Clinical Communication

Comparison between effect of etomidate and thiopentone on blood glucose in diabetic patients – A randomised controlled trial

INTRODUCTION

Several anaesthetic agents have been investigated for their effect on stress response and hyperglycaemia in diabetics and non-diabetics.[1-5] By cortisol suppression, etomidate decreases blood glucose (BG) in healthy patients.[6] The effect of etomidate on BG in diabetics is unknown. We hypothesise that etomidate lowers BG in diabetic patients. This study compared the impact of general anaesthesia (GA) induction with etomidate and thiopentone on BG in diabetic patients.

METHODS

This randomised controlled trial was conducted after obtaining Institutional Research Ethics Committee approval (No. EC/NIMS/1799/2016) and the study was registered at Clinical Trials Registry-India (CTRI/2017/02/007752, www.ctri.nic.in). Written informed consent for participation in the study and use of patient data for research were obtained. The study was carried out in accordance with the principles of the Declaration of Helsinki, 2013. One hundred diabetic patients aged between 40 and 65 years with preoperative glycosylated haemoglobin (HbA1c) <8% and undergoing less than 3 h of surgery under GA were enroled. Patients with other endocrine disorders or medications that might influence BG perioperatively, patients receiving regional anaesthesia, patients with hepatic or renal disease, and pregnant and lactating women were excluded.

Computer-generated simple randomisation was done, and the allocation was concealed using sequentially numbered, sealed, opaque envelopes. The participant, investigator, outcome assessor and data entry operator were all blinded to the drug administered. Patients were randomised to group T (n = 50) and group E (n = 50) and received intravenous (IV) thiopentone or etomidate for anaesthesia induction, respectively. If any included patients required perioperative beta-blockers, steroids or vasopressors after induction, they were excluded from the analysis.

Standard preoperative fasting orders were followed. All patients were scheduled as the first on the list. Diabetic medications were continued, and oral hypoglycaemics/insulin were withheld on the morning of surgery. After establishing standard monitors, fentanyl 2 μg/kg IV was administered. BG was recorded (T0) by pinprick using BG reagent strips (Medisense; Abbott Laboratories, Maidenhead, UK) and glucometer (Optium; Abbott Laboratories, Illinois USA). IV Ringer's lactate was infused at 2 mL/kg/h. Anaesthesia was induced with IV etomidate or thiopentone until response to verbal commands was lost. After achieving sufficient relaxation with IV atracurium 0.5 mg/kg, tracheal intubation was performed. Subsequently, anaesthesia was maintained with isoflurane 0.7–1.2 minimum alveolar concentration in 50% air and oxygen. Fentanyl 0.5 μg/kg IV bolus was administered hourly, and neuromuscular blockade was maintained with atracurium infusion 0.25 μg/kg/h IV. At the end of the surgery, residual neuromuscular blockade was antagonised with glycopyrrolate 0.02 mg/kg and neostigmine 0.05 mg/kg IV, and the trachea was extubated. In the postoperative period, Ringer's lactate 100 mL/h was continued till the commencement of oral intake.

BG was measured at 15 min, 30 min and 1, 2, 4, 8, 12 and 24 h after induction. If BG was <70 mg/dL, 50% dextrose 1 mL/kg IV was given, 5% dextrose infusion at 100 mL/h was started, and the study was discontinued. If any measurement of BG was more than 250 mg/dl, insulin infusion was started. The dose of the insulin infusion was adjusted to maintain BG less than 200 mg/dl; BG was monitored second hourly in patients who received insulin infusion until discontinuation. The requirement for insulin was noted. The systolic arterial pressure (SAP), diastolic arterial pressure (DAP), mean arterial blood pressure (MAP) and heart rate (HR) were recorded at the baseline and 1, 2, 3, 4, 5, 15, 30, 45 and 60 min after intubation. Incidences of hypotension (30% decrease in MAP from baseline), hypertension (MAP >30% from baseline), bradycardia (HR <50 beats/min), hiccups, myoclonus and pain on injection of the anaesthetic agent were noted.

The primary outcome was to find the effect of the etomidate and thiopentone on BG up to 24 h after induction of GA. The secondary outcomes were to compare the effect on haemodynamics during induction and tracheal intubation, the incidence of myoclonus and pain on IV anaesthetic induction agent injection.

The sample size calculation was done using data from a pilot study in which the mean BG in group E was 138 mg/dL and group T was 158 mg/dL with a pooled standard deviation (SD) of 34 at 4 h after induction of GA. The α error was set at 0.05 and the β error at 0.20. Accounting for a dropout of 10%, 50 patients were enroled in each group. The statistical analysis was done using the Statistical Package for Social Sciences (SPSS) software 17 version (International Business Machines, New York, USA). Paired *t*-test was done to analyse continuous data, and the Chi-square test was done for categorical data. The intragroup comparison was done by repeated measures analysis of variance (ANOVA). A *P* value of <0.05 was considered significant.

RESULTS

A total of 89 patients were analysed [Figure 1]. There was no difference in age, body mass index, surgery duration and insulin requirement. More females were present in group E [Table 1]. The mean (SD) [95% confidence interval] dose of etomidate and thiopentone was 0.19 (0.03) [0.10–0.276] mg/kg and 3.84 (1.02) [3.53–4.14] mg/kg, respectively ($P < 0.0001$). Types of surgery included were minimally invasive surgeries (percutaneous nephrolithotomy [12], ureterorenoscopy lithotripsy [5], laparoscopic cholecystectomy [12], laparoscopic oophorectomy[3] and diagnostic laparoscopy [3]]), fixation of fracture upper limb (12) and lumbar laminectomy (17) [Table 1]. There was no difference in BG levels between the groups. A significant increase in BG levels was observed in both groups 2 h after induction [Table 2]. None had haemodynamic instability at induction. Myoclonus was observed in two patients in group E. Four patients in group E and two in group T complained of pain on injection ($P = 0.322$). Hiccups were observed in 12 and one patient in groups T and E, respectively ($P = 0.001$). All patients resumed normal diet and antidiabetic regimen within 12 h following extubation.

