Effects of sliding scale insulin use on glycemic control and length of stay in hospitalized patients with Type 2 diabetes mellitus

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Objectives: To assess the effect of sliding scale insulin (SSI) use on glycemic control and length of hospital stay in patients with diabetes mellitus. **Methods:** A prospective cohort study of 182 patients with diabetes mellitus as a primary diagnosis or a comorbid condition admitted consecutively to the internal medicine wards over a 6-week period. Demographic, clinical and laboratory data were collected from in-patient medical records. Data were analyzed using Chi-square and independent t-tests and presented as the mean ± standard error of the mean. **Results:** Of the total 182 in-patients with Type 2 diabetes, 130 (71.4%) were placed on SSI (Group A) and 52 (28.6%) on standing-dose antihyperglycemic therapy without the use of SSI (Group B). While there was no difference in admission blood glucose values (mg/dl) between Group A (236 ± 14.3) and Group B (237 ± 6.4), higher average in-hospital fasting blood glucose values were recorded from Group A (168 ± 7.2) compared with Group B (139 ± 11.5), p = 0.04. Plasma glucose values at discharge were not significantly different between the two groups with an average of 172 ± 8.1 for Group A and 170 ± 18.1 for Group B. Also, there was no significant difference in the number of days of hospitalization between the two groups with an average of (7.6 ± 0.89) for Group A and (10 ± 4.7) for Group B. **Conclusion:** SSI use is associated with higher in-hospital blood glucose and does not offer any advantage in terms of duration of hospital stay as compared with standard-dose antihyperglycemic therapy.

Keywords:
blood glucose monitoring, glycemic control, outcomes, sliding scale insulin, therapy, Type 2 diabetes

Type 2 diabetes mellitus is a common, major risk factor for cardiovascular disease with rising prevalence that is approaching epidemic proportions [1–7]. In 1990, there were 2.8 million diabetes-related hospital discharges in the USA, accounting for over 1 million days of hospital stay [3–5]. Persons with diabetes have a higher risk of stroke, myocardial infarction (MI), congestive heart failure (CHF) and death after an acute MI both in the short and long-term [1–9]. In addition, in the event of stroke, diabetic patients are more likely to die or to suffer greater neurologic damage, compared with nondiabetic individuals [1,3,4,6,10]. Furthermore, in hospitalized persons with Type 2 diabetes mellitus, suboptimal glycemic control can have adverse vascular and metabolic consequences, including volume and electrolyte abnormalities, increased neurologic ischemia, delayed wound healing and increased infection rate as well as increased adverse effects on the outcome of the primary illness [3,4,9–14].

Among the different management approaches to in-patients with diabetes, the use of insulin sliding scale recipes survived, grossly unchanged, into our evidence-based medicine era, despite the lack of data on their efficacy [3,4,15–21]. The practice, which apparently became established by tradition, is so common that its efficacy is rarely questioned. As Sawin mentioned, 'it is done because it is expected' [4]. In fact, several reports discourage the use of sliding scale regimens in in-patient management of diabetes and call on more aggressive standing regimens, which may improve the overall outcomes especially in patients with MI and stroke [3–5,8,11–13,22–28].

With these important issues in mind, we conducted a prospective cohort study to examine the effect of sliding-scale insulin use on glycemic control and length of hospital stay, compared with the use of standing dose antidiabetic medications.

Methods

Study participants & data collection

The Institutional Review Boards at University Hospital of Brooklyn (NY, USA) and King's County Hospital Center (NY, USA) approved the study prior to commencement. Over a 6-week period, 182 consecutive patients admitted to either hospital with a primary or secondary diagnosis of diabetes mellitus were prospectively followed.

