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Haemodynamic Consequences after Etomidate Administration for Short Surgical Procedures in Patients Aged Above 50 Years - A Prospective Study

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Abstract

Background: Haemodynamic perturbances due to anaesthesia in various surgeries have become a great concern especially in older patients [1]. All methods used in anaesthesia induction are designed so that the haemodynamic stability is maintained throughout surgery and even postoperative period too [2]. Anaesthetic challenges are quite high in short surgical procedures same as long surgeries. Intravenous anaesthetics are preferred for induction of general anaesthesia (GA) because of more rapid and smoother action with fewer risks. Cardiovascular and Respiratory systems appear to be minimally affected by Etomidate and myocardial oxygen supply-to-demand ratio is also well maintained.

A prospective study "Use of Etomidate for short surgical procedures in patients aged above 50 years" conducted in MBS hospital and Government Medical College, Kota, Rajasthan, India; to determine the effect of etomidate on haemodynamics.

Material and Method: After institutional ethical approval and meeting of inclusion criteria, we enrolled 100 patients of more than 50 years age; who were planned for short surgical procedures. Pre-anaesthetic examination and routine investigations were done. After receiving baseline parameters, all patients were pre-medicated with injection Midazolam (0.25mg/kg), Glycopyrrolate (0.004 mg/kg) and Fentanyl (2 mcg/kg) intravenously 10 minutes prior to procedure. Patient was induced with Etomidate 0.2 mg/kg loading dose. An additional dose of Etomidate 0.1 mg/kg was given intravenously if needed. Induction of anaesthesia was confirmed by loss of verbal communication with the patient and loss of eyelash reflex. Once an adequate depth of anaesthesia was achieved, the patient was mask ventilated with 100% oxygen during operative time.

Observation and Result: Heart rate, Systolic blood pressure, Diastolic blood pressure, Mean arterial pressure and SpO_2 were recorded preoperatively before induction and intra-operatively after induction of anaesthesia at every 1 min intervals up to 5 minute and then 5 min intervals up to 20 min, then post operatively at 60 minutes. Data were reported as mean ± SD and percentage. In our study the mean systolic blood pressure, diastolic blood pressure, mean arterial blood pressure and mean heart rate observed at various time interval, they were not change significantly from baseline values in intra-operative and post-operative period. ($p>0.05$).

Conclusion: As per our prospective study and review of literature, etomidate is a relatively safe and sufficient pharmacotherapeutic agent for short surgical procedures in elderly people with minor adverse reactions.

Keywords: Etomidate; Short Surgical Procedures; Haemodynamic Stability; General Anaesthesia

Introduction

Haemodynamic instability is one of the most common problems during general anaesthesia, many factors either solely or in combination, may be predisposing factors for it. Haemodynamic changes due to anaesthesia in various surgeries have become a great concern for physicians inside the operation room and evidence show that changes in blood pressure, either increase or decrease, independently are associated with side effects and complications in patients undergoing surgery [1]. All methods used in anaesthesia induction are designed so that the haemodynamic stability is maintained especially in older patients [2]. Intravenous anaesthetics are preferred for induction of general anaesthesia (GA) because of more rapid and smoother action with fewer risks. Cardiovascular and Respiratory systems appear to be minimally affected by Etomidate and myocardial oxygen supply-to-demand ratio is well maintained. Short operative procedures like closed reductions and plasters, abscess drainage, K-wire insertion, debridement of the wounds, K-wire removal, biopsy taking, VIU, wound dressing etc. require adequate depth of anaesthesia, muscle relaxation and profound analgesia along with clear headed recovery within a short period of time with minimal side effects and minimal alterations in haemodynamics.

Present prospective study was planned to observing haemodynamic response to etomidate in patients aged above 50 years scheduled for short surgical procedures in our tertiary care centre, government medical college and attached hospitals, Kota, Rajasthan (India) during 1 year of duration from 1/11/2014 to 31/10/2015.

