

Clinical applicability of glycated hemoglobin in the evolution of patients with hospital hyperglycemia

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Abstract

Diabetes Mellitus (DM) consists of a chronic illness occasioned by hyperglycemia. It is known that this pathology is present in approximately 10% of the hospitalizations, and that a significant percentage of the patients with DM presents itself without previous diagnosis at the time of the hospitalization. Hyperglycemia can provoke deleterious effects in the organism as an inflammatory process. To evaluate glycated hemoglobin (HbA1c) as a diagnosis and predictive tool in the clinical evolution of patients with and without DM diagnosis, evaluated during the period of hospitalization and its relation with hospitalization complication. There were 100 patients evaluated during the period of one year and verified through the NUMAD (*Núcleo Multidisciplinar de Atendimento ao Paciente Diabético do Hospital Samaritano*) institutional protocol values of HbA1c in patients with hyperglycemia. The patients without previous diagnosis of DM evinced HbA1c between 5.8% and 7.5%, with a mean of hospitalization period of 9 days, without complications. The patients with DM who evolved with complications, evinced HbA1c between 7.3% and 12.4% and corresponded to 20% of the study, with a mean of period of hospitalization of 34.5 days. Studies describe the prevalence of hyperglycemia related to comorbidities and the period of hospitalization, and principally in relation to the glycated hemoglobin as marker of gravity independent of the pathology. Our study demonstrated the importance of this tool as an ally to hospital. HbA1c evinced itself in our study as a prognosis marker and an important predictor in patients with hospital hyperglycemia.

Introduction

Patients who need hospitalization due to diverse pathologies can evince hyperglycemia having had or not having had a previous DM. It is known that high levels of glycaemia can propitiate exacerbation of the systemic inflammatory process contributing to the evolution of intra hospital complications [1-3].

The hyperglycemia in a hospitalized patient can be characterized as "stress hyperglycemia", which is generally due to the occurrence of an acute sickness, which is responsible for the liberation of inflammatory cytokines and counter regulator hormones (glucagon, adrenaline, octreotide). These hormones unleash alteration in the metabolism of the carbohydrates, including resistance to insulin, endangering its production, increase of the hepatic glyconeogenoses and damage in the peripheral utilization of glucose. Recent studies identified the presence of hyperglycemia in 38% of the patients admitted in hospital, of who 1/3 did not evince a previous history at admission [1,2].

In the meantime, the glycemic elevation of the hospitalized patient can occur due to the already diagnosed or not yet diagnosed DM, through glycemic variability, due to stress hyperglycemia, or through the use of therapeutics with potential hyperglycemiants (glucocorticoides, octreotide, immune-suppressors, enteral and parenteral nutrition) [3-5]. The glycated hemoglobin (HbA1c) adjusts the differentiation occasioned due to secondary glycemic variability to other hospitalization factors and DM without previous diagnosis [2].

As of the studies Diabetes Control and Complications Trial (DCCT) in 1993 and United Kingdom Prospective Diabetes Study (UKPDS) in 1998, the utilization of the HbA1c was established as

the laboratory parameter in the control of DM. The non-enzymatic glycation of proteins or reaction of Maillard is a process connected to chronic hyperglycemia which is responsible for significant physiological alterations for the development of chronic complications related to DM. Thus, the HbA1c has a fundamental role in the monitoring of the glycemic control because it evinces information of the retrospective index of plasmatic glucose [4-7].

By virtue of the deleterious effects unleashed by hyperglycemia, our interest in the evaluation of HbA1c and its relation with the clinical evolution of hospitalized patients.

Materials and methods

To utilize HbA1c as a diagnosis and predictive tool of the clinical evolution of patients with or without a diagnosis of DM, evaluated during the hospitalization period and its relation with the hospital complications.

This is a prospective, observation analysis of the HbA1c of 100 patients hospitalized with hyperglycemia in Hospital Samaritano due to other clinical pathologies during a period of a year. According to the American Diabetes Association (ADA) DM was defined as hospital

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hyperglycemia when glycemic values were above 140 mg/dl. The HPLC method employed by Fleury laboratory with the certificate of the The National Glycohemoglobin Standardization Program was utilized. The hospital hyperglycemia was verified through capillary glycaemia by means of the Precision XTra (Abbott) glycosimeter, approved by the FDA (Food and Drug Administration).

The glycemic values were evaluated at the time of hospitalization with the measure of the capillary glycaemia, according to the protocol preconized in the NUMAD, obtaining the collection of HbA1c, as of the hospital hyperglycemia. Age, internment diagnosis, previous diagnosis or not of DM, intra-hospital permanence, the evolution or non-evolution for complications were evaluated.

