EDITORIAL (SEE UMPIERREZ ET AL., P. 2181)

Sliding-Scale Insulin

More evidence needed before final exit?

Sliding-scale regular insulin (SSI) in the management of patients with diabetes was the standard practice as early as 1934 (1) and was also used in the hyperglycemic emergency diabetic ketoacidosis (2). These earlier studies used urine glucose for sliding scale, but with demonstration of inaccuracy of urine glucose (3), blood glucose replaced urine glucose for sliding scale in diabetic ketoacidosis (4). SSI is widely used in health institutions (5,6) because it is easy and convenient, but it has the disadvantage of not delivering insulin in a physiologic manner, thereby leading to fluctuations in glycemic levels (7–9). Despite these drawbacks, the use of SSI has survived for >70 years, through many generations of physicians. Retrospective (6,9) and prospective (5) cohort studies, as well as observations and commentaries (10), have concluded that SSI should be discouraged because it has not been shown to be an effective means of achieving much-needed optimal glycemic control in hospitalized patients.

However, the issue of SSI has never been settled because of the lack of data on prospective, randomized, controlled studies. Hence, the studies reported in this issue by Umpierrez et al. (11) are a welcome addition based on which future studies could finally settle the controversies of SSI (12).

Umpierrez et al. reported on a prospective, randomized, open-label, two-center study in which two groups of relatively similar insulin-naive patients admitted to general medical wards were compared regarding efficacy of basal-bolus insulin (glargine once a day plus glulisine before meals and at bedtime) versus SSI (before each meal and at bedtime if patients were able to eat or every 6 h if they were unable to eat). Although blood glucose was better controlled with the basal-bolus regimen, the outcome of this study (except for one death in the basal-bolus group due to pulmonary embolism) showed a similar length of stay and number of hypoglycemic episodes between groups. This paper raises some important questions, which future studies will need to address.

In comparing the two protocols, one may question the accuracy of the randomization procedure, as the sex ratio was significantly different in the two groups (42/23 males/females in the basal-bolus group vs. 21/42 males/females in the SSI group). Whether sex distribution made any difference in the response to therapy elicited is not known. More importantly, however, was that the dosage of insulin in the basal-bolus arm was between 0.4 and 0.5 units/kg body wt, whereas the SSI group received insulin on an empirical schedule, the efficacy of which has never been established. Therefore, as stated by the authors, the total daily dose of insulin in the SSI group was barely one-third that received by the basal-bolus group (12.5 vs. 42 units, respectively) even though the groups had comparable BMIs. The suboptimal dose of insulin in the SSI arm may be a confirmation of the observation by Queale et al. (5) that the sliding-scale schedule on admission is most likely to remain unadjusted throughout the hospital stay despite hyperglycemic episodes. Furthermore, contrary to what has been implied (7), this study refutes the statement that the sliding-scale method is associated with frequent hypoglycemia. Additionally, this study corroborates similar findings in a smaller prospective but nonrandomized study comparing insulin 70/30 (the ratio of 70% NPH to 30% regular insulin) with SSI, in which both groups received a comparable dose of insulin (13). The superiority of the basal-bolus regimen in this study may be attributable to suboptimal insulin dosing in the SSI arm rather than to inferiority of the sliding technique per se. It is also pertinent to observe that the study of Umpierrez et al. did not include patients with newly diagnosed diabetes or hyperglycemia, patients who were being treated with insulin before hospitalization, or those on corticosteroid therapy—populations who constitute a significant proportion of hospitalized patients with hyperglycemia. Another point of concern is the comparative cost and resource utilization of the two methods.

It is now recommended that hospitalized diabetic patients who are not critically ill receive basal insulin along with scheduled preprandial doses of rapid-acting insulin and additional supplemental rapid-acting insulin to correct premeal hyperglycemia (14). Supplemental insulin may be given using a sliding-scale protocol, as was used by Umpierrez et al. in the basal-bolus arm of their study. Therefore, SSI without basal insulin must be distinguished from SSI with basal and premeal bolus in cases where SSI is only used to combat breakthrough hyperglycemia.

Hyperglycemia remains a major problem in hospitalized patients, with the prevalence of diabetes reported as high as 38% in patients admitted to a community teaching hospital (15). Uncontrolled hyperglycemia in hospitalized patients is associated with increased morbidity, mortality, and longer hospitalization, whereas optimal glycemic control results in better outcome (6–8). Therefore, it is imperative that blood glucose levels in patients with hyperglycemia be properly controlled.

