



# A Comparative Study of Valsalva Maneuver, Lidocaine, and Valsalva Maneuvers with Administration of Lidocaine to Reduce the Pain Associated with Administration of Etomidate During General Anesthesia

Behzad Nazemroaya <sup>1,2,\*</sup>, Omid Aghadavodi <sup>1</sup>, Azim Honarmand <sup>1</sup> and Sarina Ahmadian <sup>3</sup>

<sup>1</sup>Anesthesiology and Critical Care Research Center, Isfahan University of Medical Sciences, Isfahan, Iran

<sup>2</sup>Department of Anesthesiology and Critical Care, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran

<sup>3</sup>School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran

\*Corresponding author: Anesthesiology and Critical Care Research Center, Isfahan University of Medical Sciences, Isfahan, Iran. Email: behzad\_nazem@med.mui.ac.ir

Received 2021 February 06; Revised 2021 May 01; Accepted 2021 May 18.

## Abstract

**Objectives:** The purpose of this study is a comparison of Valsalva, lidocaine, and Valsalva with administration of lidocaine to reduce the pain associated with administration of etomidate.

**Methods:** The present study is a clinical trial study. The number of samples in each group was 30 and a total of 90 people were selected. This study was a clinical trial and the subjects were randomly divided into three groups: Group 1: Valsalva, 2: Lidocaine, 3: Valsalva and Lidocaine. Pain due to etomidate was rated on a VAS from 1 (painless) to 3 (worst imaginable pain) and their information was recorded. The collected information was entered into SPSS 22 and analyzed with appropriate statistical tests.

**Results:** A total of 90 subjects participated in the present study and were divided into 3 groups: Valsalva, lidocaine, and Valsalva with lidocaine. No significant difference was observed between demographic variables in the study groups. There was a significant relationship between severity of pain in the three groups. According to the results, the highest pain intensity was in the Valsalva group and the lowest pain intensity was in the Valsalva with lidocaine group.

**Conclusions:** Valsalva with lidocaine reduces the severity of pain caused by etomidate to a greater extent than other groups.

**Keywords:** Etomidate, Valsalva Maneuver, Lidocaine, General Anesthesia

## 1. Background

One of the most common non-barbiturate hypnotic agents was used in anesthesia through the intravenous (IV) mode is etomidate which is known to be an ultrashort-acting drug (1). Furthermore, etomidate is not known to possess analgesic characteristics. This medication can be solely used as an IV medicine. The reason that etomidate is a desirable medication is that Etomidate possesses acceptable hemodynamic characteristics when used during anesthesia induction, meaning that it causes a negligible extent of reduction in blood pressure, therefore etomidate is considered to be an acceptable drug in trauma anesthesia which has caused the patient to go into shock, or in patients suffering from hypovolemia, and those with a history of serious cardiovascular conditions (2, 3). Additionally, it has been safely utilized for the induction of general anesthesia and also in rapid sequence intubation. Another use for etomidate is in sedation, and also for maintenance

of general anesthesia (4). It can also be used in operative procedures that are short in length for example in reduction of dislocated joints, cardioversion, and tracheal intubation, (5) cervical conization, or dilation and curettage (6, 7). In addition, Etomidate can be utilized for ECT since it has the ability to elevate the seizure duration potential which has shown superiority in this regard compared to thiopental or propofol (8). It has also been used in patients suffering from Cushing's syndrome in the form of an off-label drug in order to suppress the production of steroids. Lidocaine is classically considered a local anesthetic but is now becoming more widely used for systemic analgesia (9).

Considering that the most common complication of etomidate is pain during injection, there have been a number of ways used to decrease the discomfort, one such way being the injection of lidocaine before the injection of etomidate, which has been proven to reduce pain (10).

Moreover, this maneuver has been known as a physio-

logical method which has been used to lower pain in different procedures (9, 10). The Valsalva maneuver reduces both somatic and physiological aspects of painful procedures (8, 9).

