Disease and Diagnosis

Dis Diagn. 2023; 12(1):29-34

doi 10.34172/ddj.2023.408

Original Article

Effects of Intravenous Anesthesia on the Plasma Glucose Level During Cataract Surgery Among Patients With Type II Diabetes

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Abstract

Background: High blood sugar is a typical reaction to stress. In the diabetic population, hyperglycemia can be a serious issue and has been linked to higher mortality rates. Recent studies have shown that anesthetics reduced glucose tolerance; however, it is still unclear how propofol, ketamine, and thiopental of Na affect glucose metabolism. The present study compared the blood glucose levels of thiopental of Na, ketamine, and propofol among patients with cataract surgery.

Materials and Methods: The study included 135 ASA II and III adult patients of both genders who were older than 65, known to have type II diabetes, receiving intravenous (IV) sedation, and scheduled for cataract surgery. The three groups were comparable with regard to patients, age, gender, weight, duration of the operation time, duration of recovery time, duration of diabetes, and anesthesiologist's physical status (based on the American Society of Anesthesiology). Patients were randomly assigned to one of three groups, including receiving IV thiopental of Na 5 mg/kg/h (group T), ketamine 2 mg/kg/h (group K), or propofol 2 mg/kg/h (group P) after the induction of IV sedation with 1-2 mic/kg fentanyl and 0.03 mg/kg midazolam. Changes in blood glucose levels were examined as dependent variables in patients with cataract surgeries while under the influence of these medications up to 6 hours after.

Results: The results showed that blood glucose concentrations increased significantly over time in all groups. Moreover, blood glucose concentrations did not differ significantly between the groups receiving the thiopental of Na ketamine or propofol at any measurement time. During the first post-administrative hour, the thiopental of Na, ketamine, and propofol groups demonstrated blood glucose levels of 114.2 ± 16.24 mg/dL, 136.2 ± 12.28 mg/dL, and 122.2 ± 13.84 mg/dL, which were not statistically significant ($P = 0.72$). Regarding the frequency and severity of blood glucose level changes during or after surgery, the groups did not significantly differ at any point in time.

Conclusion: The findings of the present study suggest that the thiopental of Na, ketamine, and propofol have equal effects on glucose metabolism.

Keywords: Intraoperative, Postoperative hyperglycemia, Thiopental sodium, Ketamine, Propofol

Received: March 16, 2022, Accepted: September 19, 2022, ePublished: November 21, 2022

Introduction

According to estimates and epidemical statistics, up to 20% of all cataract surgeries may be conducted on diabetic patients (1, 2). Thus, cataract is a well-known complication of diabetes. Evidence suggests that all types of diabetic retinopathy may worsen after cataract surgery (3). However, a large portion of the data used to support this claim came from the retrospective case note analyses of patients who had extracapsular cataract surgery (3-5). Reviewing the few controlled prospective trials that have been performed in this field makes the evidence for this claim less believable.

Diabetes mellitus has diverse effects on all body organ systems. Most importantly, insulin levels and metabolic control are far more complex than previously thought (1). The central role of insulin in metabolism is still being better understood through research, and treating hyperglycemia in diabetic patients is now recognized as being essential for preventing long-term diabetic complications (1). It has been demonstrated that preserving euglycemia and physiologically regulating insulin responses to variations in glucose levels increase

lifespan and decrease complications associated with diabetes mellitus (2). Perioperative glucose control has tightened; however, the ideal glucose level and way to administer insulin during surgery are still debatable in terms of preventing unfavorable postoperative outcomes (3). Although there is convincing evidence that shows preoperative glucose control reduces postoperative morbidity and even mortality, the science behind this issue is debatable (4, 5).

Elevated glucose is thought to contribute to coronary endothelial dysfunction, platelet dysfunction, amplifying ischemic reperfusion injury, and eradicating ischemic preconditioning (6-13). Every precaution to prevent perioperative hyperglycemia should be taken, including the appropriate choice of intravenous (IV) sedatives and anesthetics for diabetic patients, given our growing understanding of the detrimental effects of hyperglycemia on postoperative infections and neurological, renal, and cardiovascular complications. Therefore, the aim of the present study was to compare the use of three different anesthetics in diabetic patients undergoing cataract surgery. Preoperative to postoperative glucose level changes and the mean difference in the change in the glucose level between the three commonly used anesthetics were the outcomes of interest.

Our objective was to ascertain whether using these three different anesthetics increases the need for medical intervention or exposed diabetic patients to a higher risk of postoperative hyperglycemia.

