The impact of the implementation of computerized insulin order sets for the control of hyperglycemia in hospitalized cardiac patients

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Background **Glycemic control is crucial in managing hospitalized patients with type II diabetes (T2DM), and it presents as a clinical challenge in the cardiac population. Therefore, we aimed to evaluate the impact of computerized insulin order sets in T2DM hospitalized cardiac patients.**

Methods **A quasi-experimental, pre- and post-study design. We included T2DM patients who were hospitalized for at least 3 days. Patients undergoing cardiac surgery were excluded. The primary endpoint was the mean difference in random blood glucose level (BGL) before and after the implementation of insulin order sets. While the secondary endpoints were to compare the median differences in fasting BGLs and the number of hyperglycemic and hypoglycemic episodes during the first 7 days. The study consisted of three phases: pre-implementation, intervention and post-phase. In the intervention phase, insulin order sets were integrated into the electronic prescribing system, and education was provided to the cardiology department. The post-phase included the patient's post-implementations.**

Results **A total of 194 patients were enrolled during the study period. The mean random BGL was 11.17 mmol/L, 95% CI, 10.6–11.7 in the pre-phase and 9.5 mmol/L, 95% CI, 9-1 –9.9 mmol/L in the post-phase ($P<0.001$). The median fasting BGL was 9.2 mmol/L (7.4–11.8, IQR) in the pre-phase and 8.5 mmol/L (6.6–10.3, IQR) in the post-phase ($P=0.027$). The number of hypoglycemic episodes was 24 in pre-phase and 33 in post-phase ($P=0.13$).**

Conclusion **The use of computerized insulin order sets was associated with potential improvements in random and fasting glycemic control without increasing the risk of hyperglycemia or hypoglycemia. *Cardiovasc Endocrinol Metab* 13: 1–7 Copyright © 2023 The Author(s). Published by Wolters Kluwer Health, Inc.**

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Introduction

Diabetes is a global health problem that affects 537 million people worldwide, and according to the International Diabetes Federation, this number may increase to 783 million in 2045 [1]. The prevalence of diabetes in Saudi Arabia is high, accounting for 18% of the population [2].

Diabetic patients have a four-fold greater chance of developing cardiovascular disease (CVD) compared with patients without diabetes which is the major cause of death in this population [3,4]. A retrospective study of 130,011 CVD patients with type II diabetes (T2DM) in 2017 had a higher mortality rate and stroke than nondiabetic patients with CVD during admission for myocardial infarction [5]. On the other hand, tight glycemic control may lead to an incidence of hypoglycemia, which is also associated with a higher risk of mortality in hospitalized patients [6,7].

In hospitalized patients, glycemic control is crucial in T2DM and has been considered a clinical challenge [8]. Poor glycemic control in the inpatient setting is associated with unfavorable clinical outcomes, including but not limited to thrombosis, infections, acute kidney injury, increased hospitalization, and increased mortality [8,9]. A previous study in 2017 involving 3.5 million patients from 575 hospitals in the USA showed that 32% of non-ICU patients experienced hyperglycemic episodes [4].

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An insulin regimen with basal, bolus and correctional insulin is the preferred treatment for admitted non-critically ill patients with good oral intake [6,10,11]. The preferred regimen for non-critically ill patients with poor oral intake is using a basal plus correctional insulin regimen [6,10,11]. Undesirable hypoglycemia and hyperglycemia have been reported with the use of sliding scale insulin (SSI) in the hospital; hence, it is strongly discouraged for use in the inpatient setting [12]. A randomized trial compared the efficacy and safety of the basal plus bolus inulin regimen vs. SSI in patients admitted to general medicine services and reported that the blood glucose level (BGL) was <7.7 mmol/L in 55% of patients on the basal plus bolus insulin regimen after the first day of starting the therapy, whereas only 38% of patients with SSI had a BGL <7.7 mmol/L [4,13].

