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Impact of Intravenous Propofol and Intravenous Etomidate as Induction Agents on Intraoperative Blood Glucose Levels in Elective Surgical Procedures Under General Anesthesia: A Randomized Controlled Trial

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KEYWORDS
Blood Glucose; Nondiabetic patients; Diabetes mellitus; Hemodynamic parameters.

Abstract: Background: Major surgical procedures can often trigger acute hyperglycemia, which, even if it's brief, can resultin a weakening of the immune system [1]. Surgeries necessitating general anesthesia are particularly susceptible to stress- related immune system suppression and a rise in blood sugar levels during the procedure. The drugs administered during the induction and maintenance of anesthesia are also recognized for their potential to disrupt normal blood glucose levels, further contributing to the overall stress response associated with surgery, which can subsequently increase the risk of postoperative complications [2], [3]. **Material and methods**: Fifty cases, all falling within the American Society of Anesthesiology's class 1 and 2 categories, were included in this study. These patients underwent preoxygenation and received premedication drugs, followed by anesthesia induction using either Propofol at a dosage of 2 mg/kg or Etomidate at 0.3 mg/kg. Blood glucose levelswere monitored at three specific time points: before premedication, at the 6th minute, and at the 15th minute post-induction. Statistical analysis was performed using the Student t-test for continuous scale parameters and the Chi-square test for categorical scale parameters. A p-value less than 0.05 was considered statistically significant. **Results:** In the Etomidate Group, there was a notable increase in blood glucose levels when compared to the premedication values (80.7 14.37 to 90.5 18.09), and this increase was statistically significant (p-value 0.0165). Conversely, in the Propofol Group, the variation in blood glucose levels was not statistically significant (86.26 15.27 to 84.05 12.64). **Conclusion:** In this study, it was observed that the rise in blood glucose levels in non-diabetic patients following anesthesia induction was notably higher when using Etomidatecompared to Propofol.

I. INTRODUCTION

The induction of anesthesia in patients undergoing any sur- gical procedure raises concerns related to hemodynamic stability and the suppression of the body's stress response. Among the various metabolic reactions that occur during surgery, one of the most significant is the developmentof insulin resistance and the occurrence of hyperglycemia. Hyperglycemia during the perioperative period is primarily attributed to stress-induced hormonal responses, including the release of epinephrine, cortisol, and various inflammatory mediators. Diabetic patients undergoing surgery encounter several immediate challenges [4]. Firstly, surgical proce- dures trigger the secretion of catabolic hormones as part of the stress response. Secondly, surgeries involving the gastrointestinal system often lead to extended interruptions in food intake. Additionally, altered consciousness levels in patients can obscure the typical symptoms of hypoglycemia, necessitating frequent blood glucose monitoring to ensure adequate glycemic control. Finally, circulatory disturbances induced by anesthesia and surgery can disrupt the absorp- tion of

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subcutaneous insulin, raising the risk of infectious complications. This elevated risk of infections is associated with potential adverse outcomes, including increased patient mortality. The presence of acute hyperglycemia during the perioperative period is strongly linked to a notable increase in complications and a worsened prognosis, even among patients who initially showed normal results on glucose tolerance tests [5]. This hyperglycemia triggers a cascade of harmful effects, especially when it comes to the myocardium undergoing ischemia-reperfusion processes. Elevated blood glucose levels eliminate the protective mechanism of is- chemic preconditioning and intensify reperfusion injuries. Moreover, maintaining appropriate glycemic control during surgery can be challenging, despite the administration of in-sulin therapy, due to the complexities associated with intraop- erative blood glucose management. According to the guide- lines set forth by the American Diabetes Association (ADA), the diagnosis of diabetes mellitus can be established in an asymptomatic individual if a random plasma glucose value exceeds 11.1 mmol/liter. In cases where a fasting plasma glucose measurement surpasses 7.0 mmol/liter (equivalent to
6.1 mmol/liter in terms of blood glucose) in an asymptomatic individual, the test should be repeated on a different day, and a diagnosis can be made if the value remains above this threshold. [6] Furthermore, the ADA defines fasting plasma glucose concentrations falling between 6.1 and 7.0 mmol/liter (equivalent to 5.6-6.1 mmol/liter in blood glu- cose terms) as indicative of 'impaired fasting glycemia.' According to the findings of Lattermann et al. ,the use of a combined spinal epidural technique during surgery appears to have a beneficial effect in preventing hyperglycemia when compared to general anesthesia. However, it's important to note that certain surgical procedures, such as head and neck surgeries and cardio-thoracic surgeries, necessitate the useof general anesthesia. In these cases, rigorous monitoring of blood glucose levels becomes especially crucial, partic- ularly for individuals with diabetes, to effectively manage and maintain glycemic control during the surgical proce- dure. Numerous studies have explored the impact of blood glucose levels when using Propofol in comparison to other inhalational agents. However, it's worth noting that in the existing body of literature, there is a noticeable absence of studies that have directly compared the effects of Propofol and Etomidate as induction agents on blood glucose levels in elective surgeries involving non-diabetic patients. To addressthis gap in research, the current study was conducted with the aim of evaluating and comparing the influence of Propofol and Etomidate as induction agents on both blood glucose lev- els and hemodynamic parameters at specific intervals during these elective surgical procedures [7].

