

Effects of etomidate on blood cortisol, insulin, and glucose levels and PONV rates in smokers

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Aim: To observe differences in the effects of etomidate, used for anesthesia induction, on surgery-induced endocrine response and postoperative nausea and vomiting (PONV) among nonsmokers and smokers.

Materials and methods: Eighty adult patients with ASA I-II risk status were randomly divided into 2 groups: smokers (Group I, n = 40) and nonsmokers (Group II, n = 40). Patients were then further divided into subgroups according to the drug used for anesthesia induction, either propofol (Group IP and Group IIP) or etomidate (Group IE and Group IIE). Blood cortisol, insulin, glucose, and white blood cell (WBC) levels were measured and PONV scores were recorded.

Results: Blood cortisol values were significantly lower in Group IE and Group IIE compared to Group IP and Group IIP during the 1st and 2nd hours after induction. By the 8th hour, blood insulin levels had increased significantly compared to the baseline values in Groups IE, IP, and IIP. Blood glucose levels were significantly higher in Group IIE compared to both Group IP and Group IIP. There was no significant difference between the WBC levels of the different groups. PONV scores were significantly higher in Group IIE compared to the other groups.

Conclusion: We determined that the use of etomidate causes a lower stress response and more PONV compared to propofol, while smoking increases the stress response and decreases PONV.

Key words: Anesthesia, smoking, cortisol, etomidate, PONV

Introduction

The health problems arising due to smoking and the use of other tobacco products are well known. Smoking affects not only the cardiovascular and respiratory systems but also the endocrine system (1,2). Smoking is known to affect the levels of catecholamines, antidiuretic hormone (ADH), growth hormone (GH), adrenocorticotrophic hormone (ACTH), prolactin, gonadotropins, and insulin. Smoking may affect the hypothalamo-pituitary axis via central nervous system pathways; thus, an increase in vasopressin and corticotrophin-releasing hormone (CRH) also increases the release

of ACTH. Impaired glucose tolerance is another adverse effect of smoking (3-6).

Etomidate provides the best cardiovascular stability but can cause nausea, vomiting, pain on injection, and myoclonus, and has adverse effects on the endocrine system (7). Etomidate inhibits, in a dose-dependent and reversible manner, 11- β -hydroxylase, which converts 11-deoxycortisol to cortisol. Single dose etomidate inhibits 11- β -hydroxylase for 5-8 h postoperation; 11- β -hydroxylase is fully restored after 20 h (8). At the same time, etomidate leads to higher rates of nausea and vomiting (around 30%-40%) during the postoperative period (7).

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In our study, we aimed to determine the effects of using etomidate for anesthesia induction on cortisol, insulin, glucose, and WBC levels, as well as the incidence of nausea and vomiting in smokers and nonsmokers.

Materials and methods

After approval was obtained from the Medical Ethics Committee, 80 patients with ASA I-II status who were scheduled for noncardiac elective surgery were included in this study. All patients were between 30 and 60 years old. Patients were divided into 2 groups: smokers (Group I, n = 40) and nonsmokers (Group II, n = 40). Patients who smoked 20 cigarettes/day, had been active smokers for at least 10 years, and were still smoking 72 h before the operation were included in Group I. Patients were randomly divided into 2 subgroups and were administered either etomidate (Group IE, n = 20; Group IIE, n = 20) or propofol (Group IP, n = 20; Group IIP, n = 20) for anesthesia induction.

Patients with neurological, psychiatric, cardiac, or metabolic disease, diabetes mellitus, endocrine dysfunction, and/or a known allergy to the medication were excluded from this study. Patients were premedicated with 2 mg of midazolam (im) and 0.5 mg atropine (im) sulfate 45 min before the operation. Electrocardiography, noninvasive blood pressure, and peripheral oxygen saturation were monitored.