The Institute for Safe Medication Practices recommends the use of structural computerized prescriber order entry (CPOE) sets of insulins to minimize serious adverse events of hypoglycemia and hyperglycemia associated with the use of insulin to improve patient care [14,15]. A previous pre- and post-study design resulted in a reduction in hypoglycemic events after using CPOE insulin order sets [16]. Furthermore, a cluster-randomized trial supporting CPOE order sets for using basal plus bolus insulin was associated with an improvement in mean BGLs from 12.4 ± 3.1 mmol/L to 10.8 ± 3.6 mmol/L ($P = 0.004$), without increasing hypoglycemia in patients with T2DM [17].

Based on the findings of these studies, controlling the BGL in a hospital setting remains a challenge, and insulin protocols and CPOE sets provide opportunities to optimize patient care. To our knowledge, there is no published evidence to determine the effectiveness of insulin order sets to control BGLs in the cardiac population in Saudi Arabia. Therefore, we aim to study the effectiveness of CPOE insulin order sets in controlling BGL in hospitalized cardiac patients with T2DM.

Methods

Study design and setting

This study is a quasi-experimental study with a pre- and post-study design, including hospitalized cardiac patients with T2DM who were admitted to a tertiary care hospital in Jeddah, Saudi Arabia, between June 2018 and August 2019. This study was granted the approval of the Institutional Review Board from King Abdullah International Medical Research Center, number RJ18/033/J.

Sampling and study population

Using convenience sampling, we included adult patients (>18 years) with T2DM who were admitted to the hospital with at least 3 days of hospital stay. We excluded patients with type I diabetes or T2DM undergoing cardiac surgery, on enteral or total parenteral nutrition, having active malignancy, or end-stage renal disease on regular hemodialysis.

Study phases

The study is composed of three phases: pre-phase, intervention phase and post-phase (Fig. 1; study phases summary).

Pre-phase

The pre-phase included a retrospective assessment of all eligible patients who were admitted to the hospital from June to December 2018 (6-months period). We identified the list of patients admitted to the cardiac center in our hospital through our Information System Department (ISD) for the study period. Patients were screened for eligibility criteria. For patients with multiple admissions during the period, we only collected the first admission information in the study for eligible patients. BGLs were recorded starting from the day of admission until day seven or until discharge if they were less than 7 days.

Intervention phase

In the intervention phase, a subcutaneous insulin treatment protocol was designed based on previously studied protocols [11,17], reviewed by the investigators, including an endocrinologist and clinical pharmacists, and approved by the hospital pharmacy and therapeutic committee. The insulin protocol divided the patients into two groups: patients with good and poor oral intake, and each group has specific treatment guidelines and recommendations (Supplementary File A; Supplemental digital content 1, *http://links.lww.com/CAEN/A54* insulin treatment protocol). Subsequently, the protocol was integrated into the electronic prescribing system as COPE sets based on the Institute for Safe Medication Practices standards for developing order sets in December 2018 (Supplementary File B; Supplemental digital content 2, *http://links.lww.com/CAEN/A55* insulin order sets) [17,18]. Finally, several educational sessions were provided to the cardiology team on the use of the insulin order sets and included an interactive presentation and flowchart handouts to enhance the utilization of the order sets (Fig. 2; insulin protocol flow chart).

