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Original Article

Evaluation of the efficacy of the valsalva maneuver and fentanyl administration for attenuating etomidate injection pain: A double-blind clinical trial

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Abstract

Objective: Etomidate is mentioned as one of the rapid intravenous anesthetic drugs whose unique characteristics include hemodynamic stability, negligible respiratory depression, and brain protection. The most common complication of etomidate is intravenous pain during injection. The purpose of this study was to compare the effectiveness of the Valsalva maneuver and fentanyl in reducing the pain caused by etomidate injection for anesthesia induction.

Methods: This clinical trial was performed on 96 patients at Alzahra hospital, affiliated with the Isfahan University of Medical Sciences, from January to June 2021. Patients were divided into two groups of 48 people: the Valsalva maneuver group (group 1) and the fentanyl group (group 2). Blood pressure, heart rate (HR), oxygen saturation, and pain of etomidate injection using the withdrawal response score were graded on a four-point scale (no pain = zero, mild pain = 1, average pain = 2, and severe pain = 3). The collected information was entered into SPSS software version 24. Then, the pain score in the two groups was compared using the chi-square test. The significance level in the present study was $P < 0.05$.

Results: The mean HR ($P = 0.07$), mean arterial pressure (MAP) ($P = 0.33$), systolic pressure ($P = 0.90$), diastolic pressure ($P = 0.67$), and oxygen saturation level ($P = 0.27$) at different times between the two groups showed no significant difference ($P > 0.05$). However, during the etomidate injection, the HR increased and after the injection, the HR decreased in both groups ($P = 0.042$). The two groups had no significant difference regarding pain frequency.

Conclusion: There was no difference in the effect of the Valsalva maneuver and fentanyl on reducing the pain caused by etomidate injection.

Keywords: Valsalva maneuver, Etomidate, Fentanyl, Pain

Introduction

Etomidate is one of the fast-acting non-barbiturate intravenous anesthetic drugs (1). Its unique characteristics, including maintenance of hemodynamic stability, negligible respiratory depression, and brain protection, make it the most suitable medication in patients with cardiovascular disease, reactive airway disease, intracranial hypertension (IIH), hypovolemic patients, and unwell and traumatic patients (2). Intravenous etomidate administration to induce anesthesia has many advantages, including, short effect time, fast metabolism, low risk of histamine release, and hemodynamic stability in bolus injection (3). Etomidate is also used to induce general anesthesia, sedation and relaxation during anesthesia, fixing dislocated joints, rapid intubation, cardioversion, and inducing anesthesia for short surgeries such as dilation, curettage, and cervical conization (1). Etomidate is contraindicated in patients with any allergic reaction. Septic patients have a higher risk for adrenal insufficiency, which is associated with higher death rates (3). Because etomidate is mainly excreted through the kidneys, the toxicity of this drug increases in patients with kidney dysfunction, so it should be used with caution (4). Etomidate's most common side effects are pain during injection, superficial thrombophlebitis, myoclonus, hemolysis, and frequent nausea and vomiting (5). The most common side effect of etomidate is intravenous pain during drug injection (6). Etomidate is formulated in soluble propylene glycol, which causes inflammation of the vascular endothelium and pain during intravenous injection (7). Less pain is felt when the injection is done in the more proximal veins of the arm (6). Measures to reduce pain caused by etomidate injections include slower rate of injection, drug dilution, etomidate injection in the large veins of the forearm, and injection of lidocaine, ondansetron, tramadol, or opioid analgesics, such as fentanyl (8-10). Fentanyl is a short-acting opioid agonist that is commonly used for intra-operative and post-operative analgesia. Also, it has some analgesic effects when administered in the clinical dose range (11).

Fentanyl can reduce the amount of pain during etomidate injection and myoclonus when inducing anesthesia, and attenuate hemodynamic response to intubation (12,13).