Materials and Methods

Participants and Procedures

Overall, 135 adult patients of both genders, 65 years of age or older, known to have type II diabetes, receiving IV sedation, and scheduled to have cataract surgery were recruited for the present case-control study. These patients were classified as ASA II and III (Physical Status Classification System of the American Society of Anesthesiologists: ASA2: Patients with mild to moderate systemic disease, ASA3: Patients with severe disease process which limits activity but is not incapacitating). The patients undergoing surgery would have a blood sugar test sample taken from them, as it is a standard hospital procedure for all patients before surgery. However, this study is not a clinical trial. All patients in the hospital under study have received the same medications on a regular basis. These medications are commonly used in various settings. For instance, these medications were examined in a previous study (14).

Sample Size Calculation

A power calculation was used to estimate the sample size. Furthermore, G*Power revealed that at least 42 patients per group were required to achieve 80% power to identify a 20% difference between the groups. To account for any exclusions, we enrolled 45 patients in each group. Power analysis was used to determine the required number of patients for each group based on previous research (13). A 60% prevalence of hyperglycemia was predicted in this regard. Prior to the study, a power analysis demonstrated that a sample size of 42 patients in each group would have an 80% chance of detecting a significant mean difference in preoperative to intraoperative or postoperative glucose between groups of 60 mg/dL, a clinically significant change in serum glucose that would necessitate intervention in our group of patients. However, we recruited 45 patients per group to account for any exclusions. Emam Khomini hospital of Kermanshah (Iran) was the site of the study in 2013. As part of the standard protocol for the pre-operative preparation of patients, all patients, whether insulin or non-insulin dependent (on oral hypoglycemic therapy), were switched to insulin therapy using short-acting insulin to control blood glucose (80-110 mg/dL fasting and up to 140 mg/dL random).

A computer-generated randomizer was employed to choose 45 patients for each group after obtaining, reviewing, and applying the inclusion and exclusion criteria to the patient's medical file. Age, gender, number of operations, length of recovery, changes in hemodynamics and blood glucose levels, and drug complications were among the information gathered on each patient. Patients with a glucose level greater than 200 mg/100dL, a history of diabetic ketoacidosis, or diabetic nephropathy were excluded from the study. Patients requiring intraoperative insulin administration, large volumes of crystalloid (>2 L), ephedrine, or other vasoactive medications to maintain blood pressure were excluded as well. To maintain the integrity of the results, the patients received 10 mL/kg of a Ringer lactate serum before the induction of IV sedation. No patients received preanesthetic medication. Following the induction of IV sedation with 1-2 μg/kg Fentanyl and 0.03 mg/kg midazolam, patients were randomly included in one of three groups to receive IV thiopental of Na, 5 mg/kg/h (group T), ketamine, 2 mg/kg/h (group K), or propofol, 2 mg/kg/h (group P). The anesthesiologist in charge of maintaining control and keeping track of the clinical symptoms was blinded to the study drugs and prepared all three medications in identical 10-cc syringes.

Assessments

Blood glucose concentrations were measured in all groups at baseline and 1, 2, three, and 6 hours after administration in addition to the standard intraoperative monitoring techniques (i.e., electrocardiogram, noninvasive blood pressure, oxygen saturation, and temperature monitoring). The number of patients with at least one blood glucose level greater than 180 mg/dL, the incidence of hyperglycemic events, was calculated, and the anesthetic time was defined from the time of

induction until stopping the anesthetic. The recovery time was calculated as the time it took after that for the patient to respond to a verbal command. Ringer-lactate serum, and if needed, 10 mg of ephedrine were given if the systolic blood pressure fell to 20% below at baseline. Moreover, drug side effects and the lengths of anesthesia and surgery underwent assessment. Next, patients were released from the rehabilitation center using the modified Aldrete score criteria. Hemodynamic changes, nausea, vomiting, constipation, lightheadedness, dizziness, drowsiness, headaches, seizures, fever, diarrhea, rash, and itching were all noted as possible side effects of the drug. Using the Modified Observer's Assessment of Alertness/Sedation Score, post-anesthesia sedation was assessed in the postanesthesia care unit (PACU) every 20 minutes for 40 minutes and graded as 0 = Does not respond to pain, 1 = Does not respond to mild prodding or shaking, 2 = Responds only after mild prodding or shaking, 3 = Responds only after the name is called loudly and/or repeatedly, and 4 = Lethargic response to name spoken in a normal tone. The recovery room was maintained at 22-23°C.

Statistical Analysis

SPSS software, version 20 was used for statistical analysis. Quantitative and parametric data were compared between the three groups using the chi-square test and the independent ANOVA test, respectively. Non-parametric test as Mann--whitney was used and the results were deemed significant if the *P* value was less than 0.05.

