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www.jmscr.igmpublication.org Impact Factor (SJIF): 6.379 Index Copernicus Value: 71.58 ISSN (e)-2347-176x ISSN (p) 2455-0450 crossref DOI: \_https://dx.doi.org/10.18535/jmscr/v6i4.09

IGM Publication

Journal Of Medical Science And Clinical Research An Official Publication Of IGM Publication

### Comparison of Post Induction Haemodynamic Response after Induction with Etomidate versus Propofol-Ketamine Combination

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### Introduction

Anesthesia is a unique medical intervention which does not itself offer any particular medical benefit and instead enables the performance of other medical interventions. The best anesthetic is therefore one with the lowest risk to the patient that still achieves the end points required to complete the other intervention.

Endoscopic approach of spine surgery has almost entirely replaced the conventional approach of open spine surgery<sup>[1]</sup> because of its advantages over the open surgery in terms of small incision, less tissue trauma, minimal blood loss, improved illumination and visibility, early return to activity and work, easier operative approach in obese patients, easier revision surgery because of less scar tissue in the access portal, lower complication rates, lower cost due to shorter operating times shorter inpatient stay. Moreover and the postoperative pain and the need for postoperative analgesics is meagre.

Propofol is a widely administered hypnotic agent that is of unique advantages yet some disadvantages.<sup>[2,3]</sup> Satisfactory recovery, short half-life, rapid elimination from the blood circulation, lesser sedative affect and vomiting are the reasons for using this drug more commonly.<sup>[4]</sup> Induction of anesthesia with propofol is associated with significant hemodynamic instability, which is more dramatically seen in patients with known hypotension and ASA physical status more than II.<sup>[5,6]</sup>

Ketamine is another anesthetic agent used for both induction and maintenance of general anesthesia. It is known to produce sympathomimetic effects via both central and peripheral mechanisms.<sup>[7]</sup> It is known to preserve respiratory drive, and its sympathomimetic properties result in an increase in blood pressure and heart rate, making it an appropriate choice for cases in which decrease in heart rate and blood pressure is feared; for instance in old patients with compromised cardiac conditions.<sup>[8,9]</sup>

The combination of propofol and ketamine for total intravenous anesthesia has shown to minimize the side effects of each drug used alone. Total intravenous anesthesia with propofol and ketamine proved to be very satisfactory from a clinical point of view.<sup>[10]</sup>

Etomidate is an anesthesia induction agent with minimal cardiovascular side effects making it especially useful for cardiac-compromised patients and for those in whom hypotension must be avoided during induction of anesthesia.<sup>[11,12]</sup>

Hence, the present study was conducted with aim to evaluate the hemodynamic changes during induction with etomidate and ketamine + propofol combination in order to find the efficient drug in establishing more stable hemodynamic parameters during intubation and post intubation in patients undergoing endoscopic spine surgeries.

### Aim

The aim of this study is to compare haemodynamic response after induction with etomidate versus propofol-ketamine combination.

### Objectives

- 1. Assessment of variation of the baseline hemodynamic parameters, following induction – SBP, DBP, MAP, HR.
- 2. Assessment of time taken for the above parameters to come back to the baseline values.

### **Material and Methods**

### **Place of Study**

The present study was conducted in Neurosurgery Operation Theatre in Department of Anaesthesiology.

### **Study Population**

Study population consisted of all the in-patients electively posted for endoscopic spine surgery during the study period.

### Sample Size

In the present study, we had included 60 patients fulfilling all the inclusion criteria and none of the exclusion criteria. The sampling technique used for convenient sampling.

### **Study Design**

Prospective, randomized, comparative and observational study.

### Time Frame to address the Study

The study duration was one year.

### Grouping

All the patients were divided into two groups:

Group A (n=30): Patients were anaesthetized with propofol and ketamine. These patients were

induced with 0.75 mg/kg ketamine and 1 mg/kg propofol.

Group B (n=30): Patients were anaesthetized with etomidate. These patients were induced with 0.2 mg/kg etomidate.