Another method is the Valsalva maneuver. The Valsalva maneuver is a physiological and non-pharmacological method that has been proven to reduce pain caused by propofol injection, intravenous cannulation, and spinal anesthesia (14-17). The Valsalva maneuver is created with strong exhalation against a closed throat and holding the breath for at least 16 seconds (18). This maneuver reduces pain through the baroreceptor reflexive arc and the release of substance P and noradrenaline and reduces pain by distraction of the senses away from the injection site (19). In a clinical trial on 90 patients with spinal anesthesia, the postoperative pain rate in the group of patients who performed the Valsalva maneuver was 10%, while the rate was 100% in the control group (20). The advantages of the Valsalva maneuver include simplicity of this technique, rapid time of effect, and a lack of side effects (15), making it suitable for patients who are reluctant to use drugs. As no study has been conducted on the effectiveness of the Valsalva maneuver in the reduction of pain caused by etomidate injection, we compared the effect of the Valsalva maneuver and fentanyl on the pain caused by the injection of etomidate.

Methods

This randomized, controlled, double-blind clinical trial study assessed patients vesting at Alzahra Hospital, affiliated with the Isfahan University of Medical Sciences, from January to June 2021. Quantitative data were described by mean and SD, and qualitative data were described using frequency and relative frequency. Analysis of variance, chi-square, and Fisher's exact test were used in data analysis. Repeated measures ANOVA was used for data comparison between the two groups at different times. Data were analyzed using SPSS software version 24, with a statistical significance level of 0.05. Approval was obtained from the Ethics Committee (IR.MUI.MED.REC.1399.635). Patients aged 18–60 years with American Society of Anesthesiologists (ASA) I-II physical status, who were undergoing surgery under general anesthesia and were able to perform the Valsalva maneuver entered the study after providing consent. Patients with a history of psychiatric diseases, cardiopulmonary disease, chronic pain disorders, use of narcotic drugs, sensitivity to etomidate and fentanyl, and a history of drug use were identified at the time of admission by obtaining a medical history during anesthesia consultation and excluded from the study. In addition, patients who had hemodynamic instability, cardiovascular arrest, and severe sensitivity to these drugs (etomidate or fentanyl) or were unable to perform the Valsalva maneuver were removed from the study.

After obtaining the required licenses, patients requiring general anesthesia using etomidate (who met the entry criteria and lacked the exclusion criteria) were entered into the study until the sample size was achieved. After obtaining permission from the patient and explaining the research, a written informed consent was obtained. Finally, all the patients were randomly divided into two groups (A and B) using random allocation software. The following formula was used to calculate the sample size:

$$n = \frac{2\left(Z1-\frac{a}{z}+Z1-\beta\right)^2 \times (s)^2}{d^2}$$

Based on the results of similar studies, considering the first type error of 0.05 and the second type error of 0.2, the standard deviation (SD) was 2 and 1, equal to the effect of 14.1; the number of samples in each group was 48, so in total, 96 individuals were selected. For intravenous injection, an IV line was used with needle No. 18 on the back surface of the non-dominant hand in the preoperative room 1 hour before the scheduled surgery time. The patients were scheduled as the first cases between 9 and 11 am to minimize the impact of differences in pain perception at different times of the day.

The Valsalva maneuver was taught on the morning of the operation day, and patients were divided into two groups. The first group (group A) was the Valsalva and etomidate group. Patients were assigned to perform the Valsalva maneuver by blowing in a plastic tube attached to a pressure gauge and raising the mercury column to 30 mmHg for at least 20 seconds. The second group (group B), the fentanyl and etomidate group, received fentanyl at a dose of 2 μg/kg. An anesthesia technician, who was not a member of the study team, injected a 0.3 mg/kg dose of etomidate using a 10 mL syringe. All patients received ¼ of the total calculated dosages of etomidate in 5 seconds immediately in the form of an initial dosage after the subject had received the pre-injection treatment specific to their group. We interrupted the infusion for 15 seconds and assessed the pain 20 seconds after the etomidate injection. The ¾ remaining dosage was injected after the 20 seconds in 1 minute before the patient lost their alertness. A nurse unaware of the grouping of patients assessed the pain level. The pain was evaluated using the withdrawal response score, which had four degrees: 0 = no pain, 1 = mild pain (a pain that is only reported by the patient's response to the question, with no change in behavior such as changes in facial expression, retracting the hand, or crying), 2 = moderate pain (in addition to complaint of pain in response to the question, the pain was observable as a behavioral sign, or reported spontaneously and without being asked), 3 = severe pain (a pain accompanied by a loud vocal response, or in association with behavioral symptoms). Then, the information related to every patient, including the demographic information and pain score, was recorded in the designed

