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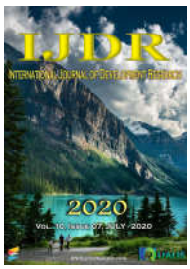

RESEARCH ARTICLE OPEN ACCESS

ANALYSIS OF GLYCEMIC CONTROL IN ELDERLY OCTOGENARIANS USING ORAL HYPOGLYCEMIC AGENTS

Phellipe Fabbrini Santos Lucas[1] and Vicente Paulo Alves[2]

[1]Graduação em Medicina, Universidade Católica de Brasília, Brasília - DF, Brasil
[2]Programa de Pós-Graduação em Gerontologia, Universidade Católica de Brasília, Brasília - DF, Brasil

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Corresponding author:
Karla Helena Coelho Vilaça e Silva

ABSTRACT

Aims: Consider the glycemic level of elderly octogenarians with diabetes mellitus when using oral hypoglycemic agents. **Methods:** Descriptive study carried out by reviewing data collected from patients treated on an outpatient basis at the Hospital da Universidade Católica de Brasília - HUCB. The patients were submitted to medical evaluation through an anamnesis in a first consultation, where diseases that had already been diagnosed and the medications that are taken under medical prescription were reported. The elderly were subsequently referred to a Clinical Analysis Laboratory for the blood collection of laboratory tests. We assessed glycemia and glycated hemoglobin in patients diagnosed with diabetes mellitus II and the drug therapy used for glycemic control. **Results:** Data on 139 elderly people aged 80 years and over were analyzed. Of these, 36 (25.9%) had diabetes mellitus II and 29 (20.9%) were using oral hypoglycemic agents. Patients who did not present information on the diagnosis of DM II and use of oral hypoglycemic agents, who used insulin or who did not have results of laboratory tests were excluded from the analysis. It was observed that, among diabetic patients using oral hypoglycemic agents, 19 (52.8%) presented increased glycemia and 10 (27.8%) normal glycemic index. In the analysis of Glycated Hemoglobin (HbA1c), 13 patients (36.1%) presented normal results and 16 (44.4%) increased rates. The presence of 16 patients with concomitantly increased glycemic indexes and HbA1c was found, with 6 using Metformin + Gliclazide and 8 using Metformin up to a dose of 2550 mg / day. **Conclusion:** A small portion of patients using drug therapy had goals for glycemic control. Age and accompanying metabolic changes interfere with the effectiveness of drugs in the body. Greater individualization of treatments and greater monitoring of the prescription of oral hypoglycemic agents is necessary in this portion of the population, always analyzing the risks of possible hypoglycemia and the chronic effect of high glycemic levels in the body.

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INTRODUCTION

The ongoing increase in longevity among elderly Brazilians poses challenges to society and individuals who age. The physiological mechanisms of aging result in physical decline with neural and endocrine disruption, modification of body composition, decreased immune function, decreased resistance to stressors in addition to loss in psychomotor speed (FRIED *et al*, 2001). The functions of different organs become deficient, and the physiological decline translates into changes in pharmacokinetic and pharmacodynamic patterns that lead to changes in the effectiveness of medications and increased susceptibility to adverse effects in this portion of the population. Among the most prevalent disorders in this age group, diabetes mellitus II stands out, which directly or indirectly is among the top ten causes of deaths and hospitalizations among elderly people aged 80 years and over in Brazil (BRASIL, 2010). Type II Diabetes Mellitus (DM II) is a disorder characterized by insulin resistance and a progressive decrease in its secretion, which results in hyperglycemia. The prevalence of a chronic state of hyperglycemia can lead to micro and macrovascular complications, diabetic retinopathy and nephropathy, in addition to other complications resulting from diabetes

(PANAROTTO *et al*, 2008). Control of blood glucose levels is achieved with lifestyle changes and pharmacological therapy (ROVARIS *et al*, 2010). According to the Brazilian Diabetes Society (SBD), robust studies aimed at the treatment of individuals with DM II and older than 75 years are lacking, so that the treatment of the elderly obeys the same principles applied to younger age groups. In addition, there are few studies found in the literature to study the direct effects of drugs on the glycemic profile of elderly octogenarians. These patients are subject to a decrease in renal function, with decreased glomerular filtration, decreased hepatic blood flow and, consequently, changes in phases I and II of drug metabolism, changes in motility of the gastrointestinal tract, decreased body composition of water that influences in the volume of drug distribution (SOUZA *et al*, 2012). In search of study and explanation to the above, the work aims to evaluate the effectiveness of therapies used with oral hypoglycemic agents in the glycemic control of elderly octogenarians, in order to know the clinical reality of these patients and seek further evidence on the effects of this therapy in this portion of the population.