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Baseline demographic characteristics and outcome of the 182 patients are shown in Table 1. Our cohort had Type 2 diabetes as per chart documentations and/or current or previous use of oral antidiabetic medications. Patients with Type 1 diabetes were not included. Participants were patients who had been admitted consecutively to the internal medicine service of two urban hospitals for a 6-week period in 2002. Data collectors were trained to review the medical records for data on glucose control including finger stick (FS) monitoring and plasma glucose levels obtained for routine care, as well as other data regarding the existence of diabetic macrovascular and microvascular disease. FS measurements were carried out by nursing staff using a handheld glucose meter (Life scan, California, Milpitas, One Touch II) which was calibrated at least daily. Also, records were examined for the use of sliding scale insulin (SSI), standing insulin and/or oral antidiabetic regimens and prescribed diet. All patients were seen by a certified dietitian and prescribed diabetic diets. Patients were included in the study if a history of Type 2 diabetes mellitus was volunteered, or was found in the medical records, documented in the admitting physician's or in the emergency physician's notes, or if patients were on antidiabetic medications. The management of diabetes with or without the use of SSI regimens was decided by the treating physicians. Those who received SSI (± standing-dose insulin and/or oral antidiabetic agents), were designated as Group A. Those who received only standing-dose therapy without the use of SSI, were designated Group B.

Data analysis

Using SPSS version 10.0 (SPSS Inc. IL, USA), a Student t-test (independent) was applied for comparison of the continuous variables, such as age, length of hospitalization and blood glucose (BG) values between the two groups of patients, that is, those on SSI (Group A) and those on standing orders of antidiabetic medications (Group B). Chi-square analysis was utilized for comparison of the two groups with regards to categorical variables, such as gender and presence of cardiovascular disease.

Results

In group A, the lowest dose of insulin of two units was started at a glucose level of 8.3 mmol/L (150 mg/dl) in 8.3%, at 11 mmol/L (200mg/dl) in 85.6% and at 13.8 mmol/L (250) mg/dl) in 6.1%. The insulin dose was increased by increments of two units per increment of BG level (L) of 2.8 mmol/L (50 mg/dl). The relatively small variability in the style of writing SSI orders reflects the fact that house staff and the majority of the attending physicians rotate between the two affiliated hospitals where the study was performed. This may also be indicative of the tradition with which practice of using SSI insulin is being transmitted.

For the entire cohort, age (years) mean = 60.8 ± 1.0, time since diagnosis of diabetes (years) = 13.3 ± 1.2. 57.1% were female, and 49.9% male. Plasma glucose (PG) on admission = 237 ± 14.6 mg/dl and hemoglobin (Hb)A1c = 8.7 ± 0.28. Of the total of 182 patients, 130 (71.4%) were placed on SSI (Group A) and 52 (28.6%) were treated with

Table 1. Baseline characteristics of diabetic patients treated with sliding scale insulin compared with those treated with standing regimen.

Baseline characteristics of study participants	Patients treated with SSI alone or in combination with standard insulin regimen and/or OHA (Group A) n = 130 (71.4%)	Patients treated with standing dose of insulin and/or OHA (Group B) n = 52 (28.6%)	p§
Age (years) mean ± SEM	60.5 ± 1.1	62.8 ± 2.0	NS
Time since diagnosis of DM (years)	12.4	15.9	NS
% performing SHGM	56.1	64.7	NS
% with comorbid conditions§§	50.3	49.7	NS
Hemoglobin A1C (HbA1C) %	8.8 ± 0.3	8.2 ± 0.4	NS
Admission PG (mg/dl)	236 ± 14.3	237 ± 6.4	NS

BG: Blood glucose; DM: Diabetes mellitus; OHA: Oral hypoglycemic agents; PG: Plasma glucose; SEM: Standard error of the mean; SHGM: Self home glucose monitoring; SSI: Sliding scale insulin.

§: p significant at < 0.05, §§: Additional admitting diagnosis (primary or secondary) besides diabetes, including cardiac disease, stroke, infections, respiratory, gastrointestinal, hematologic, renal and neurologic disorders.

Table 2. Glycemic control and hospital length of stay of diabetic in-patients treated with sliding scale insulin compared with those treated with standing regimen.

