A COMPARATIVE STUDY OF ETOMIDATE LIPURO (0.2%) AND PROPOFOL (1%) FOR INDUCTION OF ANESTHESIA AND HAEMODYNAMIC CHANGES IN VARIOUS DAY CARE SURGICAL PROCEDURES

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ABSTRACT
BACKGROUND: To evaluate the effect of Etomidate and Propofol by comparing certain parameters such as change in blood pressure, heart rate during induction and intubation as a primary outcome and post operative nausea and vomiting, pain on injection, myoclonus and thrombophlebitis as a secondary outcome. Materials and Methods: 80 patients ASA grade I and II of age 20 to 60 years undergoing various day care surgical procedures were taken and randomly divided into two groups each of 40. Etomidate Group 1 was given 0.3 mg/kg body weight of etomidate. Propofol Group 2 was given 2.5 mg/kg body weight of propofol. Conclusion: We have concluded from the present study that 0.2% of Etomidate Lipuro in the dose of 0.3mg/kg body weight is afer for day care surgical procedure and especially in hemodynamically compromised patients.

KEYWORDS
Day care surgery, Etomidate, Propofol.

Introduction
Day care surgical procedures are known as “an operation or procedure, an office or outpatient operation/procedure, where the patient is discharged on same working day” by an international association of ambulatory surgery.

The advantages of day care surgical procedures includes better use of resources and also a cut of cost, minimal psychological disturbances for patient, hospital acquired infection and venous thromboembolism and early mobilization.

Propofol, 2,6 di-isopropylphenol, is most popular induction agent with its favorable characteristic of rapid and smooth recovery and decreased incidence of nausea and vomiting. 1-3 The major drawbacks are decrease in blood pressure, dose dependent depression of ventilation, pain on injection.

Etomidate Lipuro is a carboxylated imidazole derivative, achieve rapid intravenous induction with hemodynamic stability, cerebral protection and minimal respiratory depression. Etomidate Lipuro 1,2,3 lacks effect on sympathetic nervous system, baroreceptor reflex regulatory system and it increases coronary perfusion even in moderate cardiac dysfunction patients makes it an induction agent of choice in cardiac disease patient. Drawbacks are pain on injection, thrombophlebitis and myoclonus. 4-7

This study was attempt to evaluate the effect of Etomidate and Propofol by comparing certain parameters such as change in blood pressure, heart rate during induction and intubation as a primary outcome and post operative nausea and vomiting, pain on injection, myoclonus and thrombophlebitis as a secondary outcome.

Materials and method
The study was conducted in the Department of Anaesthesia, National institute of medical sciences and research, jaipur, after taking approval from the ethical committee. The study included 80 patients ASA grade I and II of age 20 to 60 years undergoing various day care surgical procedures.

Uncooperative patient, patients with h/o convulsions, allergy to the drugs used, bleeding disorders, severe neurological deficit or respiratory, cardiac, hepatic or renal failure were not included. A complete pre anaesthetic check-up with all the basic investigations was done a day before surgery. Informed consent was obtained for performance of surgical procedure under anaesthesia after complete explanation about the study protocol.

The patients were randomly divided into two groups each of 40 persons. The patients were preoxygenated with 100% O2 for at least 3 minutes. Etomidate Group 1 was given 0.3 mg/kg body weight of etomidate and premedication of midazolam (0.02 mg/kg) and fentanyl (2µg/kg). Propofol Group 2 was given 2.5 mg/kg body weight of propofol and premedication of midazolam (0.02 mg/kg) and fentanyl (2µg/kg). The loss of consciousness was assessed by the help of eyelash reflex, breath holding and muscle relaxation.

Myoclonus was given score according to the following grading scale 1.
0. No myoclonus
1. Minor myoclonus
2. Moderate myoclonus
3. Severe myoclonus

Pain was measured by using four grading scale 1.
0. No pain
1. Verbal complain of pain
2. Withdrawal of arm
3. Both verbal complain and withdrawal of arm

Anaesthesia was maintained with O2 and N2O with light fitting face mask via Bain circuit. Intraoperative drug was repeated if required. Administration of muscle relaxant in the form of short acting NDMR was done in case it is required. Intraoperatively BP, pulse rate and spo2 was monitored 1st to five minute continuously then every 5 min up to 15 mins. Rest of the anaesthesia was continued according to standard clinical practice.