The Valsalva maneuver is very effective and useful in reducing pain because it is easily applicable and physiologically effective, time and cost effective, painless, without side effects and compatible with the patient, which can be effective in reducing pain in patients who refuse medication.

Considering that no study has previously been done on the effectiveness of the Valsalva maneuver in reducing the pain caused by etomidate injection and comparing it with the effectiveness of lidocaine, we decided to study this effect by designing a study.

## 2. Objectives

Therefore, the purpose of this study is a Comparison of the Valsalva, lidocaine, and Valsalva with lidocaine in reducing the pain associated with etomidate.

## 3. Methods

The present study is a clinical trial study that was performed in Al-Zahra hospital in 2019.

### 3.1. Inclusion Criteria

Ages 18 to 65 years and induction of general anesthesia with etomidate.

### 3.2. Exclusion Criteria

Unavailability and Incompleteness of information, using corticosteroids, seizures, inability to perform Valsalva maneuver and dissatisfaction with continuing the study.

Beforehand, approval from Ethics Committee (IR.MUI.REC.1399.378) of the University and informed consents was obtained from the patients or the legal guardians were obtained. The study was listed at www.irct.ir with a documentation code of IRCT (IRCT 20160307026950N26). The handmade device used in the present study for the Valsalva maneuver. (Figure. 1)

### 3.3. Sample Size Estimation

The sampling method was a non-probabilistic sampling. The equation seen below was utilized in order to obtain the number of subjects needed:

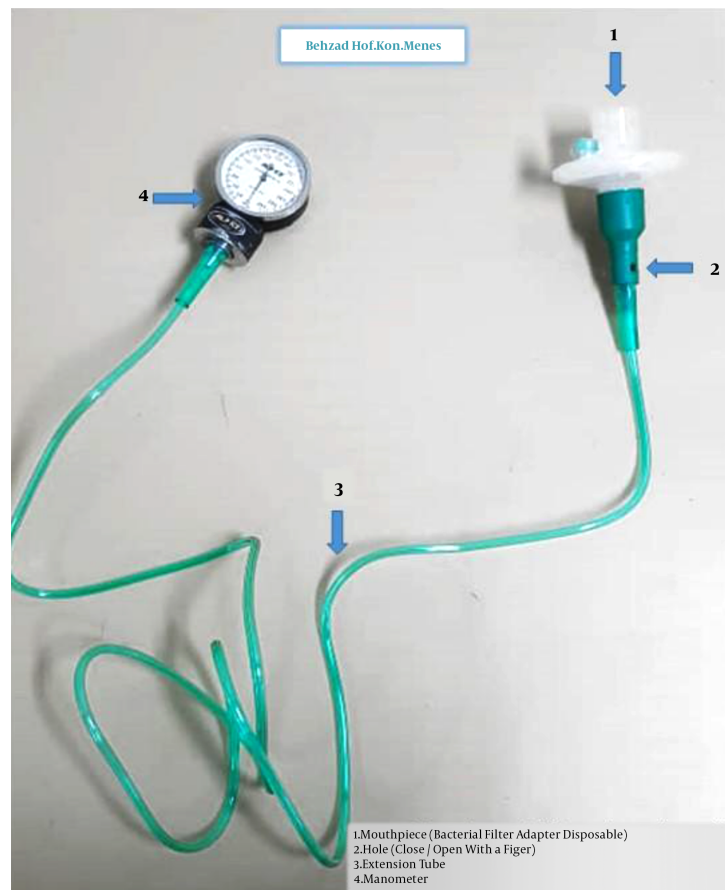
$$N = \frac{\left(Z_{1-\frac{\alpha}{2}} + Z_{1-\beta}\right)^2 (\delta_1^2 + \delta_2^2)}{d^2} \quad (1)$$

According to similar studies, considering the first type error of 0.05 and the second type error of 0.2, the deviation of criteria 2 and 1 was equal to the effect of 14.1 and the number of samples in each group was calculated to be 30 hence a total of 90 patients were selected.