Outcome of study participants	Patients treated with SSI alone or in combination with standard insulin regimen and/or OHA (Group A) n = 130 (71.4%)	Patients treated with Standing dose of insulin and/or OHA (Group B) n = 52 (28.6%)	p§
Discharge BG (mg/dl)	172 ± 8.1	170 ± 18.1	NS
Fasting BG during hospitalization (mg/dl)	168 ± 7.2	139 ± 11.5	0.04
Mean BG during hospitalization (mg/dl)	189 ± 6.6	168 ± 9.2	0.001
Hypoglycemic episodes n (%)§§	3 (2.2)	4 (9.3)	NS
Length of hospitalization (days)	7.6 ± 0.89	10 ± 4.7	NS

BG: Blood glucose; DM: Diabetes mellitus; OHA: Oral hypoglycemic agents; SSI: Sliding scale insulin.

§ p significant at < 0.05, §§ Hypoglycemia defined as BG < 60 mg/dl occurring at anytime during hospitalization.

standing dose antidiabetic medications without the use of SSI (Group B). Of the Group A patients, 29.7% also received oral antidiabetic medication(s), 19% received standing-dose insulin in addition to SSI and 14% received both oral agent(s) and standing-dose insulin.

There was no difference between the two groups in age, time since diagnosis of diabetes, PG on admission, BG on discharge or HbA1c values (**Table 1**).

There were no significant differences between the two groups in the incidence of hypoglycemic episodes, as defined as BG (or PG) less than 60 mg/dL occurring anytime during hospitalization (**Table 2**). Overall, the incidence of hypoglycemia was 3.8% with four cases occurring in Group B representing 9.3%, and three cases occurring in Group A representing 2.2%, p = 0.055.

Group A had a higher in-hospital fasting BGL (168 ± 7.2) when compared with Group B (139 ± 11.5), p = 0.04 and a higher mean in-hospital BGL; Group A (189 ± 6.6mg/dl) compared with Group B (168 ± 9.2 mg/dL, p = 0.001). Mean in-hospital BG was defined by the sum of the BG values divided by the number of measurements carried out. Days of hospitalization (mean ± SD) were 7.6 ± 0.89 for Group A and 10 ± 4.7 for Group B (p = 0.98), (**Table 2**).

There was no difference in the percentage of comorbidity conditions enlisted as primary or secondary admission diagnosis with diabetes (**Table 1**), (50.3 versus 49.7%, p = NS) for Group A and Group B respectively.

Discussion

SSI is commonly prescribed for hospitalized patients with diabetes mellitus. In this study, 71.4% of the patients received SSI therapy. This is consistent with prospective cohort data of 171 diabetic patients by Queale and colleagues [3], where 76% of the patients were treated with SSI, indicating that its use is still very common practice. This might also explain the large difference in sizes of the groups, SSI versus standard antidiabetic regimen. Consistent with our data also, Queale and colleagues demonstrated a higher risk of hyperglycemia with the use of SSI [3]. However, in contrast to our study, Queale and colleagues showed a higher risk of hypoglycemic episodes in association with SSI use [3]. Furthermore, the study by Queale and colleagues did not provide specific data regarding hospital stay [3].

In our study, when SSI was administered, it was initiated 85.6% of the time at a BGL of 11 mmol/L (200)mg/dl and 6.1% of the time at 13.8 mg/dl (250 mg/dl) thus allowing high in-hospital BGLs to occur prior to the administration of insulin. Such high in-hospital BGLs have been shown to lead to unfavorable outcomes. For instance, hyperglycemia was reported to adversely affect stroke outcome in both diabetic and nondiabetic patients [29,30]. In fact, hyperglycemia increases brain lactate production and facilitates conversion of hypoperfused at-risk tissue into infarction [29]. In addition, glucose levels of more than 140 mg/dl, reduced the beneficial effect of early restoration of blood flow, leading to worse outcome despite tissue plasminogen activator-induced recanalization [31]. Furthermore, in critically ill patients, normalization of BG with intensive insulin therapy reduced morbidity and mortality [32]. One possible explanation for the higher in-hospital BG values with the use of SSI, is that it allows for the hyperglycemia to occur first before giving any insulin, while the use of standing dose antidiabetic therapy prevents hyperglycemia from occurring in the first place [33].

