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LETTER TO THE EDITOR

Role of incretin-based therapy in hospitalized patients with type 2 diabetes

Hyperglycemia in hospitalized patients is a common, serious and costly healthcare problem. Randomized clinical trials in critically ill and non-critically ill patients have reported that improved glycemic control can reduce the number of hospital complications. Based on this, clinical guidelines from professional organizations recommend the use of subcutaneous insulin as the preferred therapy in hospitalized patients in a non-intensive care unit setting. The most recommended regimen is basal–bolus insulin therapy. However, the complexity and hypoglycemia risk of this approach has limited its use. A 2018 Cochrane systematic review that analyzed 1,048 participants with type 2 diabetes in a hospital setting with eight trials showed that a basal–bolus insulin strategy might result in better short-term glycemic control, but could increase the risk for severe hypoglycemic episodes[1].

The use of non-insulin antihyperglycemic agents in hospitalized patients is limited, because few data are available regarding their safety and efficacy[2]. However, evidence that treatment with incretin-based therapy (glucagon-like peptide-1 [GLP-1], GLP-1 receptor agonist and dipeptidyl peptidase-4 inhibitors) in hospitalized patients with type 2 diabetes has increased in the past 15 years.

Since 2004, many studies have investigated the use of GLP-1 or GLP-1 receptor agonist in an inpatient setting, although these protocols included a limited number of patients and heterogeneous populations (individuals with or without history of diabetes, with acute myocardial infarction and left ventricle systolic dysfunction, with chronic heart failure, postmajor surgery and critically ill patients). The results did not show a better glycemic control, requiring therapy with rescue insulin, with no difference in the rate of hypoglycemic events, and also, in two-thirds of the cases, gastrointestinal side-effects (nausea, vomiting, constipation) were present[3]. However, Fushimi *et al.*[4], in a randomized controlled pilot study, showed that dulaglutide (dose 0.75 mg) combined with insulin therapy (insulin glargine dose 0.25 U/kg), compared with a basal-plus regimen, achieved superior glycemic control (mean blood glucose 162 ± 30 vs 183 ± 29 mg/dL, $P < 0.05$) with reduced frequency of hypoglycemia (0.4% vs 2.3%, $P < 0.001$), lower supplemental doses of regular insulin and without difference of gastrointestinal symptoms (11% vs 6%, $P = 0.241$).

Instead, treatment with a dipeptidyl peptidase-4 inhibitor has been shown to be effective in achieving glycemic control without increasing the risk of hypoglycemia in medical and surgical patients with type 2 diabetes. The use of sitagliptin (dose 25–100 mg/day) or saxagliptin (2.5–5 mg/day), alone or in combination with glargine insulin (dose 0.15–0.25 U/day), reported a mean daily blood glucose after the first day ranging from 154.2 to 171.2 mg/dL, with a blood glucose aim <180 mg/dL ranging from 57 to 78% and an incidence of hypoglycemia ranging from 0.4 to 9%[2].

In conclusion, based on the available evidence, dipeptidyl peptidase-4 inhibitors should be considered for hospitalized patients with type 2 diabetes and an algorithm for this is proposed (Figure 1). In relation to the use of GLP-1 and GLP-1 receptor agonist, further research is required to help define their role in the inpatient setting.

DISCLOSURE

The author declares no conflict of interest.

