Original Article

A retrospective analysis of blood gases with two different insulin infusion protocols in patients undergoing cardiovascular surgery

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Abstract

Aim: Intraoperative blood glucose concentration is known to be an independent risk factor for morbidity and mortality in patients undergoing cardiovascular surgery. Arterial blood gas analysis is an important investigation to monitor the acid-base balance and gas exchange in these patients. Hyperglycemia leads to a series of metabolic changes which affect acid-base balance and serum electrolytes. In this study, we aimed to look into the effect of glycemic control on arterial blood gas parameters, serum electrolytes, and hemoglobin (Hb).

Materials and Methods: We collected data from diabetic patients who underwent cardiovascular surgery between 2010 and 2014. The patients were divided into two groups according to the insulin infusion protocols applied such as with conventional (180–250 mg/dl) (n = 17) (Group 1) and tighter glycemic targets (121–180 mg/dl) (n = 51) (Group 2). We retrospectively analyzed arterial blood gas results taken at different perioperative time points from these patients.

Results: We found that pH HCO_3 and base excess, serum sodium, potassium, calcium, and Hb were similar in both groups.

Conclusion: Our study showed that a tighter intraoperative glycemic control does not affect arterial blood gas parameters, serum electrolytes, or Hb when compared to the conventional glycemic control.

Key words: Base excess, cardiovascular surgery, diabetes mellitus, electrolytes, perioperative insulin infusion

Date of Acceptance: 20-Dec-2015

Introduction

Diabetes mellitus (DM) is a significant risk factor for coronary artery disease.[1-3] Intraoperative blood glucose concentration is known to be an independent risk factor for morbidity and mortality in surgical patients.[4-6] Several studies demonstrated the benefit of continuous insulin infusion regarding perioperative morbidity and mortality.[7-9] A significant mortality benefit was shown in surgical Intensive Care Unit with tight glycemic control (target blood glucose: 80–110 mg/dl) in a prospective study.[10] However, results of some other studies showed increased mortality with tight glycemic control, probably due to increased incidence of hypoglycemia.[11-13] Due to these conflicting data, guidelines about perioperative management of diabetes state different

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Access this article online	
Quick Response Code:	**Website**: www.njcponline.com
	DOI: 10.4103/1119-3077.178943

How to cite this article: Kuşkonmaz ŞM, Kurtipek Ö, Aydın ME, Erbatur ME, Alkan M, Ünal Y, *et al*. A retrospective analysis of blood gases with two different insulin infusion protocols in patients undergoing cardiovascular surgery. Niger J Clin Pract 2016;19:742-6.

target blood glucose values, ranging from 108–180[14] to 140–200 mg/dl.[15]

DM is implied as a risk factor for intraoperative bleeding or blood transfusion after cardiovascular surgery.[16-19] There are only a few studies looking into the effect of tight glycemic control on these outcomes. A recent prospective study reported no difference in the incidence of bleeding in patients undergoing cardiovascular surgery, whether they received intraoperative insulin infusion, thus achieved a tight glycemic control, or not. The study included both diabetic and nondiabetic patients.[20]

Arterial blood gas analysis is an important investigation to monitor the acid-base balance and gas exchange in a patient who undergoes cardiovascular surgery.[21] Hyperglycemia leads to a series of metabolic changes which affect acid-base balance and serum electrolytes.[22] In this study, we aimed to compare arterial blood gas parameters, serum electrolytes, and hemoglobin (Hb) values in diabetic patients who had undergone cardiovascular surgery with two different intraoperative insulin infusion protocols.

Materials and Methods

This study was approved by the Ethics Committee of Gazi University Hospital (Gazi University Ethics Committee for Clinical Research. Decision Number: 22). The study is carried out in a university hospital setting, in which 100–130 major cardiovascular surgeries are performed per year. We analyzed the blood glucose levels and blood gas parameters derived from diabetic patients who underwent major cardiovascular surgery (coronary artery bypass grafting, valve replacement, and aortic aneurysm) between 2010 and 2014. Patients with Type 1 diabetes, chronic renal failure, chronic liver disease, New York Heart Association Class II–IV heart failure, and active malignant disease are not included in the study. Between 2010 and 2012, we had preferred to initiate insulin infusion only when blood glucose level exceeds 200 mg/dl and we had targeted a target blood glucose value of 180–250 mg/dl. After 2012, we began to initiate insulin infusion directly preoperatively and used a more intensive approach to keep blood glucose between 121 and 180 mg/dl. The details of these two protocols are given in Table 1. Patients in the conventional insulin infusion protocol are named as Group 1 (n = 17) and patients in the intensive glucose control group as Group 2 (n = 51). The perioperative Hb, serum electrolytes (calcium [Ca], sodium [Na], and potassium [K]) blood glucose, arterial blood gas parameters (pO_2, pCO_2, HCO_3, base excess [BE], and pH) obtained in 11 different time points (T0: Initial blood glucose, T1–T10: Blood glucose measurements 60 min apart intraoperatively, and T11: Blood glucose measurement at the end of surgery) perioperatively were retrospectively analyzed. All parameters were measured by an arterial blood gas analyzer (Radiometer. Blood gas analyzer, ABL835 Flex, I902-754R0288N0008, Copenhagen, Denmark).

