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Studying the efficacy of insulin sliding scale: Clinical pharmacy approach

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Abstract: Over more than 40 years, many clinical studies are questioning the efficacy of Insulin Sliding Scale (ISS) in controlling blood sugar levels in hospitalized diabetic patients. Its efficacy remains suboptimal and many treatment guidelines recommending its discontinuation. No studies were conducted to explore the impact of clinical pharmacy services in this area. This study aimed to detect the efficacy of ISS in controlling blood sugar level and convince the physicians about ISS failure in an attempt to change to the Basal / Bolus technique. Methods: a total of 99 cardiovascular patients were enrolled in this study and during clinical pharmacist's round, responses to the ISS were recorded and discussed with the treating physicians. The physician's acceptance was also recorded. Specific patients' characteristics that may potentially affect the blood sugar levels control were detected for every patient. Results: ISS failed to control the blood sugar level in 98% of the patients. Only 12% of patients had elevated serum creatinine. Elderly patients accounted for 49% of the patients and 54% of patients were obese. Physician's response rate to change to the basal / bolus technique was 54%. Conclusion: ISS failure in controlling blood sugar levels necessitates its discontinuation.

Keywords: Glycemic control, insulin sliding scale, basal / bolus insulin technique, clinical pharmacy.

INTRODUCTION

Glycemic control in many diabetic hospitalized patients still under control because of the resistance to its discontinuation despite more than 40 years' warnings in many studies about its ineffectiveness (Boord *et al.,* 2009). ISS failure in controlling blood sugar levels was proven in many large cohort studies. These studies concluded that 76% of in-patients hospitalized in medical wards received ISS, which failed not only in controlling their hyperglycemia but also its use resulted in many episodes of hypoglycemia and increased the length of hospitalization. In addition, the blood sugar levels of >300 mg/dl were recorded at a higher rate (3 times higher) in patients treated with ISS than patients on other insulin regimens (Queale *et al.,* 1997). Physicians' failure to adjust ISS to enhance glycemic control is problematic in both hospitalized and nursing home patients. Another observational retrospective study in a large medical center resulted in; 84% of patients developed hyperglycemia during their treatment with ISS, adjustment of the doses occurred only in 18 % of these patients (Golightly *et al*., 2006). This difficulty to achieve the optimal glycemic control is affected by many factors. The failure of ISS in burn patients resulted in an increase in their mortality, the mortality rates increased also in intensive care unit's patients with myocardial infarction, open heart surgery and ischemic stroke (Gore *et al.,* 2001; Malmberg *et al.,* 1995; Bruno *et al.,* 1999; Kalin *et al.,* 1998; Marcus *et al.,* 1998; Van Den Berghe *et al.,* 2001). Delayed wound healing with an increased risk of infections also was resulted from poor glycemic control due to the failure of ISS (Bistrian, 2001). ISS use is considered as the cornerstone in the management of diabetic inpatients (Queale *et al.,* 1997). While ISS use is associated with an increase in the insulin demand during the course of illness and unexpected insulin requirement during intervals of low calories intake. ISS regimens can cause inadequate blood sugar control because it permitting hyperglycemia to occur before insulin administration. ISS role in the management of diabetic inpatients and optimizing its regimens to achieve these goals still need to be identified (Bergenstal, 1998; Gaster, 1998; Lorber, 2001; Trochtenberg, 1997). Individualizing insulin requirements and bolus insulin doses before meals cannot be achieved with ISS. Because adjusting insulin dosing before meals depend on the patient's essential metabolic requirements, the quantities of consumed food, the weight of the patient and many other factors that may affect the insulin requirements such as previous insulin requirements, sensitivity or resistance to insulin (Umpierrez *et al.,* 2007). A typical ISS depends on the exaggerated elevation in the insulin premeal and bedtime requirement, the insulin dose is calculated according to only the patient's finger-stick sugar level at this time. ISS depends on repeating the finger-stick sugar levels every six hours or before meals and bed-time. Measurement of sugar concentrations before meals will not explore the required insulin at this time. It reflects the effect of insulin that was given before. If the patient received rapid-acting insulin with the previous meal and the effects of this insulin last only 3-4 hours, the patient will have elevated sugar

