

Severe Hypoglycemia in an Emergency Department of a General Hospital in Costa Rica

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ABSTRACT

Objective: To report the frequency of severe hypoglycemic events (SHGE) admitted into the Emergency Department (ED) of Hospital San Juan de Dios.

Methods: We recorded demographic, clinical characteristics, finger-stick glucose level, co-morbidities and length of stay of diabetics treated with anti-hyperglycemic agents suffering SHGE. Healthcare costs linked to admission into ED with SHGE were assessed.

Results: From March to July 2018, 55620 patients were attended at the ED. Of them, 4434 had non-communicable conditions including 961 diabetics, of those 61 had SHGE. Females ($n = 37$, aged 70 ± 16.01 yo) and males ($n = 24$, aged 62.9 ± 13.4 yo) (mean \pm SD) constitute the study population. The reported co-morbidities were: cardiovascular disease (16.3 %), cerebrovascular disease (11.4 %), renal disease (19.6%) and chronic liver disease (1.6 %). In females finger-stick glucose level was 42 ± 15.44 mg/dl and in males 32.6 ± 8.8 mg/dL (mean \pm SD, $p=ns$). Four patients had 2 episodes of SHGE and another patient presented seizures. SHGE was associated with insulin in 56 patients, 2 cases associated to glibenclamide and in three the medication was unknown. Of those on insulin, 22 also received metformin. All received IV dextrose and none required hospitalization. The length of stay in ED was 3.46 ± 5.3 hours. The costs per patient's visits were 693 ± 303 dollars representing an overall cost of 42.3000 US dollars. Patient's costs due to loss of working hours were not evaluated.

Discussion: This is the first study, which explores the significance of SHGE in the ED of a tertiary hospital in Costa Rica. Recurrent and severe hypoglycemia could trigger future cardiovascular events and aggravates cognitive dysfunction in elderly diabetics.

Conclusion: Hypoglycemia represents an unexplored complication associated to diabetes treatment in Costa Rica. Better ambulatory glycemic management and evaluation of current pharmacologic approaches is recommended in this country.

Keywords

Diabetes complications, Severe hypoglycemia, Emergency department, Diabetes treatment.

Introduction

Diabetes represents a worldwide health problem associated with

macrovascular and microvascular complications and premature death [1,2]. Diabetes prevalence is increasing in Costa Rica [3,4] and in Latin America all cause mortality among persons with type 2 diabetes is more than double as compared to people without diabetes [5]. The objectives of diabetes treatment focus to achieve metabolic control improve quality of life and prevent

or delay chronic complications [6,7]. By treating hyperglycemia microvascular complications can be avoided, while aggressive lipid and hypertensive management impact primarily on macrovascular complications [8-10]. Recent data indicate that newer therapeutic strategies can improve glycemic control with fewer side effects and have cardio-renal protection [11-16]. Some commonly used oral agents and intensification of insulin treatment aimed to reach strict glycemic goals can induce hypoglycemia and glucose variability [17-22].

In addition, hypoglycemia represents a barrier to achieve optimal glycemic control and it is associated with a number of complications including falls, fractures, cognitive dysfunction, arrhythmias, and cardiovascular morbidity and cardiovascular death [17-23]. A number of risk factors for hypoglycemia include advance age, strict glucose control, glucose variability, duration of insulin treatment, impaired awareness of hypoglycemia, previous severe hypoglycemia, renal insufficiency and decreased cognitive ability [17-23]. While hypoglycemia has emerged as a serious condition associated with diabetes treatment, little is known about the prevalence of hypoglycemia in Costa Rica. In view of this, we performed an exploratory evaluation of the frequency of hypoglycemic events in diabetic patients attended in the ED of a tertiary facility in this country. In addition, the health care costs associated with such events was analyzed.

Material and Methods

We retrospectively reviewed charts of diabetic patients treated with anti-hyperglycemic agents who presented SHGE at the ED of the Hospital San Juan de Dios. SHGE were recorded as an adverse event according to the regulation of the National System of Surveillance [24]. The clinical data, age, sex, and the patient's co-morbidities were obtained from the daily epidemiologic report of the Department of Epidemiology. Finger-stick glucose levels were measured with a Freestyle Optium glucometer from Abbott. Hypoglycemia was diagnosed based on the clinical presentation and with glucose levels below 70 mg/dL [25]. Additionally, we estimated the healthcare costs linked to admission into ED with SHGE.