For the descriptive analyses of the data, the category variables were expressed as absolute frequencies and percentiles, compared with the Qui Squared test. The continuous variables were expressed in mean and standard of deviation and compared with the Student test t or the Fisher exact test. The level for the rejection of the null hypothesis was fixed at 0.05 or 5% ($\alpha \leq 0.05$), pointing out the significant values with an asterisk (*).

Results

The study was carried out through 100 patients with a mean age of 63 years, being that 75% evinced a previous diagnosis of DM (Table 1). Out of 25 of the patients with hyperglycemia, but with no previous DM diagnosis, 14 were subsequently diagnosed with DM, domicile treatment being introduced at the time of discharge (Table 2). The patients without previous DM diagnosis evinced HbA1c between 5.8% and 7.5%, with a mean time of hospitalization of 9 days. The patients with DM who evolved with complications, evinced HbA1c between 7.3% and 12.4% and corresponded to 20% of the study, with hospitalization of 34 days. The DM patients with no complications evinced HbA1c between 5.9% and 11.5% with internment time of 11 days (Table 3). The complications were pulmonary infections (50%), septic shock (15%), skin infection (15%), urinary tract infection (10%), and renal insufficiency (10%) (Figure 1).

Discussion

In our institution, a protocol for attendance and treatment of patients with hospital hyperglycemia is preconized in the treatment of, aside from the previous diagnosis of DM. Little is known regarding the importance of HbA1c as a prognosis marker in patients submitted

Table 1. Basal characteristics.

Patients	100
Woman	45
Man	55
Age (years)	63 +- 4
DM previously	75

Table 2. Patients without DM previously.

Total	25
Evaluated with DM	14
Not Evaluated	11

Table 3. Relation of HbA1c.

	HbA1c	Time hospitalization
With DM	5,9 until 11,5%*	11 days +- 3 *
Without DM	5,8 until 7,5% *	9 days +- 2 *
With DM and Compl.	7,3 until 12,4%*	34,5 days +-3 *

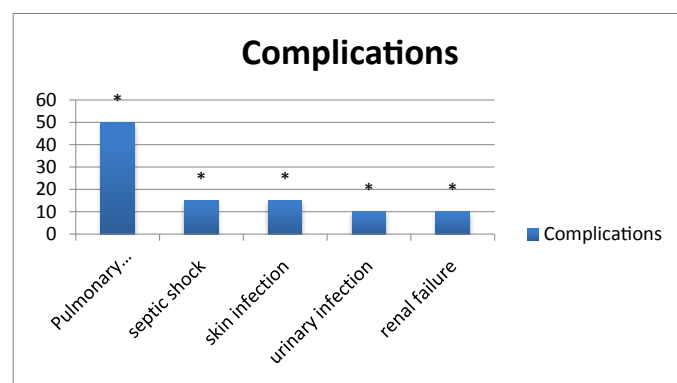


Figure 1. Prevalence of complications.

to hospital internment. This is the reason for our interest in analyzing the protocol and the relationship of the HbA1c values and the clinical evolution of the patient.

Our study demonstrated that the increase of HbA1c was relative to the increase of hospital complications regardless of the pathology associated to the patient. It is known that the deleterious effects of hyperglycemia affect the immunity and healing, increase of oxidative stress, endothelial dysfunction, increase of pro-inflammatory and pro-thrombotic factors, increase of the mitogenesis, hydroelectrolytic alterations and potential exacerbation of myocardial and cerebral ischemia, thus providing the increase of these complications [8-12].

Our evidence relating glycemic control with decrease of complications corroborates some studies such as that of Funary e col, which attended patients hospitalized for heart surgery for a long time and concluded that it is important to keep the postoperative in all DM patients submitted to heart surgery, because in this manner they attained a 77% reduction of a deep infection in the sternum scar.

In this context, studies demonstrated that the patient with DM evinced an absolute risk 8% greater than any type of infection or complications when compared to the general population and the level of hospitalization for diagnosis of infectious disease and twice greater, different form of study which was almost 4 time greater in patients with DM and a higher HbA1c9.10.

However, even so, there are few reports in the literature comparing the control of HbA1c with the need of hospitalization or not, as well as the clinical evolution of the patients with or without hyperglycemia.

Some studies in critical patients evince that aggressive glycemic control can decrease mortality, multiple organ failure, systemic infections, time in the hospital, in addition to hospitalization costs [4,5]. Now the NICE-SUGAR [13], characterized as an important multicenter, multinational, controlled and randomized study tested the effect of rigorous glycemic control, being that mortality was significantly greater in the intensive treatment group. The exact reason for the increase of mortality remains unknown. In the meantime, still in regards to the establishment of a glycemic objective in the infirm, there is controversy and scarcity of studies, as well as in the utilization of HbA1c as a prognosis marker for these patients.