Material and Methods

After institutional ethical committee approval and written informed consent, in this prospective study, we enrolled 100 consecutive adults, aged more than 50 years, scheduled for elective as well as emergency short duration surgeries (less than 15 minutes). Exclusion criteria were: restricted mouth opening, history of obstructive sleep apnea, longer duration of surgery (>10 min), allergy or known hypersensitivity reaction to etomidate, pregnant female, nursing mother, patients with seizure

disorder and patients with presence of primary and secondary steroid deficiency. A detailed history regarding physical health, coexisting medical problems, current medications, allergies, previous anaesthetic and surgical experience were noted before surgery. Relevant laboratory investigations were reviewed.

The primary end point of this study was to determine the effects of Etomidate on heart rate, systolic blood pressure, diastolic blood pressure and mean blood pressure during anaesthesia induction, surgery and at 1 hour in post operative period in above mentioned group of patients and in enrolled patients with co-morbidities.

Secondary end points were evaluating the any complications regarding etomidate and required mean doses for completion of such surgeries.

Anaesthetic technique

On arrival of the patient in the operating room, after consent, fasting status and PAC checked, prior to induction anaesthesia machine, oxygen supply, suction resuscitation equipment and emergency drugs kept ready. After obtaining venous access with normal sized vein flow as per vein size an infusion of Ringer solution was started. The patient was connected to multi parameter monitor who records HR, non-invasive measurements of SBP, DBP, MAP, $EtCO_2$, SpO_2 and continuous ECG monitoring. The baseline readings were recorded. After that, all patients were pre-medicated with injection Midazolam (0.25mg/kg), Glycopyrrolate (0.004mg/kg) and Fentanyl (2 mcg/kg) intravenously 10 minutes prior to procedure. Then patient was preoxygenated with 100% oxygen for 3 minutes via a face mask with Bain's circuit. Patient was induced with Etomidate 0.2 mg/kg loading dose. An additional dose of Etomidate 0.1 mg/kg was given intravenously if needed. Induction of anaesthesia was confirmed by loss of verbal communication with the patient and loss of eyelash reflex. Once an adequate depth of anaesthesia was achieved the patients were mask ventilated with 100% oxygen throughout operative time. Injection ondansetron 4 mg used to all for postoperative vomiting prophylaxis.

Recorded parameters

Haemodynamic parameters were recorded in all patients. Parameters were recorded at pre-operatively, 1 min, 2 min, 3 min, 4 min, 5 min, 10 min, 15 min and 20 minutes after induction. All parameters were also recorded post-operatively at 1 hour after completion of surgery. At the end of the operation, anaesthetic agents were discontinued allowing smooth recovery of consciousness. When the patient responded to verbal command to open the eyes, he was shifted to recovery room.

Statistical analysis

The data were analyzed using SPSS version 20 software for windows 7. All recorded data were expressed as mean ± S.D or mean (range) as appropriate. Paired t test was used for analysis of numerical data (HR, SBP, DBP, and MAP) in Intra-group comparison. The data of patients with co-morbid conditions were also analyzed for changes in a heart rate, systolic blood pressure, diastolic blood pressure, and mean arterial pressure. P-value of less than 0.05 was taken to be statistically significant.

Observation and Results

In this study we enrolled 108 patients, in which 100 patients were included while eight patients were excluded from study because of non-meeting of the inclusion criteria (patient refusal {n=1} and prolonged surgical time {n=7} who were managed with laryngeal mask airway; were the reason for these excluded patients). The results of 100 patients were observed and analyzed.

Demographic details of the participants (Table 1).

Mean age of patients was 63 years (62.94 ± 9.2691), while majority of the patients were male (62%) and belong to the age group of 51-60 years. Mean weight (kilograms) of patients was 64.64 kg ± 6.6447. In this study enrolled 83 patients were of ASA physical status-II; while 17 patients were of ASA physical status-III.