### Randomization

The randomization of the patients was done using computer generated numbers.<sup>[13]</sup> Available from: https://www.random.org/integers/

Here are your random numbers:

Group A	Group B
483	978
671	88
373	358
466	57
497	412
842	781
325	225
677	895
639	215
220	995
808	25
19	88
787	310
359	858
847	781
568	275
655	221
175	621
821	640
305	116
134	769
765	258
318	997
722	769
452	263
474	675
502	611
124	164
878	146
703	296

### **Inclusion Criteria**

- 1. 60 patients of ASA physical status I and II
- 2. Age between 20 to 60 years undergoing endoscopic spine surgery
- 3. Patient and/or his/her legally acceptable representative willing to provide their voluntary written informed consent for participation in the study

### **Exclusion Criteria**

- 1. Emergency surgery
- 2. Patients who received sedatives and anti psychotic drugs in the last month.
- 3. Patients with personality disorder.
- 4. Patients with contraindications to etomidate, ketamine or propofol.
- 5. Patients with autonomic neuropathy or inherent unstable haemodynamics.
- 6. Patient and/or his/her legally acceptable representative not willing to provide their voluntary written informed consent for participation in the study

### Methodology

Each patient and/or his/her legally acceptable representative was explained in the detail about the study, its risks / benefits, procedures, etc. in detail and after getting their verbal consent, a voluntary written informed consent was obtained.

A detailed history, thorough physical examination, routine investigation and any special investigation if required was done for the study.

After careful pre anaesthetic examination and investigations, the patient was shifted to operation theatre. After shifting patients to operation theatre, routine monitoring devices such as ECG leads, non invasive BP cuff, pulse oximetry probe was setup.

Patients were allowed overnight fasting for at least 8 hrs, before surgery and an intravenous access will be established. Patients received fentanyl (1mcg/kg), midazolam (0.03 mg/kg) intravenously as premedication. Then patients were randomly assigned into groups receiving either ketamine+ propofol (ketofol) (n=30) or etomidate (n=30). In ketofol group, patients were induced with 0.75 mg/kg ketamine and 1 mg/kg propofol. Etomidate group patients were induced with 0.2 mg/kg etomidate. Intubation and maintenance was facilitated with injection vecuronium.

Isoflurane was used as an inhalation agent for maintenance of anaesthesia. At the end of the procedure, neuromuscular blockade was reversed with neostigmine 0.05mg/kg and glycopyrrolate 80mcg/kg intravenously. Patients were extubated when they regained spontaneous respiration and obeyed simple verbal commands.

### **Outcome Measures**

Demographic findings were recorded for each patient. Hemodynamic variables including systolic blood pressure (SBP) and diastolic blood pressure (DBP), mean blood pressure (MAP) and heart rate (HR) were recorded before induction, and after induction at two, four, six, eight, ten, fifteen, twenty and thirty minutes.

### **Data Collection Methods**

A customized proforma was designed for the purpose of the study, which was approved by the Ethics Committee was used for collection of the data.

### **Statistical Analysis**

The data from the customized proforma was entered into the Microsoft Excel. The statistical software IBM SPSS (Chicago) Version 21.0.0.0.was used for analysis. The mean comparisons between the groups was done using unpaired 't' test and within the group was done using paired 't' test. A p value of < 0.05 was taken as statistically significant. The final data was presented in the form of graphs and tables.

### **Ethical Considerations**

The protocol of the study was submitted to the Ethics Committee of our institution. After getting the approval from the committee, the study was initiated in the institution. Also prior to enrollment of the patient into the study, a written voluntary informed consent was obtained from the patient and/or his/her legally acceptable representatives. This informed consent was in addition to the other consents that are routinely taken for the management of the condition.

### **Financial Inputs and Funding**

There was no additional test / procedure conducted for the specific purpose of the study, hence there was no additional financial burden

either on the patient and/or the institution. All the costs towards the conduct of the study were borne by the investigator. Also this study was not funded by any pharmaceutical company or institution.

### Results

In the present study there were 60 patients of ASA grade more than II, divided into 30 patients in each group – Group A (n=30) and Group B (n=30).

In both the groups there was a male preponderance in comparison to the females (66.7% versus 33.3%), with a mean age of  $41.60 \pm$  9.39 years in Group A and  $41.87 \pm 12.03$  years in Group B. The difference was found to be statistically not significant (P>0.05), showing a comparable age between the two groups.

The mean height in Group A was  $158.40 \pm 3.14$  cm and in Group B it was  $158.30 \pm 2.98$  cm. The difference was found to be statistically not significant (P>0.05), showing a comparable height between the two groups.