DISCUSSION

In the present study, there was no difference in BG levels measured up to 24 h after induction of GA with either etomidate or thiopentone.

People with diabetes are at increased risk of endothelial dysfunction, surgical site infections and postoperative stroke.[7-9] The choice of anaesthetic techniques and agents is essential in glycaemic control. Although not commonly used, etomidate may be used for cardiovascular stability. With the revival of interest in etomidate as an induction

Table 1: Demographic data

Demographic data	Group E (*n*=42)	Group T (*n*=47)
Age (years)	53 (10.8)	53.11 (8.49)
Male/female	10/32	23/24
Body mass index (kg/m^2)	26.8 (3.7)	25.67 (3.24)
Duration of surgery (min)	122.5 (41.9)	123.4 (50.3)
Patients given insulin	4	5
Type of surgery		
Endoscopic procedures	12	23
Surgeries on breast	8	8
Thyroidectomy	2	3
Other surgeries	20	13

Data are expressed as mean (standard deviation) or numbers

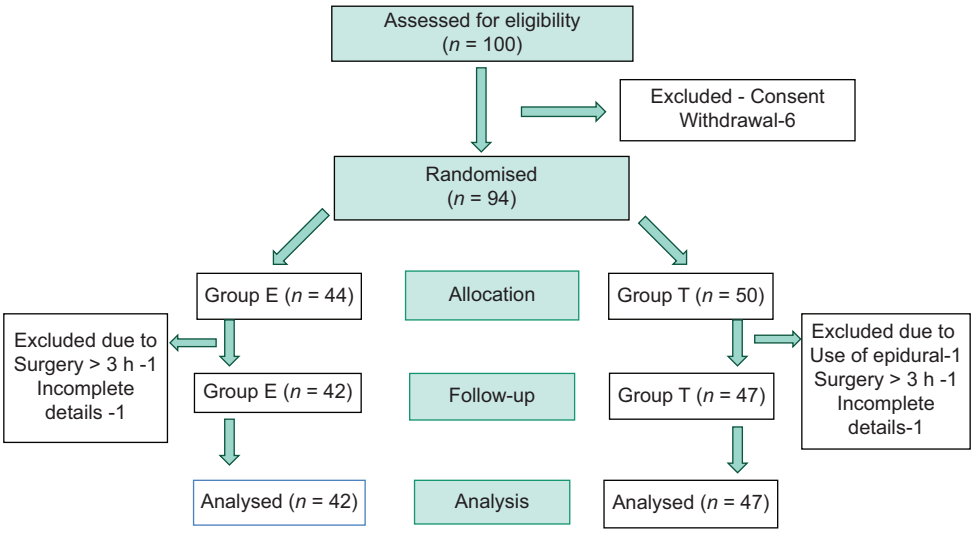

Figure 1: Consolidated standards of reporting trials diagram of the study

Table 2: Comparison of blood glucose levels (mg/dL) between groups E and T

Time intervals	Group E (*n*=42) Mean (SD) (95% CI)	Group T (*n*=47) Mean (SD) (95% CI)	*P*
0	133.57 (40.81) (125.50–141.64)	134.47 (40.93) (126.81–142.12)	0.560
15 min	133.29 (37.78) (125.81–140.76)	134.72 (46.94) (125.94–143.49)	0.528
30 min	136.98 (41.00) (128.87–145.08)	140.17 (42.35) (132.25–148.08)	0.378
60 min	157.52 (38.74) (149.85–165.18)	160.23 (52.27) (150.45–170.00)	0.539
2 h	187.88 (52.81)* (177.43–198.32)	192.55 (57.57)* (181.78–203.31)	0.307
4 h	200.12 (53.57)* (189.52–210.71)	218.66 (81.65)* (203.39–233.92)	0.100
8 h	210.88 (52.67)* (200.47– 221.22)	218.00 (71.98)* (204.54–231.45)	0.365
12 h	195.14 (70.76)* (200.46–221.29)	203.89 (65.01)* (191.73–216.04)	0.395
24 h	176.90 (58.15)* (165.40–188.39)	170.02 (54.43)* (159.84–180.19)	0.861

CI=confidence interval, SD=standard deviation. *P<0.05 from the baseline within the group

agent, there is a need to reassess its endocrine and metabolic effects, especially in patients with diabetes, which this study has partially addressed. Etomidate reduces BG levels by 18 mg/dL in non-diabetics.[10] A single induction dose of etomidate suppresses hormone production for 6–12 h, while infusion for 1–2 h blocks cortisol synthesis up to 24 h.[11,12] In this study, the primary outcome measured was BG at 4 h, a time point chosen based on the duration of cortisol suppression by etomidate. There was no difference in BG levels either at 4 h or at any other time up to 24 h in either group. This may be because the surgeries included were mostly superficial or minimally invasive. The other reason may be the smaller dose of etomidate used in the current study compared to the reported decrease in BG with 0.35 mg/kg etomidate.[10]

Uniform protocol, scheduling all study participants first on the list and standardisation of fasting duration and IV fluids were the strengths of this study. The study's limitations included subjective endpoint for induction and non-standardisation of the surgical procedures.

CONCLUSION

The induction of GA with etomidate does not affect blood sugar levels in diabetic patients compared to thiopentone.

Study data availability

De-identified data may be requested with reasonable justification from the authors (email to the corresponding author) and shall be shared after approval as per the authors' institutional policy.

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Conflicts of interest

There are no conflicts of interest.

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