The present study supports the results of a randomized controlled multicenter trial involving 153 Type 2 diabetic patients [34], in which no difference in hospital length of stay was found between the SSI treated group and the standard antidiabetic group [34]. However, in contrast to the study of Dickerson and colleagues [34], our data showed higher levels of intrahospital hyperglycemia, consistent with several other previous reports [3,21].

Finally, our study is limited by being nonrandomized, due to a lack of specific information on nutritional status, medication use and frequency of BG measurements in each group. Nonetheless, our data raises very important questions regarding the possible hazards involved with the use of SSI, especially in view of the accumulating evidence indicating poor outcomes are associated with high intra-hospital BG levels [1,2,9,12] and decreased morbidity and mortality, conversely, with intensive glycemic control [34]. However, the present study did not assess morbidity and mortality outcomes associated with SSI. Further studies are needed to specifically address this important question.

Highlights

- Sliding scale insulin (SSI) is a very common practice in the management of hospitalized diabetic patients. In our study, 71.3% of the cohort was treated with sliding scale insulin.
- SSI treatment was associated with increased intra-hospital hyperglycemia, which is potentially detrimental.
- SSI treatment did not offer any advantages over standing-dose antidiabetic therapy, in terms of length of hospitalization.
- Routine use of SSI in the management of diabetes in hospitalized patients should be discouraged.

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Bibliography

Papers of special note have been highlighted as either of interest (•) or of considerable interest (••) to readers.

1. Wahab NN, Cowden EA, Pearce NJ *et al.* Is blood glucose an independent predictor of mortality in acute myocardial infarction in the thrombolytic era? (Clinical study: acute coronary syndromes). *J. Am. Coll. Cardiol.* 40, 1748–1754 (2002).
2. Hammoud T, Tanguay JF, Bourassa MG. Management of coronary artery disease: therapeutic options in patients with diabetes. *J. Am. Coll. Cardiol.* 36, 355–365 (2000).
• Queale WS, Seidler AJ, Brancati FL. Glycemic control and sliding scale insulin use in medical in-patients with diabetes mellitus. *Arch. Intern. Med.* 157, 545–553 (1997).
3. Sawin CT. Action without benefit: the
• sliding scale of insulin use. *Arch. Intern. Med.* 157, 489 (1997).
4. US Department of Health and Human Services, Public Health Service. Diabetes Surveillance. Atlanta, Centers for Disease Control and Prevention. GA, USA (1993).
5. Castro JP, El-Atat FA, McFarlane SI, Aneja A, Sowers JR. Cardiometabolic syndrome: pathophysiology and treatment. *Curr. Hypertens. Rep.* 5, 393–401 (2003).
6. McFarlane SI, Banerji M, Sowers JR. Insulin resistance and cardiovascular disease. *J. Clin. Endocrinol. Metab.* 86, 713–718 (2001).
7. Fischer KF, Lees JA, Newman JH.
• Hypoglycemia in hospitalized patients: causes and outcomes. *N. Engl. J. Med.* 315, 1245–1250 (1986).
8. Walters E, Hallam L. Association of hyperglycaemia with hyponatraemia. *Br. Med. J.* 288, 1146 (1984).
9. Trachtman H. Cell volume regulation: a review of cerebral adaptive mechanisms and implications for clinical treatment of osmolal disturbances. *Pediatr. Nephrol.* 6, 104–112 (1992).
10. Malouf R, Brust JC. Hypoglycemia: causes, neurological manifestations and outcome. *Ann. Neurol.* 17, 421–430 (1985).
11. Rossini AA. Why control blood glucose
• levels? *Arch. Surg.* 111, 229–233 (1976).
12. Hostetter MK, Lorenz JS, Preus L, Kendrick KE. The iC3b receptor on *Candida albicans*: subcellular logalization and modulation of receptor expression by glucose. *J. Infect. Dis.* 161, 761–768 (1990).
13. Lilley SH, Levine GI. Management of
• hospitalized patients with Type 2 diabetes mellitus. *Am. Fam. Physician* 57, 1079–1088 (1998).
14. Katz CM. How efficient is sliding scale
•• insulin therapy? Problems with a 'cookbook' approach in hospitalized patients. *Postgrad. Med.* 89, 46–57 (1991).
15. Hirsch IB. In-patient management of adults with diabetes. *Diabetes Care* 18, 870–878 (1995).
16. MacMillan DR. The fallacy of insulin
•• adjustment by the sliding scale. *J. Ky Med. Assoc.* 68, 577–579 (1970).
17. Bergman M, Felig P. Self-monitoring of blood glucose levels in diabetes. *Arch. Intern. Med.* 144, 2029–2034 (1984).
18. Queale WS, Seidler AJ, Brancati FL. The
• use of sliding scales in medical in-patients with diabetes mellitus. *J. Gen. Intern. Med.* 10(Suppl), 47 (1995).
19. Kletter GG. Sliding scale fallacy. *Arch. Intern. Med.* 158, 1472 (1998).
20. 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, 313–322 (1994).
21. Hostetter MK. Handicaps to host defense: effects of hyperglycemia on C3 and *Candida albicans*. *Diabetes* 39, 271–275 (1990).
22. McFarlane SI, Jacober SJ, Winer N *et al.* Control of cardiovascular risk factors in patients with diabetes and hypertension at urban academic medical centers. *Diabetes Care* 25, 718–723 (2002).