checklists. Patient information was handled according to the principle of confidentiality. Anesthesia occurred 1 minute after the Valsalva maneuvers by injecting 0.3 mg/kg etomidate. After 3–4 minutes, the cisatracurium besylate bolus dosage was injected, and 3 min later, intubation was performed by an anesthesiologist after complete anesthesia was achieved, morphine was used for analgesia at a dosage of 0.1 mg/kg, and to maintain anesthesia, 1.2% isoflurane was used and 2 µg/kg fentanyl (only in group A) was injected.

The hemodynamic factors included systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), heart rate (HR), and oxygen saturation SpO_2 before and immediately after each group's intervention and immediately after the delivery of the primary dosage of etomidate (¼ of the etomidate dosage). The parameters were measured at minutes 1, 2, 3, 10, and 15 after the primary etomidate dosage injection.

Results

Ninety-six subjects (48 patients in each group) were studied (Figure 1). According to Table 1, the average age of the subjects was 53.71 years in the Valsalva group and 54.56 years in the fentanyl group. The average age and BMI in the two groups did not differ significantly ($P > 0.05$). However, the mean height and weight were significantly different in the two groups ($P \leq 0.05$). Also, the chi-square test indicated that the distribution frequency of gender was significantly different in the groups (Table 1).

The average HR, SBP, DBP, moderate blood pressure, and oxygen saturation at different times in the two groups showed that in all variables, the interaction of time and group was not significant and that the two groups had almost similar behaviors over time. Also, the group's effect was insignificant in all variables, indicating that the mean variables were almost identical over time in the two groups. During the etomidate injection, the HR showed an incremental trend, and after the end of the injection, a decrease in HR was observed in both groups. Therefore, time did not impact the other variables significantly, except for HR. (Table 2).

Also, the chi-square test showed that the frequency distribution of gender in the two groups was significantly different. The chi-square test for pain frequency in the two groups showed that there was no difference between the two groups in terms of pain (P value = 0.549). The result of the repeated measures test to investigate the average HR, SBP, DBP, MAP, and SpO_2 at different times between the two groups indicated that in all variables, the interaction of time and group was not significant, indicating that both groups had almost similar behaviors over time. Also, the group's effect was not significant in any of the variables, indicating that the mean variables over time in the two groups were almost identical.

The effect of time was not significant in any of the variables except for HR. As in systolic, diastolic, and

