

Intraoperative Insulin Infusion Regimen versus Insulin Bolus Regimen for Glucose Management during CABG Surgery: A Randomized Clinical Trial

Rami Alqassieh¹, Mohanad Odeh^{2,3*}, Feras Jirjees⁴

¹ Faculty of Medicine, Hashemite University, Jordan.

² Pharmacy Management and Pharmaceutical Care Innovation Centre, Hashemite University, Jordan.

³ Department of Clinical pharmacy and Pharmacy Practice, Faculty of Pharmaceutical Sciences, Hashemite University, Jordan.

⁴ College of Pharmacy, University of Sharjah, United Arab Emirates.

ABSTRACT

Background and Aim: The stress induced by surgery disrupts the delicate balance between hepatic glucose production and glucose utilization in the body. Despite the significance of intraoperative glycaemic control for diabetic patients, limited attention has been given to this aspect. Two methods for administering insulin to manage glucose levels during surgery exist. This study aimed to compare intraoperative glucose levels in diabetic patients undergoing Coronary Artery Bypass Graft (CABG) surgery using either insulin infusion or the bolus method.

Method: This was a Randomized Clinical Trial (RCT). Seventy diabetic patients aged 40 or older scheduled for CABG surgery were enrolled in the trial. They were randomly assigned, using block randomization, to receive intraoperative insulin via either infusion or the bolus method. The primary outcome measure was intraoperative glucose levels. Subsequent insulin unit requirements and intraoperative potassium levels were secondary outcomes. Data was monitored throughout the CABG procedure and recorded at six different checkpoints.

Results: Male patients constituted the majority in both groups, with no significant differences in the preoperative characteristics of patients, including HbA1c levels and comorbidities. The infusion regimen demonstrated a statistically significant reduction in glucose levels (-19.12 mg/dL, 95% CI: -27.68 to -10.55, $P < 0.001$, Cohen's $d = 1.06$) compared to the bolus regimen. The total insulin units administered in the infusion group were 480 units, as opposed to 600 units in the bolus group ($P = 0.001$, Cohen's $d = 0.85$). Importantly, no cases of hypoglycemia or hyperkalemia were reported among the patients.

Conclusion: Intraoperative glucose control using insulin was effective for CABG patients with diabetes. However, the infusion regimen exhibited statistically superior results compared to the bolus regimen.

Clinical Trials Registry and Registration Number: The trial received approval from the Ethics Committee on 2/1/2019/2020 and was registered on Clinicaltrials.gov under ID: NCT04824586.

Keywords: Type 2 diabetes mellitus; cardiac surgery; glucose levels; insulin infusion; insulin bolus.

HIGHLIGHTS:

- Most studies typically focus on pre- and post-operative glucose levels. This is the first Randomized Clinical Trial to compare

intraoperative glucose level performance between infusion and bolus regimens.

- The use of insulin for glucose control in CABG patients helps prevent intraoperative hyperglycemia and potassium disturbances.
- The insulin infusion regimen in diabetic patients during CABG surgery yielded superior outcomes compared to the bolus regimen.

*Corresponding author: Mohanad Odeh

mohanad_odeh@hu.edu.jo

Received: 7/12/2022 Accepted: 19/1/2023.

DOI: <https://doi.org/10.35516/jjps.v16i3.708>

INTRODUCTION

In cardiac surgery patients, a significant association between intraoperative hyperglycaemia (glucose greater than 200 to 250 mg/dL) and increasing odds of morbidity and mortality has been documented^{1,2}. At such high glucose levels, there are increased risks of pulmonary and renal complications, infection, atrial fibrillation, heart failure, myocardial infarction, pericarditis, and neurological complications³⁻⁷.

Nevertheless, the optimal glucose management strategy during operations remains undetermined^{8,9}. There is some evidence supporting the superiority or at least equivalence of moderate glycaemic control (100–140 mg/dL, or 140–180 mg/dL) compared to intensive control (80–110 mg/dL) in patients undergoing cardiac surgery^{10,11}. It was found that glucose levels ranging from 140-170 mg/dL had the lowest risk of adverse outcomes¹⁰. The established and widely approved treatment strategies in cardiac surgery are still predominantly insulin-based¹²⁻¹⁴. Nevertheless, to the best of our knowledge, there is no universal agreement on the best specific protocol to be used. A considerable body of literature compares the impact of infusion insulin versus the sliding scale on postoperative parameters including surgical site infections and readmission rates¹⁴⁻¹⁵. Despite that, no published research, including a review of existing literature from sources such as PubMed, CINAHL, EMBASE, and CENTRAL, has compared the practical aspects and intraoperative parameters between infusion insulin and bolus insulin protocols in cardiac surgery for patients with diabetes. Reviewers, such as Duggan and colleagues, have confirmed the lack of data comparing subcutaneous insulin to IV insulin infusion in the operative setting¹⁵⁻¹⁷.

Accordingly, the primary objective of the present trial was to explore which insulin-based regimen, either infusion or bolus regimen, is superior for intraoperative management of glucose levels in patients with diabetes undergoing Coronary Artery Bypass Graft (CABG) surgery. Secondary objectives include comparing the

relative amounts of insulin required during the operation, the subsequent cost impact, and comparing potassium levels between the two groups.

METHODS AND MATERIALS

Study Design

This study was a parallel group, randomized clinical trial (RCT) with a 1:1 allocation ratio. The study was designed and reported in accordance with CONSORT guidelines.

Ethical Approval and Study Registration

Ethical approval for the study was obtained from the Office for Research Ethics Committees at Hashemite University and Prince Hamza Hospital in Jordan, with reference number 2/1/2019/2020. The study was also registered on Clinicaltrials.gov (ID: NCT04824586)¹⁸.