In this prospective study 46 patients presented with co-morbid illnesses i.e. Diabetes Mellitus, Hypertension, Chronic obstructive pulmonary disease, Ischemic heart disease and pulmonary tuberculosis etc. Majority of the patients were hypertensive (15 Hypertensive + 9 Diabetic-Hypertensive patients). We only enrolled patients undergoing short duration surgical procedures. The observed mean time in our study was 7.05 ± 1.707 minutes for completion of these surgical procedures. Majority of operative procedures were Visual internal urethrotomy (26%), swelling excision (22%) and closed joint reductions (17%).

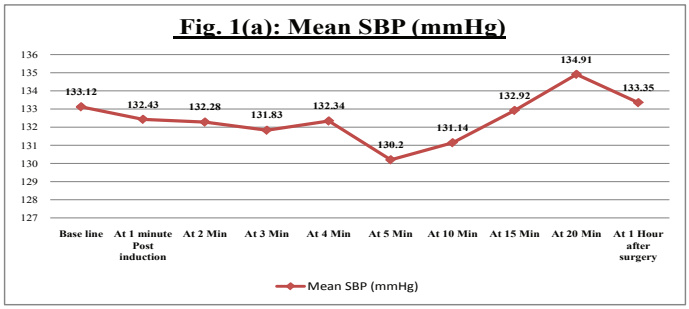
Haemodynamic stability

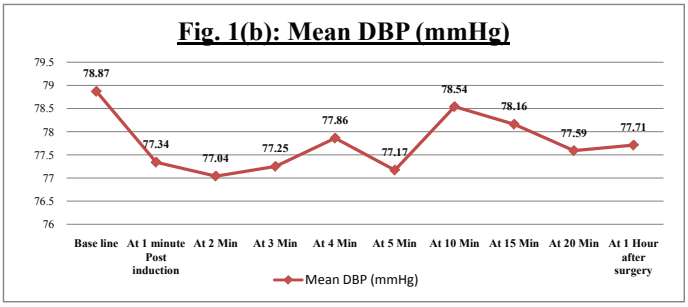
The comprehensive and statistical analysis of changes in mean heart rate, mean SBP, mean DBP, and mean MAP values in response to administration of Etomidate at various time intervals were observed [Table 1, Figure 1(a,b,c,d)).

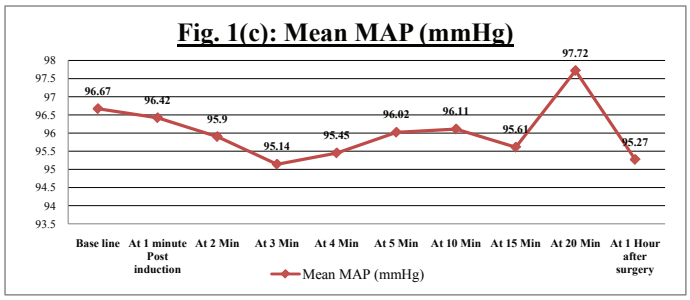
Baseline mean heart rate was 81.34 ± 11.29 beats per minute. Mean heart rate remained near to baseline values from the pre-operative time to till 1 hour of completion of surgical procedures. When the differences in changes of mean heart rate at various intervals were compared with baseline mean heart rate, it was found to be statistically insignificant (P>0.05). Baseline systolic blood pressure was 133.12 ± 12.86 mmHg. Mean SBP values remained near to baseline values from the pre-operative time to till 1 hour of completion of surgical procedures. When the differences in changes of mean systolic blood pressure at various intervals were compared with baseline Mean SBP, it was found to be statistically insignificant (P>0.05). Mean DBP values remained near to baseline values

Table 1: Changes in mean values of haemdynamic parameters from base line readings after administration of Etomidate for completion of short surgical procedures.