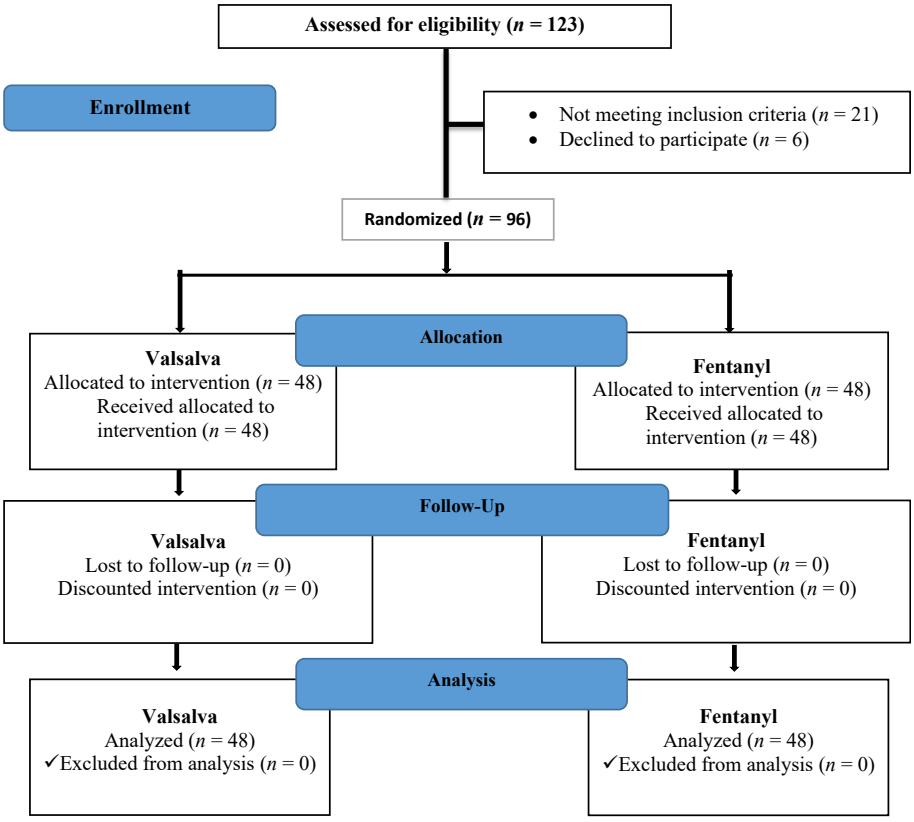

Figure 1. Study Flow Diagram

moderate blood pressure variables, we witnessed a decreasing trend and an incremental trend in the SpO_2 variable over time in the two groups. In the case of HR, we observed an incremental trend during the etomidate injection but a decreasing trend in both groups after the injection (Figure 2). Also, the independent t-test comparing different times in the two groups (Table 3) showed that there was a significant difference between the variables 2 min after intervention.

Discussion

The purpose of this study was to compare the severity of pain caused by etomidate administration when preceded by the Valsalva maneuver or fentanyl administration. According to the study results, there was no significant difference between the demographic variables in the

Table 1. The Demographic Characteristics of the Participants and the Relationship Between Pain Intensity in Study Groups

Variable	Valsalva	Fentanyl	*P* Value
Age (y)	53.71 ± 10.23	54.56 ± 11.49	0.701
Height (cm)	166.67 ± 5.45	164.33 ± 5.28	0.05
Weight (kg)	72.02 ± 7.61	68.44 ± 9.71	0.036
BMI (kg/m^2)	25.52 ± 2.58	24.81 ± 3.37	0.251
Gender, No. (%)	*N* (%)	*N* (%)	
Male	31 (64.6)	22 (45.8)	0.05
Female	17 (35.4)	26 (54.2)	
Pain intensity			
Mild	0.17 ± 0.09	0.14 ± 0.02	
Moderate	0.10 ± 0.06	0.11 ± 0.04	0.549
Severe	0.06 ± 0.02	0.03 ± 0.01	

Table 2. Results of Repeated Measures Test of Systolic Blood Pressure, Diastolic Blood Pressure, Mean Arterial Pressure, Heart Rate, and Oxygen Saturation in the Two Groups

Variable		*P* Value
Systolic blood pressure	Time	0.008
	Group	0.772
	Time / Group*	0.902
Diastolic blood pressure	Time	0.563
	Group	0.141
	Time / Group*	0.678
Mean arterial pressure	Time	0.675
	Group	0.754
	Time / Group*	0.331
Heart rate	Time	0.443
	Group	0.270
	Time / Group*	0.069
Oxygen saturation	Time	0.265
	Group	0.650
	Time / Group	0.276