Statistics

The statistical analyses were performed using (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.), and $P < 0.05$ was considered statistically significant. Variations in blood glucose levels and blood gas parameters between study groups were assessed using the Student's t-test. The results were expressed as mean ± standard deviation and minimum–maximum.

Results

A total of 420 major cardiovascular surgeries -all on pump- were performed within the study period. Sixty-eight of

Table 1: Insulin infusion protocols for conventional and intensive perioperative glucose control

Conventional insulin infusion protocol
0.45% NaCl (50 ml/h) is initiated, and blood glucose is measured every 60 min
Initial blood glucose
>200 mg/dl: Continuous regular insulin infusion through an electronic pump
200–300 mg/dl: Insulin infusion 1–2 U/h
>300 mg/dl: 2–4 U insulin bolus + insulin infusion 1–2 U/h
Measure blood glucose every 60 min
Blood glucose
<70 mg/dl: Withhold insulin for 60 min, give 50 ml of 50% DW bolus, measure glucose 15 min later, continue with infusion if blood glucose >70 mg/dl, repeat the procedure if blood glucose ≤70 mg/dl
71–200 mg/dl: Withhold insulin for 60 min
200–300 mg/dl: Continue with the same insulin infusion dose
>300 mg/dl: Give 2–4 U insulin bolus, increase insulin infusion to 3 U/h
Insulin infusion protocol for intensive glycemic control
Continuous regular insulin infusion through an electronic pump, 0.45% NaCl (50 ml/h) and 10% DW (50 ml/h) and potassium are infused separately
Initial blood glucose
100–200 mg/dl: Insulin infusion 2 U/h
>200 mg/dl: 2–4 U insulin bolus + insulin infusion 1–2 U/h
71–100 mg/dl: Insulin infusion 1 U/h
Measure blood glucose every 60 min
Blood glucose
<50 mg/dl: Withhold insulin for 30 min, give 50 ml of 50% DW bolus, measure glucose 15 min later, continue with infusion if blood glucose >70 mg/dl, repeat the procedure if blood glucose ≤70 mg/dl
50–70 mg/dl: Withhold insulin for 30 min, continue with 10% DW
71–120 mg/dl: Decrease insulin infusion to 1 U/h
121–180 mg/dl: Continue with the same insulin infusion dose
181–250 mg/dl: Increase insulin infusion to 2 U/h
>250 mg/dl: Give 2–4 U insulin bolus, increase insulin infusion to 3 U/h

DW=Dextrose in water

Table 2: Demographic properties of the patients (mean±SD (minimum-maximum))

	Group 1 (*n*=17)	Group 2 (*n*=51)	*P*
Age (years)	59.66±8.35 (41-78)	58.22±9.21 (33-80)	0.414
Sex (male/female)	11/6	37/14	0.822
Duration of anesthesia (min)	285.00±38.25 (220-360)	265.67±42.75 (200-320)	0.625
RBC transfusion (unit)	3.08±1.24 (1-6)	3.18±1.06 (1-7)	0.666

RBC=Red blood cell; SD=Standard deviation

Table 3: Perioperative blood glucose measurements of the patients (mean±SD (minimum-maximum))