Heart rate	Mean HR ± S.D. (BPM)	Mean SBP ± S.D. (mmHg)	Mean DBP ± S.D. (mmHg)	Mean MAP ± S.D. (mmHg)
Base line	81.34 ± 11.29	133.12 ± 12.86	78.87 ± 7.14	96.67 ± 8.37
At 1 minute Post induction	82.89 ± 10.06	132.43 ± 11.56	77.34 ± 6.71	96.42 ± 7.77
At 2 Min	82.48 ± 9.34	132.28 ± 11.45	77.04 ± 7.12	95.9 ± 7.96
At 3 Min	83.25 ± 9.38	131.83 ±10.14	77.25 ± 7.42	95.14 ± 7.97
At 4 Min	83.57 ± 9.40	132.34 ± 11.06	77.86 ± 7.39	95.45 ± 7.94
At 5 Min	84.04 ± 8.95	130.2 ± 10.11	77.17 ± 7.35	96.02 ± 7.47
At 10 Min	83.94 ± 8.82	131.14 ± 9.17	78.54 ± 6.30	96.11 ± 6.40
At 15 Min	83.84 ± 8.93	132.92 ± 9.25	78.16 ± 6.13	95.61 ± 6.95
At 20 Min	82.92 ± 10.07	134.91 ± 8.70	77.59 ± 6.56	97.72 ± 6.42
At 1 Hour after completion of surgery	82.02 ± 9.72	133.35 ± 8.76	77.71 ± 6.38	95.27 ± 6.44







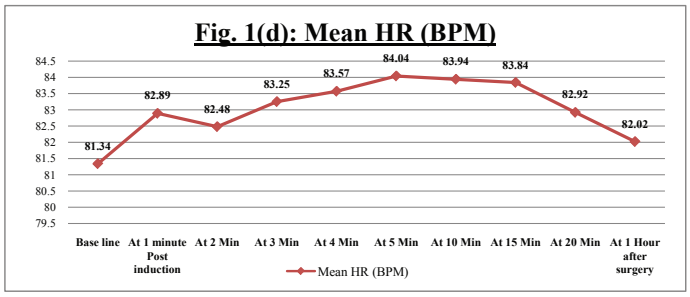


Figure 1(a-d): Graphical changes in mean values of haemdynamic parameters from base line readings after administration of Etomidate for short surgical procedures

(78.87 ± 7.14) from the pre-operative time to till 1 hour of completion of surgical procedures. When the differences in changes of mean diastolic blood pressure at various intervals were compared with baseline mean DBP, it was found to be statistically insignificant (P>0.05). Baseline MAP was 96.67 ± 8.37 mmHg. Mean MAP values remained near to baseline values from the pre-operative time to till 1 hour of completion of surgical procedures. When the differences in changes of mean MAP at various intervals were compared with baseline mean MAP, it was found to be statistically insignificant (P>0.05). We have not found any significant difference in SpO_2 at different time intervals in intra-operative period and post-operative period compared to baseline value.

As evident from the observation and result in our study, we observed and conservatively managed few of known complications. These were apnea (4%), myoclonus (18%), pain on injection (24%) and PONV (12%).

Discussion

Induction of anaesthesia is a critical part of anaesthesia practice, sudden hypotension, arrthymias, cardiovascular collapse are threatening complications, following administration of most of induction agents in haemodynamically unstable, old aged patients and even in haemodynamically stable patients. It is desirable to use a safe agent with least adverse effects of this purpose. An ideal intravenous anesthetic induction agent should provide a rapid but pleasant abolition of consciousness with minimal cardiovascular alterations, possess no side effects and have a short duration of action. Currently anaesthetic agents for induction are available in India as well as in United States are propofol, thiopentone sodium, ketamine and etomidate. Unfortunately, no one is ideal induction agents due to their own side effects. Myocardial and respiratory depression are very common with both propofol and sodium thiopental while ketamine has its specific bad emergence properties. [4-6].

Etomidate has minimal haemodynamic and ventilatory depression effects and does not trigger histamine release. Cardiovascular and Respiratory systems appear to be minimally affected and there is no indication of organ toxicity or other biochemical or haematological drug-induced disturbance. [7,8].