$P < 0.05$ is statistically significant

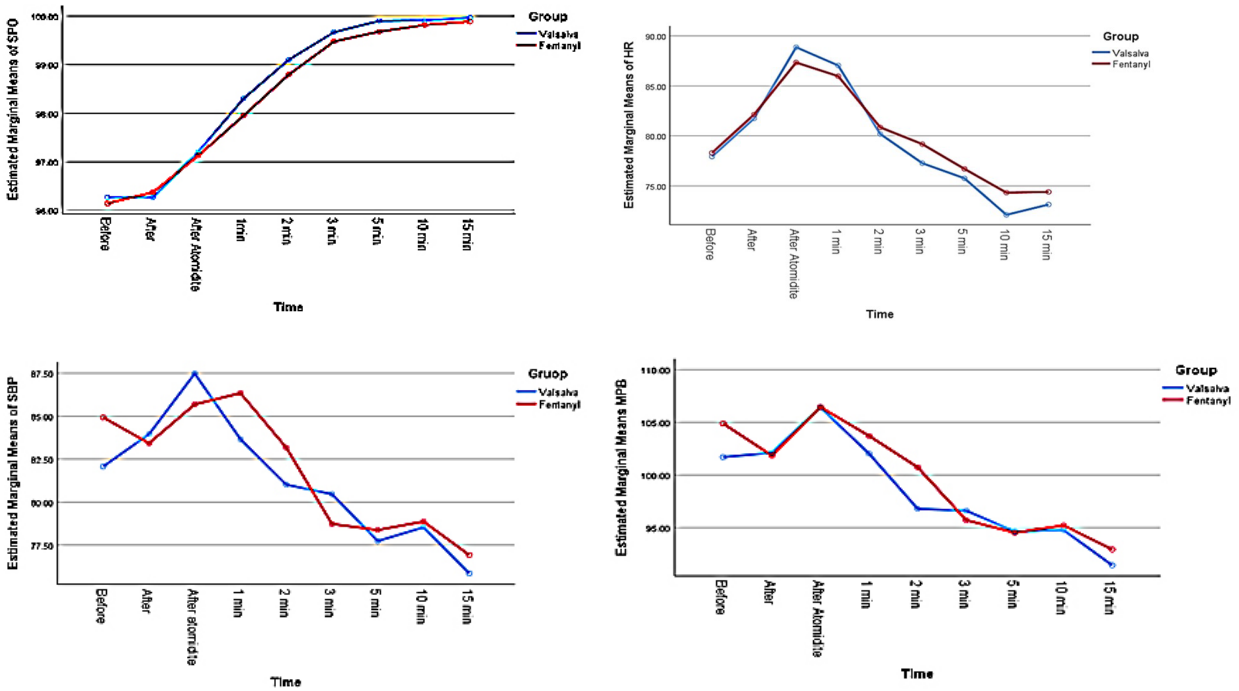

Figure 2. Changes in MAP, SBP, HR, and SpO_2 in the Two Groups at Eight Points in Time

Table 3. Changes in Mean Blood Pressure, Heart Rate, and Arterial Oxygen Saturation in the Two Groups at Eight Points in Time

Variable	Time of Assessment	Valsalva	Fentanyl	*P* Value[a]
Mean arterial pressure	Before injection	13.30 ± 02.10	138.98 ± 20.17	0.488
	After injection	102.0.2 ± 13.15	134.69 ± 19.74	0.821
	After etomidate injection	106.31 ± 16.94	140.73 ± 19.92	0.659
	1 min after injection	102.27 ± 15.39	138.40 ± 20.05	0.432
	2 min after injection	96.81 ± 14.67	129.04 ± 18.76	0.407
	3 min after injection	95.21 ± 14.96	125.15 ± 21.81	0.806
	5 min after the injection	95.25 ± 13.65	125.54 ± 17.28	0.807
	10 min after injection	91.52 ± 12.65	125.02 ± 14.19	0.812
	15 min after injection	102.10 ± 13.30	138.98 ± 20.17	0.488
Heart rate	Before injection	77.50 ± 12.60	78.73 ± 14.92	0.534
	After injection	81.13 ± 11.59	82.75 ± 14.18	0.602
	After injection etomidate	88.63 ± 11.65	87.58 ± 12.71	0.641
	1 min after injection	86.62 ± 15.09	86.40 ± 13.85	0.510
	2 min after injection	77.02 ± 12.57	79.42 ± 16	0.938
	3 min after injection	75.60 ± 13.26	76.85 ± 14.57	0.546
	5 min after injection	71.98 ± 9.72	74.44 ± 13.29	0.568
	10 min after injection	72.92 ± 9.50	74.60 ± 11.58	0.782
	15 min after injection	77.50 ± 12.60	78.73 ± 14.92	0.534
Oxygen saturation	Before injection	96.17 ± 1.55	96.25 ± 1.73	0.812
	After injection	96.19 ± 2.73	96.46 ± 1.74	0.460
	After injection etomidate	97.15 ± 1.24	97.19 ± 1.75	0.979
	1 min after injection	98.23 ± 0.99	98.02 ± 1.21	0.947
	2 min after injection	99.65 ± 0.53	99.50 ± 0.68	0.247
	3 min after injection	99.88 ± 0.39	99.71 ± 0.62	0.680
	5 min after injection	99.90 ± 0.31	99.83 ± 0.52	0.712
	10 min after injection	100 ± 0.20	99.9 ± 0.30	0.867
	15 min after injection	96.17 ± 1.55	96.25 ± 1.73	0.607