II. MATERIALS AND METHODS

The study was designed as a double-blind, prospective, ran- domized comparative study, spanning a duration of one year. Prior to commencing the study, approval from the Insti- tutional Ethical Committee was obtained to ensure ethical standards were met. Furthermore, all patients participating in the study group provided oral and informed consent, demonstrating their voluntary agreement to be part of the research. To ensure the study had adequate statistical power to detect a 20% change in blood glucose levels, the neces- sary sample size was calculated. It was determined that a minimum of 25 patients in each group would be required. Importantly, there were no dropouts or withdrawals from the study group during the course of the research. The study group comprised individuals aged between 20 and 60 years, without any associated comorbidities, who were scheduled for elective surgeries. The standard deviation of the study was found to be 34% of the mean. The study was designed to have a statistical power of 80% and an alpha error (sig- nificance level) of 0.005, ensuring robustness in the analysis and conclusions drawn from the research [8]. In this study, several exclusion criteria were applied to ensure a focused and controlled research environment. Patients with specific comorbidities, including those falling into ASA Grade II or higher, individuals scheduled for emergency surgeries, those with preexisting diabetes, psychiatric conditions, metabolic disorders, or endocrine dysfunction, as well as individuals with known allergies to the study drugs or impaired co- agulation profiles, were excluded from participation. Ad- ditionally, patients taking medications that could influence blood glucose levels, such as steroids, within the week preceding surgery were also excluded. The study population was then randomized using a random number table, and the participants were divided into two distinct groups for further analysis and comparison. 1. Group P: Thisgroup comprised 25 individuals, and the induction dose used was Propofol at 2 mg/kg. 2. Group

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E: Similarly, this group consisted of 25 participants, and the induction dose employedwas Etomidate at 0.3 mg/kg A comprehensive preanesthetic assessment was conducted, encompassing a thorough review of the patients' medical history and pertinent investigations. These investigations involved a complete hemogram, renal function tests, serum electrolytes, bleeding time and clottingtime assessments, electrocardiogram (ECG), and randomblood glucose levels for all individuals. [9] Patients falling within ASA Grade 1 and ASA Grade 2 were the focus ofthe study and included for further analysis. In preparation for surgery, patients were required to observe a fasting period of at least 8 hours prior to the procedure. Upon arrival in the operating room, essential monitoring equipment including ECG, non-invasive blood pressure (NIBP) cuff, and pulse oximeter were applied to ensure continuous monitoring of vital parameters such as pulse rate, oxygen saturation, sys- tolic and diastolic blood pressure, and mean arterial pressure [10]. This meticulous preoperative monitoring was crucial for ensuring the safety and readiness of patients for the upcoming surgical procedure. In the preoperative phase, all patients received premedication with Inj. Midazolam at a dose of 1 mg intravenously and were preoxygenated with 100% oxygen for a duration of 5 minutes. Blood glucose levels were monitored prior to induction, at 6 minutes, and at 15 minutes following induction using the respective study drugs. For Group P, patients were induced using Inj. Propofol at a dose of 2 mg/kg, while for Group E, induction was achieved using Inj. Etomidate at a dose of 0.3 mg/kg. Following the administration of the induction agent, succinylcholine was administered at a dose of 1.5 mg/kg. These induction procedures were essential steps in preparing patients for the surgical intervention [11].