Results:
80 patients were taken for day care surgical procedures. Observation during intra operative period includes readings of baseline heart rate, systolic blood pressure, diastolic blood pressure, mean blood pressure, readings of clinical variables at 1-5 minutes continuously thereafter at 10th minute and at 15th minutes in both groups. Postoperatively nausea and vomiting, myoclonus, pain on injection and thrombophlebitis were observed.
Mean age in years in Etomidate group was 30.9±8.3 and mean age in years in Propofol group was 32.3±10.2. (Table 1,2) The mean and standard deviation of Baseline HR was 89.2±9.9 in etomidate group and 86.6±11.1 in group propofol. Baseline SBP was 129.8±12.7 in Group 1 and 130.3±10.0 in group 2. Baseline DBP was 87.5±5.1 in group 1 and Baseline DBP was 85.7±1.0 in group 2. (Table 1,2) The mean and standard deviation of heart rate at 1st minute was 91.0±13.3. Systolic Blood Pressure was 126.9±13.1, Diastolic Blood Pressure was 85.6±6.4 and Mean BP was 85.6±6.4 in Etomidate group and HR was 81.7±11.7, Systolic Blood Pressure was 126.4±9.9, Diastolic Blood Pressure was 81.7±7.3 and Mean BP was 96.6±7.5 in Propofol group.

There is no significant difference in the heart rate of etomidate group in comparison to baseline (p value >0.05), and there is significant difference in HR, SBP, DBP and MBP in the propofol group in comparison to baseline (p value <0.05). (Table 1,2)

In 2nd minute mean and standard deviation of heart rate was 86.3±10.1, Systolic Blood Pressure was 125.8±10.5, Diastolic Blood Pressure was 85.2±5.1 and Mean BP was 98.7±5.1 in Etomidate group and HR was 71.8±10.0, Systolic Blood Pressure was 115.3±11.2, Diastolic Blood Pressure was 75.4±7.0 and Mean BP was 88.7±7.7 in Propofol group.

There was significant difference in HR, SBP, DBP and MBP in both groups in comparison to baseline (P value <0.05). (Table 1,2)

In 3rd minute mean and standard deviation of heart rate was 87.3±10.1, Systolic Blood Pressure was 126.8±10.5, Diastolic Blood Pressure was 86.2±5.1 and Mean BP was 99.7±5.1 in Etomidate group and HR was 71.8±10.0, Systolic Blood Pressure was 106.6±11.4, Diastolic Blood Pressure was 70.9±6.8 and Mean BP was 82.8±7.7 in Propofol group.

There is no significant difference in the diastolic blood pressure of the etomidate group (p value >0.05) in comparison to baseline. And there is significant difference in all the other parameters of both the groups (p value <0.05). (Table 1,2)

In 4th minute mean and standard deviation of heart rate was 89.3±9.8, Systolic Blood Pressure was 128.7±10.8, Diastolic Blood Pressure was 88.0±4.9 and Mean BP was 101.6±5.2 in Etomidate group and HR was 69.0±9.3, Systolic Blood Pressure was 100.6±11.2, Diastolic Blood Pressure was 67.9±6.5 and Mean BP was 78.4±7.6 in Propofol group.

There is no significant difference in any parameter in etomidate group (p value >0.05) but in propofol group there is significant difference in all the parameters (p value <0.05). (Table 1,2)

In 5th minute mean and standard deviation of heart rate was 89.4±9.5, Systolic Blood Pressure was 128.8±10.7, Diastolic Blood Pressure was 88.3±5.0 and Mean BP was 101.8±5.2 in Etomidate group and HR was 69.5±8.3, Systolic Blood Pressure was 102.3±8.2, Diastolic Blood Pressure was 69.9±5.6 and Mean BP was 80.7±6.5 in Propofol group.

In etomidate group, there is no significant difference in any clinical variables (p value >0.05) but there is significant difference in all the clinical variables in propofol group (p value <0.05). (Table 1,2)

In 10th minute mean and standard deviation of heart rate was 86.4±11.4, Systolic Blood Pressure was 116.3±12.5, Diastolic Blood Pressure was 78.0±5.2 and Mean BP was 90.8±6.6 in Etomidate group and HR was 73.9±9.0, Systolic Blood Pressure was 106.1±7.6, Diastolic Blood Pressure was 74.8±6.5 and Mean BP was 95.2±5.8 in Propofol group.

There is no significant difference in the heart rate of the etomidate group (p value > 0.05) but there is significant difference in all the parameters in propofol group, (p value <0.05). (Table 1,2)

In 15th minute mean and standard deviation of heart rate was 89.4±11.4, Systolic Blood Pressure was 119.3±12.5, Diastolic Blood Pressure was 81.60±5.1 and Mean BP was 94.1±6.6 in Etomidate group and HR was 78.6±10.0, Systolic Blood Pressure was 117.6±8.1, Diastolic Blood Pressure was 78.8±6.6 and Mean BP was 91.7±6.4 in Propofol group.