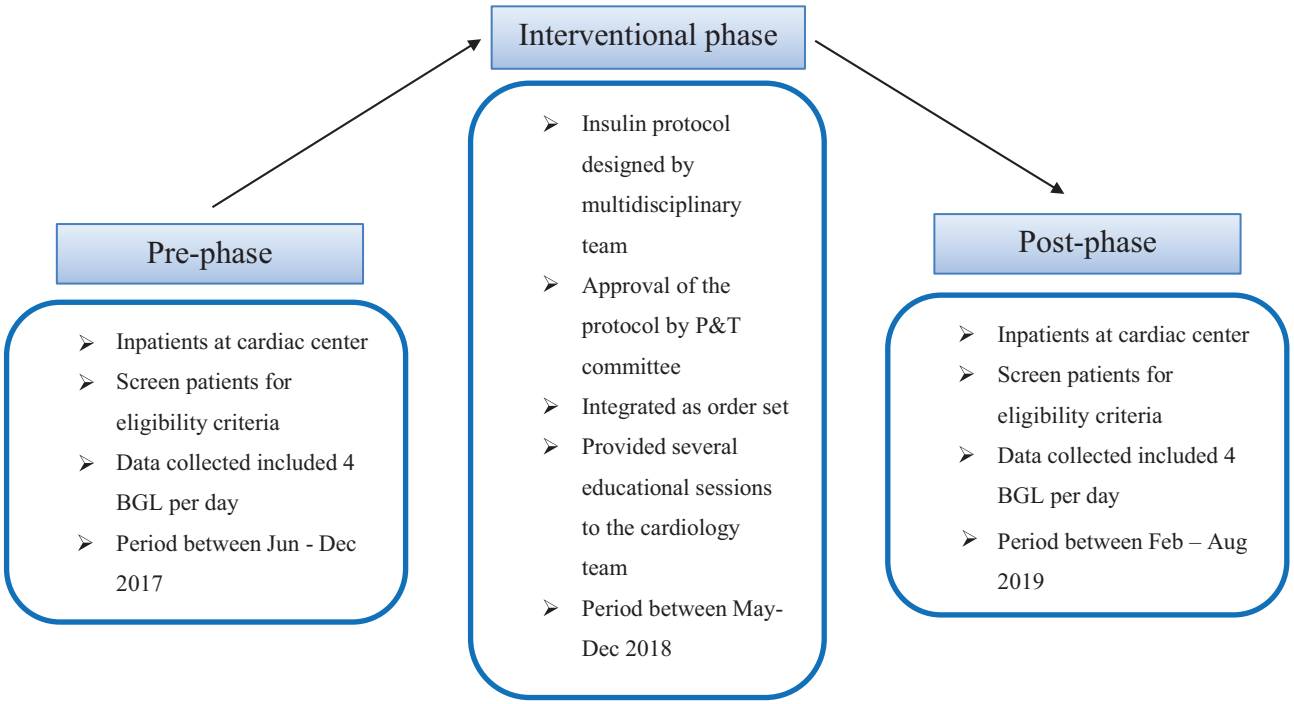
Post-phase

In the post-phase, the list of patients admitted to the hospital was generated by ISD on a regular monthly basis. Patients were recruited from February to August 2019 as per the eligibility criteria. We collected data for eligible hospitalized patients after the implementation of the insulin order sets, similar to the pre-phase.

Data collection

The following data were collected: baseline characteristics such as age, gender, body mass index (BMI), primary

Fig. 1



Phases summary.

diagnosis and comorbidities. Laboratory data such as Hgb, A1c, renal profile (i.e. creatinine clearance), liver function tests (i.e. alanine transaminase) and glycemic parameters were documented and reported in the electronic health records. Glycemic parameters were identified on a daily basis and included three random BGLs and one fasting BGL.

Outcomes

The primary outcome was the mean difference in random BGL before and after the implementation of computerized insulin order sets. The secondary outcomes included: (1) the median difference in the fasting BGLs, (2) the proportions of patients achieving target random BGL defined as BGL < 10 mmol/L[6], (3) the number of hyperglycemic episodes defined as BGL > 10 mmol/L[6], (4) the number of hypoglycemic episodes defined as BGL < 3.8 mmol/L[6], (5) length of hospital stay, (6) number of consultations to the endocrine team before and after the implementation of computerized insulin order sets, (7) physician's adherence to the insulin order sets, which was defined by using the order sets for >75% of the time during prescribing insulin for admitted cardiac patients enrolled in the study.