METHODS

The present study used data contained in the electronic bank of the multicenter research "Patterns of cognitive and psychosocial physical aging in long-lived elderly people living in different contexts", a cross-sectional study financed by the National Program for Academic Cooperation (PROCAD) of CAPES (Commission for the Improvement of Higher Education Personnel), which proposed to investigate the relationships between demographic and socioeconomic risk variables, stressful events experienced in old age, indicators of cognitive reserve, physical health, social resources and elements of psychological resilience. The data were collected in an outpatient setting at the Hospital of the Catholic University of Brasilia - HUCB. The participants were subjected to medical evaluation through an anamnesis in a first consultation, where diseases that had already been diagnosed and medications that were taken under medical prescription were raised. The elderly were subsequently referred to a Clinical Analysis Laboratory for the blood collection of laboratory tests, which together with other results they should bring to the return visit. The tests performed in this laboratory were used for analysis in the present study, which were: Fasting glycemia and Glycated Hemoglobin. The research project was submitted to and approved by the Research Ethics Committee - REC (CAAE nº 50075215.2.0000.0029) of the Catholic University of Brasília, under opinion No. 1,290,368 and carried out after informing the elderly about the research objective, the voluntary nature of their participation and signature of the Free and Informed Consent Form (ICF) by the elderly or responsible caregiver.

Sample: Elderly men and women participated in the study, who were part of a previous list of visits by geriatric doctors and those scheduled by the SUS Appointment and Examination Scheduling Center, where only those who were 80 years old or older were invited to participate in the research. In total, 226 participants were recruited, who received information, either in person or by telephone, about the nature of the research and were instructed to appear on the day and time scheduled at the geriatric clinic at HUCB, alone or with a companion. The study included elderly people who could understand and answer the instruments applied from March 2016 to May 2018. Elderly people who did not sign the Informed Consent Form (ICF), elderly people who were unable to respond were excluded. to the questionnaires, elderly people who died during the research period or who refused to continue in the subsequent stages and elderly people without conditions to travel to the places for multi-professional assessment, thus totaling 190 long-lived elderly people in the analyzed sample, with 36 elderly people fitting for different situations in this relationship of exclusion. After standardizing the data, 51 patients were excluded for not presenting information on the diagnosis of DM II, use of oral hypoglycemic agents, or results of laboratory tests, totaling 139 patients in the final sample used.

Definitions: Biochemical measurements were performed using methods standardized by the Clinical Analysis Laboratory. The parameters: "decreased", "normal and" increased "used in the present study were defined by the reference values used by the laboratory for the interpretation of biomarkers. For the analysis of blood glucose, it was considered: Decreased: <70 mg / dl; Normal: 70 to 99 mg / dl; Increased:> or equal to 100 mg / dL according to the new criteria recommended by the American Diabetes Association, 2003. For the analysis of HbA1c it was considered: Normal: <6.0%; Increased:> or equal to 6.0%. The method used in this measurement of glycated hemoglobin is certified by the National Glycohemoglobin Standardization Program (NGSP). The elderly, diagnosed with DM II and using oral hypoglycemic agents were divided into 2 groups according to the dosage and medication used. For the analysis of drug therapy, it was considered: Therapy 1: Metformin (use of 1000mg to 2550mg / day) and Therapy 3: metformin and gliclazide in any dose.

Data Analysis: Statistical analyzes were performed using the SPSS® for Windows program (SPSS Inc., Chicago, IL, USA). Categorical variables were presented as proportions. An attempt was made to establish a relationship between the diagnosis of by a doctor, before the first consultation, self-reported by the elderly, the results of tests performed at the Clinical Analysis Laboratory and the therapy used, which was also self-reported.