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concentrations for many hours before the next insulin dose. Instead of being proactive in alleviating large fluctuations in blood sugar levels, ISS is treating hyperglycemic after its occurrence (Hirsch, 2009). If the patient has a normal blood sugar level, he will not receive insulin. In this situation, another scenario with ISS will occur, after a few hours, the blood sugar level will increase, leaving the patient with prolonged durations of elevated sugar concentrations. Insulin will be given with the next blood sugar level check, and blood sugar level returns to normal. These fluctuations in blood sugar levels are more harmful physiologically than blood sugar levels that are continuously elevated (Nalysnyk *et al.,* 2010). Nowadays, the updated guidelines recommend the use of structured insulin regimens: basal insulin, nutritional insulin, and correctional insulin. The blood sugar level is maintained normally by the normal physiology of the body which secretes insulin to maintain the blood sugar level even if without food intake. The basal insulin requirement which adjusts and stabilize the blood sugar levels between meals and during the night, and stabilizes these levels throughout the whole day. Bolus insulin is secreted based on the body's requirement after food intake. (Perez *et al.,* 2014) The basal-bolus insulin technique is the preferred therapy technique because it mimics the normal physiology of the patient's body (Freeland, 2016). Changing from ISS to the new basal-bolus technique is a challenging situation because of many barriers. The obstacles to change include physician's resistance to change, clinicians may afraid from hyperglycemia overcorrection which may be resulted in hypoglycemia, inadequate sugar levels monitoring, difficulty to obtain the patient's body weight in certain situations, work overload and spending a lot of time calculating the correctional insulin dosages, calculation errors associated with insulin dosages, and lack of knowledge about the risks resulted from ISS usage (DeYoung *et al.,* 2011). Clinical pharmacist's role was documented in managing diabetic patients. Patient self-management and patient education are the most common clinical pharmacist's interventions in diabetic management (Gagnon *et al.,* 2017; Mohamed *et al.,* 2015). No studies were conducted to explore the impact of clinical pharmacist's intervention in changing the clinical practice from using ISS to using the basal-bolus insulin technique. This study aimed to detect the efficacy of ISS in controlling blood sugar levels of diabetic cardiac patients and to convince the physicians about ISS failure in an attempt to change to the newer physiological insulin regimens.

MATERIALS AND METHODS

Study design

This is a prospective evaluation with descriptive analysis study.

Patients

The study was conducted on a total of 99 cardiovascular patients admitted to the critical care cardiac unit (CCU) and cardiology ward of Prince Sultan Cardiac Center, Saudi Arabia.

Inclusion and exclusion criteria

Patients enrolled in this study if they have a history of type I or II diabetes mellitus or receiving any oral hypoglycemic agent before hospital admission. Patients were excluded if they have any factor that may affect the blood sugar levels or influence the glycemic control of the patients. These factors include; patients receiving corticosteroids due to any medical condition before hospitalization, patients have acute infections receiving any antibiotic during hospitalization or patients receiving hydration intravenous fluids containing dextrose. All the included patients were receiving the hospital's diabetic diet.

Sampling technique

All patients admitted to the care cardiac unit or cardiology ward of Prince Sultan Cardiac center from the 1st of February 2015 to 31st of July, 2015 were included in this study. These patients were admitted the CCU post cardiac events (acute myocardial infarction (AMI), acute decompensated heart failure, atrial fibrillation…etc.)

Study tool

The Accu-Chek(R) Performa blood glucose meter was used to detect the blood sugar levels for each patient. Blood sugar levels were measured every 6 hours and Insulin doses were given according to the detected values. This tool was designed to provide rapid and accurate results within 5 seconds. The test strip should be inserted into the meter which will turn on automatically. The blood sample (only 1 small drop) will be applied to the yellow window of the tool, then the tool will provide the result within approximately 5 seconds.

Methodology

Specific patients' characteristics that may potentially affect the blood sugar levels control were detected for every patient. These patients' characteristics include patient's age, sex, Insulin use before admission (using of Insulin alone, using of Insulin + any oral hypoglycemic drug, oral hypoglycemic drug only or diabetic diet only), presence or absence of obesity and presence or absence of abnormal kidney functions. ISS regimen is defined as the administration of regular or lispro insulin doses based on the measured capillary blood sugar levels every 6 hours. Nurses' documentation of the measured blood sugar levels was used to assess the patients' glycemic control. All the blood glucose values whether normal or abnormal were recorded for all patients during the hospitalizations' periods. Insulin dose adjustments based on the detected blood sugar levels were also recorded to detect the

Table 1: Patients' characteristics

Parameter	Value
Demographic characteristics	
age, years (mean ± SD)	58.3 ± 12.7
male/female (n)	70/29
Clinical characteristics prior to admission, n (%)	
insulin only	43 (44)
insulin + oral agent	28 (28)
oral agent only	24 (24)
diet controlled	4 (4)
Admission unit, n (%)	
Cardiac care unit	69 (69)
Cardiology ward	30 (30)
Obesity, n (%)	
BMI > 30	54 (54)
BMI < 30	45 (45)
Kidney functions, n (%)	
Normal serum creatinine	88 (88)
Elevated serum creatinine	11 (12)