Sample size

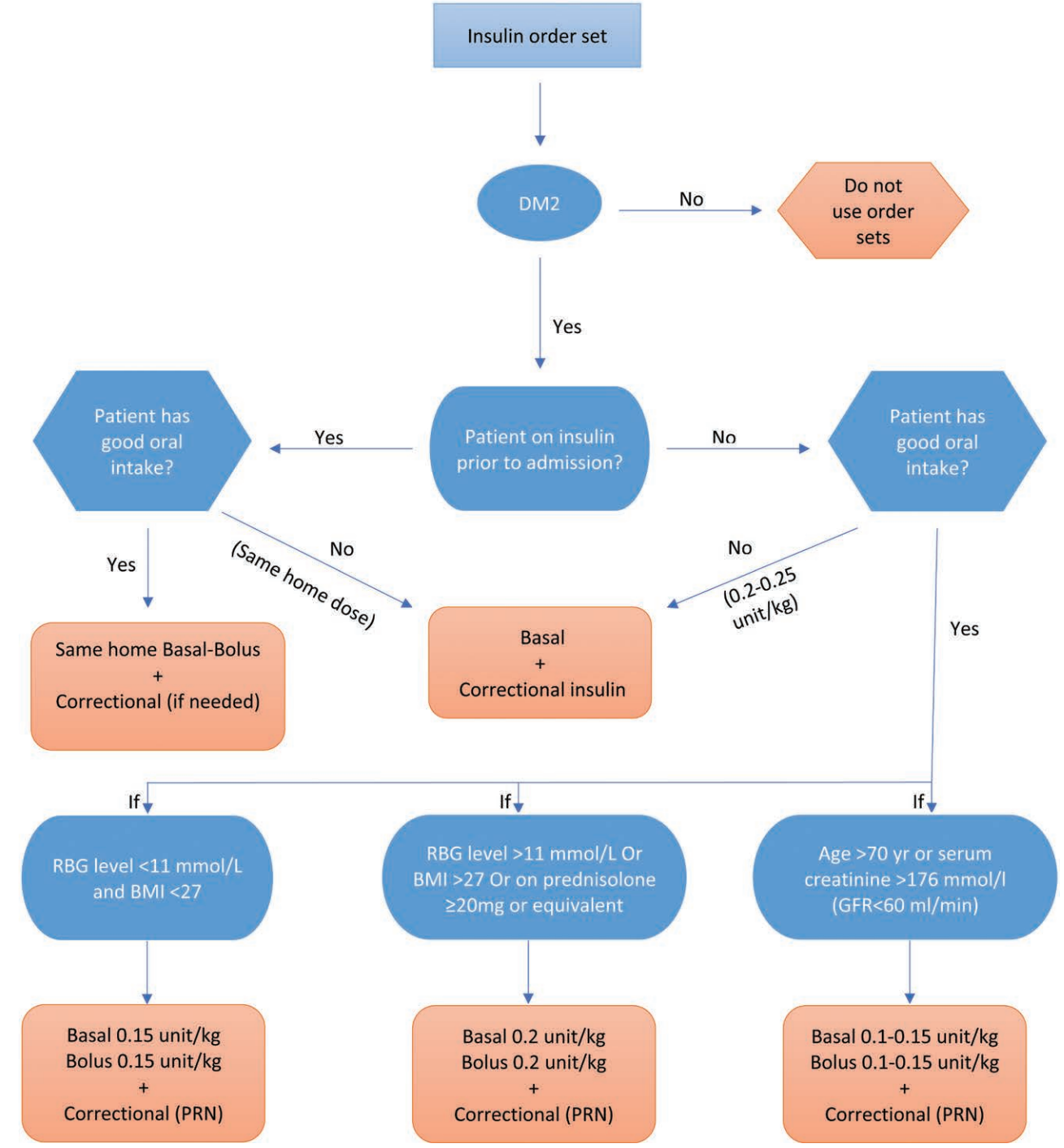
A sample of 97 patients per phase was estimated to provide 90% power to detect a mean difference of 1.6 mmol/L of BGL before and after the intervention with an alpha of 0.05 [17].

Statistical analysis

Descriptive statistics were used as deemed necessary for baseline characteristics.