[a] t-test; $P < 0.05$ is statistically significant.

study groups. No significant difference in pain intensity was observed in the two groups, which can be associated with the pain control methods. The severity of pain in the Valsalva maneuver group was not different from that of the fentanyl group.

In a clinical trial study on 90 patients undergoing spinal anesthesia, postoperative pain in patients who performed the Valsalva maneuver reached 10%, while in the control group, it was reported to be 100% (20). In another study, the effect of the Valsalva maneuver on the reduction of pain caused by propofol injection was investigated. This study showed a significant difference in pain in the Valsalva maneuver group compared to the control group (15). On the other hand, Vijay et al reported a reduction in the severity of pain in the Valsalva group compared to the control group (14). Soltani Mohammadi et al also found that the Valsalva maneuver reduced pain compared to the control group. In their study, a decrease in HR was recorded at the time of cannulation until the third minute, which was insignificant. On the other hand, this decrease in HR was significant in the first, third, and tenth minutes of our study. Of course, one of the limitations of their study was that vital signs was recorded only two times after the intervention, while in our study, vital signs were recorded at nine points in time (17). In the study of Akdas et al, which was performed on children aged 5 to 15 years, pain reduction in the Valsalva group was not significant compared to the control group, which can be due to the inability of children to perform the Valsalva maneuver or the misunderstanding of visual criteria in pain measurement (21). Another study on hemodialysis patients indicated that the severity of pain in the Valsalva maneuver intervention group was significantly reduced (22). In an article, Memiş et al studied the prevention of pain caused by rocuronium injection by ondansetron, lidocaine, tramadol and fentanyl. In this study, ondansetron was the most effective in reducing pain, and fentanyl was the least effective. The drug that caused the pain was rocuronium in their study, which is different from the drug we used. On the other hand, the pain level caused by the administration of rocuronium is higher in women than in men, which is one of the limitations of the mentioned

study (8). Ahmad et al examined the effect of fentanyl and lidocaine on the pain caused by rocuronium, and fentanyl was reported to be more effective than lidocaine in pain reduction (9). In another study by Babamohamadi et al, the pain caused by etomidate injection was reduced by the Valsalva maneuver and lidocaine (23). Helmers et al reported a significant reduction in pain during propofol injection from 40 to 16% when fentanyl was administered before it (24). In the study of Ray et al, lignocaine pre-treatment was more effective in preventing the pain of propofol injection compared to fentanyl (25). In the study of Vijayaragavan et al, the administration of 5 µ/kg of fentanyl before etomidate injection decreased the occurrence of pain caused by the injection, myoclonus, HR, and blood pressure (26).

Conclusion

According to this study's findings, the Valsalva maneuver and fentanyl are equally effective in reducing the severity of pain caused by etomidate injection, and neither treatment disrupted hemodynamic stability. Regarding the selection of an appropriate method of pain reduction, conditions such as age and the ability to perform the maneuver should be considered.