Anesthesia was induced using 0.3 mg kg⁻¹ etomidate, 0.1 mg kg⁻¹ vecuronium, and 2 µg kg⁻¹ fentanyl in Group IE and Group IIE. In Group IP

and Group IIP, anesthesia was induced using 2-2.5 mg kg⁻¹ propofol, 0.1 mg kg⁻¹ vecuronium, and 2 µg kg⁻¹ fentanyl. In all of the groups, anesthesia was maintained using 6% desflurane in a 50% O₂-50% air mixture, and additional doses of vecuronium and fentanyl were administered if required. At the end of surgery, in order to remove any residual muscle relaxation agent, 0.04 mg kg⁻¹ neostigmine and, if needed, 0.5 mg atropine were administered intravenously.

Blood samples for cortisol, insulin, glucose, and white blood cell (WBC) measurements were collected from patients 10 min before induction and 10 min, 1 h, 2 h, and 8 h after induction. Patients were monitored for at least 1 h in the postoperative recovery room and records were kept of their postoperative nausea vomiting (PONV) scores (0: no nausea or vomiting; 1: mild nausea, no vomiting, and no treatment required; 2: moderate nausea, minimal vomiting, and treatment required; 3: severe vomiting) and postanesthesia recovery scores (PAS) (9) 1, 15, 30, 45 and 60 min after surgery.

The Statistical Package for the Social Sciences 17.0 software was used for statistical evaluation. One-way ANOVA, the post hoc Tukey HSD test, and Dunnett's test were used to compare groups. The paired samples t-test and Wilcoxon's test were used for comparisons within groups. Results with a P value less than 0.05 were considered statistically significant.

Results

Demographic data did not differ significantly among the groups (Table).

Table. Demographic data of groups (mean ± SD).

	Group IE (n = 20)	Group IP (n = 20)	Group IIE (n = 20)	Group IIP (n = 20)
Age (years)	34.45 ± 5.34	38.00 ± 8.54	38.15 ± 9.28	34.75 ± 7.26
Operation duration (min)	104.00 ± 11.07	100.00 ± 8.58	102.00 ± 10.18	101.50 ± 11.82
Anesthesia duration (min)	117.00 ± 9.65	115.75 ± 8.47	118.75 ± 8.86	119.50 ± 12.23
Gender	Female	13	12	12
	Male	7	8	8

At 1 h and 2 h postinduction, blood cortisol levels were significantly lower than before induction in Group IE and Group IIE ($P < 0.05$). No statistically significant difference was found in either Group IP or IIP. Blood cortisol levels were significantly lower in Group IE compared to Group IIP, and in Group IIE compared to Group IIP, 1 h after induction ($P < 0.05$). Cortisol levels were significantly lower in Group IE and Group IIE compared to Group IP and Group IIP by the 2nd hour ($P < 0.05$). No statistically significant difference was demonstrated between groups before induction, 10 min after induction, or 8 h after induction (Figure 1).

Blood insulin levels were significantly higher 8 h after induction than before induction in Group IE, Group IP, and Group IIP ($P < 0.05$). Blood insulin levels were significantly higher in Group IP compared to Group IE and Group IIE 8 h postinduction ($P < 0.05$). No significant difference was found between groups during any of the other periods (Figure 2).

In all of the groups, blood glucose levels were significantly higher at all points after induction compared to before induction ($P < 0.05$). Blood glucose levels were significantly higher in Group IIE compared to Group IP and Group IIP after the induction period ($P < 0.05$). Blood glucose levels were also significantly higher in Group IIE compared to Group IP 1 h and 2 h after induction and were higher in Group IIP compared to Group IE 8 h after induction ($P < 0.05$; Figure 3).

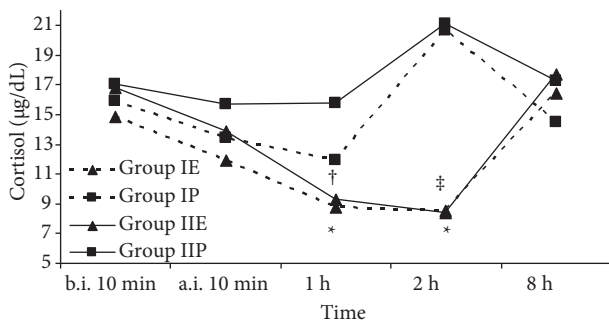


Figure 1. The serum cortisol values of the groups.

