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Original Research Article

Comparative Analysis of Hemodynamic Variability and Level of Blood Cortisol while Induction with Propofol and Etomidate

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Abstract:

Background and Aim: The selection of an anesthetic for inducing anaesthesia is primarily based on its pharmacodynamic characteristics. One of the most often used drugs for inducing general anaesthesia is propofol, or 2,6-diisopropyl phenol. The goal of the current study is to determine how serum cortisol levels, hemodynamic parameters, discomfort during injection, myoclonus, and apnea during induction affect patients undergoing laproscopic cholecystectomies.

Material and Methods: A prospective, randomized, double-blind clinical trial was used in this investigation. 50 patients each were randomly assigned to Group A, which received an IV injection of propofol (2 mg/kg), and Group B, which received an IV injection of etomidate (0.3 mg/kg). Vital signs were recorded during induction, laryngoscopy, and thereafter. Carefully observed were pain upon injection, myoclonus, and apnea during induction. One hour prior to induction, two hours after induction, and 24 hours following induction, serum cortisol levels are assessed.

Results: there were no statistically significant differences in the groups' age, sex, or weight, the demographic data for the two groups were equivalent. In comparison to the etomidate group, the propofol group exhibits a considerable reduction in heart rate and mean blood pressure following induction. Group A experienced more injection-related pain, but Group B experienced more myoclonus activity. After induction, Group B's serum cortisol level is much lower than Group A's, which rises to above baseline after 24 hours but remains below normal limits.

Conclusion: When used as an induction drug, etomidate is hemodynamically more stable than propofol and is linked to a lower incidence of discomfort during injection but a substantially larger incidence of myoclonic movements. Additionally, it was discovered that etomidate caused adrenocortical insufficiency to appear chemically for a shorter period of time before returning to normal within 24 hours in patients with ASA grades I and II undergoing elective laparoscopic surgery under general anesthetic.

Keywords: Etomidate, Laparoscopic Surgery, Propofol, Serum Cortisol.

Introduction

The process of going from being awake to being unconscious, known as induction of anaesthesia, is difficult.[1] Various induction agents, such as inhalational agents and intravenous agents, are currently available. Nowadays, intravenous anesthetics are more frequently used to produce anaesthesia, with the exception of youngsters, who prefer inhalational anaesthetics.[2,3] The selection of an anesthetic for causing anaesthesia is primarily based on its pharmacodynamic characteristics.

Hemodynamic changes result from the stress reaction during laryngoscopy and intubation, particularly in patients with cardiac risk factors such hypertension and ischemic heart disease.[4] Dysrhythmia, hypertension, myocardial ischemia, infarction, hypoxia, hypercapnia, laryngospasm, bronchospasm, and a few uncommon side effects like increased intracranial pressure and increased intraocular pressure are all unavoidable consequences of laryngoscopy and tracheal intubation.

Cardiovascular effects had been the primary deciding factor up until this point. The depth of anaesthesia and effects on cortisol production, for example, can alter this oversimplified perspective. Since

the development of general anaesthesia, the optimal inducing drug for maintaining stable hemodynamics during laryngoscopy and endotracheal intubation has not yet been identified.

One of the most often used drugs for inducing general anaesthesia is propofol, or 2,6-diisopropyl phenol. This intravenous anaesthetic has a brief duration of action. Propofol for induction is advised at a dose of 1-2.5 mg/kg. Hemodynamic instability and cardiovascular issues, such as an erratic heartbeat and low blood pressure, are unwelcome side effects linked to this medication. By increasing the generation and release of nitrous oxide, propofol can cause bradycardia. It also causes pain at the injection site and, as a respiratory depressant, commonly induces apnoea.[5-7] Propofol has been suggested to work via a number of different mechanisms, including sodium channel blocking and potentiating GABA receptor activation. Recent studies have also revealed that the endocannabinoid system may play a substantial role in the anaesthetic effect and special features of propofol. After surgery, cortisol levels were not decreased by propofol.