Participants

The eligibility criteria for participants were adult patients with type 2 diabetes mellitus admitted to the hospital for CABG surgery. These patients were asked to provide informed consent and met the following criteria: ages ranging from 40 to 70 years, a regular need for insulin according to dosing guidelines, and preoperative glucose levels between 200 mg/dL and 300 mg/dL.

The following patients were excluded from the trial: insulin-sensitive patients¹⁹, insulin resistance patients (Body Mass Index (BMI) > 35 kg/m², total daily insulin dose > 80 units, and/or daily steroids therapy > 20 mg prednisone), age > 70 years, Glomerular Filtration Rate (GFR) < 45 ml/min, individuals with no history of diabetes, patients at high risk of complications, and those whose operations were to be supervised by a specialized team. Patients unable to provide written informed consent and those with ≥ 4 emergency admissions within the six months prior to the index admission were also excluded.

Setting

Patients were recruited from the tertiary care center at Prince Hamza Hospital in Amman, Jordan. Patients with diabetes who had scheduled cardiac surgery and met the

study criteria were invited to participate. Patients who accepted participation and provided their consent were enrolled by well-trained research assistants who were trained in ethical standards and a patient-centered approach.

The Intervention

All patients in the two groups, the infusion and bolus groups, received doses of fast-acting human insulin (Regular insulin, Actrapid®). The insulin regimen protocol and its details were executed following the insulin standardization protocol in the hospital¹⁷.

Primary and Secondary Outcomes

The primary outcome was the intraoperative glucose level. It was monitored six times during the operation (see Table 1). The checkpoints were as follows: induction measurement before surgery, glucose levels post-heparin, and then every 30 minutes for two hours while the patient's blood was circulated through the Coronary Artery Bypass Machine (CABM). Insulin doses and potassium levels were recorded for use in the analysis of secondary outcomes.

Table 1 Baseline demographic and clinical characteristics of patients for two groups (n=70)

Variables	Infusion Group (n=35)	Bolus Group (n=35)	P-Value
Age (years) Mean (±SD)	57.6 (±6.98)	58.3 (±7.52)	0.69 ^a
Gender: Male (%)	28 (80.00%)	29 (82.86%)	0.76 ^b
Duration of diabetes (years) Mean (±SD)	10.06 (±7.80)	7.06 (±6.90)	0.09 ^a
HbA1c % Mean (±SD)	9.7 (±2.37)	9.2 (±2.88)	0.40 ^a
Induction glucose level mg/dL Mean (±SD)	244.77 (±26.56)	241.29 (±23.65)	0.56 ^a
No. of patients on insulin preoperatively (%)	9 (25.71%)	4 (11.43%)	0.12 ^b
No. of patients on oral hypoglycaemic agents (%)	24 (68.57%)	29 (82.82%)	0.16 ^b
No. of patients on both insulin and hypoglycaemic agents (%)	2 (5.71%)	2 (5.71%)	1.00 ^b
Hypertension (%)	22 (62.86%)	27 (77.14%)	0.19 ^b
Duration of Hypertension (years) Mean (±SD)	9.7 (±7.43)	11.8 (±7.58)	0.35 ^a
Duration of ischemic heart disease (weeks) Mean (±SD)	25 (±8)	31 (±5)	0.07 ^b
Duration of ischemic heart disease (years) Mean (±SD)	1.3 (±1.58)	1.1 (±1.46)	0.73 ^a
Kidney Disease (%)	2 (5.71%)	1 (2.86%)	1.00 ^c
Thyroid Disease (%)	1 (2.86%)	0	1.00 ^c

Sample Size

To detect a difference of at least 25 mg/dL between the infusion and bolus groups (the standard deviation of the two groups is expected to be 35 mg/dL, i.e., the variance is 1225 mg/dL), the study recruited and collected complete data for a minimum of 31 patients in each group. This provided a confidence level of (95%) and the power of

80%. $n = (Z\alpha/2 + Z\beta)^2 * 2 * \sigma^2 / d^2$. where $Z\alpha/2$ is the critical value of the Normal distribution at $\alpha/2$ (for a confidence level of 95%, α is 0.05, and the critical value is 1.96), $Z\beta$ is the critical value of the Normal distribution at β (for a power of 80%, β is 0.2, and the critical value is 0.84), σ^2 is the population variance, and d is the difference needed to be detected²⁰.

Statistical Methods

Standard independent-samples t-tests or separate variances t-tests (Welch t-tests) were used to compare the results between the two arms of the study. A General Linear Model and one-way repeated measures ANOVA were conducted to determine whether there was a statistically significant difference within groups.

Cost analysis and cost-effectiveness were employed for the pharmacoeconomic analysis^{21,22}. The incremental cost-effectiveness ratio (ICER) was calculated using the following equation:

$$ICER = \frac{\text{Cost of insulin in the infusion protocol} - \text{Cost of insulin in the bolus protocol}}{\text{Drop in glucose level by infusion} - \text{Drop in glucose level by bolus}}$$

Equation 1

Randomization, Allocation and Blinding

During patient enrollment, concealed allocation to either the infusion group or bolus group was ensured by using a closed envelope system prepared by an

independent investigator²³. Block randomization with random block sizes was employed to ensure allocation balance and prevent selection bias by avoiding allocation prediction²⁴. Researchers and physicians were blinded to the block size sequence and randomization. The envelopes remained unopened until the registration of patients was completed. Hospital staff responsible for monitoring glucose levels and administering insulin were also blinded to the primary and secondary outcomes of the study.

RESULTS

Out of 179 screened patients, 93 patients were invited to participate in the study, and ultimately, 70 patients were recruited and randomized into two arms. No losses or exclusions were documented after recruitment in the study. Please refer to Figure 1 below for the flow of participants through the trial based on eligibility criteria. The patient recruitment process took place from June 1, 2019, to January 30, 2020. Follow-up was not carried out as the study's focus was on intraoperative glucose control.