- *: $P < 0.05$ when the 1st and 2nd hours were compared with measurements taken 10 min before induction (b.i. 10 min) in Group IE and Group IIE.
- †: $P < 0.05$ when Group IE and Group IIE were compared with Group IIP at 1 h.
- ‡: $P < 0.05$ when Group IE and Group IIE were compared with Group IP and Group IIP at 2 h.

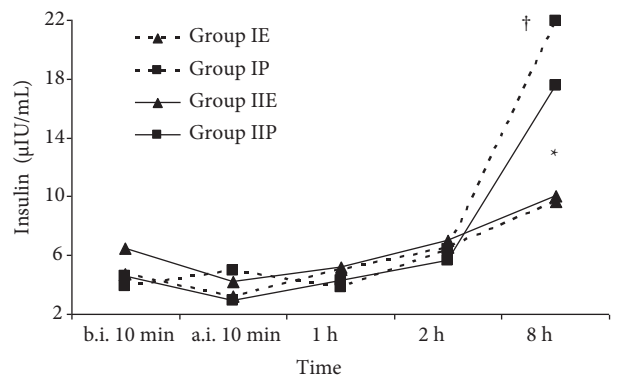


Figure 2. The serum insulin values of the groups.

- *: $P < 0.05$ when the 8th h was compared with measurements taken 10 min before induction (b.i. 10 min) in Group IE, Group IP, and Group IIE.
- †: $P < 0.05$ when Group IP was compared with Group IE and Group IIE at 8 h.

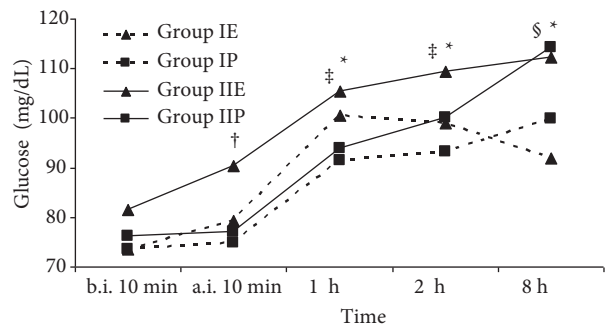


Figure 3. The serum glucose values of the groups.

- *: $P < 0.05$ when the 1st, 2nd, and 8th hours were compared with measurements taken 10 min before induction (b.i. 10 min) in Group IE, Group IP, Group IIE, and Group IIP.
- †: $P < 0.05$ when Group IIE was compared with Group IP and Group IIP before induction.
- ‡: $P < 0.05$ when Group IIE was compared with Group IP at 1 and 2 h.
- §: $P < 0.05$ when Group IIP was compared with Group IIE at 8 h.

The WBC levels did not significantly differ within or between groups at any point. PONV scores were significantly higher in Group IIE compared to Group IE, Group IP, and Group IIP 1 min, 15 min, and 30 min after surgery ($P < 0.05$; Figure 4). PAS scores were significantly higher in Group IE compared to Group IP 1 min after induction ($P < 0.05$).

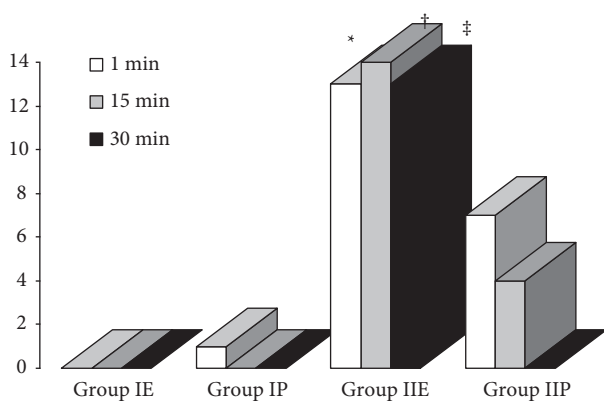


Figure 4. The PONV scores of the groups.

*: $P < 0.05$ when Group IIE was compared with Group IE at 1 min.

†: $P < 0.05$ when Group IIE was compared with Group IE, Group IP, and Group IIP at 15 min.