N: number

Table 2: SSI Regimens Used by Blood Glucose Concentration Treated and Insulin Doses

If blood sugar is	SSI Regimens Used	Number of times prescribed / day for all patients (%)
151 to 200	Give 2 units regular insulin	498 (37.5)
201 to 250	Give 4 units regular insulin	366 (27.5)
251 to 300	Give 6 units regular insulin	216 (16)
301 to 350	Give 8 units regular insulin	186 (14)
351 to 399	Give 10 units regular insulin	59 (4.5)
≥ 400	Contact prescriber; check finger-stick blood sugar in one hour	3 (0.5)
Total		1328

different rates of hypo- or hyperglycemia for every patient.

Clinical pharmacists' interventions

Patients were followed up daily by the clinical pharmacist (The principal investigator) who raised recommendations to the treating physicians about the risks associated with poor glycemic control in critically ill cardiac patients. The principal investigator of this current study was a clinical pharmacy consultant and she was responsible for monitoring therapeutic plans for patients. All patients started on an ISS regimen were monitored daily to detect their responses to the administered insulin during routine clinical pharmacy rounds, with data recorded every 24 h. During these interventions, the clinical pharmacist explained in details the advantages of the bolus- basal technique in a trial to convince the treating physicians about ISS failure in controlling the blood sugar levels.

Physician's acceptance

All cases were discussed with physicians (12 physicians from different medical specialties) during bed rounds to convince them to change from the sliding scale to basal-bolus technique. Many educational lectures were arranged in collaboration with the endocrine department in the hospital to highlight the difference between ISS and the basal-bolus technique. The physician's acceptance rate was recorded and calculated as the number of cases in which the physician agreed to change the ISS to the basal-bolus technique/ total number of cases.

Ethical approval

The study was approved by the Head of the Research and Training Center of Prince Sultan Cardiac Center, Qassium, Saudi Arabia.

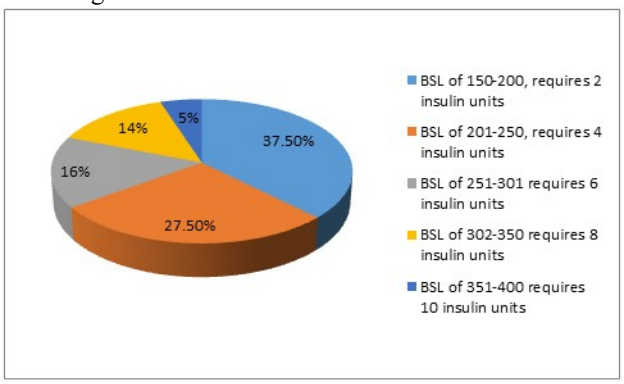
STATISTICAL ANALYSIS

Data analysis was done by SPSS Statistics- version 21

RESULTS

Data were collected from 99 patients after the exclusion of 7 patients who were receiving corticosteroids and 9 patients who were receiving antibiotics because of severe infection. Table 1 shows the baseline characteristics of the

patients. The median number of blood sugar levels recorded for each patient was 14 (mean +/- SD = 14.6 +/- 3.9). As shown in table 1; about 71% of the included patients were males. Their age ranged from 43-78 years (mean = 58.3 years). Seventy-two of the included patients were received insulin +/- other oral hypoglycemic agents before the hospital's admission. About 54% of the included patients were obese (BMI > 30) and 12% had elevated serum creatinine during the hospital's admission. All patients received regular insulin to adjust their blood sugar levels by using the ISS technique. ISS was started if the patient's blood sugar level was ≥ 150 mg/dl. Table 2 shows the ISS regimens used according to the measured blood sugar levels and the required Insulin doses. Table 2 also shows that different insulin doses were prescribed 1328 times for all of the patients according to their blood sugar levels. Blood sugar levels adjustments based on the measured suboptimal capillary glucose levels occurred in 81% of the total measured blood sugar levels. Figure 1 represents the percentages of number of times during which insulin was prescribed/ day according to different blood sugar levels.



BSL: Blood sugar level

Fig. 1: Percentages of detected blood sugar levels and insulin requirements.