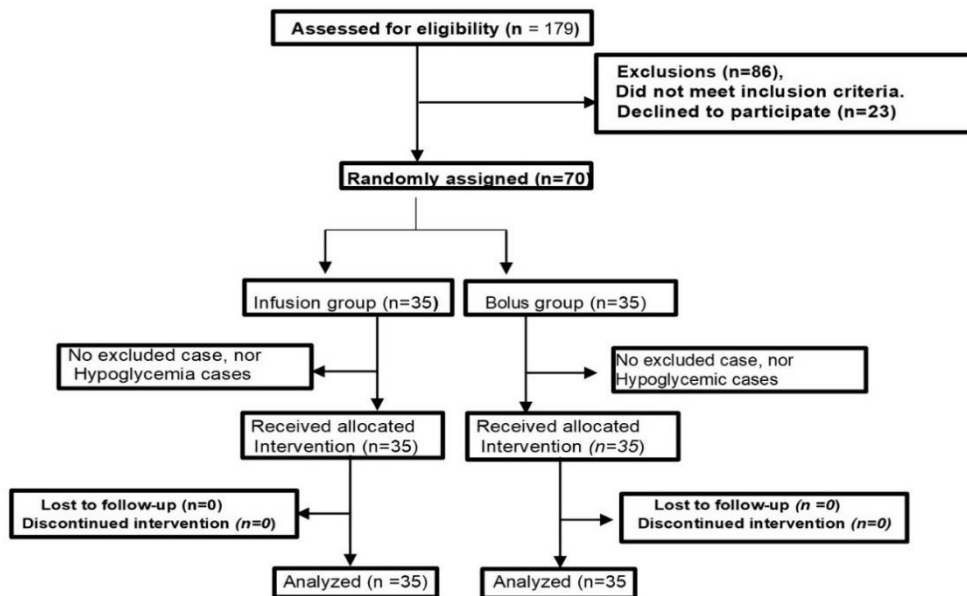


Figure 1 Participation flow diagram. Patients recruited and randomized (n=70); in the infusion group (n=35) and bolus group (n=35)

Characteristics of Study Participants

The baseline characteristics of the 70 subjects presented in Table 1, with no statistically significant differences were noted in all characteristics of the two groups: infusion group (n=35) and bolus group (n=35). There were more male participants than female participants in the two groups with an average age 57.6 and 58.3 years old, respectively. Mean HbA1c for the two groups were between 9.7 and 9.2, respectively. Induction glucose levels were much closed with 244.77 and 241.29 mg/dL. In addition, there were no significant differences in the presentation of other chronic diseases.

Surgery Characteristics

The number of diseased vessels (blocked coronary arteries) in patients was 3 in 91.4% and 94.3% in the infusion group and the bolus group, respectively. The remaining patients had 4 diseased vessels. The number of grafts performed was equal to the number of diseased vessels in all patients in the two groups. There were no significant differences in the number of diseased vessels and grafts performed between the two groups.

The average surgery time for patients with three grafts

in both groups was 5.0 ± 0.4 hours, and 5.3 ± 0.5 hours for patients with four grafts. There were no significant differences in operative time between the two groups.

A team consisting of surgeons, anesthesiologist, and surgical nurses conducted the CABG surgeries for all patients included in this trial.

Pre- and Intraoperatively Glucose Levels

Table 2 displays the mean glucose levels between the two insulin groups. Variances were found to be homogeneous, as assessed by Levene's test for equality of variances. Glucose levels across the operation were statistically significantly lower in the infusion group compared to the bolus group. The maximum difference was observed at the second checkpoint, where the mean difference was -24.91 mg/dL (95% CI: -40.73 to -9.10; P=0.002) with a medium effect size (Cohen's d value = 0.75). The minimum statistically significant difference was reported at checkpoint 5, where the difference was -17.6 mg/dL (95% CI: -29.07 to -6.13; P=0.003, d=0.73). At the end of operation mean glucose levels for the infusion group was 19.12 mg/dL less than mean for the bolus group (95% CI: -27.68 to -10.55, P<0.001, d=1.06).

Table 2 Primary outcome, glucose level as measured at six checkpoints through the operation and insulin units used in the CABG operations (n=70)

Checkpoint ts	Variables between-group analysis	Mean glucose level (±SD) (mg/dL)	Mean glucose level (±SD) (mg/dL)	Levene's Test for Equality of variances	Mean difference	P value	95% Confidence Interval of the difference		Effect size Cohen's d
		Infusion Group (n=35)	Bolus Group (n=35)				Lower	Upper	
1	Induction Glucose level	244.77 (±26.56)	241.29 (±23.65)	0.326 ^a	3.48	0.564 ^b	-8.51	15.45	0.14
2	Glucose / Post Heparin	193.06 (±33.71)	217.97 (±32.59)	0.243 ^a	-24.91	0.002 ^b	-40.73	-9.10	0.75
3	1 st on CABM	169.46 (±31.55)	191.49 (±30.88)	0.972 ^a	-22.03	0.004 ^b	-36.92	-7.13	0.71
4	2 nd on CABM	158.00 (±25.42)	176.11 (±28.71)	0.398 ^a	-18.11	0.007 ^b	-31.05	-5.18	0.67
5	3 rd on CABM	156.71 (±25.37)	174.31 (±22.66)	0.661 ^a	-17.60	0.003 ^b	-29.07	-6.13	0.73
6	4 th on CABM post-protamine	152.37 (±19.31)	171.49 (±16.48)	0.540 ^a	-19.12	< 0.001 ^b	-27.68	-10.55	1.06
		Mean (±SD) Insulin Unit	Mean (±SD) Insulin Unit						
		480 [13.71 (±4.29)]	600 [17.14 (±3.80)]	0.354	-3.43	0.001	-5.36	-1.50	0.85

CABM: Coronary Artery Bypass Machine

^a Population variance of both groups is equal

^b Standard independent-samples t-test

No cases of hypoglycaemia (glucose level < 60 mg/dL) were reported during the trials in either of the two groups.