Authors' Contribution

Conceptualization: Behzad Nazemroaya.
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Funding acquisition: Golshan Mazaheri Tehrani.
Investigation: Behzad Nazemroaya, Azim Honarmand.
Methodology: Behzad Nazemroaya, Azim Honarmand.
Project administration: Behzad Nazemroaya.
Resources: Azim Honarmand, Golshan Mazaheri Tehrani.
Supervision: Behzad Nazemroaya.
Validation: Behzad Nazemroaya, Azim Honarmand.
Writing–original draft: Behzad Nazemroaya, Golshan Mazaheri Tehrani.
Writing–review & editing: Behzad Nazemroaya, Azim Honarmand.

Competing Interests

None.

Ethical Approval

This study was performed in accordance with the CONSORT (consolidated standards of reporting trials) 2010 guidelines after acquiring the permission of the Ethics Committee of Isfahan University of Medical Sciences (IR.MUI.MED.REC.1399.635) and registration in the Iranian Registry of Clinical Trials (IRCT20160307026950N33).

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References

1. Dumps C, Bolkenius D, Halbeck E. [Etomidate for intravenous induction of anaesthesia]. Anaesthesist. 2017;66(12):969-80. doi: 10.1007/s00101-017-0381-6. [German].
2. Saliminia A, Azimaraghi O, Javadi A, Abdoulahpoor M, Movafegh A. Comparison of granisetron and lidocaine on reducing injection pain of etomidate: a controlled randomized study. Braz J Anesthesiol. 2017;67(6):615-8. doi: 10.1016/j.bjane.2017.04.001.
3. Erdoes G, Basciani RM, Eberle B. Etomidate--a review of robust evidence for its use in various clinical scenarios. Acta Anaesthesiol Scand. 2014;58(4):380-9. doi: 10.1111/aas.12289.
4. Ruth WJ, Burton JH, Bock AJ. Intravenous etomidate for procedural sedation in emergency department patients. Acad Emerg Med. 2001;8(1):13-8. doi: 10.1111/j.1553-2712.2001.tb00539.x.
5. Liu J, Liu R, Meng C, Cai Z, Dai X, Deng C, et al. Propofol decreases etomidate-related myoclonus in gastroscopy. Medicine (Baltimore). 2017;96(26):e7212. doi: 10.1097/md.0000000000007212.
6. Canessa R, Lema G, Urzúa J, Dagnino J, Concha M. Anesthesia for elective cardioversion: a comparison of four anesthetic agents. J Cardiothorac Vasc Anesth. 1991;5(6):566-8. doi: 10.1016/1053-0770(91)90007-g.
7. Doenicke AW, Roizen MF, Hoernecke R, Lorenz W, Ostwald P. Solvent for etomidate may cause pain and adverse effects. Br J Anaesth. 1999;83(3):464-6. doi: 10.1093/bja/83.3.464.
8. Memiş D, Turan A, Karamanlioğlu B, Süt N, Pamukçu Z. The prevention of pain from injection of rocuronium by ondansetron, lidocaine, tramadol, and fentanyl. Anesth Analg. 2002;94(6):1517-20. doi: 10.1097/00000539-200206000-00026.
9. Ahmad N, Choy CY, Aris EA, Balan S. Preventing the withdrawal response associated with rocuronium injection: a comparison of fentanyl with lidocaine. Anesth Analg. 2005;100(4):987-90. doi: 10.1213/01.ane.0000147790.76114.3a.
10. Brown PM, Moss E. Reduction of pain on injection of etomidate. Anaesthesia. 1981;36(8):814-6. doi: 10.1111/j.1365-2044.1981.tb08823.x.
11. Basaranoglu G, Erden V, Delatioglu H. Reduction of pain on injection of propofol: a comparison of fentanyl with remifentanil. Anesth Analg. 2002;94(4):1040-1. doi: 10.1097/00000539-200204000-00053.
12. Holdcroft A, Morgan M, Whitwam JG, Lumley J. Effect of dose and premedication on induction complications with etomidate. Br J Anaesth. 1976;48(3):199-205. doi: 10.1093/bja/48.3.199.
13. Stockham RJ, Stanley TH, Pace NL, King K, Groen F, Gillmor ST. Fentanyl vs. etomidate plus fentanyl for induction of anaesthesia in high-risk patients. Ma Zui Xue Za Zhi. 1986;24(3):160-5.
14. Vijay VR, Agnihotri M, Kaur S, Bhalla A. Effect of Valsalva maneuver prior to peripheral intravenous cannulation on intensity of pain. Nurs Midwifery Res J. 2013;9(4):143-51. doi: 10.33698/nrf0166.
15. Kumar S, Khuba S, Agarwal A, Gautam S, Yadav M, Dixit A. Evaluation of efficacy of Valsalva maneuver for attenuating propofol injection pain: a prospective, randomized, single blind, placebo-controlled study. Korean J Anesthesiol. 2018;71(6):453-8. doi: 10.4097/kja.d.18.00017.
16. Kumar S, Gautam SK, Gupta D, Agarwal A, Dhirraj S, Khuba S. The effect of Valsalva maneuver in attenuating skin puncture pain during spinal anesthesia: a randomized controlled trial. Korean J Anesthesiol. 2016;69(1):27-31. doi: 10.4097/kjae.2016.69.1.27.
17. Soltani Mohammadi S, Ghasemi Pajand A, Shoeibi G. Efficacy of the Valsalva maneuver on needle projection pain and hemodynamic responses during spinal puncture. Int J Med Sci. 2011;8(2):156-60. doi: 10.7150/ijms.8.156.
18. Walters S, Hoffman B, MacAskill W, Johnson MA, Sharpe GR, Mills DE. The control of respiratory pressures and