After just one dose of etomidate, there is known to be a decrease in blood cortisol levels, which can last for up to twenty-four hours.[8] To the extent that it does not last during the postoperative phase, when the body's circulatory reflexes must remain intact for the maintenance of hemodynamic parameters, the drop in blood cortisol levels offered by etomidate may be advantageous. Etomidate has less adverse effects on the respiratory system or cardiovascular system than thiopental, propofol, or midazolam, and it can be used safely in patients with hemodynamic instability or cardiac ischemia. It is a perfect agent for patients with head traumas since it is cerebrally protective, has the capacity to lower intracranial pressure, and preserve cerebral perfusion.[9-11] Steroidogenesis suppression caused by a reversible and concentration-dependent inhibition of 11-hydroxylase and 17-hydroxylase is one of the uncommon but significant side effects of etomidate.[12-13] Approximately 30 minutes after induction, the cortisol and aldosterone levels are decreased as a result of the adrenal suppression, which may persist up to 24 hours. Although there have been no reports of clinically significant cortisol suppression with a single induction dosage, adrenal suppression is a possible issue when etomidate is used as a continuous infusion drug for days or weeks in ICU settings.

To the extent that it does not last during the postoperative phase, when the body's circulatory reflexes must remain intact for the maintenance of hemodynamic parameters, the drop in blood cortisol levels offered by etomidate may be advantageous.

The goal of the current study is to determine how serum cortisol levels, hemodynamic parameters, discomfort during injection, myoclonus, and apnea during induction affect patients undergoing laproscopic cholecystectomies.

Material and Methods

A prospective, randomized, double-blind clinical trial was used in this investigation. The patient was between the ages of 18 and 60 and of either sex and ASA physical status I or II. Ethical approval was taken from the institutional ethical committee and written informed consent was taken from all the participants. 50 patients each were randomly assigned to Group A, which received an IV injection of propofol (2 mg/kg), and Group B, which received an IV injection of etomidate (0.3 mg/kg). The following patients were disqualified from the study: ASA physical status III and IV, emergency surgery, patient refusal to GA Patient has a history of bronchial asthma, hypersensitivity to propofol/etomidate, Mallampati grades 3 and 4, significant pathology in the larynx and pharynx, Patient on steroids, GERD patient severe acute cholecystitis and acute pancreatitis brought on by gallstones. A day before surgery, patients underwent a pre-anesthetic assessment and received advice on proper fasting, sedation, local anaesthesia, and surgical technique. The institution's protocol was followed when conducting the investigations. Prior to surgery, the patients were maintained nil by mouth for 8 hours. The night before surgery, tabs of ranitidine 150 mg and alprazolam 0.25 mg were administered to each patient. 45 minutes prior to induction in the preoperative ward, all patients received an injection of glycopyrrolate (0.2 mg IM). Standard anaesthesia monitors, such as an electrocardiogram (ECG), a non-invasive blood pressure (NIBP), and a pulse oximeter, were attached when the patient entered the operating room. Hemodynamic parameters such as heart rate, mean blood pressure, and oxygen saturation were recorded prior to induction, during induction, and at the five, ten, fifteen-, thirty-, forty-five-, and sixty-minute marks following laryngoscopy. An 18 G intravenous (IV) cannula was inserted into the right hand and an injection of ringer's lactate began. Midazolam 0.025 mg/kg IV and fentanyl 2 g/kg IV were administered two minutes prior to induction. Depending on their group, either propofol 2 mg/Kg iv or etomidate 0.3 mg/Kg iv were used to produce anaesthesia. Adverse effects such as discomfort on injection, apnea on induction, and myoclonus were noted after induction. Grade 0 - No myoclonus movements, Grade 1 - Minor myoclonic movements, Grade 2 - Moderate myoclonic movements, and Grade 3 - Major myoclonic movements are the grades for myoclonus movements at the time of induction. Measurement of injection-related pain during induction as: No pain is graded as grade 0;

verbal complaints of pain are grade 1; arm withdrawals are grade 2; and both verbal complaints and arm withdrawals are grade 3 60 seconds after losing consciousness, which was proven by the loss of the eyelid reflex and unable to respond to spoken directions. Vecuronium injection (0.1 mg/kg intravenous), After three minutes, laryngoscopy and endotracheal intubation were performed, and this was verified by capnometry and bilateral chest auscultations. Midazolam injections of 0.25 to 1 g/kg/minute were used to maintain anaesthesia throughout the procedure, coupled with equal mixes of oxygen and nitrous oxide and periodic boluses of vecuronium as needed. Extubation was carried out when breathing was sufficient and the patient could accept verbal orders. Remaining neuromuscular block was neutralised by injections of neostigmine (0.05 mg/kg) and glycopyrolate (0.01 mg/kg) intravenously at the conclusion of the procedure. 2ml of blood is drawn under aseptic conditions into a serum separating tube (SST) vial before, after, and 24 hours of induction. The blood is then sent to a lab to be analysed using a chemiluminescent assay.

