and oral antidiabetics to this MRH.

With great respect, we suggest performing such an analysis or taking these comments into consideration if the continuation of this relevant study is planned.

## ARTICLE INFORMATION

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**TABLE 1** Drug-induced hypoglycemia by the medication(s) used in 116 diabetic geriatric patients

Drugs	Hypoglycemia (n = 40)	No hypoglycemia (n = 76)	P value <sup>a</sup>
Metformin	22 (55)	34 (44.7)	0.29
Sulfonylureas	16 (40)	21 (27.6)	0.17
Any oral antidiabetics	31 (77.5)	45 (59.2)	0.048
Insulin	14 (35)	18 (23.7)	0.2
Any oral antidiabetics + insulin	5 (13)	11 (14)	0.77
Number of drug classes taken before admission	0 (diabetes diagnosed in the hospital)	24 (31.6)	<0.001
	1	28 (70)	32 (42.1)
	2	12 (30)	19 (25)
	3	0	1 (1.3)

Data are presented as number (percentage) of patients.

**a**  $\chi^2$  Pearson test

**Author's reply** Indeed, drug-induced hypoglycemia is one of the most prevalent medication-related harms in comorbid geriatric patients that it is worth being a subject of a debate. In the presented study,<sup>1</sup> this iatrogenic syndrome concerned 40 out of 116 patients with diabetes, ie, 34.5% of those taking antidiabetic medications before hospital admission (13.3% of all geriatric study patients). These figures are extremely high and unbelievable.

Could the type of diabetes have an influence on such a high rate of hypoglycemia? Possibly, it could, but, in clinical practice, the vast majority of older adults has type 2 diabetes.<sup>2</sup> Although quite high numbers of individuals with type 1 diabetes are living into old age,<sup>3</sup> this discussion concerns the late-onset type 2 diabetes, which is most commonly observed in the older population.<sup>4</sup> Differently from middle-aged individuals, diabetes in older people is associated with the combined effects of increasing insulin resistance and impaired pancreatic islet function with aging. Age-related insulin resistance appears to be primarily associated with adiposity, sarcopenia, and physical inactivity.<sup>5</sup> Age is one of the main risk factors for type 2 diabetes. For this reason, it was not our intention to differentiate between the 2 types of diabetes in patients at a mean age of over 80 years.

The second point raised by the commentators concerns the risk of hypoglycemia depending on the type of antidiabetic medications used before hospitalization. In my article, separate drugs (metformin, sulfonylureas, insulin) were combined into the joint group of antidiabetic medications, mainly due to the complex treatment and statistical approach. Some detailed data on hypoglycemia depending on the drugs used before hospitalization are presented in [TABLE 1](#).

The data show that some risks of drug-related hypoglycemia relate to all classes of drugs; to a minor extent to metformin, to a greater extent to sulfonylureas. Surprisingly, oral antidiabetics, irrespectively of classes or numbers,

seem to carry an even higher risk of hypoglycemia than insulin itself. The highest proportion of antidiabetic-related harm referred to a single drug item (70% of patients in the hypoglycemic group), which indicates that, more than the type of a drug, the dose makes a difference. Most likely, the oldest patients, unable to visit a specialist regularly, stay a long time on the same (too high) doses of antidiabetics although they actually need lesser doses (due to weight loss, sarcopenia, comorbidity, frailty, etc). They manifest hypoglycemia atypically (fall, confusion, cognitive worsening, syncope, and cardiac arrhythmia). Therefore, according to the American Diabetes Association (2018), the treatment goals include hemoglobin A<sub>1c</sub> levels below 7.5% for healthy adults with few comorbidities and normal cognitive function and 7.5% to 8.5% for those with multiple comorbidities and cognitive impairment.<sup>2</sup>

**ARTICLE INFORMATION**

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