neuromuscular activation to increase force production in trained martial arts practitioners. Eur J Appl Physiol. 2021;121(12):3333-47. doi: 10.1007/s00421-021-04800-7.
19. Gupta D, Agarwal A, Dhiraaj S, Tandon M, Kumar M, Singh RS, et al. An evaluation of efficacy of balloon inflation on venous cannulation pain in children: a prospective, randomized, controlled study. Anesth Analg. 2006;102(5):1372-5. doi: 10.1213/01.ane.0000205741.82299.d6.
20. Agarwal A, Sinha PK, Tandon M, Dhiraaj S, Singh U. Evaluating the efficacy of the Valsalva maneuver on venous cannulation pain: a prospective, randomized study. Anesth Analg. 2005;101(4):1230-2. doi: 10.1213/01.ane.0000167270.15047.49.
21. Akdas O, Basaranoglu G, Ozdemir H, Comlekci M, Erkalp K, Saidoglu L. The effects of Valsalva maneuver on venipuncture pain in children: comparison to EMLA® (lidocaine-prilocaine cream). Ir J Med Sci. 2014;183(4):517-20. doi: 10.1007/s11845-013-1037-4.
22. Davtalab E, Naji S. The evaluation of Valsalva maneuver on pain intensity within the needle insertion to the arteriovenous fistula for patients undergoing hemodialysis in the selected hospitals in Isfahan in 2015. Ann Trop Med Public Health. 2017;10(5):1322-7. doi: 10.4103/atmph.atmph_202_17.
23. Babamohamadi H, Ameri Z, Asadi I, Asgari MR. Comparison of the effect of EMLA™ cream and the Valsalva maneuver on pain severity during vascular needle insertion in hemodialysis patients: a controlled, randomized, clinical trial. Evid Based Complement Alternat Med. 2022;2022:8383021. doi: 10.1155/2022/8383021.
24. Helmers JH, Kraaijenhagen RJ, van Leeuwen L, Zuurmond WW. Reduction of pain on injection caused by propofol. Can J Anaesth. 1990;37(2):267-8. doi: 10.1007/bf03005485.
25. Ray S, Pal R, Pal S, Kirtania J, Sarbapalli D, Sarkar U, et al. Preclusion of pain on injection with propofol: evaluating the effects of lignocaine or fentanyl pretreatment. Anesth Essays Res. 2011;5(1):33-8. doi: 10.4103/0259-1162.84180.
26. Vijayaragavan S, Balamurugan M, Vasanth K. Comparison of different doses of fentanyl for attenuating stress response and side effects of etomidate during induction and intubation: a randomized control study. Int J Sci Study. 2017;5(1):100-3.