Within-group analysis

Figure 2A illustrates the decrease in glucose levels in the infusion group from 244.77 (± 26.56) mg/dL pre-intervention to 152.37 (± 19.31) mg/dL (i.e. reduction of 92.4 mg/dL, 95% CI: 75.7–109.1, $p < 0.001$) and in the bolus group from 241.29 (± 23.65) mg/dL to 171.49 (± 16.48) mg/dL (i.e. reduction of 69.8: 95% CI: 56.9–82.7, $p < 0.001$) by the end of intervention. Both the infusion and bolus interventions elicited statistically significant changes in glucose concentration over time, $F(2.9, 97.9) = 97.86$, $p < 0.001$ and $F(2.6, 89.4) = 75.07$, $p < 0.001$, respectively.

Mauchly's test of sphericity indicates that the assumption of sphericity has been violated in both the infusion group $\chi^2(14) = 58.34$, $p < 0.001$ and the bolus group $\chi^2(14) = 76.74$, $p < 0.001$, so results were interpreted by using the Greenhouse-Geisser correction (estimated epsilon (ϵ) less than 0.75). The sample effect size based on within-subjects factor variability, partial eta squared effect size η^2 was = 0.74 in the infusion group, and 0.67 in the bolus group. The estimated effect size (partial ω^2) was = 0.697 in the infusion group and 0.638 in the bolus group.

Post hoc pairwise analysis, adjusted for multiple comparisons Bonferroni correction, revealed that glucose concentration was statistically significantly decreased within the infusion group between pairwise at checkpoints 1, 2, and 3 ($p < 0.05$). A similar pattern has also resulted in post hoc pairwise analysis for the bolus group.

Insulin Units Used Pre- and During Surgical Operations

As shown in Figure 2B, patients in the infusion group received fewer insulin units compared to the bolus group, with 13.71 (± 4.29) units and 17.14 (± 3.80) units, respectively (Table 2). The difference was statistically significant (-3.43 units of insulin, 95% CI: -5.35 to -1.50, $P = 0.001$, $d = 0.85$).

Cost Effectiveness Analysis

Economic evaluation ICER = (480 unit * \$0.15/unit – 600 unit * \$0.15/unit) - (92.4 - 69.8). In other terms = $72 - 90 / 22.6 = -18/22.6 = -0.79$. (See Equation 1).

As the incremental cost is negative (-18) and the incremental effect is positive (22.6), the infusion intervention is unequivocally cost-effective when compared with the bolus intervention. It is dominant, achieving better outcomes at a lower cost^{21,22}.

Potassium Levels

Generally, there was no case of hypokalaemia, and potassium levels reached the upper limit only once (at checkpoint 5) in the bolus infusion group. However, the results showed that there were no statistically significant differences between the two groups with regards to potassium levels throughout the operations. Within-group analysis revealed that the mean potassium levels fluctuated between 4.13 (± 0.39) and 4.43 (± 0.38) among the infusion group and 4.09 (± 0.32) and 4.51 (± 0.41) among the bolus group. Figure 3 illustrates the intraoperative levels of potassium across six operation checkpoints.

Both groups reported within-group statistically significant differences in potassium levels. Post hoc pairwise analysis, adjusted for multiple comparisons using Bonferroni correction, revealed that statistically significant results were driven by checkpoint 5 in both groups (see Figure 3). The maximum fluctuation and statistically significant mean difference in the infusion group were observed at 5, 1 Δ mean = 0.29 (95% CI: 0.06 – 0.53, $P=0.006$) and points 5,6: Δ mean = 0.30 (95% CI: 0.08 – 0.52, $P=0.002$). In the bolus group, the maximum mean difference was observed at points 5, 1: Δ mean = 0.42 (95% CI: 0.14 – 0.70, $P=0.001$) and points 5,6: Δ mean = 0.33 (95% CI: 0.004 – 0.66, $P=0.045$). The maximum mean difference in the bolus group was larger than that in the infusion group. However, all potassium readings intraoperatively were almost within the normal potassium range.