We calculated the daily mean of random and fasting BGLs, and then we determined the overall mean of random and fasting BGLs for each patient, which depended on the number of days during hospital admission. We performed Student's *t*-tests and the Mann–Whitney test to determine differences between means and medians of the continuous and non-normally distributed variables. The chi-square test or Fisher's exact test was used for categorical variables. We used regression analysis to adjust for potential confounders based on age, gender, baseline admission A1c, atrial fibrillation, ischemic heart disease (IHD), categories of BMI, insulin home doses, hypertension (HTN), dyslipidemia, heart failure with preserved and reduced ejection fraction, deep vein thrombosis, pulmonary embolism, chronic kidney disease, anemia, cerebrovascular accident, and baseline creatinine clearance between the pre-phase and post-phase. We used two-sided tests and a *P* value of 0.05, and 95% confidence intervals (CIs) were used as cutoff levels for significance in all analyses. The analysis was performed using Excel (MAC 2015, version 10.13.6) and STATA 14.

Fig. 2



Insulin flow chart.

Results

A total of 986 patients were screened; 194 patients (97 patients in each group) were enrolled based on the study eligibility criteria. The majority of the admitted patients were men (65%) in both groups. The most common admission diagnoses were IHD (48.4%) and acute decompensated heart failure (40.2%) (Table 1; baseline characteristics). HTN was the most prevalent comorbidity (82%) in both arms, followed by IHD with 50.5% (Table 2; patient comorbidities)

Primary outcome

The mean random BGL was 11.17 mmol/L, 95% CI, 10.6–11.7 in the pre-phase vs. 9.5 mmol/L, 95% CI,

Table 1 Baseline characteristics

Baseline characteristics	Pre-phase (n=97)	Post-phase (n=97)	P value
Age (year) (mean±SD)	66.64±10.35	68±11.04	0.24
Male, *n* (%)	65 (67)	65 (67)	0.31
BMI (Kg/m^2)			
Underweight, *n* (%)	1 (1.03)	1 (1.03)	1
Normal weight, *n* (%)	17 (17.53)	15 (15.46)	0.69
Overweight, *n* (%)	30 (30.93)	27 (27.84)	0.63
Obese, *n* (%)	49 (50.52)	54 (55.67)	0.47
Serum creatinine (mmol/L) (Mean±SD)	117±65.32	127±72.36	0.15
Hgb (g/dl) (Mean±SD)	12.42±2.39	12.21±2.29	0.36
Glycosylated hemoglobin A1c (Mean±SD)	8.59[a]±2.29	8.14[b]±1.90	0.16
T2DM home medications			
Metformin, *n* (%)	33 (34.02)	35 (36.08)	0.76
Sulfonylurea, *n* (%)	18 (18.56)	25 (25.77)	0.22
Dipeptidyl peptidase-4 inhibitor, *n* (%)	12 (12.37)	14 (14.43)	0.67
Rapid-acting insulin, *n* (%)	32 (32.99)	38 (39.18)	0.37
Short-acting insulin, *n* (%)	2 (2.06)	1 (1.03)	1
Intermediate-acting insulin, *n* (%)	9 (9.28)	4 (4.12)	0.25
Long-acting insulin, *n* (%)	35 (36.08)	51 (52.58)	0.02
Median total daily insulin units at admission, (interquartile range)	60[c] (49–80)	53[d] (36–85)	0.31
Admission diagnosis			
Acute decompensated heart failure, *n* (%)	43 (44.33)	35 (36.08)	0.24
Ischemic heart disease, *n* (%)	44 (45.36)	50 (51.54)	0.39
Atrial fibrillation, *n* (%)	2 (2.06)	5 (5.15)	0.28
Others, *n* (%)[e]	8 (8.25)	7 (7.21)	0.79

[a]Mean A1c for 69 patients.
[b]Mean A1c for 94 patients.
[c]44 patients were on insulin prior to admission.
[d]53 patients were on insulin prior to admission.
[e]Hypertensive crisis, pneumonia.