Results

From March to July 2018, 55620 patients were attended at the ED. 4434 of them had chronic non-communicable conditions including 961 diabetics. SHGE was documented in 61 cases representing 6.34 % of the diabetic patients admitted in the ED during a six-month period. Baseline characteristics of the 61 patients with SHGE were analyzed descriptively. There were 37 females aged 70 ± 16.01 years and 24 males aged 62.9 ± 13.4 years (mean \pm SD). The most frequent co-morbidities were cardiovascular disease (16.3 %), cerebrovascular disease (11.4 %), renal disease (19.6%) and chronic liver disease (1.6 %). As shown in Figure 1 there were a cluster of comorbidities in the same patient. At admission, 28 patients were receiving NPH plus regular insulin; 24 patients were treated with NPH alone; in two patients the type of insulin was not specified and one patient used only regular insulin. In three patients the hyperglycemic treatment was not reported and

2 patients were on glibenclamide.

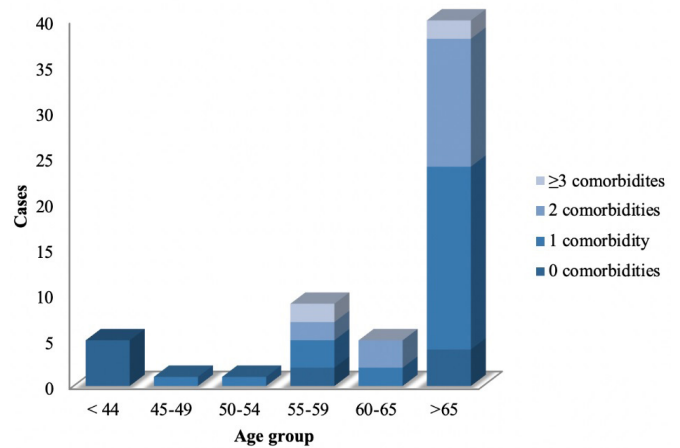


Figure 1: Clustering of comorbidities in diabetic patients admitted with severe hypoglycemia into the Emergency Department.

Finger-stick glucose levels were obtained in 56 patients. In females glucose level was 42 ± 15.44 mg/dl and in males 32.6 ± 8.8 mg/dL ($p=ns$). Two patients with severe symptomatic hypoglycemia, who were treated in the ambulance prior to ED admission, had a glucose concentration above 70 mg/dL. Hypoglycemic events according to patient's age (A) and distribution of glucose concentration (B) are shown in Figure 2.

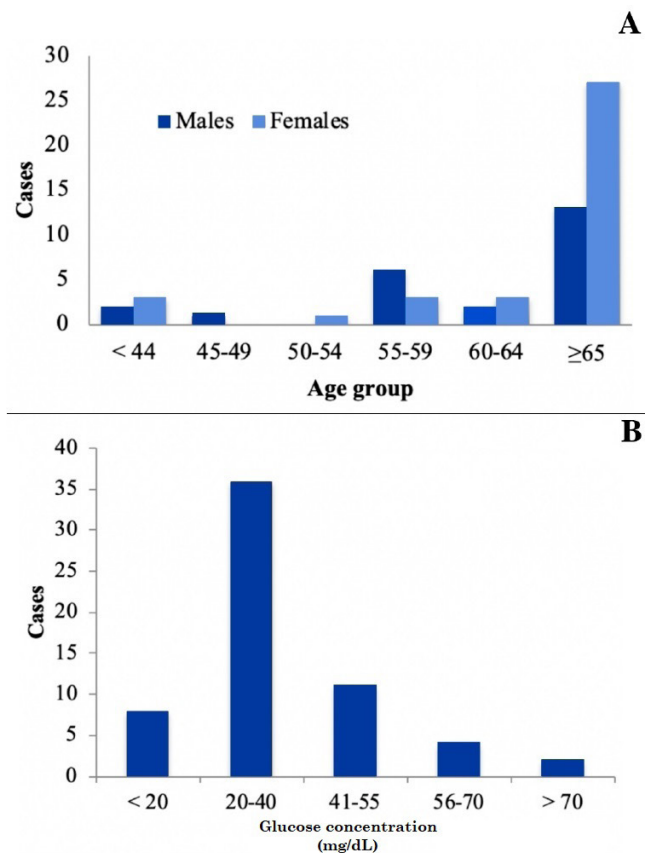


Figure 2: A. The majority of hypoglycemic events occurred in diabetic patients older than 65 years of age. B. Distribution of glucose concentration (mg/dL).