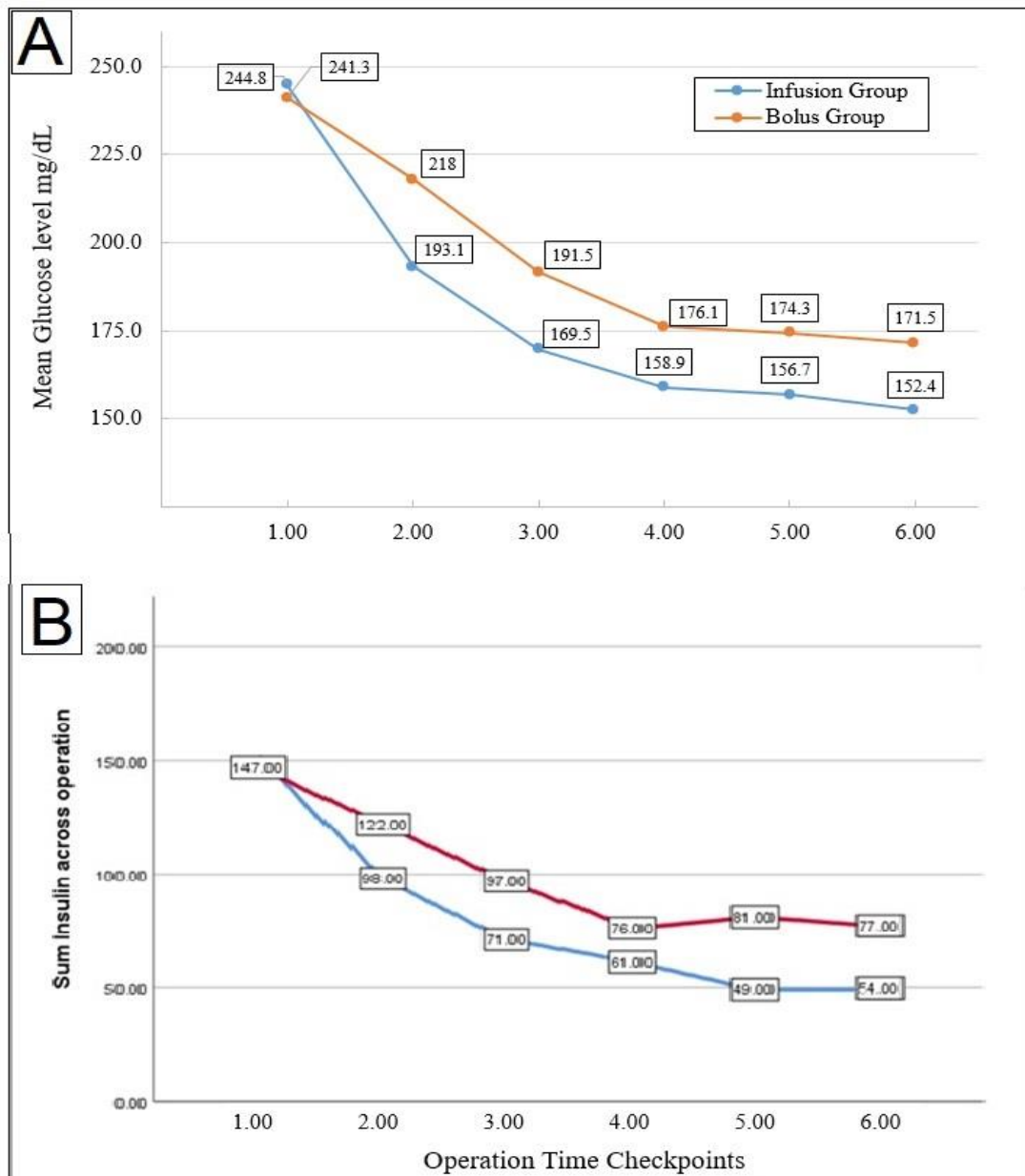


Figure 2A: Intraoperative mean glucose levels across six operation checkpoints infusion (n=35) or bolus (n=35) groups. By the end of the intervention, the decrease in glucose levels was significant within both the infusion group, $p < 0.001$, and bolus group $p < 0.001$ by one-way repeated measures ANOVA. **2B:** Intraoperative insulin units used across six checkpoints operation. Patients within the infusion group received fewer total insulin units than those in bolus group. $P = 0.001$ by the standard independent-samples t-test.

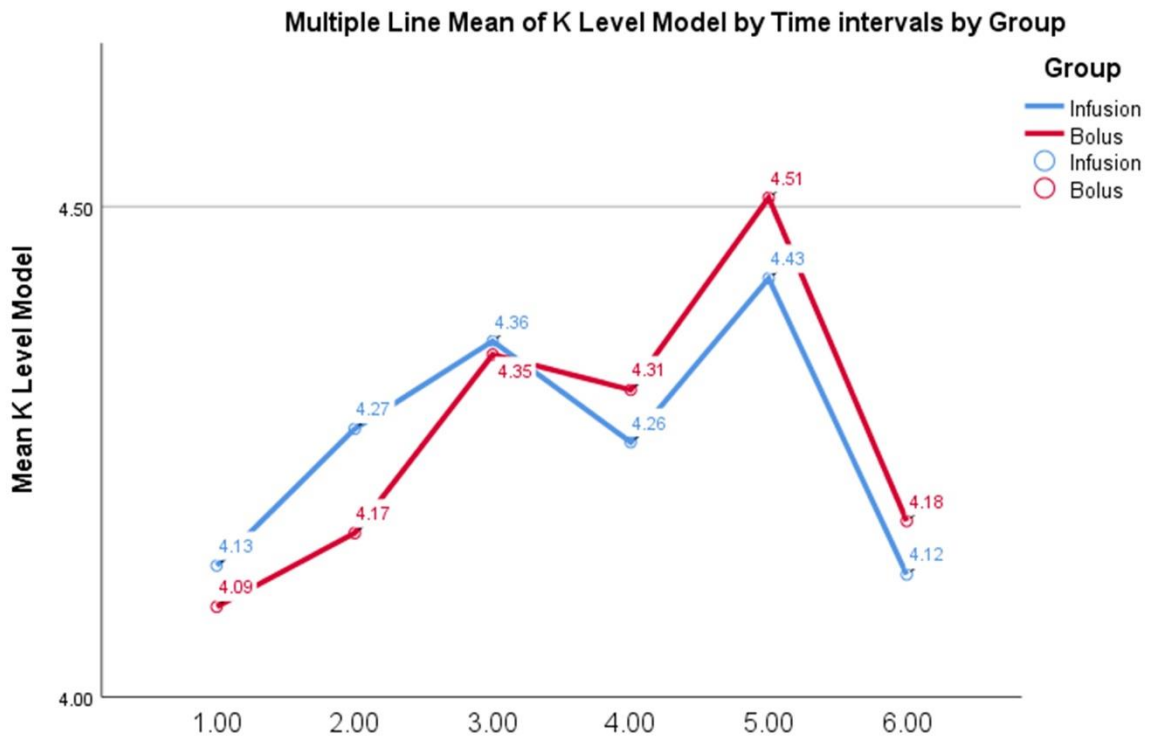


Figure 3 Intraoperative levels of potassium across six operation checkpoints. Patients received insulin as infusion (n=35) or bolus (n=35). By the end of the intervention, change in potassium levels was significant within both the infusion group, $p < 0.001$, and bolus group $p < 0.001$, one-way repeated measures ANOVA.