### 3.4. Randomization, Intervention and Blinding

For the purpose of randomization, a sequence used for random allocation using a computer model, concealed in 90 closed packets with consecutive numbers mentioning the group distribution, was prepared by a nurse employed in the center who was not a stake holder in this study. Intravenous cannulation was performed 1 h before surgery using an 18 G cannula on the back of the non-dominant hand vein in the ward. On the morning of surgery, dedicated envelopes were opened for group assignment of registered patients. Monitoring started using blood pressure measurements, electrocardiography capnography and pulse oximetry. The amount of 0.2mg/kg etomidate (B. Braun Medical S.R.L, Romania) and 30 mg of lidocaine 1% (Caspian Tamin Pharmaceutical Co. Rasht, Iran) were administered separately into a 20 ml syringe by an expert anesthesia technician who was not involved in the study. Patients assigned to carry out the Valsalva maneuver blew into a rubber tube attached to a sphygmomanometer, raising the Barometer hands for a period of at least 20 s to 30 mmHg (Group I, Valsalva group). In group II (lidocaine group) the tube was placed between the lips, however, the maneuver did not perform in this group and only 30 mg of lidocaine 1% was administered. In group 3 Valsalva maneuver was performed along with receiving 30 mg of lidocaine 1%. All patients received a quarter of the total calculated dose of etomidate within 5 seconds as the initial dose, immediately after the group-specific intervention. Following this, the infusion was ceased for 15s. Pain assessment was started 20 seconds after the start of etomidate injection. The remaining 75 percent of the dose were injected over 1 minute after 20 seconds, prior to patients losing awareness. The person in charge of information collection who assessed the level of discomfort was left blind as follows: the technician prescribing the drug and the person in charge who gathered information about the level of pain were not aware of the group's special intervention as the patient's head was hidden by a curtain from them. After the intervention that was special to each group, the person in charge of gathering the information went to the side of the patient's head (the far side of the curtain) to evaluate the pain level. The intensity of the pain was assessed with a questionnaire for assessment of the withdrawal response score and a ruler as the visual analogue scale (VAS). A stopwatch was applied in order to record the duration of etomidate injection in a few seconds. Patients were educated about the VAS ruler which shows the numbers on one side and the relative facial expressions to each number, on the other side. The VAS score was between 0 and 10, with 0 meaning there is no pain and 10 showing the highest level of comprehended pain.

Patients learned to show a point on the VAS ruler that indicated the severity of their pain. The pain score was specified by counting the distance in mm between 0 and



**Figure 1.** The handmade device used in the present study for the Valsalva maneuver

the patient-marked point on the ruler.

Twenty seconds after administration of etomidate, withdrawal response was evaluated using standard questions including verbal response, convenience during drug administration, and changes in the patient expression such as facial frowning, tears, and/or withdrawal of the arm. Evaluation of pain was graded on a 4-point scale using the withdrawal response scoring: 0 = no pain, 1 = mild pain (pain that is expressed solely in response to a question without any changes in behavior), 2 = moderate pain (pain that is expressed in response to a question and is associated with changes in behavior or aching that is reported suddenly before even asking), and 3 = severe pain (strong vocal response or response that is associated with facial grimacing, arm pulling, or tears).

Anesthesia was performed 1 min after the Valsalva maneuver with intravenous etomidate administration of 0.2 mg/kg and fentanyl 3  $\mu$ g/kg. Intubation of the trachea was carried out by a committed experienced resident who was not one of the participants in the study, 3 - 4 min sub-

sequent to receiving a bolus dose of Cisatracurium and 5min after receiving etomidate. General anesthesia was maintained using isoflurane. Withdrawal response score and VAS were evaluated by a committed anesthesiologist who was blinded to group assignment and had no role in the project. On day 1 postoperatively, the etomidate injection site was evaluated for signs of inflammation including edema, wheal, pain, and flare by a clinical pain recorder unaware of the research procedure or the prescribed drugs.