Table 2 Patients comorbidities

Comorbidity	Pre-phase	Post-phase	P value
HTN (%)	82 (84.5)	82 (84.5)	1
IHD	57 (58.8)	41 (42.3)	0.02
DLP	44 (45.4)	38 (39.2)	0.38
CKD	22 (22.7)	29 (29.9)	0.25
HFrEF	21 (21.7)	21 (21.7)	1
AF	15 (15.5)	4 (4.1)	0.014
CVA	7 (7.2)	8 (8.3)	0.79
HFpEF	4 (4.1)	8 (8.3)	0.25
Anemia	4 (4.1)	3 (3.1)	1
PE	2 (2.1)	0 (0)	0.5
Liver diseases	1 (1)	3 (3.1)	0.62
DVT	0 (0)	4 (4.1)	0.12
Others[a]	59 (60.8)	47 (48.4)	<0.001

AF, atrial fibrillation; CKD, chronic kidney disease; CVA, cerebrovascular accident; DLP, dyslipidemia; DVT, deep vein thrombosis; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; HTN, hypertension; IHD, ischemic heart disease; PE, pulmonary embolism.
[a]Others (Hypothyroidism, bronchial asthma, pneumonia, benign prostatic hyperplasia).

9.1–9.9 mmol/L in the post-phase (P<0.001). The mean difference in BGL was −1.8 mmol/L; 95% CI, −0.88 to 2.72; P<0.001, in post-phase vs. pre-phase.

Secondary outcome(s)

The median fasting BGL was 9.2 mmol/L (7.4–11.8, IQR) in the pre-phase and 8.5 mmol/L (6.6–10.3, IQR) in the post-phase (P=0.027). The proportion of patients achieving target random BGL was 29% in the pre-phase and 63% in the post-phase (P<0.001). The number of hyperglycemic episodes was 867 in the pre-phase and 548 in the post-phase (P<0.0001). The number of hypoglycemic episodes was 24 in the pre-phase and 33 in the post-phase (P=0.48). The median length of hospital stay was 6 days (IQR: 5–7) in the pre-phase vs. 5 days (IQR: 4–7) in the post-phase (P=0.42). The physician's adherence to the insulin order sets was 70%.(Table 3; study outcomes). The target random BGL was achieved in 56.8% of patients who were adherent to the protocol and in 43.1% of patients who were not adherent. The incidence of hypoglycemia in the non-adherent group (29 patients) was 13.7%, and 22% in the adherent group (68 patients).

Table 3 Outcomes

Outcome	Pre-phase	Post-phase	P value
Mean random BGL (mg/dl), 95% CI	201.11; 95% CI (190.8–211.4)	171.7; 95% CI (164–179.3)	<0.001
Median fasting blood glucose level (mg/dl), IQR	166.8 (133.5–213.7)	153 (119.4–186.3)	0.027
Random blood glucose in target, *n* (%)	29 (29.9)	63 (63.9)	<0.001
Number of hyperglycemic episodes, *n*	867	548	<0.0001
Number of hypoglycemic episodes, *n*	24	33	0.48
Adherence to insulin order sets, *n* (%)	NA[a]	68 (70.1)	NA[a]
Length of hospital stays, median (IQR)	6 (5–7)	5 (4–7)	0.42
Endocrine consultations, *n* (%)	10 (10.31)	5 (5.15)	0.28

BGL, blood glucose level; CI, confidence interval; IQR, interquartile range.
[a]NA: not applicable as the Insulin order set was designed prospectively.

Discussion

In this quasi-experimental, pre- and post-study, we found that the designed subcutaneous insulin treatment protocol integrated as order sets into the hospital CPOE system had a positive impact on improving random and fasting BGLs in cardiac diabetic patients without increasing the risk of hypoglycemia.

In our study, the mean random BGL was above 10 mmol/L in the pre-phase indicating that the standard of care did not adequately control BGLs in cardiac patients. In the post-phase, random BGL was reduced, reaching its target, which demonstrates that the standardized insulin order sets integrated into CPOE and continuous education are helpful tools to guide physicians in dosing and calculating the insulin requirements in cardiac T2DM patients. This result is consistent with the findings of previous studies [16,17,19]. However, all of these studies have failed to reach the target random BGL with modest improvement in mean random BGL [16,17]. Moreover, the previous research included all non-critically ill patients and was not specified to cardiac patients.