Results

One hundred and twenty-eight patients completely participated in the study, and seven were excluded from the study. In terms of age, gender, body mass index, duration of diabetes mellitus, and ASA status, all the study groups were comparable; however, there was a male predominance in each group. All additional intraoperative variables, including hemodynamic parameters and the length of the patient's stay in the operating room, the duration of anesthesia, and the procedure's start and end temperatures, were comparable and statistically insignificant (Table 1).

In all groups, the median blood glucose levels increased significantly over time (from the median baselines of 108 to 132 mg/dL to maximum medians ranging from 141 to 191.5 mg/dL, all $P > 0.001$). At any measurement time, there were no appreciable differences in blood glucose levels between the groups receiving the thiopental of Na ketamine or propofol. None of the groups experienced a different incidence of hyperglycemic events (18-23%, $P = 0.607$). Blood glucose levels in the thiopental of Na, ketamine, and propofol groups during the first post-administrative hour were 114.2 16.24 mg/dL, 136.2 12.28 mg/dL, and 122.2 13.84 mg/dL, respectively. These ANOVA test were not statistically significant ($P = 0.72$). In the thiopental Na, ketamine, and propofol groups, the mean changes between preoperative, intraoperative, and postoperative blood glucose levels were 23.5 52.76 mg/dL, 37.6 48.49 mg/dL, and 20.4 60.18 mg/dL, respectively.

Discussion

Patients with diabetes are known to have worse morbidity and mortality when undergoing surgery, and hyperglycemia is associated with worse patient outcomes (9-12). Hyperglycemia is an important risk factor for both intraoperative and postoperative complications, including infection such as wound infection, urinary tract infection, or septicemia (13). Moreover, stroke, persistent respiratory issues, heart attack, cardiac arrest, and even death can be attributed to hyperglycemia (13). The present study aimed to compare the effects of the thiopental of Na, ketamine, and propofol, three commonly used anesthetics, on changes in blood glucose levels following cataract surgery.

A large body of evidence confirmed that surgery-related trauma causes a rise in stress hormone production, the degree of which depends on how difficult the surgery was or whether there were any complications afterward. Insulin sensitivity is decreased by the rise in cortisol and catecholamine levels associated with surgery, whereas insulin secretion is decreased by sympathetic activity. Surgery changes the body's natural metabolic processes, causing gluconeogenesis, glycogenolysis, proteolysis, lipolysis, and ketogenesis, leading to hyperglycemia and ketosis (15). In this regard, Gandhi et al (16) examined 409 cardiac surgery patients and found that intraoperative hyperglycemia was associated with postoperative morbidity and mortality. A 1.11 mg/dL (20 mg/dL) increase in glucose concentration was associated with a 34% increase in the number of postoperative adverse events when the blood glucose concentration was greater than 5.55 mg/dL (100 mg/dL). Further, Lazar et al demonstrated that actively maintaining tight glucose control during cardiac surgery improved clinical outcomes in 141 patients undergoing coronary artery bypass grafting (17-20). According to a recent study by Kitamura et al (20), blood glucose levels significantly increased during sigmoid colostomy under sevoflurane anesthesia, but they remained comparatively stable under propofol anesthesia.

After cataract surgery, it is critical to maintain normal blood glucose control to stop the progression of diabetic retinopathy and maculopathy. Due to the increased risk of infection, inflammation, and inadequate wound healing, perioperative hyperglycemia was more of a concern than intraoperative hypoglycemia. There are currently no internationally recognized standards for the postoperative care of diabetic patients having cataract surgery (21). Nevertheless, there are some examples. For

Table 1. Demographic and Operative Details of Patients in Three Groups

Groups	Thiopental Sodium Group (n = 43)	Ketamine Group (n = 42)	Propofol Group (n = 43)	*P* value
Age (y)	71.2 ± 11.3	67.8 ± 7.3	69.4 ± 5.3	0.66
Height (cm)	162.1 ± 7.6	166.3 ± 5.6	169.6 ± 4.8	0.69
Weight (kg)	61.4 ± 7.6	66.4 ± 4.6	59.4 ± 9.6	0.68
Male/Female	29/14	27/15	28/15	0.78
ASA II	28	29	31	0.75
ASA III	15	13	12	0.78
Duration of Anesthesia (min)	45 ± 7.1	49 ± 5.3	38 ± 9.4	0.76
Duration of recovery (min)	105 ± 12.6	115 ± 9.8	125 ± 7.5	0.86
Intraoperative blood glucose level (mean)	122 ± 11.5	142 ± 16.7	152 ± 9.1	0.78
First hour postoperative blood glucose level (mean)	152 ± 11.1	162 ± 7.6	172 ± 9.8	0.72
Sixth hour postoperative blood glucose level (mean)	132 ± 7.1	132 ± 6.8	142 ± 9.6	0.83