While we commend the effort of Umpierrez et al., further studies that would address the limitations of the current one are necessary to settle the issue of SSI. Such a study must use comparable doses of insulin in matched control and experimental groups, preferably with comparative evaluation regarding the cost-effectiveness of the two methods.

ABBAS E. KITABCHI, PHD, MD
EBENEZER NYENWE, MD

From the Division of Endocrinology, Diabetes, and Metabolism, Department of Medicine, University of Tennessee Health Science Center, Memphis, Tennessee.

Address correspondence to Abbas E. Kitabchi, PhD, MD, Division of Endocrinology, Department of Medicine, University of Tennessee, Health Science Center, 956 Court Ave., Suite D334, Memphis, TN 38163. E-mail: akitabchi@utmem.edu.

A.E.K. has received grant support from Sanofi-Aventis.

DOI: 10.2337/dc07-1141

References

1. Joslin EP: *A Diabetic Manual for the Mutual Use of Doctor and Patient.* Philadelphia, Lea & Febiger, 1934, p. 108
2. Kitabchi AE, Ayyagari V, Guerra SM: The efficacy of low-dose versus conventional therapy of insulin for treatment of diabetic ketoacidosis. *Ann Intern Med* 84:633–638, 1976
3. Morris LR, McGee JA, Kitabchi AE: Correlation between plasma and urine glucose in diabetes. *Ann Intern Med* 4:469–471, 1981
4. Kitabchi AE, Rumbak MJ: Diabetic ketoacidosis: diagnosis; diabetic ketoacidosis: treatment; hyperglycemic hyperosmolar nonketotic coma; and maintenance treatment after hyperglycemic crisis. In *Decision Making in Emergency Medicine*. Callaham M, Ed. Philadelphia, B.C. Decker, 1990, p. 178–185
5. Queale WS, Seidler AJ, Brancati FL: Glycemic control and sliding scale insulin use in medical inpatients with diabetes mellitus. *Arch Intern Med* 157:545–552, 1997
6. Baldwin D, Villanueva G, McNutt R, Bhatnagar S: Eliminating inpatient sliding-scale insulin. *Diabetes Care* 28:1008–1011, 2005
7. Clement S, Braithwaite SS, Magee MF, Ahmann A, Smith EP, Schafer RG, Hirsch IB: Management of diabetes and hyperglycemia in hospitals. *Diabetes Care* 27:553–591, 2004
8. Garber AJ, Moghissi ES, Bransome ED, Clark NG, Clement S, Cobin RH, Furnary AP, Hirsch IB, Levy P, Roberts R, Van den Berghe G, Zumudio V; American College of Endocrinology Task Force on Inpatient Diabetes Metabolic Control: American College of Endocrinology position statement on inpatient diabetes and metabolic control. *Endocr Pract* 10 (Suppl. 2):4–9, 2004
9. Gearhart JG, Duncan JL 3rd, Replogle WH, Forbes RC, Walley EJ: Efficacy of sliding-scale insulin therapy: a comparison with prospective regimens. *Fam Pract Res J* 14:313–22, 1994
10. Sawin CT: Action without benefit: the sliding scale of insulin use. *Arch Intern Med* 157:489, 1997
11. Umpierrez GE, Smiley D, Zisman A, Prieto LM, Palacio A, Ceron M, Puig A, Mejia R: Randomized study of basal-bolus insulin therapy in the inpatient management of patients with type 2 diabetes: the RABBIT 2 Trial. *Diabetes Care* 30:2181-2186, 2007
12. Umpierrez GE, Palacio A, Smiley D: Sliding scale insulin use: myth or insanity? *Am J Med* 120:563–567, 2007
13. Schoeffler JM, Rice DAK, Gresham DG: 70/30 insulin algorithm versus sliding scale insulin. *Ann Pharmacother* 39:1606–1610, 2005
14. American Diabetes Association: Standards of medical care in diabetes (Position Statement). *Diabetes Care* 30 (Suppl. 1): S4–S41, 2007
15. Umpierrez GE, Isaacs SD, Barzargan N, You X, Thaler LM, Kitabchi AE: Hyperglycemia: an independent marker of in-hospital mortality in patients with undiagnosed diabetes. *J Clin Endocrinol Metab* 87:978–982, 2002