Blood glucose	Group 1 (*n*=17)	Group 2 (*n*=51)	*P*
T1	178.77±65.71 (112-320)	157.37±48.99 (69-290)	0.051
T2	248.79±67.73* (135-375)	149.94±39.48 (93-247)	<0.0001
T3	233.14±66.96* (156-350)	146.24±32.76 (92-232)	<0.0001
T4	242.21±62.63* (171-381)	149.20±27.95 (100-237)	<0.0001
T5	238.93±79.67* (138-433)	154.43±24.70 (105-205)	<0.0001
T6	238.07±72.25* (125-445)	156.47±26.15 (100-206)	<0.0001
T7	235.25±89.82* (124-496)	156.81±27.67 (84-216)	<0.0001
T8	248.50±71.79* (154-433)	153.29±31.92 (57-204)	<0.0001
T9	242.86±70.61* (122-365)	158.08±37.98 (98-246)	0.011
T10	241.75±30.93* (210-273)	155.50±18.64 (140-189)	0.010
T11	209.33±48.29* (122-273)	154.57±28.46 (87-216)	<0.0001

**P*<0.05: When compared to Group 1. SD=Standard deviation

Table 4: Arterial blood gas parameters at different perioperative time points in two groups (mean±SD (minimum-maximum))

	Group 1 (*n*=17)	Group 2 (*n*=51)	*P*
T1			
pH	7.41±0.06 (7.33-7.49)	7.42±0.05 (7.23-7.52)	0.769
pO_2 (mmHg)	170.03±95.73 (64-432)	154.87±81.04 (34-403)	0.567
pCO_2 (mmHg)	32.73±4.95 (23.6-40.7)	34.20±5.40 (25.4-51.7)	0.614
HCO_3 (mmHg)	21.06±2.88 (16.6-25)	21.67±2.18 (16.4-28.2)	0.282
BE	−3.52±2.97 (−8.5-0.7)	−2.42±2.29 (−7.6-4.7)	0.140
T6			
pH	7.46±0.04 (7.35-7.51)	7.44±0.06 (7.28-7.53)	0.212
pO_2 (mmHg)	222.00±83.66 (34.5-316.1)	214.49±70.89 (90.6-340)	0.575
pCO_2 (mmHg)	32.46±4.48 (27.8-42)	31.97±3.95 (21.5-40.9)	0.994
HCO_3 (mmHg)	21.81±2.50 (17.7-25)	20.37±1.85 (16.1-25.5)	0.080
BE	−2.39±2.74 (−6.9-1.2)	−3.48±1.97 (−8.5-3)	0.161
T11			
pH	7.39±0.06 (7.28-7.49)	7.40±0.05 (7.30-7.52)	0.758
pO_2 (mmHg)	147.13±69.79 (69.9-308)	148.56±76.29 (64.4-380)	0.894
pCO_2 (mmHg)	34.15±8.18 (20.4-52.7)	33.10±4.26 (24.8-44.5)	0.537
HCO_3 (mmHg)	20.35±2.48 (14.5-24.6)	20.22±1.70 (16.1-24.6)	0.387
BE	−4.43±2.43 (−10-−2)	−3.88±1.90 (−9-0.3)	0.982

SD=Standard deviation; BE=Base excess

them were eligible for our study (regarding the inclusion criteria explained above). Of those, 52 were cardiovascular bypass surgeries and 16 were valvular operations. The demographic properties of the patients were similar in two groups [Table 2].

Table 5: Hemoglobin and electrolytes at different perioperative time points in two groups (mean±SD (minimum-maximum))

	Group 2 (*n*=17)	Group 1 (*n*=51)	*P*
T1			
Hb (g/dl)	11.24±2.648 (7.2-16.2)	11.96±1.94 (8.2-15.3)	0.230
Na (mmol/L)	138.83±3.92 (132-145.3)	141.33±4.77 (132-161)	0.100
K (mmol/L)	3.54±0.37 (2.93-4.33)	3.67±0.35 (3-4.40)	0.345
Ca (mmol/L)	0.98±0.19 (0.65-1.34)	0.93±0.19 (0.54-1.18)	0.332
T6			
Hb (g/dl)	8.76±1.13 (7-10.9)	8.33±0.75 (6.8-9.5)	0.281
Na (mmol/L)	135.39±5.23 (124-144.2)	137.91±5.40 (125-158)	0.141
K (mmol/L)	3.97±0.80 (2.92-5.79)	4.18±0.64 (3.30-5.90)	0.305
Ca (mmol/L)	1.11±0.14 (0.98-1.34)	1.05±0.13 (0.75-1.19)	0.711
T11			
Hb (g/dl)	8.88±1.69 (5.3-11.3)	8.42±0.84 (7.0-10.1)	0.223
Na (mmol/L)	137.92±4.95 (129-145.4)	141.19±5.06 (132-158)	0.059
K (mmol/L)	3.78±0.69 (2.90-5.40)	3.94±0.56 (3-5.40)	0.157
Ca (mmol/L)	1.08±0.14 (0.88-1.32)*	0.93±0.17 (0.56-1.21)	0.007

**P*<0.005: When compared to Group 1. Hb=Hemoglobin; SD=Standard deviation

Perioperative blood glucose measurements are shown in Table 3. Initial blood glucose measurements (T0) were similar in both groups. Blood glucose measurements in Group 1 were significantly lower than that of Group 2 in all other time points (T1–T11).