Additionally, the use of insulin order sets as CPOE was associated with a reduction in fasting BGL, which is an important BGL reading that reflects the efficacy of the basal insulin regimen and appropriate modification of the doses if indicated. On the other hand, all of the previous studies did not measure fasting BGL [16,17,19]. However, we did not achieve the target fasting BGL. Our fasting glucose level does not always reflect 8 h of fasting; a major contributing factor is that some patients lose their appetite at the scheduled dinner time or eat late at night, which may affect the number of fasting hours before the morning BGL, leading to unreliable fasting BGL.

Regarding the number of hyperglycemic episodes, our study showed a greater reduction in the number of hyperglycemic episodes in the post-phase compared with the pre-phase. This optimum glycemic control could be explained by the simplicity of the insulin order sets, optimum utilization, and accurate dosing recommendations provided by our protocol. In contrast to this finding, a previous study reported by Kravchenko *et al.* [16] stated that the number of hyperglycemic episodes was similar between the two phases [17].

In regard to the proportion of patients achieving target random BGL, the percentage was only 29.9% in the pre-phase and significantly increased to 63.9% in the post-phase which demonstrates the impact of using the insulin order sets. Another important finding in our study is that there was an increase in the number of hypoglycemic episodes in the post-phase compared with the pre-phase, but it was not statistically significant. The adherence to the insulin order sets by the physicians was 70%, and this may have been attributed to some rotating medical residents from different specialties joining the cardiology team on a monthly basis without attending the educational sessions.

Despite the fact that the adherent group had a higher target random BGL than the non-adherent group which demonstrates the utility of the protocol, we need to interpret these findings with caution as we are not able to conduct formal statistical subgroup analysis due to a lack of power. Moreover, although there was no difference in the length of hospital stay between the two groups. Patients in the post-phase had fewer days of hospital stay than those in the pre-phase without complete adherence to our insulin order sets. The number of endocrine consults was reduced by half in the post-phase compared with the pre-phase.

Our study has several strengths. First, the quasi-experimental design is a useful tool to assess practice changes after the implementation of a new intervention; second, we were able to detect the differences in all the study outcomes; third, the insulin treatment protocol can be generalized to be used in other wards for non-cardiac diabetic patients in different medical units; fourth, we were able to increase the physician's awareness about the use of insulin in hospitalized diabetic patients, which improved the patient care. Finally, to our knowledge, this is the first study in Saudi Arabia to assess the impact of insulin order sets on inpatient glycemic control in a cardiac setting.

There are several limitations to our study. First, a single-center experience which may affect the generalizability of the results. Second, due to retrospective design, we conducted a multivariant regression analysis to control potential confounders between pre- and post-phases. Third, the insulin order sets were not known or accessible to some rotating medical residents initially which affected adherence. Then we ensured accessibility by sharing the sets with the general hospital access. Finally, some patients did not have four BGL readings due to several factors, such as having an urgent interventional or diagnostic procedure at the time of blood glucose test or patient refusing blood sampling.

Potential future improvements to this intervention include conducting monthly educational sessions to increase the physician's adherence to the insulin order sets. In addition, adding an alert tool to the insulinorder sets to remind the physician about daily insulin dosing adjustments could improve order sets use, which can optimize glycemic control.

Future research directions are to design insulin treatment protocols for glycemic control in the critical care setting, implement the protocol as an order sets and then to assess the impact of the insulin order sets in this population.

Conclusion

The pharmacist-led implementation of computerized insulin order sets was associated with an improvement in random and fasting glycemic control without increasing the risk of hyperglycemia or hypoglycemia among hospitalized cardiac patients with T2DM.

Acknowledgement

Conflicts of interest

There are no conflicts of interest.

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