Post-operative data

As per the trial protocol, data regarding patients were collected in the Cardiac Intensive Care Unit (CICU) for six hours post-operatively, focusing on the general health status of the patients. Both groups exhibited controlled glucose and potassium levels, and no insulin-related complications were observed. Additionally, during these hours in the CICU, patients in both groups received a nearly identical amount of insulin as that administered during the last intraoperative checkpoint. Furthermore, patients from both groups remained stable at the sixth hour post-operatively.

DISCUSSION

This RCT included two groups with 1:1 allocation ratio. Seventy patients with diabetes who underwent This

randomized controlled trial (RCT) featured two groups with a 1:1 allocation ratio, including seventy patients with diabetes who underwent CABG surgery. The patients in the infusion regimen group (n=35) demonstrated a statistically significant impact on blood glucose level reduction compared to the bolus group (n=35). Moreover, the infusion group received a lower total amount of insulin units than the bolus group. Notably, there were no reported cases of hypoglycaemia and hyperkalaemia in any of the patients receiving the two regimens.

This study represents the first evaluation, to the best of our knowledge, comparing bolus versus infusion methods in patients with diabetes undergoing cardiac (CABG) surgery. These findings align favorably with the joint French diabetology and anesthesiology position statement,

which recommended fewer insulin units with the infusion method compared to the bolus method, even though substantial evidence supporting such a recommendation was lacking²⁴.

The findings of the present study contrast with results in published research that compared the two insulin regimens in non-cardiac surgeries²⁵. Arun et al. concluded that the intravenous insulin bolus regimen, compared to the insulin infusion regimen for intraoperative blood glucose management in non-cardiac surgery, provided better glycaemic control measured in terms of the proportion of intraoperative duration during which the patients remained within the target blood glucose levels²⁵. This somewhat contradictory result may be attributed to differences in patient characteristics and variations in perioperative blood glucose levels.

Hyperglycemia commonly observed during cardiac surgery results from a combination of exogenous glucose administration, glucose utilization during prolonged anesthesia, and the relative insulin resistance that develops in response to the stress of surgery²⁶. While there is strong evidence that preoperative and postoperative glucose control for patients undergoing cardiac surgery impacts surgical-related complications^{27,28}, there is limited data on methods of intraoperative insulin administration. Glucose management has been assessed in a few types of cardiac surgery using both bolus insulin and insulin infusion. In the Kruger et al. study, the use of a timely insulin dosing method in patients with diabetes during cardiopulmonary bypass (CPB) surgery was effective but raised some safety concerns in preventing hyperglycemia during surgery²⁶.

The findings related to insulin unit consumption align with the performance of blood glucose levels during heart surgery. The results regarding potassium levels were not unexpected. Albacker et al., in their study comparing 44 patients undergoing elective CABG, who received titrated intravenous insulin infusion (n = 22) or a fixed high-dose systemic insulin infusion (n = 22), did not find any differences in potassium levels between the two groups

and did not observe any hypo- or hyperkalaemia during the study¹³. Despite differences in study design, this may provide insights into the results related to potassium level performance.

Limitation of the study

The present study has limitations. It was conducted at a single center, which is a constraint. Additionally, the study design had limitations, with a short follow-up after the operation. However, post-operative follow-up may relate to glucose levels or other variables rather than the method of insulin administration. Furthermore, the trial's inclusion criteria were limited to stable patients requiring regular insulin, making the results applicable primarily to patients within similar groups. The study did not explore perioperative treatment modalities, as inclusion criteria focused on glucose levels between 200 – 300 mg/dL. Finally, while a cost-effectiveness analysis of the cost of insulin was performed, no other cost factors were considered.

CONCLUSION

Using insulin in both infusion and bolus regimens intraoperatively in patients with type 2 diabetes mellitus undergoing CABG surgeries was effective in controlling glucose levels during the operation without influencing potassium levels. However, the present randomized clinical trial demonstrated that providing insulin through the infusion regimen delivers statistically significantly better intraoperative glucose control for patients with diabetes undergoing CABG surgery when compared to the bolus regimen. Consequently, the infusion regimen required fewer units of insulin and exhibited dominant cost-effectiveness, achieving better outcomes at a lower cost.

ACKNOWLEDGMENT: Special thanks are extended to Pharmacist Ayah Yousef Banat for her invaluable assistance in data collection and electronic data transfer.

Conflicts of interest: The authors declare no conflicts of interest.

Funding: This study received no external funding.

DISCLOSURE OF ETHICAL STATEMENTS

- Research Protocol Approval: The research protocol was approved by the Office for Research Ethics Committees at Hashemite University and Prince Hamza Hospital, Jordan, with reference number 2/1/2019/2020.

- Informed Consent: All participants signed the consent form.
- Approval date of Registry and the Registration No. of the study/trial: The study was registered on Clinicaltrials.gov (ID: NCT04824586).
- Animal Studies: N/A