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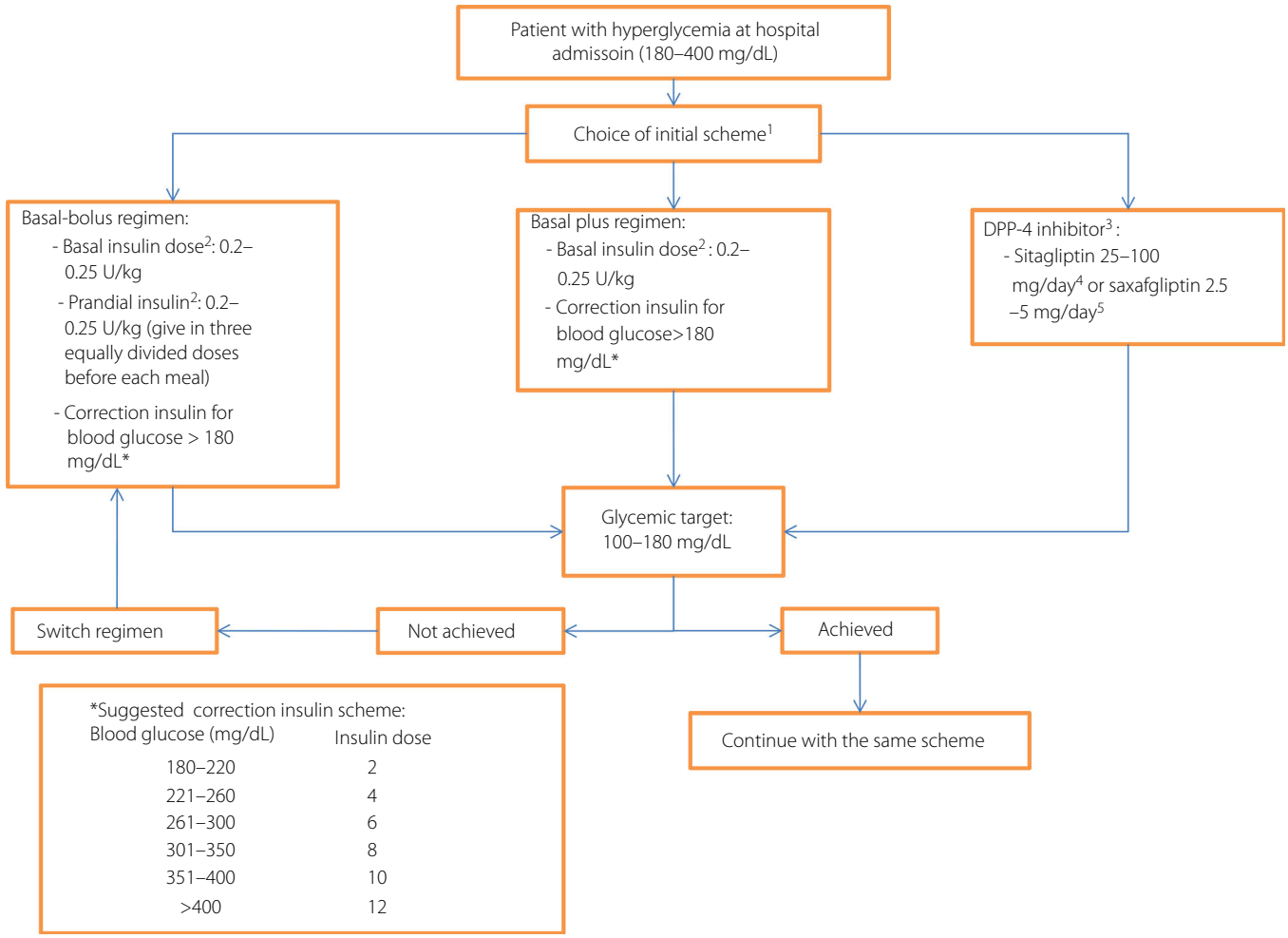

Figure 1 | Algorithm proposed for the management of hyperglycemia in hospitalized patients with type 2 diabetes based of evidence. [1]The choice of scheme is based on individual characteristics of patients: (i) use basal–bolus regimen considering the following: mean daily glucose >250 mg/dL, glycated hemoglobin ≥9%, previous insulin therapy at a daily dose ≥0.4 U/kg; (ii) use basal-plus regimen or dipeptidyl peptidase-4 (DPP-4) inhibitor as follows: mean daily glucose between 180 and 250 mg/dL, glycated hemoglobin <9%, fasting C-peptide index at hospital admission ≥1.103 ng/mL, no previous insulin therapy or at a daily dose <0.4 U/kg, fasting patients or with low food intake, elderly patients or with renal failure. [2]In patients aged ≥70 years and those with estimated glomerular filtration rate (eGFR) <30 mL/min per 1.73 m^2, reduce the dose to 0.15 U/kg. [3]Use alone or in combination with the basal-plus regimen. [4]For patients with eGFR >50 mL/min per 1.73 m^2, use the dose of 100 mg/day; if eGFR is between 30 and 50 mL/min per 1.73 m^2, use 50 mg/day; and if eGFR is <30 mL/min per 1.73 m^2, use 25 mg/day. [5]Use 2.5 mg/day in patients with eGFR <50 mL/min per 1.73 m^2 or if using strong CYP3A4/5 inhibitors.