RESULTS

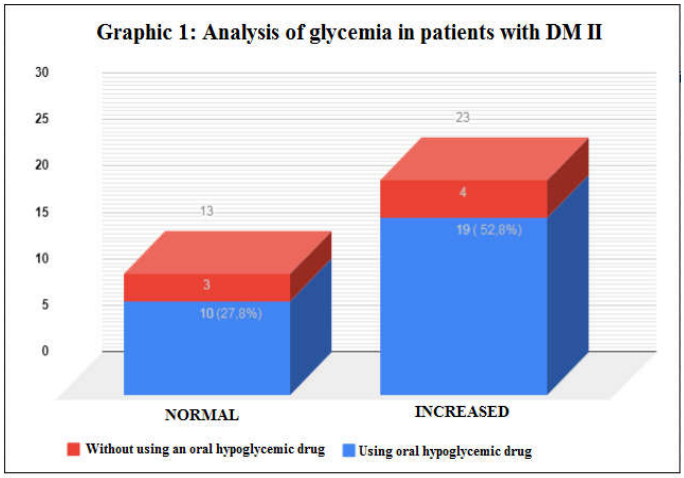
Data from 139 elderly people aged 80 years or older, treated on an outpatient basis, were included in the analysis. Of these, 36 patients (25.9%) had Diabetes Mellitus. Table 1 makes an analysis of the glycemia found in the study group and already allows initial considerations regarding the management of the disease in this age group. Among diabetic patients, 23 (63.9%) had increased glycemic indexes and only 13 (36.1%) normal glycemic indexes. A number that draws attention in this initial approach is that 12.9% of the total sample has increased blood glucose without however having a diagnosis of diabetes mellitus or even glucose intolerance. Regarding medication use, it was found that 20.9% of the sample were using therapy with oral hypoglycemic agents, revealing the high prevalence of the use of these drugs in the age group. When analyzing the most prevalent therapy, it was noted that the use of Metformin (Dose: up to 2550 mg / day) is the most used, corresponding to 65.5% of patients who are using oral hypoglycemic agents. Then, 34.4% using Metformin + Gliclazide. You can also see in Table 2 that 7 patients with a previous diagnosis of DM II were not using therapy even in outpatient follow-up.

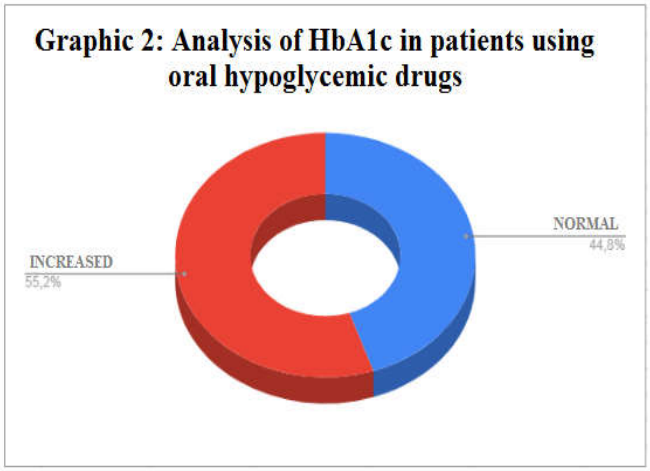
Table 1. Analysis of the general glycemic profile