Statistical analysis

The collected data was organized, inputted, and exported to the data editor page of SPSS version 15 (SPSS Inc., Chicago, Illinois, USA) after being combined and entered into a spreadsheet programme (Microsoft Excel 2007). The level of significance and confidence level for each test were set at 5% and 95%, respectively.

Results

Given that there were no statistically significant differences in the groups' age, sex, or weight, the demographic data for the two groups were equivalent. (Table 1) The averages for heart rate (HR), mean arterial pressure (MAP), and mean oxygen saturation % are comparable between the two groups. After induction, the mean heart rate is much lower in Group A than Group B, and it is higher in Group A after 5 minutes following intubation, although the difference between the two groups is not statistically significant.

The mean MAP is significantly lower in both groups ($p<0.05$), with group A seeing a greater decline. After 5 minutes after intubation, MAP is higher in both groups, and after 10 minutes, it is equivalent in both groups. (Table 2) At induction and following laryngoscopy, the mean % oxygen saturation in the two groups stays comparable. The mean baseline blood cortisol levels in the two groups were identical. After two hours of induction, mean serum cortisol is considerably lower in group B ($p<0.05$), but it is significantly higher in group A. The mean serum cortisol level after 24 hours is higher than the initial value but still within normal limits and the difference between the two groups is very significant. (Table 3)

Comparing the side effects, it was discovered that 48 out of 50 patients in Group A experienced no pain after receiving injection Etomidate while 33 out of 50 patients in Group A experienced pain after receiving injection Propofol.

No myoclonic movements were observed in group A during induction with injections of propofol, but 25% of patients displayed Grade I myoclonic movements and 7% displayed Grade II myoclonic movements after induction with injections of etomidate. Compared to Group B, 36 out of 50 patients in Group A experienced apnea upon injection of propofol, while 30 out of 50 patients experienced apnea upon injection of etomidate.

Table 1: Demographic Distribution of study participants

Variables	Group A	Group B	P value
Gender (M:F)	11:39	15:25	0.25
Age	33.10 ± 5.48	34.98 ± 8.10	0.10
ASA Grade (I/II)	45/5	43/7	0.7

Statistically significance at $p\leq0.05$

Table 2: Comparison of mean arterial pressure between the groups A and B

Variables	Group A Mean±SD	Group B Mean±SD	P value
Baseline	82.54±5.12	83.10±2.49	0.06
At induction	73.11±5.2	82.1±4.63	0.002*
5 min	80.05±2.32	82.84±4.64	0.01*
10 min	81.10±5.32	81.41±3.40	0.32
15 min	84.12±4.45	84.64±3.2	0.09
30 min	81.51±5.23	82.21±4.45	0.10
45 min	79.03±5.10	79.66±4.12	0.44
60 min	79.01±3.22	78.74±5.14	0.32

* indicates statistically significance at $p\leq0.05$

Table 3: Comparison of effects on serum cortisol between groups A and B

S. Cortisols	Group A (Mean±SD)	Group B (Mean±SD)	P value
1 hr before induction	13.05±4.22	13.98±3.14	0.09
2 hrs after induction	15.98±2.24	8.04±2.49	0.002*
24 hrs after induction	19.05±3.14	16.04±4.11	0.003*

* indicates statistically significance at p≤0.05

Discussion

In our investigation, both groups' hemodynamic metrics and demographic characteristics were equivalent. After induction, there was a non-significant (p >.0.05) decrease in heart rate in Group B patients with a mean value of 79.20±8.10 bpm, as opposed to Group A patients who saw a substantial decrease with a mean heart rate of 74.50±09.78 bpm. We discovered a drop in heart rate from baseline following induction in both groups, although this difference was not statistically significant. (p>0.05). The results of this study are consistent with those of Sarkar Molly et al. (2005)14, Shagun Bhatia Shah et al. (2015) [15], Kaushal Ram Prasad et al. (2015)[11], and Binod Pegu et al. (2017) [16], which found that a decrease in heart rate is more pronounced when propofol is administered intravenously rather than etomidate, which was compared and found to be non-significant.