For practical purposes, we preferred to compare T1, T11, and a mean of intraoperative measurements (T2–T10). We did not find a statistically significant difference between pH, HCO_3, and BE levels in different perioperative time points between two groups [Table 4]. We did not find a statistically significant difference between two groups when hemoglobin, Na, K, or Ca levels are compared in different perioperative time points between two groups [Table 5] except a significantly higher calcium in Group 2 in T11 measurements.

Discussion

Arterial blood gas analysis provides important data about the metabolic status of a patient who is under surgical stress. Although the adverse effects of hyperglycemia on various surgical outcomes are well established, there are a few studies that looked into the association between glycemic management and perioperative arterial blood gas parameters.[23,24]

Rucka *et al*. hypothesized that insulin may influence the genes associated with surfactant and, in turn, have an effect on pulmonary gas exchange. They investigated the effect of insulin infusion on oxygenation in patients undergoing lung resection. The study was conducted in a cohort of 64 patients (15 had diabetes). The authors did not find a difference in pO_2 or pCO_2 in patients who received intraoperative insulin infusion.[24] Masoumi *et al.* investigated the effect of intraoperative insulin infusion on arterial blood gas parameters in patients undergoing cardiovascular surgery.[20] In this prospective study, 61 patients (17 had diabetes) were divided into two groups such as one group received insulin infusion with tight glycemic control (target blood glucose value between 90 and 150 mg/dl) and the other group was followed without insulin infusion. The authors reported that pO_2, PCO_2, and pH values obtained at different time points preoperatively were similar in both groups. Our results were consistent with the results of these two studies. We thought that gas exchange is more dependent on patient-related factors such as respiratory function and surgical technique used (on-pump or off-pump) in cardiovascular surgery.

In our study, we also evaluated serum Na, K, and Ca. Hyperglycemia itself and insulin infusion are both known to affect serum electrolyte levels.[25] We found that a tighter intraoperative glycemic control does not influence serum electrolytes. We should remind that potassium infusion is given with insulin at appropriate doses in our protocols.

Intraoperative blood loss is an important cause of morbidity in cardiovascular surgery. Several studies implied DM as a risk factor for intraoperative bleeding or blood transfusion after cardiovascular surgery.[16-19] In a large multicenter study, in patients undergoing coronary artery bypass grafting surgery, no significant difference was found between postoperative Hb values of diabetic patients on oral anti-diabetic medications or insulin and nondiabetic patients.[26] In the study mentioned above, Masoumi *et al.* failed to find a difference in the risk of bleeding from surgical site between patients who were given insulin infusion and patients followed without insulin infusion.[20] In our preliminary study, we showed that a tighter glycemic control does not affect postoperative Hb values in cardiovascular surgery. Although diabetes increases the risk of intraoperative bleeding, the way and degree of glycemic control do not seem to be related to bleeding. To our opinion, bleeding may be more related to the baseline health status of the diabetic patient. Further studies are needed to clarify the effect of glucose control on intraoperative bleeding.

Our study has some limitations. First, we were unable to evaluate important parameters such as the incidence of hypoglycemic episodes in this retrospective design. Second, data about short-term and long-term morbidity and mortality of these patients are not analyzed in this study. The absence of a prestudy power analysis is also a potential limitation of our study. Finally, the small study group precludes a more powerful statistical analysis to be done.

Conclusion

This preliminary study on diabetic patients undergoing cardiovascular surgery showed that a tighter intraoperative glycemic control does not affect arterial blood gas parameters, serum electrolytes, BE, or Hb when compared to the conventional glycemic control. Intraoperative tight glycemic control does not seem to be superior to conventional insulin regimens in diabetic patients as far as the electrolyte and acid-base balance are concerned. Tight glycemic control does not influence gas exchange and the risk of intraoperative bleeding either. Further studies are warranted to detect the impact of intraoperative tight glycemic control on short-term and long-term morbidity and mortality in diabetic patients undergoing cardiovascular surgery.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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