REFERENCES

1. Sathya B., Davis R., Taveira T., Whitlatch H., Wu WC. Intensity of peri-operative glycemic control and postoperative outcomes in patients with diabetes: a meta-analysis. *Diabetes Res Clin Pract*, 2013; 102(1): 8-15. doi: 10.1016/j.diabres.2013.05.003
2. Shah NJ., Leis A., Kheterpal S., Englesbe MJ., Kumar SS. Association of intraoperative hyperglycemia and postoperative outcomes in patients undergoing non-cardiac surgery: a multicenter retrospective study. *BMC Anesthesiol*. 2020; 20: 106. <https://doi.org/10.1186/s12871-020-01022-w>
3. Gandhi GY., Nuttall GA., Abel MD., Mullany CJ., Schaff HV., Williams BA., Schrader LM., Rizza RA., McMahon MM. Intraoperative Hyperglycemia and Perioperative Outcomes in Cardiac Surgery Patients. *Mayo Clin Proc*, 2005; 80(7): 862–866.
4. Abuloha S., Alabbadi I., Albsoul-Younes A., Younes N., Zayed A. The Role of Clinical Pharmacist in Initiation and/or Dose Adjustment of Insulin Therapy in Diabetic Patients in Outpatient Clinic in Jordan. *Jordan J Pharm Sci*. 2016; 9(1): 33–50.
5. Hua J., Chen G., Li H., Fu S., Zhang LM., Scott M., Li Q. Intensive Intraoperative Insulin Therapy Versus Conventional Insulin Therapy During Cardiac Surgery: A Meta-Analysis. *J Cardiothorac Vasc Anesth*. 2012; 26(5): 829–834.
6. Omar S., Albsoul A., Alabbadi I. Hypoglycaemia Fear among Diabetics. *Jordan J Pharm Sci*. 2016; 9(2): 77–88.
7. Duncan AE., Abd-Elseyed A., Maheshwari A., Xu M., Soltesz E., Koch CG. Role of Intraoperative and Postoperative Blood Glucose Concentrations in Predicting Outcomes after Cardiac Surgery. *Anesthesiology*, 2010; 112(4): 860–871.
8. Lazar HL. Glycemic Control during Coronary Artery Bypass Graft Surgery. *ISRN Cardiol*, 2012. doi:10.5402/2012/292490
9. Cha S., Whitman G. Glycemic Control Does Matter in the Cardiac Surgery Patient. *5th EAI International Conference*, Portugal, 2018. DOI: 10.1007/978-3-030-04146-5_29
10. Boreland L., Scott-Hudson M., Hetherington K., Frussinetty A., Slyer JT. The effectiveness of tight glycemic control on decreasing surgical site infections and readmission rates in adult patients with diabetes undergoing cardiac surgery: A systematic review. *Hear Lung*. 2015; 44(5): 430–440.
11. Hulst AH., Plummer MP., Hollmann MW., DeVries JH., Preckel B., Deane AM, Hermanides J. Systematic review of incretin therapy during perioperative and intensive care. *Crit Care*. 2018; 22(1): 299.
12. Yeldandi RR., Lurie A., Baldwin D. Comparison of once-daily glargine insulin with twice-daily NPH/regular insulin for control of hyperglycemia in inpatients after cardiovascular surgery. *Diabetes Technol Ther*. 2006; 8(6): 609–616.
13. Albacker TB., Carvalho G., Schrickler T., Lachapelle K. Myocardial Protection During Elective Coronary Artery Bypass Grafting Using High-Dose Insulin Therapy. *Ann Thorac Surg*. 2007; 84(6): 1920–1927.

14. Polderman JAW., van Steen SCJ., Thiel B., Godfried MB., Houweling PL., Hollmann MW., DeVries JH., Preckel B., Hermanides J. Perioperative management of patients with type-2 diabetes mellitus undergoing non-cardiac surgery using liraglutide, glucose-insulin-potassium infusion or intravenous insulin bolus regimens: a randomised controlled trial. *Anaesthesia*. 2018; 73(3): 332–339.
15. Hoo GW. *Intravenous Insulin Therapy*. 2020. Medscape Available online: <https://emedicine.medscape.com/article/2049152-overview#a11> (access on 1st of June 2020)
16. Wilson M., Weinreb J., Hoo GW. Intensive insulin therapy in critical care: a review of 12 protocols. *Diabetes Care*. 2007; 30(4): 1005-11. doi: 10.2337/dc06-1964. Epub 2007 Jan 9. PMID: 17213376.
17. Duggan EW., Carlson K., Umpierrez GE. Perioperative Hyperglycemia Management. *Anesthesiology*. 2017; 126(3): 547–60.
18. Clinicaltrials.gov. 2021. U.S. National library of Medicine (NIH). Available online <https://clinicaltrials.gov/ct2/show/NCT04824586?term=Insulin&cntry=JO&draw=2&rank=1>
19. Gutch M., Kumar S., Razi S., Gupta K., Gupta A. Assessment of insulin sensitivity/resistance. *Indian J Endocrinol Metab* [Internet]. 2015; 19(1): 160. Available from: <https://journals.lww.com/10.4103/2230-8210.146874>
20. Meysamie A., Tae F., Mohammadi-Vajari MA., Yoosefi-Khanghah S., Emamzadeh-Fard S., Abbasi M. Sample size calculation on web, can we rely on the results? *J Med Stat Informatics*. 2014; 2(1): 3.
21. Reeder CE. Overview of pharmacoeconomics and pharmaceutical outcomes evaluations. *Am J Health Syst Pharm*. 1995; 52(19 Suppl 4), S5-8.
22. Ahuja J., Gupta M., Gupta AK., Kohli K. Pharmacoeconomics. *Natl Med J India*. 2004; 17(2): 80–83.
23. Elkins M. Concealed allocation in randomised trials. *J Physiother*. 2013; 59(2): 134–136.
24. Efird J. Blocked Randomization with Randomly Selected Block Sizes. *Int J Environ Res Public Health*. 2010; 8(1): 15–20.
25. Cosson E., Catargi B., Cheisson G., Jacqueminet S., Ichai C., Leguerrier A., Ouattara A., Tauveron I., Bismuth E., Benhamou P., Valensi P. Position Statement/Recommendations Practical management of diabetes patients before, during and after surgery: A joint French diabetology and anaesthesiology position statement. *Diabetes Metab*. 2018; 44: 200–216.
26. Arun P., Krishna HM. Comparative study between insulin bolus regimen and glucose insulin infusion regimen on effectiveness of intraoperative blood glucose control in patients with type 2 diabetes mellitus undergoing non-cardiac surgery. *Sri Lankan J Anaesthesiol*. 2019; 27(2): 110.
27. Kruger C., Sidebotham D., Brown AJ., Singh H., Merry AF. Timely bolus insulin for glucose control during cardiopulmonary bypass. *J Extra Corpor Technol*. 2012; 44(1): 34-38.
28. Navaratnarajah M., Rea R., Evans R., Gibson F., Antoniadis C., Keiralla A., Demosthenous M., Kassimis G., Krasopoulos G. Effect of glycaemic control on complications following cardiac surgery: literature review. *J Cardiothorac Surg*. 2018; 13(10). <https://doi.org/10.1186/s13019-018-0700-2>
29. Furnary AP., Gao G., Grunkemeier GL., Wu Y., Zerr KJ., Bookin SO., Floten HS., Starr A. Continuous insulin infusion reduces mortality in patients with diabetes undergoing coronary artery bypass grafting. *J Thorac Cardiovasc Surg*. 2003; 125(5): 1007-21. doi: 10.1067/mtc.2003.181. PMID: 12771873