### 3.5. Statistical Analysis

The collected information was entered into SPSS 22 and analyzed with appropriate statistical tests. The pain score in the three groups was compared by chi-square test.

## 4. Results

Overall 90 patients participated in the present study and were divided into three groups: Valsalva, lidocaine,

and Valsalva with lidocaine. As the results show, no significant difference was observed between demographic variables in the study groups ( $P > 0.05$ ).

**Table 1** examines the relationship between pain intensity in the three study groups. As the results of **Table 1** show, there is a significant relationship between severity in the three groups ( $P < 0.05$ ). Also, the highest pain intensity was in the Valsalva maneuver alone group and the lowest pain intensity was in the Valsalva maneuver with lidocaine group. (**Table. 1**)

## 5. Discussion

The objective of this research was to determine the severity of pain due to etomidate administration in the Valsalva alone, Lidocaine, and Valsalva maneuver with lidocaine groups. Based on the preliminary results of the study, there was no significant difference between the demographic variables in the study groups. Therefore, the significant differences observed in the intensity of pain in the three groups could be related to the type of injectable drug used.

According to the results of the study, the severity of pain in the Valsalva maneuver with lidocaine groups was lower than other groups. Therefore, the results of the present study show that administration of Valsalva maneuver in combination with lidocaine can significantly reduce the pain of etomidate administration.

Based on the results performed by Pourmehdi et al, it has been shown that the amount of pain caused by the administration of etomidate is reduced by injecting lidocaine (11).

Kumar et al., which examined 80 patients in two groups and measured pain during propofol injection, one group performed the Valsalva maneuver during the injection. They concluded that the Valsalva maneuver was an effective method of reducing pain caused by propofol injection and can be used. (12)

In another study, the results showed that the Valsalva maneuver reduced pain (13).

Davtalab et al., reported the two methods of Valsalva maneuver and ice massage in reducing the pain caused by the needle entering the AVF and concluded that Valsalva maneuver reduced pain more effectively than massage (14).

In a clinical trial study in 90 patients under spinal anesthesia, the rate of postoperative pain reached 10% in the group of patients with maneuvering Valsalva, compared with 100% in the control group (12).

In another study, the effect of Valsalva maneuver on reducing pain caused by propofol injection was investigated. In this study, the amount of pain in Valsalva group was significantly different from the control group (15).

Agrawal et al, in one study showed that the effect of lidocaine in reducing propofol-induced pain was greater than that of etomidate injection pain (16).

Vijay et al, in another study reported a reduction in pain intensity in the Valsalva group compared with the control group (17).

Also, Mohammadi et al, reported a reduction in aching in the Valsalva group compared to the control group (18).

In the study by Akdas et al, which was performed on children aged 5 to 15 years, the reduction of pain in the Valsalva group was not significant compared to the control group, which could be due to the inability of children to perform the Valsalva maneuver or misunderstanding of visual pain measurement criteria (19).

By comparing the publications and studies conducted about the Valsalva Maneuver and lidocaine and findings that show both of these measures to be efficacious in decreasing pain, it appears that combination therapy using both of these methods in an intervention group as a means of reducing pain has definitely been effective.

### 5.1. Limitations

Because of the limited number of subjects used in our research there needs to be more research done in this regard in order to compare the various amounts of etomidate and also the possible complications that may be caused at different drug levels.

### 5.2. Conclusion

In this study, it was shown that the use of Valsalva maneuver with lidocaine reduces the severity of pain caused by the administration of etomidate to a greater extent than other groups.

## Footnotes

**Authors' Contribution:** Author Contributions: Study concept and design, Acquisition of data, Analysis and interpretation of data, Critical revision of the manuscript for important intellectual content, Statistical analysis: B. N.; Administrative, technical, and material support, Study supervision: O.A.; Drafting of the manuscript: S.A.