DISCUSSION

This study aimed to determine the efficacy of ISS in controlling the blood sugar levels, as shown in table 2 more than 80% of the times, patients required more insulin to control their blood sugar levels by using the sliding scale technique. The findings of this present study were compared with those of Queale and his colleagues (Queale *et al.,* 1995) who conducted a study to detect the predisposing factors for hypo and hyperglycemic attacks in inpatients. Hyperglycemia is considered if the blood sugar level was ≥ 300 mg/dl. In this current study, a blood sugar level of ≥ 200 mg/dl was selected to define hyperglycemia because it is associated with adverse consequences. Another study (Bergenstal, 1998), recorded 40% and 23% rates for hyperglycemia and hypoglycemia, respectively. The results of this current study revealed that 98% of the patients had hyperglycemia as shown in table 2. No episodes of hypoglycemia were detected in any patient and the lowest detected blood glucose level was 75 mg/dl. This study detected a higher rate of hyperglycemia compared to Queale and his colleagues' results. Dailey and his colleague also reported a 50% incidence of hyperglycemia and 15% incidence of hypoglycemia, the selected blood sugar level in this study was ≥ 200 mg/dl (Dailey and Lutomski, 2013). Queale and his colleagues' study documented that there are many risk factors associated with patient's hyperglycemia. These factors included: the severity of the disease, elevated blood sugar levels during admission, use of corticosteroids and concurrent infections. Queale and his colleagues concluded that; the risk of hyperglycemia decreases if the patient receives any oral hypoglycemic drug with insulin therapy or if the patient on dialysis. The hyperglycemia rate with ISS alone was 3 times more than ISS with other oral hypoglycemic drugs. Queale and his colleagues' results were extracted from all diabetic patients in all medical departments. The results also included patients with other oral hypoglycemic drugs (Queale *et al.,* 1995). This current study couldn't analyze the same parameters since we only included cardiovascular patients admitted to the critical care unit post cardiac events (AMI, acutely decompensated heart failure, atrial fibrillation…etc.). It was not possible to use any oral hypoglycemic agents in these patients' conditions. All the included patients were initiated on an ISS regimen after hospital admission without any other oral hypoglycemic agents. Patients were excluded if they have infections, on dialysis or receiving corticosteroids. The overall glycemic control according to the blood sugar levels is presented in fig. 1. About 37.5% of times, patients prescribed 2 Insulin units/day because the blood sugar levels were 151- 200 mg/dl. Patients required 2 Insulin units / day, 4 Insulin units / day, 6 Insulin units / day, 8 Insulin units / day and 10 Insulin units / day according to their blood sugar levels which were ≥ 150, ≥ 200 mg/dL, ≥250 mg/dL, ≥300 mg/dL and ≥350 mg/dL respectively. Fig. 1 also shows that about 37.5% of times, patients prescribed 2 Insulin units/day. This rate was lower than the rate of 73% which was detected by Dailey and his colleague. About 27.5 % of times, patients required 4 Insulin units/day and 16% of times, they required 6 Insulin units/day. These rates were higher than the rates recorded by Dailey and his colleague (Dailey and Lutomski, 2013). This study (Dailey and Lutomski, 2013) reported a lower need for insulin doses 2.6% and 1.3% for 4 and 6 Insulin units/day respectively. Clinical pharmacist's role in diabetic management was documented by many studies. There are an ever-growing body of evidence demonstrates that clinical pharmacists, through a range of extended services can participate effectively in improving the clinical and humanistic outcomes of internal medicine disease patients (Abuelsoud, 2018) Further, these services can be delivered cost-effectively in diabetic patients (Hughes *et*

al., 2016). Numerous studies worldwide have documented the effectiveness of pharmacy-based interventions in supporting people with Diabetes mellitus (Aguiar *et al.,* 2016; Wang *et al.,* 2016). The main role of pharmacists is medication provision included enhancements in supporting adherence to medications (Dhippayom, 2015). Physician's acceptance to the clinical pharmacist recommendations were recorded in this current study. After discussion with the clinical pharmacist (the principal investigator) and attending the endocrine's department educational sessions which were conducted by the clinical pharmacist, many physicians changed ISS to the basal-bolus technique. The physician's acceptance rate was 54%. This is the first study concerned about recording the acceptance rate in this specific intervention. Because controlling the blood sugar levels for hospitalized cardiac patients is very serious and considered a challenging situation for many physicians. This study recorded a high acceptance rate among the other studies, Foroughinia and colleagues performed a study aimed to assess the impact of the clinical pharmacy services in the neurology specialty in Iran. The acceptance rate to their interventions was 41.91% among physicians (Foroughinia *et al.,* 2016). Another study was conducted by Anderegg and colleagues to detect the acceptance rate to inpatient pharmacy case managers recorded a lower acceptance rate of 48% (Anderegg *et al.,* 2013)

CONCLUSIONS

Clinical pharmacy interventions were very successful in achieving the best practice effectiveness through convincing the physicians to change from the failed ISS which was questionable in many studies over > 40 years-period to the more effective basal/bolus technique.

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