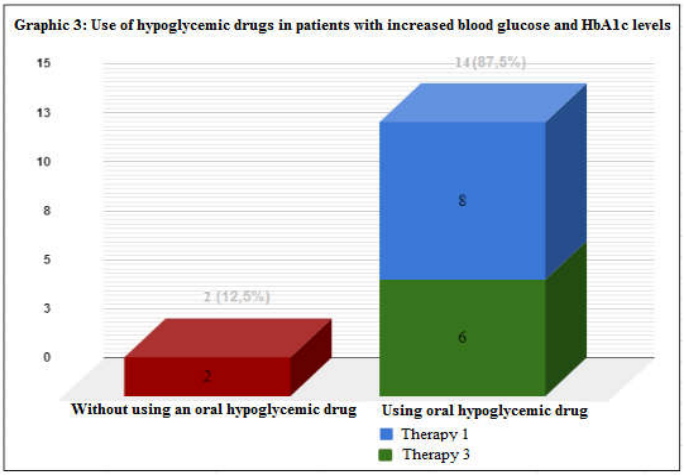
			Diabetes		TOTAL
			Yes	No	
Glucose	Normal	Count	13	83	96
		% within Glucose	13,5%	86,5%	100,0%
		% within Diabetes	36,1%	80,6%	69,1%
		% of Total	9,4%	59,7%	69,1%
	Increased	Count	23	18	41
		% within Glucose	56,1%	43,9%	100,0%
		% within Diabetes	63,9%	17,5%	29,5%
		% of Total	16,5%	12,9%	29,5%
	Decreased	Count	0	2	2
		% within Glucose	0,0%	100,0%	100,0%
		% within Diabetes	0,0%	1,9%	1,4%
		% of Total	0,0%	1,4%	1,4%
Total		Count	36	103	139
		% within Glucose	25.9%	74,1%	100,0%
		% within Diabetes	100,0%	100,0%	100,0%
		% of Total	25,9%	74,1%	100,0%

Table 2. Use of Oral Hypoglycemic

			Diabetes		TOTAL
			Yes	No	
Oral Hypoglycemic	Yes	Count	29	1	30
		% within Oral Hypoglycemic	96,7%	3,3%	100,0%
		% within Diabetes	80,6%	1,0%	21,6%
		% of Total	20,9%	0,7%	21,6%
	No	Count	7	102	109
		% within Oral Hypoglycemic	6,4%	93,6%	100,0%
		% within Diabetes	19,4%	99,0%	78,4%
		% of Total	5,0%	73,4%	78,4%
Total		Count	36	103	139
		% within Oral Hypoglycemic	25.9%	74,1%	100,0%
		% within Diabetes	100,0%	100,0%	100,0%
		% of Total	25,9%	74,1%	100,0%







When analyzing the Glycemia and Hba1c values of patients diagnosed with DM II using oral hypoglycemic agents, it was expected to find a larger portion of the elderly with values within the established goals for the management of the disease. A large percentage of these patients were observed with increased values of biochemical markers, suggesting that the therapies used are not being effective for the control of glycemic levels in this age group or that there is a failure in the use of these drugs according to the dosage prescribed for the oldest old. Graph 1 allows the visualization of this scenario, among patients with DM II and using oral hypoglycemic agents 19 (52.8%) had high blood glucose levels, whereas in only 10 (27.8%) the levels found were within the reference values. In relation to diabetic patients, but who were not using therapy at the time of the consultation, a close value was found between the groups, 4 elderly people had high blood glucose and 3 elderly people had their blood glucose levels unchanged. When he switched his research to Glycated Hemoglobin, he found even more exciting numbers. When analyzing the sample of diabetic patients, 18 (50%) of them had levels above the reference limit and 18 (50%) had a normal index. But when specifying this analysis only to diabetic patients who were using oral hypoglycemic agents, a slight increase in the percentage of increased levels of HbA1c was noted, 16 (55.2%) of these elderly people were found to have elevated levels against 13 (44 , 8%) with values within the reference limit (Graphic 2).

Finally, it was found that 16 out of 36 patients with diabetes had both high blood glucose levels and increased HbA1c values in the tests performed. It was considered an important number, since approximately half (44.4%) of diabetic patients undergoing outpatient follow-up presented themselves at the time of the research without proper control of the disease. Of the 16 patients without adequate control of the indices, 14 (87.5%) were using oral hypoglycemic agents at the time of the consultation, whether using Metformin - 1000mg up to 2,550mg / day (8 patients) or using combination therapy, in this study represented by the use of Metformin + Gliclazide (6 patients). Only 2 elderly people had a concomitant change in biochemical markers and were not using any therapy. The considerations can be analyzed in Graphic 3.