‡: $P < 0.05$ when Group IIE compared with Group IE, Group IP, and Group IIP at 30 min.

Discussion

In our study, we evaluated the effects of etomidate and smoking on blood cortisol, insulin, glucose, and WBC levels as well as on PONV. We also investigated the relationship between etomidate and smoking and the effect of smoking on PONV and PAS scores.

Etomidate causes a decrease in blood cortisol levels and an increase in cortisol precursor levels via dose-dependent, reversible inhibition of 11- β -hydroxylase, which converts 11-deoxycortisol to cortisol (7). Decreased cortisol levels increase or return to normal values within the 1st hour postoperation or 6-8 h after anesthesia induction (10-12).

Although propofol has been demonstrated to inhibit adrenal steroidogenesis in vitro (13), it has been shown to increase cortisol levels in in vivo studies. As a result, propofol was thought not to affect adrenocortical inhibition (14). Though previous studies have demonstrated that smoking increases plasma and salivary gland cortisol levels (6,15), we did not find a significant difference between the cortisol levels of smokers and nonsmokers at any time in our study.

Previous studies have demonstrated an increased risk for diabetes among smokers (16) and a link between insulin resistance and smoking (17,18). However, another study found no correlation

between smoking and insulin resistance (19). A previous study also reported that etomidate does not increase insulin levels (20). In our study, insulin levels were increased in smokers 8 h after induction, especially in the propofol-treated group.

Increased blood glucose levels indicate a stress response to anesthesia. Studies have demonstrated that blood glucose levels increase in patients who are administered propofol for anesthesia induction and maintenance (21,22). Moore et al. (23) showed that patients who received etomidate anesthesia had higher glucose levels throughout their procedure.

Studies of WBC levels during the postoperative period have indicated both increased (24) and unaffected (25,26) WBC levels depending on the anesthesia and surgical technique used (27). As in our study, Kulacoglu et al. (24) demonstrated that general and spinal anesthesia did not affect WBC levels although local anesthesia increased WBC levels during the first 24 h postoperation. Other studies have also focused on the first postoperative day to demonstrate the increase in WBCs, unlike the present study (24,26,27). Brohee et al. (28) showed that cortisol and epinephrine increased the WBC level in a healthy volunteer. Two differences between these previous studies and our study may explain why we did not observe any significant changes in WBC levels. First, the sampling time interval was different in the other studies and, second, the cortisol level was not high in all groups.

Smoking has been shown to have a protective effect against postoperative nausea and vomiting. Although the underlying mechanism is still unknown, it is a fact that nicotine is an antiemetic (29). The type of anesthesia used and the method of administration influence the frequency of PONV most (30). Many antiemetic medications are used for preventing PONV (31). Propofol regulates nausea and vomiting by interacting with dopaminergic D2 receptors. When propofol is used for general anesthesia, it causes less postoperative nausea and vomiting relative to inhalation anesthetics and it decreases the use of antiemetic drugs (32).

In our study, the number of patients complaining of nausea and vomiting was significantly higher among nonsmoking patients who were administered etomidate. Thus, we concluded that smoking and

anesthesia induction with propofol decrease the frequency of PONV. We observed that smoking counteracted the effects of etomidate on PONV. In our study, the frequency of PONV was significantly lower for smoking patients, who had high cortisol levels, compared to nonsmoking patients with low blood cortisol levels. Therefore, we concluded that the increased blood cortisol levels may have decreased the frequency of PONV. Smokers who received etomidate for anesthesia induction also had significantly higher PAS values during the recovery period compared to the patients who received propofol. We determined that this finding was related to the use of desflurane for anesthesia maintenance in all groups.

In conclusion, in our study, we determined that the surgical stress response is lower when etomidate anesthesia is administered rather than propofol anesthesia. The stress response is higher in smokers anesthetized with etomidate. However, we observed that anesthesia induction with propofol caused significantly lower rates of PONV compared to anesthesia induction with etomidate. Smokers anesthetized with etomidate had rates of PONV comparable to those of nonsmokers anesthetized with propofol. Additional studies are required to examine endocrine system changes, PONV, and the comfort of smoking patients during and following anesthesia.

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