Variable	Group P	Group E	p - value
Age (years)	32.36 ± 14.33	33.36 ± 11.85	0.72
Sex (male/female)	13/16	18/11	-
Weight (kgs)	55.78 ± 9	57 ± 10.42	0.65
ASA I	14	17	-
ASA II	16	13	-

III. RESULTS

The demographic data, including age, sex, weight, and ASA grading, for the study groups are presented in Table 1. The average age for patients in our study was 32.36 ± 14.33 years for Group P and 33.36 ± 11.85 years for Group E, demonstrating statistical comparability between the two groups. Additionally, the weights of patients in both groups were comparable, with an average weight of 55.78 ± 9 kg in Group P and 57 ± 10.42 kg in Group E. These findings suggest that the two groups were well-matched in terms of age and weight distribution. [12] The study results indicate that there was no statistically significant increase in heart rate at various time intervals when compared to the premedicationbaseline values in both Groups P (p-value 0.72) and E (p- value 0.05). Likewise, changes in mean arterial pressure (MAP) values were comparable and exhibited no statistically significant differences when compared to the premedication baseline values in both Groups P (p-value 0.72) and E (p- value 0.05). These findings suggest that the administration of Inj. Propofol or Inj. Etomidate did not lead to significant alterations in heart rate or MAP, signifying hemodynamic stability during the induction phase in both groups. In Group E, the blood glucose levels exhibited a statistically significant increase compared to the premedication baseline values (p- value 0.0165). In contrast, for Group P, the variations in blood glucose levels at the 6th and 15th minute were not statistically significant (p-value 0.7470) when compared to the premedication baseline values, as indicated in Table 3. Importantly, no major adverse effects were observed during the course of the study, suggesting that the administration ofInj. Propofol or Inj. Etomidate had a generally well-toleratedeffect on blood glucose levels in both groups [13]. Table 1: The demographic data showing age, sex, weight and ASA grading of the study groups

Fig 1: Blood glucose values which were measured following usage of Propofol and Etomidate at different time intervals. P-Propofol, E-Etomidate.

IV. DISCUSSION

Based on the evidence gathered concerning the ASA I-II status of patients scheduled for surgeries involving general anesthesia, a statistically significant finding indicates that the administration of Etomidate as an induction agent led to an elevation in blood glucose levels (p-value 0.0165). In contrast, the use of Propofol as an induction agent did not result in a similar increase in blood glucose levels (p-value 0.72). The reason for hyperglycemia during surgery may be surgical pain and metabolic response to surgical stress that even deeper plane of anesthesia cannot block the response. But with enough analgesia we can maintain blood glucose

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in normal limits and prevent hyperglycemia [14]. In the research conducted by Diltoer M and Camu, they explored the impact of isoflurane anesthesia on glucose tolerance tests,both with and without the added factor of surgical stress. Their study revealed that during surgical stress, concentrations of growth hormone and norepinephrine increased, leading to insulin secretion in response to hyperglycemia. However, under isoflurane anesthesia without surgical stress, this response was impaired, resulting in impaired glucose tolerance. Notably, during surgery under isoflurane anesthesia, concentrations of cortisol, growth hormone, norepinephrine, and epinephrine increased, potentially contributing to insulin resistance and/or increased glucose production, further im- pairing glucose tolerance [15]. It's important to note that our study did not assess the effects of propofol or etomidate for maintenance, and additional research is needed to investigate this aspect further. In the study conducted by Kitamura Tet al., which involved approximately 150 participants under sevoflurane anesthesia and 62 under propofol anesthesia, they observed changes in blood glucose levels during anesthetic management. Their findings suggested that propofol had a significantly milder impact on glucose metabolism compared to sevoflurane. While their study had a larger sample size compared to ours, the conclusion aligns with our own re- search, reinforcing the beneficial effects of propofol in termsof glucose metabolism.

V. CONCLUSION

Based on the observations and results obtained in our study, we can confidently conclude that intravenous propofol is effective in preventing hyperglycemia when compared to in- travenous etomidate, particularly when comparing the values to the baseline readings [16]. Additionally, it's noteworthy that hemodynamic parameters did not show statistically sig- nificant differences between the two groups. Furthermore, it's important to highlight that no significant adverse effects wereobserved during the course of our study.

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CONFLICTS OF INTEREST

The authors declared no conflict of interest.

AUTHORS' CONTRIBUTIONS

All authors equally contributed to preparing this article.

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