**Clinical Trial Registration Code:** IRCT 20160307026950N26.

**Conflict of Interests:** The authors declare that they have no competing interests.

**Ethical Approval:** IR.MUI.REC.1399.378.

**Funding/Support:** This work was supported by Isfahan University of Medical Sciences.

**Informed Consent:** Informed consent from the patients/legal guardians was obtained.

**Table 1.** Relationship between Pain Intensity in Study Groups<sup>a</sup>

Intensity of Pain (VAS)	Group V (N = 30)	Group L (N = 30)	Group VL (N = 30)	P_Value
0	2 (%6.7)	19 (%63.3)	26 (%86.7)	0.001
1	7 (%23.3)	5 (%16.7)	4 (%13.3)	
2	13 (%43.3)	4 (%13.3)	0	
3	8 (%26.7)	2 (%6.7)	0	

<sup>a</sup>Chi-square test was used to compare the results. The P < 0.05 indicate the significance of the comparison of the results.

## 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](https://doi.org/10.1007/s00101-017-0381-6). [PubMed: [29147790](https://pubmed.ncbi.nlm.nih.gov/29147790/)].
2. Gooding JM, Corssen G. Etomidate: an ultrashort-acting nonbarbiturate agent for anesthesia induction. *Anesth Analg*. 1976;**55**(2):286–9. doi: [10.1213/00000539-197603000-00035](https://doi.org/10.1213/00000539-197603000-00035). [PubMed: [943993](https://pubmed.ncbi.nlm.nih.gov/943993/)].
3. Nazemroaya B, Mousavi SM. Comparison of premedication with low-dose midazolam versus etomidate for reduction of etomidate-induced myoclonus during general anesthesia for electroconvulsive therapy: A randomized clinical trial. *Anesth Pain Med*. 2019;**9**(6). e94388. doi: [10.5812/aapm.94388](https://doi.org/10.5812/aapm.94388). [PubMed: [32280614](https://pubmed.ncbi.nlm.nih.gov/32280614/)]. [PubMed Central: [PMC7118685](https://pubmed.ncbi.nlm.nih.gov/PMC7118685/)].
4. Adinehmehr L, Shetabi H, Moradi Farsani D, Salehi A, Noorbakhsh M. Comparison of the sedation quality of etomidate, propofol, and midazolam in combination with fentanyl during phacoemulsification cataract surgery: A double-blind, randomized, controlled, clinical trial. *Anesth Pain Med*. 2019;**9**(2). e87415. doi: [10.5812/aapm.87415](https://doi.org/10.5812/aapm.87415). [PubMed: [31341824](https://pubmed.ncbi.nlm.nih.gov/31341824/)]. [PubMed Central: [PMC6616865](https://pubmed.ncbi.nlm.nih.gov/PMC6616865/)].
5. 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](https://doi.org/10.1111/aas.12289). [PubMed: [24588359](https://pubmed.ncbi.nlm.nih.gov/24588359/)].
6. 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](https://doi.org/10.1111/j.1553-2712.2001.tb00539.x). [PubMed: [11136141](https://pubmed.ncbi.nlm.nih.gov/11136141/)].
7. 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.00000000000007212](https://doi.org/10.1097/MD.00000000000007212). [PubMed: [28658112](https://pubmed.ncbi.nlm.nih.gov/28658112/)]. [PubMed Central: [PMC5500034](https://pubmed.ncbi.nlm.nih.gov/PMC5500034/)].
8. Wismeijer AA, Vingerhoets AJ. The use of virtual reality and audiovisual eyeglass systems as adjunct analgesic techniques: a review of the literature. *Ann Behav Med*. 2005;**30**(3):268–78. doi: [10.1207/s15324796abm3003\\_11](https://doi.org/10.1207/s15324796abm3003_11). [PubMed: [16336078](https://pubmed.ncbi.nlm.nih.gov/16336078/)].