The Diabetes Control and Complications Trial (DCCT) and United Kingdom Prospective Diabetes Study (UKPDS), determined the utilization of the HbA1c as a laboratory parameter in the control of DM [14,15]. A study by Umpierrez et al. [1] regarding the algorithm of patients with DM at hospital discharge, evaluated that the verification

of HbA1c is beneficent in the adaptation of the treatment regimes at the time of discharge. Now in our study, the HbA1c evinced a significant importance in relation with regard to the patients who needed hospitalization, demonstrating that it can also be used as an independent prognosis tool of the pathology of the patient.

In conclusion, the analysis of the HbA1c presents itself as an important prognosis and foreseeable tool to evaluate time of hospitalization and the risk of hospital complications aside from the pathology of the patient.

References

1. Umpierrez GE, Isaacs SD, Bazargan N, You X, Thaler LM, et al. (2002) Hyperglycemia: an independent marker of in-hospital mortality in patients with undiagnosed diabetes. *J Clin Endocrinol Metab* 87: 978-982. [[Crossref](#)]
2. CDC-Diabetes Public Health Resource: Disponível: <http://www.cdc.gov/diabetes/statistics/index.htm> (acessado em janeiro de 2015)
3. Kosiborod M, Inzucchi SE, Krumholz HM, Xiao L, Jones PG, et al. (2008) Glucometrics in patients hospitalized with acute myocardial infarction: defining the optimal outcomes-based measure of risk. *Circulation* 117: 1018-1027. [[Crossref](#)]
4. Van der Berghe G, Wouters P, Weekers F, Verwaest C, Bruyninckx F, et al. (2001) Intensive insulin therapy in the critically ill patients. *N Engl J Med* 345:1359-67. [[Crossref](#)]
5. Van der Berghe G, Wilmer A, Hermans G, Meersseman W, Wouters PJ, et al. (2006) Intensive insulin therapy in the medical ICU. *N Engl J Med* 354: 449-61. [[Crossref](#)]
6. Clement S, Braitwaite SS, Magee MF, Ahmaam A, Smith EP, et al. (2004) Management of diabetes and hyperglycemia in hospitals. *Diabetes care* 27: 553-91. [[Crossref](#)]
7. Gustafsson I, Malmberg K, Rydén L, Wedel H, Birkeland K, et al. (1995) Randomized study of insulin-glucose infusion followed by subcutaneous insulin treatment in diabetic patients with acute myocardial infarction (DIGAMI study): effects on mortality at 1 year. *J Am Coll Cardiol* 26: 57-65.
8. Krinsley JS (2003) Association between hyperglycemia and increased hospital mortality in a heterogeneous population in critically ill patients. *Mayo Clin Proc* 78: 1471-8. [[Crossref](#)]
9. American Diabetes Association (2014) Standards of Medical Care in Diabetes Care / ADA 2014. *Diabetes Care* 34: S11-S61. [[Crossref](#)]
10. Moghissi ES, Korytkowski MT, DiNardo M, Einhorn D, Hellman R, et al. (2009) American Association of Clinical Endocrinologists and American Diabetes Association consensus statement on inpatient glycemic control. *Diabetes Care* 32: 1119-31.
11. Kosiborod M, Inzucchi SE, Krumholz HM, Xiao L, Jones PG, et al. (2008) Glucometrics in patients hospitalized with acute myocardial infarction: defining the optimal outcomes-based measure of risk. *Circulation* 117: 1018-27. [[Crossref](#)]
12. SACKS DB, Arnold M, Bakris GL, Bruns DE, Horvath AR, et al. (2002) Guidelines and recommendations for laboratory analysis in the diagnosis and management of diabetes mellitus. *Clin Chem* 48: 436-72. [[Crossref](#)]
13. NICE-SUGAR Study Investigators (2009) Intensive versus conventional glucose control in critically ill patients. *N Engl J Med* 360:1283-97.
14. DCCT Research Group (1993) Diabetes Control and Complications Trial (DCCT). The effect of intensive treatment of Diabetes on the development and progression of the long term complications in insulin-dependent diabetes mellitus. *N Engl J Med* 329: 977-86.
15. UK Prospective Diabetes Study Group (1998) Intensive blood glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in the patients with type 2 Diabetes. *Lancet* 352: 837-53. [[Crossref](#)]