The mean weight in Group A was  $61.10 \pm 3.91$  kg and in Group B it was  $59.77 \pm 4.64$  kg. The difference was found to be statistically not significant (P>0.05), showing a comparable weight between the two groups.

### **Heart Rate**

There was statistically no significant difference in the mean heart rate between the groups at all the time intervals (P>0.05), showing a comparable mean heart rate. The mean heart rate till 10 minutes was significantly higher in Group A in comparison to the preoperative level (P<0.05), while in Group B it was significantly higher till 20 minutes (P<0.05). [Graph 1]

### Systolic Blood Pressure

There was statistically no significant difference in the mean systolic blood pressure between the groups at all the time intervals (P>0.05), showing a comparable mean systolic blood pressure. The mean systolic blood pressure was significantly higher at 2 min, while it was significantly lower till 20 minutes in Group A in comparison to the preoperative level (P<0.05), while in Group B it was significantly higher at 2 min, while it was significantly lower till 15 minutes (P<0.05). [Graph 2]

### **Diastolic Blood Pressure**

There was statistically no significant difference in the mean diastolic blood pressure between the groups at all the time intervals (P>0.05), showing a comparable mean diastolic blood pressure. The mean diastolic blood pressure was significantly lower till 20 minutes in Group A in comparison to the preoperative level (P<0.05), while in Group B it was significantly lower till 15 minutes (P<0.05). [Graph 3]

### **Mean Arterial Pressure**

There was statistically no significant difference in the mean arterial pressure between the groups at all the time intervals (P>0.05), showing a comparable mean arterial pressure. The mean arterial pressure was significantly lower till 15 minutes in Group A in comparison to the preoperative level (P<0.05), while in Group B it was significantly lower till 15 minutes (P<0.05). [Graph 4]

### **Return To Baseline Values**

The mean time taken (min) for all the hemodynamic parameters (viz. heart rate, systolic blood pressure, diastolic blood pressure, and mean arterial pressure) to return to baseline values in Group A was  $27.57 \pm 3.18$  min, while in Group B it was  $26.10 \pm 2.59$ . [Graph 5]

81.03 80.57

**Beats Per Mins** 

*'*5.07

74.40

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74.97

<del>74</del>:37







### **Diastolic BP Monitoring** ----Group A ----Group A 80.60 79.40 79.00 78:63 79.07 78.40 78.10 77.17 77.03 76.03 75.93 mmHg 75.13 74.83 74.27 4.93 72.83 8min PRE OP 2min 4min 6min 10min 15min 20min 30min

Graph 3



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# Time taken for the parameters to come back to the baseline values (Min) 27.57 26.10 100</



### Discussion

Hemodynamic parameters (viz. heart rate, systolic blood pressure, diastolic blood pressure, and mean arterial pressure) were comparable in both the groups at all the time intervals in our study. These results corroborate with the studies done by Hosseinzadeh et al (2013)<sup>[14]</sup>, Aghdaii et al (2015).<sup>[15]</sup>

In our study, we found an initial rise in heart rate and then fall in the heart rate in both the groups. Our study show the same trend as shown by the study done by Bajwa et al (2010)<sup>[10]</sup> and Joghataie et al (2009).<sup>[16]</sup>

In our study, we found and initial fall in systolic as well as diastolic blood pressure, then a rising trend was seen in both the groups. The systolic and diastolic blood pressure reached preoperative baseline values after 20 minutes approximately. Our study results are in accordance with the study done by Hosseinzadeh et al (2013)<sup>[14]</sup> and Nahidaghdaii et al (2015)<sup>[15]</sup>.

In our study, we found and initial fall in mean arterial pressure, then a rising trend was seen in both the groups. The mean arterial pressure reached preoperative baseline value in approximately 20 minutes in Group A and in 15 minutes in Group B, post induction. Our study results are in accordance with the study done by Hosseinzadeh et al  $(2013)^{[14]}$  and Nahidaghdaii et al  $(2015)^{[15]}$ .

### Conclusion

We conclude that both Ketamine+Profofol combination and Etomidate alone showed comparable hemodynamic stability in endoscopic spinal surgery. Thus, either of them can be used in endoscopic spinal surgery without any hemodynamic instability.

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