9. Tully J, Jung JW, Patel A, Tukan A, Kandula S, Doan A, et al. Utilization of Intravenous Lidocaine Infusion for the Treatment of Refractory Chronic Pain. *Anesth Pain Med*. 2020;**10**(6). e112290. doi: [10.5812/aapm.112290](https://doi.org/10.5812/aapm.112290). [PubMed: [34150583](https://pubmed.ncbi.nlm.nih.gov/34150583/)]. [PubMed Central: [PMC8207879](https://pubmed.ncbi.nlm.nih.gov/PMC8207879/)].
10. Ghasemi M, Mosaffa F, Hoseini B, Behnaz F. Comparison of the Effect of Bicarbonate, Hyaluronidase, and Lidocaine Injection on Myofascial Pain Syndrome. *aapm*. 2020;**10**(3). doi: [10.5812/aapm.101037](https://doi.org/10.5812/aapm.101037).
11. Pourmehdi Z, Soltanzadeh M, Soltani F, Leilatan J. comparing the efficacy of Lidocaine versus Magnesium sulfate on pain associated with intravenous administration of Etomidate. *Journal of Iranian Society Anaesthesiology and Intensive Care*. 2015;**37**(2).
12. 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](https://doi.org/10.4097/kja.d.18.00017). [PubMed: [29843507](https://pubmed.ncbi.nlm.nih.gov/29843507/)]. [PubMed Central: [PMC6283717](https://pubmed.ncbi.nlm.nih.gov/PMC6283717/)].
13. Babaei M, Jalali R, Jalali A, Rezaaei M. The effect of valsalva maneuver on pain intensity and hemodynamic changes during intravenous (IV) cannulation. *Iran Journal of Nursing*. 2017;**30**(108):52–9. doi: [10.29252/ijn.30.108.52](https://doi.org/10.29252/ijn.30.108.52).
14. Davtalab E, Naji S, Shahidi S. Comparing the effects of valsalva maneuver and ice massage at Hoku point methods on pain intensity within the needle insertion to the arteriovenous fistula (AVF) for patients undergoing hemodialysis in the selected hospitals in Isfahan in 2015. *Int J Med Res & Helth Sci*. 2016;**5**(5):101–7.
15. 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](https://doi.org/10.4097/kjae.2016.69.1.27). [PubMed: [26885298](https://pubmed.ncbi.nlm.nih.gov/26885298/)]. [PubMed Central: [PMC4754262](https://pubmed.ncbi.nlm.nih.gov/PMC4754262/)].
16. Agarwal A, Dhiraj S, Raza M, Pandey R, Pandey CK, Singh PK, et al. Vein pretreatment with magnesium sulfate to prevent pain on injection of propofol is not justified. *Can J Anaesth*. 2004;**51**(2):130–3. doi: [10.1007/BF03018771](https://doi.org/10.1007/BF03018771). [PubMed: [14766688](https://pubmed.ncbi.nlm.nih.gov/14766688/)].
17. Vijay VR, Agnihotri M, Kaur S, Bhalla A. Effect of Valsalva Maneuver Prior to Peripheral Intravenous Cannulation on Vital Signs. *JoNSP*. 2013;**3**(3):16–20.
18. Mohammadi SS, Pajand AG, 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](https://doi.org/10.7150/ijms.8.156). [PubMed: [21369370](https://pubmed.ncbi.nlm.nih.gov/21369370/)]. [PubMed Central: [PMC3047080](https://pubmed.ncbi.nlm.nih.gov/PMC3047080/)].
19. 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((R)) (lidocaine-prilocaine cream). *Ir J Med Sci*. 2014;**183**(4):517–20. doi: [10.1007/s11845-013-1037-4](https://doi.org/10.1007/s11845-013-1037-4). [PubMed: [24243080](https://pubmed.ncbi.nlm.nih.gov/24243080/)].