DISCUSSION

It was considered a limiting factor of this study to obtain data through an electronic bank in which the analysis of the biochemical markers used was made in a qualitative way and, due to this reason, a more robust relationship between the biomarkers and the use of medicines was not fulfilled. A new analysis and update with the numbers found in the exams performed by the elderly is necessary. It was also necessary to exclude a considerable number of patients who presented incomplete data in relation to the analyzed parameters. This study aimed to evaluate the control of diabetes mellitus II found in clinical practice in long-lived patients, as well as to understand the interaction of physiological factors resulting from aging in the process of metabolizing drugs used to manage the disease. Regarding the point prevalence of the disease in the sample studied, a higher number than that described in the literature was found. In the present study, 36 long-lived, which corresponds to 25.9% of patients, had diabetes mellitus II, while there is a prevalence in the elderly over 60 years, estimated by ISA-SP at 15.4 % and 14.6% by the Bambuí Project - Population-based Cohort Study of Elderly Health 7. The number can be explained by the fact that the elderly studied had previously undergone outpatient follow-up, making the sample more likely to present a diagnosis at the time of the research. The analysis of blood glucose among the total sample, found in Table 1, shows that 41 patients had elevated blood glucose levels, and only 23 had reported a previous diagnosis of DM II. This may be due to a high number of elderly people with glucose intolerance or may suggest underdiagnosed cases, which would make these numbers worrying, since the interviews were conducted in an outpatient setting. Maintaining a hyperglycemic state can lead to micro and macrovascular complications, diabetic retinopathy and nephropathy, in addition to other complications resulting from DM II (PANAROTTO *et al*, 2008).

It is interesting to note that the most prevalent therapy among patients using oral hypoglycemic agents is Metformin (up to 2550 mg / day), corresponding to 65.5% of this sample and then the use of Metformin + Gliclazide (34.4%) . Metformin is an oral antidiabetic product widely used in clinical practice and among its different mechanisms of action, the most relevant is the reduction of hepatic glucose production (Sociedade Brasileira de Diabetes, 2019). It is estimated that its use, dose up to 2550 mg (maximum dosage), causes a 60 to 70 mg / dl reduction in fasting blood glucose and a 1.5 to 2% reduction in HbA1c values (Sociedade Brasileira de Diabetes, 2019). It is a drug with extensive experience in clinical practice, and in addition to the reduction of glycemic indexes it is related to improved lipid profile and weight loss. Some situations contraindicate the use of this medication in the elderly, such as renal failure, chronic obstructive pulmonary disease, liver failure and chronic alcoholism (Sociedade Brasileira de Diabetes, 2019). Thus, the importance of a careful evaluation before the start of therapy is emphasized and periodic monitoring is recommended since high doses, as found in the most prevalent therapy in the sample, for prolonged periods are related to the reduction of vitamin levels B12 in the body and can generate hematological disorders and neurological syndromes. In a final analysis, it was found that 16 of the 36 patients with diabetes had both high blood glucose levels and increased HbA1c values in the tests performed. It is important to highlight that 87.5% of the patients with the increased indexes were using oral hypoglycemic agents. In other words, they presented altered values even with an estimated reduction of 60 to 70 mg / dl of fasting blood glucose and a reduction of 1.5 to 2% in the HbA1c values. In this scenario, it should be noted that the recommendation of the first measure in the treatment of DM II by scientific societies is the association of metformin with diet and physical activities (SociedadeBrasileira de Diabetes, 2019). The assessment of changes in lifestyle among patients was not found in the electronic bank, thus, they were not analyzed at work. However, 6 elderly people with increased glycemic indexes were already using therapy with a combination of drugs, such a strategy is used when the predetermined glycemic target cannot be reached. Even so, they did not present the goals for the control of the disease.

Conclusion

The majority of patients using drug therapy did not present glycemic levels within the reference values established for the management and control of the disease. Despite the orientation that the treatment of the elderly obeys the same principles

applied to younger age groups, attention should be paid in clinical practice to the factors that make the monitoring of this disease in the octogenarians more closely and judiciously. It is important that knowledge about the physiological mechanisms of aging at an advanced age, and about the variables that can contribute to healthy longevity in the elderly, be evidenced and disseminated in the clinical setting. Therefore, it is mandatory to choose therapy individually in these patients, in addition to the widespread assessment of liver and kidney function before the choice of medication, it is necessary to be aware of the increase in life expectancy in this age group and the possible harmful effects that a chronic state of hyperglycemia can cause the quality of life of these people.

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