Haemodynamic stability has been a hallmark of the induction of anesthesia with etomidate since this drug was introduced into clinical practice in the late 1970s. Etomidate produces minimal cardiovascular effects in healthy patients, as it maintains autonomic nervous system reflexes and preserves myocardial contractility [8-10]

At typical anesthetic induction doses produces minimal blood pressure and heart rate changes in patients, including those with valvular or ischemic heart disease [8,9,11-13].

Our findings of etomidate on mean heart rate corroborates with the comparative study of Mousumi Das, Basant ku Pradhan, Ramesh ch Samantray et al, 2015 [14]. As from their study; In etomidate group, pre induction heart rate was 82.10 ± 5.24 bpm. In post induction heart rate was 80.76 ± 5.27 and after intubation 0 min, 1min, 3min, 5min and 10 min heart rate were 83.56 ± 5.06, 82.2 ± 4.91,82.73 ± 4.98,81.63 ± 4.8 and 82.33 ± 5.2 respectively. There were no significant changes in heart rate in post induction and after intubation as compared with pre induction. Also, there were no significant changes after intubation as compared with post induction. Our findings of etomidate on SBP corroborates with the comparative study of Mousumi Das, Basant ku Pradhan, Ramesh ch Samantray et al, 2015 [14]. As from their study; In etomidate group pre induction SBP was 123.7 ± 5.54 mm Hg. In post induction SBP found 121.93 ± 5.43. Again, SBP after intubation 0 min, 1min, 3min, 5min, 10min were 124.03 ± 5.65, 123.93 ± 5.66, 123.43 ± 5.3, 122.56 ± 5.13, and 123.13 ± 5.7 respectively. There were no significant changes in SBP in post induction and after intubation compared to pre induction value and also no significant change after intubation compared to pre induction and post induction value.

Our findings of etomidate on DBP corroborates with the comparative study of Mousumi Das, Basant ku Pradhan, Ramesh ch Samantray et al, 2015 [14]. As from their study; In etomidate group, pre induction DBP was 81.5 ± 4.82. In post induction, DBP was 79.16 ± 4.68 mm Hg. After intubation 0 min, 1min, 3min, 5min, 10min DBP were 81.36 ± 4.77, 81.32 ± 4.78, 81.3 ± 4.7, 79.9 ± 4.9 and 81.93 ± 5.0 respectively. There were no significant changes in DBP in post induction and after intubation compared to pre induction and after intubation compared to post induction. Our

findings of etomidate on MAP corroborates with the comparative study of Mousumi Das, Basant ku Pradhan, Ramesh ch Samantray et al, 2015 [14]. In etomidate group pre induction MAP was 95.99 ± 4.88 mm Hg. In post induction MAP was 93.4 ± 4.7 and after intubation 0 min, 1min, 3min, 5min and 10 min MAP were 95.85 + 4.82, 95.29 + 4.65, 95.29 ± 4.64, 95.29 ± 4.64 and 95.99 ± 4.8 respectively. There were no significant changes in MAP in post induction and after intubation compare to pre induction and after intubation compare to post induction.

These haemodynamic findings on mean HR, mean SBP, mean DBP and Mean MAP of this study corroborates with the study reports of Ebert TJ, Muji M, Berens R et al, 1992, [8] Gooding JM, Corssen G et al, 1977, [15] Vanacker B, Wiebalck A, Vanaken H et al, 1993, [16] Kulka PJ, Bremer F, J Schuttler et al, 1993,[17] Zaugg M, Luccinetti E et al, 2002, [18] and Paris A, Philipp M, Tonner PH et al, 2003 [19].

Etomidate blocks adrenal steroidogenesis and hence cortisol synthesis, by its action on 11β-hydroxylase and cholesterol cleavage enzymes, and consequently decreases the hyperglycaemic response to surgery by approximately 1 mmol per litre in non-diabetic subjects [20]. The effects of etomidate on diabetic patients have not been established.

Conclusion

Short recovery time, lack of hemodynamic instability at usual doses, relative low frequency of adverse drug reactions during the use of etomidate, provides optimal and safe conditions for short surgical procedures in critically ill, hemodynamic unstable patients and >50 years age group population with co-morbid illnesses.

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