23. Straus SE, Majumdar SR, McAlister FA. New evidence for stroke prevention. *JAMA* 288, 1388–1395 (2002).
24. Gorelick PB. Stroke prevention. *Arch. Neurol.* 52, 347–355 (1995).
25. Sacco RL, Benjamin EJ, Broderick AJ *et al.* American Heart Association Prevention Conference IV prevention and rehabilitation of stroke: risk factors. *Stroke* 28, 1507–1517 (1997).
26. Goldstein LB, Adams R, Becker K *et al.* Primary prevention of ischemic stroke: a statement for healthcare professionals from the stroke council of the American Heart Association. *Circulation* 103, 163–182 (2001).
27. D'Agnostino RB, Wolf PA, Belanger AJ *et al.* Stroke risk profile: adjustment for antihypertensive medication: the Framingham Study *Stroke* 25, 40–43 (1994).
28. Parsons MW, Barber PA, Desmond PM *et al.* Acute hyperglycemia adversely affects stroke outcome: a magnetic resonance imaging and spectroscopy study. *Ann. Neurol.* 52, 20–28 (2002).
29. Capes SE, Hunt D, Malmberg K, Pathak P, Gerstein HC. Stress hyperglycemia and prognosis of stroke in nondiabetic and diabetic patients: a systematic overview. *Stroke* 32, 2426–2432 (2001).
30. Alvarez-Sabin J, Molina CA, Montaner J *et al.* Effects of admission hyperglycemia on stroke outcome in reperfused tissue plasminogen activator-treated patients. *Stroke* 34, 235–241 (2003).
31. •• van den Berghe G, Wouters P, Weekers F *et al.* Intensive insulin therapy in the critically ill patients. *N. Engl. J. Med.* 345, 1359–1367 (2001).
32. Shagan BP. Does anyone here know how to make insulin work backwards? *Practical Diabetol.* 9, 1–4 (1990).
33. Dickerson LM, Ye X, Sack JL, Hueston WJ. Glycemic control in medical in-patients with Type 2 diabetes mellitus receiving sliding scale insulin regimens versus routine diabetes medications: a multicenter randomized controlled trial. *Ann. Fam. Med.* 1, 29–35 (2003).

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