Four patients had 2 episodes of SHGE in different days and one patient presented seizures. The length of stay in ED was 3.46 ± 5.3 hours, however, some patients had longer stay at the ED including one patient due to suspicious of ischemic heart disease. Fifteen patients were evaluated for urinary tract infection and sepsis, 16 patients had hemodynamic and metabolic instability requiring cardiovascular evaluation including arterial blood gases. All the patients were treated with IV glucose infusion and managed at the ED and none required hospitalization. Fifty percent of SHGE arrived at the ED around noon and the rest between early evening hours until midnight. The patients were discharged without modification of medical treatment but were advised to seek further attention at the primary care setting [4]. The costs for the health care system per patient's visits were approximately 693 ± 303 dollars representing an overall cost of 42,3000 US dollars. Patient's costs due to loss of working hours or potential disability due to SHGE were not evaluated.

Discussion

In this report we describe the occurrence of SHGE in diabetic patients attended at the ED of one of the largest tertiary hospitals in San José, Costa Rica. SHGE predominantly occurred in elderly female type 2 diabetic patients with multiple chronic complications. Risk factors for hypoglycemia, were advanced age, the presence of cardiovascular, renal and hepatic disease and in those treated with insulin. Noteworthy, the health-care system of Costa Rica represented by the Caja Costarricense de Seguro Social (CCSS) provides universal medical care [3,4]. Diabetic patients are mainly seen in the primary care setting while those with complications are referred to specialists in tertiary hospitals [3,4]. Anti-hyperglycemic medication available in the CCSS includes metformin, glybenclamide and human insulin. Insulin pens are not available thus; administration of insulin is done using syringes and needles.

Greco et al. prospectively studied 99 type 2 diabetics aged 80 years or older admitted with severe hypoglycemia. Most of the episodes were linked to oral agents, while insulin associated hypoglycemia was reported in only 12 patients [26]. Furthermore, in a retrospective multicenter study including 520 older patients, 85.4 % of them with type 2 diabetes developed severe hypoglycemia. Of those patients 42.8 % were on insulin and 13.6 % were on combined therapy [27]. In our report, however, the majority of SHGE occurred in diabetics taking human insulin alone or in combination with metformin and only two were taken glibenclamide. Similarly, to a previous report [28] half of our patients arrived at the ED in a bimodal fashion, approximately half of them at noon and the rest in the evening hours. As the usual insulin dosing in diabetic patients is before breakfast and before the evening meal, one may presume that the time when the patients arrived to the ED corresponded to the peak of action of human insulin. In our study, none of the patients had SHGE associated with insulin analogues as in the public health care system the patients only have access to human insulin.

Noteworthy, in Taiwan more than fifty percent of patients with

hypoglycemia seen at the ED had concomitant complications including urinary tract infection or pneumonia requiring hospitalization [29]. Likewise, our patients were evaluated for urinary tract infections but following the ED protocol, the majority of our patients were discharged less than 4 hours after admission. Of note, in the ED our patients did not receive indications to modify insulin treatment in order to prevent further hypoglycemic episodes. Accordingly, some patients suffered of recurrent hypoglycemic events in different occasions. One patient presented seizures suggesting the existence of impaired autonomic responses and risk of unawareness hypoglycemia [19]. Patients with hypoglycemic events treated with oral anti-hyperglycemic agents had a greater risk than individuals taking insulin alone for recurrent hypoglycemia within 48 h after discharge [30]; however, this was not the case in our patients who mainly received human insulin.

Potential causes linked to SHGE in our patients were prolonged fasting, excessive physical activity, concomitant illness, inadequate insulin dosing, mistakes of insulin administration, scantiness of glucose monitoring, lower initial blood glucose or high glucose variability. It is important to mention that, when basal NPH and bolus regular insulin is prescribed, our patients usually to mix both insulin in the same syringe using the same 12.7 mm needles [4]. By doing this, elderly patients with impaired visual acuity may retrieve inadequate amounts of insulin.