Note. Values are presented as mean ± SD or the number of patients. No significant differences were noted between the three groups

instance, Amer et al (22) evaluated 60 controlled insulin-dependent diabetic patients who had cataract surgery. They were randomly assigned to either receive general anesthesia (GA) using I-gel or LA by sub-block Tenon's (LA group, n = 30). Both heart rate and mean arterial blood pressure were examined, and other parameters such as basal blood sugar levels and plasma cortisol levels, as well as those after local anesthesia induction or block, nuclear extraction, at the conclusion of surgery, and 30, 60, 120, and 240 minutes postoperatively were measured in the mentioned study. They found that blood glucose and cortisol levels in the two groups did not differ significantly. In both groups, blood sugar levels rose by inducing anesthesia. The use of I-gel was not associated with an increase in the heart rate or mean arterial blood pressure (MBP) compared to the LA group. Using I-gel, both local and GA are relatively safe without marked changes in hemodynamics, blood glucose, or cortisol level in insulin-dependent diabetic patients (22).

Conclusion

The present study examined the effects of thiopental of Na, ketamine, and propofol on blood glucose levels during cataract surgery. It was revealed that these drugs do not impair glucose use. The differences between the effects of some IV anesthetics and inhalation anesthetics on glucose metabolism during surgery may be partly explained by these findings. Insulin secretion is controlled by ATP-sensitive potassium (KATP) channel-dependent and KATP channel-independent pathways (e.g., 2-adrenergic signaling). Volatile anesthetics can inhibit insulin secretion (23). According to a recent study (24), isoflurane-induced hyperglycemia involves pancreatic sarcolemmal KATP channels but not mitochondrial KATP channels or 2-adrenergic receptors. Considering that the effects of propofol on insulin secretion are unknown, future research could focus on the pancreatic sarcolemmal KATP channel to investigate the mechanisms underlying the differences in the effects of sevoflurane and propofol on glucose metabolism (25). Propofol can inhibit sympathetic nerve activity, and plasma catecholamine concentrations during surgery under propofol/sufentanil anesthesia are significantly lower than those under enflurane anesthesia (26). More research is needed to determine whether catabolic hormones play a role in the differences in the effects of sevoflurane and propofol on glucose metabolism. Several studies have demonstrated that intraoperative hyperglycemia is associated with a high rate of postoperative complications, and strict control of blood glucose levels during surgery may reduce the risk of morbidity and mortality (23-28).

In general, perioperative hyperglycemia and changes in blood glucose levels were frequent in diabetic patients undergoing cataract surgery with three different frequently used anesthetics, thiopental sodium, ketamine, or propofol. However, there were no statistically significant differences between them, indicating that their effects on glucose metabolism are not noticeably different.

Limitations

The results of the present study confirmed that IV sedation with the thiopental of Na, ketamine, or propofol can prevent hyperglycemia related to surgery, implying the possibility that anesthetic management might be better for the management of blood glucose levels during surgery using these agents. However, we must acknowledge the study's limitations. Within each group, there was a significant difference in preoperative and postoperative blood glucose levels. This wide range could be attributed to a variety of factors, including poor preoperative blood glucose control, intraoperative hemodynamic changes, and differences in the length of time between preoperative and postoperative blood glucose measurements. These factors could be better controlled by performing a prospective study in which each test subject is served as a control or by increasing the study's power. The small sample size and the short-term follow-up (only six hours after surgery) were the other

limitations of the study. However, in light of these factors, the results seem especially solid. Finally, we propose that similar studies compare the effects of different doses of thiopental of Na, ketamine, or propofol, as well as other anesthetics, on changes in blood glucose levels in patients with type I and type II diabetes.

Acknowledgements

We also extend our thanks to clinical research development center of Imam Khomeini and Mohammad Kermanshahi and Farabi Hospitals affiliated to Kermanshah University of Medical Sciences for their kind support.

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Conflict of Interests

There are no conflicts of interests.

Ethical Approval

this study was approved by the code of ethics IR.KUMS.REC.1401.145 at Kermanshah University of Medical Sciences. The protocol of the study was approved by the Institutional Review Board of the Kermanshah University of Medical Sciences and conducted in accordance with the Declaration of Helsinki. All participants or their guardians provided informed consent after being informed of the study's protocols, objectives, benefits, and risks.

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