The mean MAP is considerably lower in group A than in group B (p<0.05), and MAP increases in both groups at 5 minutes after intubation before becoming equivalent at 10 minutes in both groups. At induction and following laryngoscopy, the mean % oxygen saturation in the two groups stays comparable. Propofol causes hypotension, which is mostly caused by a decrease in sympathetic activity, which results in vasodilatation, or by its direct impact on vascular smooth muscles. Patients with coronary artery disease, valvular stenosis, uncontrolled hypertension, and shock are at risk for developing sudden hypotension and bradycardia, which can have detrimental implications on sustaining the circulation to important organs. This is consistent with our observations of elevated blood pressure in the etomidate group after intubation. Etomidate was shown to be the least effective at reducing the stress reaction to intubation, according to Singh R et al. [17]

This is also consistent with other research by Baude C et al and Winn NN et al, which found that the use of propofol or etomidate had little to no effect on HR.[18,19] Our results were consistent with those of Mehrdad et al [20], who utilized propofol and etomidate for the induction of anaesthesia and discovered that propofol considerably decreased the MAP. Schmidt et al. [21] discovered that the hypotension brought on by propofol is produced by a decrease in the preload and afterload of the heart, which aren't timed with the heart's compensatory reactions like increased cardiac output and heart rate.

The baseline serum cortisol difference between the two groups is not statistically significant. Two hours after induction, there is a highly significant (p0.05) increase in the level of serum cortisol in Group A, reaching 15.98±2.24 g/dl from the baseline but still within the normal range. Serum cortisol levels after 24 hours were 19.05±3.14 g/dl, which likewise fall within the normal range. At 2 hours after induction, blood cortisol levels in Group B are significantly lower (8.04±2.49 g/dl; p<0.05). Serum cortisol levels after 24 hours were determined to be 16.04±4.11g/dl, which is within the normal range. The catabolic hormone cortisol mobilises proteins, carbs, and fat in order to significantly raise blood glucose levels, which are thus difficult to manage with insulin. By stabilising lysosomal membranes, reducing capillary permeability, reducing white blood cell migration to the inflamed area, and limiting phagocytosis of injured cells, increased cortisol also reduces the inflammatory response. It inhibits the immune system, which significantly lowers the generation of lymphocytes. The white blood cells emit less interleukin than before. Exogenous injection also results in a decrease in chronic inflammation. Additionally blocked is the inflammatory response to allergy responses. Our investigation is in line with the results of Pandey A. K. et al [22], who discovered that serum cortisol levels were significantly lower in the etomidate group than in the propofol group while still being within normal levels. Within 24 hours, the serum cortisol level had nearly returned to normal. On the other hand, this transient suppression of adrenal cortisol synthesis in septic patients has been shown to be a risk factor for increased mortality and can be harmful in septic patients who may already have a baseline adrenal insufficiency as a result of critical illness, despite the fact that it lasts for at least 24 hours after a single dose of etomidate administration. This is supported by Chan et al[23], who found that rapid sequence induction with etomidate is linked to greater rates of death and adrenal insufficiency in sepsis patients. As a result, patients with serious conditions like septicemia, which impact systemic vascular resistance, should use etomidate with caution. Our investigation is in line with the findings of Pandey A. K. et al. B, who discovered that the blood cortisol level after weaning the patient was much lower in the etomidate group than in the

propofol group but was still within normal levels.[22]

No myoclonic movement was observed during induction with inj. propofol in Group A, whereas in Group B, 25% of patients, displayed Grade I myoclonic movements after induction with inj. etomidate, and 7% patients displayed Grade II myoclonic movements. This conclusion was corroborated by Miner et al. [24], who found that the etomidate group had a higher incidence of myoclonus than the propofol group did. Myoclonus was detected in 20% of patients in group E of James R. Minor's study for procedural sedation in the emergency room, but only in 1.8% of patients in group P.[25] Alka Lunia et al. conducted a study on 100 adult patients receiving general anaesthesia. They observed myoclonus to occur in 26% of patient in group E while no equivalent signs were noted in group P.[25]

Conclusion

When used as an induction drug, etomidate is hemodynamically more stable than propofol and is linked to a lower incidence of discomfort during injection but a substantially larger incidence of myoclonic movements. Additionally, it was discovered that etomidate caused adrenocortical insufficiency to appear chemically for a shorter period of time before returning to normal within 24 hours in patients with ASA grades I and II undergoing elective laproscopic surgery under general anesthetic. When compared to propofol, etomidate offers more stable hemodynamic parameters during the induction of anaesthesia. To establish a link between etomidate use and a higher risk of death, more frequent use of vasopressors, a longer time spent on mechanical ventilation, or longer stays in the intensive care unit (ICU) or hospital, more research in this particular patient population is required.

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