Unfortunately, due to the characteristics of this study we cannot capture such potential causes for SHGE, which remained unanswered. Not either, the impact of SHGE on the patient's health and quality of life after the hypoglycemic event was evaluated in our report. However, the estimated cost associated with the patient's attention during a short period was surprisingly elevated. In developed countries, hypoglycemia represents enormous costs, which has declined over the last years [31,32]. Consequently, supplementary investigation to evaluate the total expenditure associated with the attention of patients with hypoglycemia at the ED is required in Costa Rica.

This report has a number of limitations. Namely, the data were recorded retrospectively as an adverse effect, thus it was not possible to document home monitoring, insulin dosing, the mode of insulin administration including type of syringes and needles used. Likewise, we did not assess the patient's meal patterns; exercise level, the presence of unawareness hypoglycemia or other factors, which predispose to hypoglycemia.

Finally, considering that this report comprises data from only one tertiary hospital, the magnitude of hypoglycemia and its implications remains largely unknown. Besides, the economic impact of hypoglycemia warrants further investigation to better estimate the expenditure associated with the attention of patients with hypoglycemia. Despite the limitations of this report, we highlighted hypoglycemia as a risky event with potential consequences in elderly diabetic patients in Costa Rica.

In conclusion, in view of this alarming findings, revision of clinical practice protocols, evaluation of current pharmacologic approaches together with diabetes education and adherence to international guidelines are mandatory actions, which need to be implemented in Costa Rica as recommended previously [33].