مقارنة تأثير طرق إعطاء الإنسولين ببطء أو بدفعة واحدة على إدارة مستويات الجلوكوز أثناء العمليات الجراحية لتوصيل شرايين القلب التاجية : دراسة سريرية عشوائية محكمة

رامي القيسية¹، مهند عودة*^{2,3}، فراس جرجيس⁴

¹ قسم الجراحة العامة والمتخصصة، كلية الطب، الجامعة الهاشمية، الزرقاء، الاردن.

² مركز الإدارة الصيدلانية والابتكار في الرعاية الصيدلانية، الجامعة الهاشمية، الزرقاء، الاردن.

³ قسم الصيدلانية السريرية والممارسة الصيدلانية، كلية العلوم الصيدلانية، الجامعة الهاشمية، الزرقاء، الاردن.

⁴ قسم الممارسة الصيدلانية والعلاجات، كلية الصيدلة، جامعة الشارقة، الامارات العربية المتحدة.

ملخص

الإطار العام والهدف: إجراء العمليات الجراحية يؤثر على التوازن المنظم بين إنتاج الجلوكوز في الكبد واستخدامه في الجسم. على الرغم من أهمية مراقبة مستوى الجلوكوز أثناء العمليات الجراحية لمرضى السكري، إلا أن هناك قليل من الدراسات التي بحثت في هذا الأمر. هناك طريقتان لإعطاء الإنسولين للسيطرة على مستوى الجلوكوز في المرضى أثناء الجراحة (إما ببطء أو دفعة واحدة). هدفت هذه الدراسة إلى مقارنة مستويات الجلوكوز لمرضى السكري أثناء عمليات جراحة القلب لتوصيل الشرايين التاجية باستخدام الإنسولين ببطء أو بالجرعة الواحدة.

الطريقة: دراسة سريرية عشوائية محكمة. تم انتقاء سبعون مريضاً مصاباً بالسكري (يعمر أكثر من 40 عاماً) والذين كانوا في مواعيد لعملية جراحة القلب. تم تعيينهم باستخدام طريقة بحثية متوازنة لتلقي الإنسولين أثناء العملية إما ببطء أو بنظام الجرعة الواحدة. كان مؤشر النتائج الأساسي هو قياس مستوى الجلوكوز أثناء العملية. وكانت كمية وحدات الإنسولين المستخدمة ومستويات البوتاسيوم أثناء العملية مؤشرات نتائج ثانوية. تم مراقبة البيانات خلال العملية وسُجّلت على مدى ست نقاط تقييمية أثناء العملية الجراحية.

النتائج: كانت نسبة المرضى الذكور أعلى في المجموعتين مع عدم وجود فروق ذات دلالة إحصائية في خصائص المرضى قبل العمليات. أظهرت الطريقة العلاجية بإعطاء الإنسولين ببطء أنها أدت إلى انخفاضاً ذو دلالات إحصائية معتمدة في مستويات الجلوكوز مقارنة بذلك الانخفاض من خلال إعطاء الإنسولين دفعة واحدة. (-19.12 mg/dL, 95% CI: -10.55, P<0.001, Cohen's d=1.06) كانت كمية وحدات الإنسولين الإجمالية للمجموعة التي تم استعمال الإنسولين ببطء 480 وحدة مقارنة بـ 600 وحدة للمجموعة التي أخذت الإنسولين بالجرعة الواحدة، و هذا الفارق كان ذو دلالة إحصائية معتمدة (فرصة الاحتمالية أقل من واحد بالالف). وأخيراً، لم تتم اية ابلاغات عن حدوث انخفاض في مستوى الجلوكوز أو ارتفاع مستوى البوتاسيوم في المرضى.

الخلاصة: كانت السيطرة على مستوى الجلوكوز أثناء عمليات القلب الجراحية باستخدام الإنسولين فعالة لمرضى السكري. وأظهرت هذه الدراسة أن طريقة إعطاء الإنسولين ببطء تعطي نتائج أفضل وبدلالة إحصائية معتمدة من طريقة إعطاء الإنسولين بالدفعة الواحدة.

الكلمات الدالة: مرض السكري من النوع الثاني؛ جراحة القلب؛ مستويات الجلوكوز؛ طريقة إعطاء الإنسولين ببطء؛ طريقة إعطاء الإنسولين بالجرعة الواحدة؛ إدارة مستويات الجلوكوز؛ إدارة مستويات الجلوكوز خلال العمليات الجراحية.

* المؤلف المراسل: مهند عودة

mohanad_odeh@hu.edu.jo

تاريخ استلام البحث 2022/12/7 وتاريخ قبوله للنشر 2023/1/19.