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References

1. Whiting DR, Guariguata L, Weil C, et al. IDF diabetes atlas: global estimates of the prevalence of diabetes for 2011 and 2030. *Diabetes Research and Clinical Practice*. 2011; 94: 311-321.
2. Stamler J, Vaccaro O, Neaton JD, et al. Diabetes, other risk factors, and 12-yr cardiovascular mortality for men screened in the Multiple Risk Factor Intervention Trial. *Diabetes Care*. 1993; 16: 434-444.
3. Barcelo A, Gregg EW, Gerzoff RB, et al. Prevalence of Diabetes and Intermediate Hyperglycemia Among Adults From the First Multinational Study of Noncommunicable Diseases in Six Central American Countries The Central America Diabetes Initiative (CAMDI). *Diabetes Care*. 2012; 35: 738-740.
4. <https://www.paho.org/salud-en-las-americas-2017/costa-rica>
5. Carrillo-Larco R, Barengo NC, Albitres-Flores L, et al. The risk of mortality among peoples with type 2 diabetes in Latin America: A systematic review and meta-analysis of population-based cohort studies. *Diabetes Metab Res Rev*. 2019; 35: e3139.
6. Nathan DM, Genuth S, Lachin J, et al. The Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med*. 1993; 329: 977-986.
7. UK Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). *Lancet*. 1998; 352: 837-853.
8. Ohkubo Y, Kishikawa H, Araki E, et al. Intensive insulin therapy prevents the progression of diabetic microvascular complications in Japanese patients with non-insulin dependent diabetes mellitus: a randomised prospective 6-year study. *Diabet Res Clin Pract*. 1995; 28: 103-117.
9. Nathan D, Bayless M, Cleary P, et al. For the DCCT/EDIC Research Group. Diabetes Control and Complications Trial/ Epidemiology of Diabetes Interventions and Complications Study at 30 Years: Advances and Contributions. *Diabetes*. 2013; 62: 3976-3986.
10. Gerstein HC, Bosch J, Dagenais GR, et al. The ORIGIN Trial Investigators. Basal insulin and cardiovascular and other outcomes in dysglycemia. *N Engl J Med*. 2012; 367: 319-328.
11. Zinman B, Wanner C, Lachin JM, et al. Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. *N Engl J Med*. 2015; 373: 2117-2128.
12. Neal B, Perkovic V, Mahaffey KW, et al. Canagliflozin and cardiovascular and renal events in type 2 diabetes. *N Engl J Med*. 2017; 377: 644-657.
13. Wiviott SD, Raz I, Bonaca MP, et al. Dapagliflozin and cardiovascular outcomes in type 2 diabetes. *N Engl J Med*. 2019; 380: 347-357.
14. Perkovic V, Jardine MJ, Neal B, et al. Canagliflozin and renal outcomes in type 2 diabetes and nephropathy. *N Engl J Med*. 2019; 380: 2295-2306.
15. Marso SP, Daniels GH, Brown-Frandsen K, et al. Liraglutide and cardiovascular outcomes in type 2 diabetes. *N Engl J Med*. 2016; 375: 311-322.
16. Marso SP, Bain SC, Consoli A, et al. Semaglutide and cardiovascular outcomes in patients with type 2 diabetes. *N Engl J Med*. 2016; 375: 1834-1844.
17. Adler GK, Bonyhay I, Failing H, et al. Antecedent Hypoglycemia impairs autonomic cardiovascular function: implications for rigorous glycemic control. *Diabetes*. 2009; 58: 360-366.
18. Dunning T, van den Heuvel I, Dickmann A, et al. Hypoglycemia aggravates critical illness-induced neurocognitive dysfunction. *Diabetes Care*. 2010; 33: 639-644.
19. Garg R, Hurwitz S, Turchin A, et al. Hypoglycemia, with or without insulin therapy, is associated with increased mortality among hospitalized patients. *Diabetes Care*. 2013; 36: 1107-1110.
20. Shorr RI, Ray WA, Daugherty JR, et al. Incidence and risks factors for serious hypoglycemia in older persons using insulin or sulphonylureas. *Arch of Intern Med*. 1997; 157: 1681-1686.
21. Frier BM. Hypoglycaemia in diabetes mellitus: epidemiology and clinical implications. *Nat Rev Endocrinol*. 2014; 10: 711-722.
22. Torimoto K, Okada Y, Hajime M, et al. Risk Factors of Hypoglycemia in Patients with Type 2 Diabetes Mellitus: A Study Based on Continuous Glucose Monitoring. *Diabetes Technol Ther*. 2018; 20: 603-612.
23. Souza C, Salazar, H, Cheong B, et al. Association of hypoglycemia and cardiac ischemia: a study based on continuous monitoring. *Diabetes Care*. 2003; 26: 1485-1489.
24. Reglamento de Buenas Practicas de Farmacovigilancia. N° 39417-S 29/07/2016.
25. Cryer PE. Individualized Glycemic Goals and an Expanded Classification of Severe Hypoglycemia in Diabetes. *Diabetes Care*. 2017; 40: 1641-1643.
26. Greco D, Pisciotta M, Gambina F, et al. Severe hypoglycemia leading to hospital admission in type 2 diabetic patients aged 80 years or older. *Exp Clin Endocrinol Diabetes*. 2010; 118: 215-219.
27. Mantovani A, Grani G, Chiona L, et al. Severe hypoglycemia in patients with known diabetes requiring emergency department care: A report from an Italian multicenter study.

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- Journal of Clinical and Translational Endocrinology. 2016; 5: 46-52.
28. Kumar GJ, Abbilash KPP, Saya RP, et al. A retrospective study on epidemiology of hypoglycemia in Emergency Department. Indian Journal of Endocrinology and Metabolism. 2017; 21: 119-124.
29. Jan Su Y, Jung Lio C. Hypoglycemia in Emergency Department. Journal of Acute Disease. 2015; 1: 59-62.
30. Betten DP, Castle DJ, Hughes MJ, et al. Frequency of return visits to the emergency department in patient discharged following hypoglycemic episodes. Int J Emer Med. 2018; 11: 28-30.
31. O'Connor L, Kue RC, O'Connor MJ. Characteristics of Patients with Recurrent Emergency Medical Services Utilization for Symptomatic Hypoglycemia in an Urban Setting. Prehosp Emerg Care. 2019; 20: 1-8.
32. Zhao Y, Shi Q, Wang Y, et al. Economic burden of hypoglycemia: Utilization of emergency department and outpatient services in the United States (2005-2009). J Med Econ. 2016; 19: 852-857.
33. Mechanick JI, Harrel RM, Allende-Vigo M, et al. AACE/ACE Transculturalization Recommendations for Developing Latin American Clinical Practice Algorithms in Endocrinology- Proceedings of the 2015 Pan-American Workshop by the American Association of Clinical Endocrinologists and American College of Endocrinology. Endocrine Practice. 2016; 2: 476-501.