There is no significant difference in heart rate of etomidate group (p value >0.05) but in propofol group there is significant difference in all the parameters (p value <0.05). (Table 1,2)

The nausea and vomiting present in 4 patients out of 40 patients in etomidate group and absent in all patients in propofol group and p value between groups is (0.0578). (Table 3)

The Myoclonus present in 2 patients out of 40 patients in etomidate group and absent in all patients in propofol group and p value between groups is (0.2468). (Table 3)

The Thrombophlebitis present in 3 patients out of 40 patients in etomidate group and absent in 4 patients in propofol group and p value between groups is (0.2842). (Table 3)

The pain on injection was reported by 3 patients in etomidate group and by 8 patients in propofol group. There was early awakening in the propofol group. (Table 3)

There was significant difference in the side effect of nausea and vomiting, myoclonus and thrombophlebities. (Table 3)

Discussion
Etomidate is an ultra short acting non barbiturate hypnotic agent which is used for induction of general anaesthesia. Etomidate lipuro is a pharmaceutical formulation in which the water insoluble active ingredient Etomidate is dissolved in an emulsion – containing medium and long chain triglyceride which acts as drug vehicle. Etomidate causes good and readily controlled induction of anesthesia with rapid onset of action and pleasant induction phase. With etomidate lipuro, some adverse effects like phlebitis, thrombosis and thrombophlebities have been eliminated while other e.g. myoclonus have been substantially reduced.

Effect on Pulse Rate and blood pressure
In both the groups pre-operatively a basal; tachycardia was noted. This could be attributed to the anxiety of anaesthesia and surgery. After induction with etomidate, these changes in pulse rate were statistically insignificant. Etomidate showed more stability in pulse rate than propofol.

Fall in blood pressure was observed after etomidate as well as propofol induction. Partly it could be due to removal of anxiety of anaesthesia and surgery and partly due to effect of drugs on the cardiovascular system. This transient fall in blood pressure was statistically insignificant in etomidate group and significant in propofol group. These finding are in agreement with those of various worker like Fatma saricaoglu et al (2011) and James R Miner et al(2007). They also concluded that pulse rate and blood pressure were found to be more stable in etomidate group then the propofol group.

Time to Loss of Consciousness
After administration of etomidate and propofol in their respective group, loss of consciousness time was faster in etomidate group than the propofol group. This finding is in agreement with J. Schaeuble, et al(2005) and fatma saricoglu et al(2011).

Nausea and Vomiting
Nausea and vomiting was reported in 4 patients out of 40 patients in etomidate group and no such complained was reported in propofol group. This finding was similar with M. St Pierre et al (2000), who concluded that the intensity of nausea was very low in both the groups. The incidence of vomiting was higher in women receiving etomidate and it does not increase nausea during the early postoperative period.
**Myoclonus**

Myoclonus present in 2 patients out of 40 patients in etomidate group and absent in all patients in propofol group and p value between groups is (0.2468). the result of our study comply with Fatma Saricagolu et al (2011), who concluded that higher incidences of myoclonic activity were seen in Etomidade Lipuro group when compared with Propofol and Etofol and also comply with Aaggarwal S et al (2016).

**Thrombophlebitis**

This finding was positive in 3 patients out of 40 patients in Etomidade group and 4 patients in Propofol group.

**Pain on Injection**

Pain on injection was reported by 3 patients in etomidate group and by 8 patients in propofol group. This finding was similar with the studies of Fatma Saricaoglu et al (2011) and Tan CH et al (1998).

**Conclusion**

We have concluded from the present study that 0.2% of Etomidade Lipuro in the dose of 0.3mg/kg body weight is safer for day care surgical procedure and specially in hemodynamically compromised patients because in the present study we found that in etomidate group heart rate, systolic blood pressure, diastolic blood pressure and mean blood pressure remain stable throughout the procedure in comparison to propofol. There were fewer incidences of nausea and vomiting, pain on injection, myoclonus and thrombophlebitis in comparison to propofol and previous preparation of etomidate.

**Table 1. Clinical variables mean±SD in Etomidade group at different time intervals**

<table>
<thead>
<tr>
<th>Clinical variables</th>
<th>1st min</th>
<th>2nd min</th>
<th>3rd min</th>
<th>4th min</th>
<th>5th min</th>
<th>10th min</th>
<th>15th min</th>
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<tbody>
<tr>
<td>Heart rate</td>
<td>89.2±9</td>
<td>91.0±9</td>
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<tr>
<td>Diastolic blood pressur e</td>
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<td>85.6±5.4</td>
<td>85.2±5.1</td>
<td>86.2±5.1</td>
<td>88.0±4.9</td>
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<tr>
<td>Mean blood pressur e</td>
<td>103±7.6</td>
<td>99.2±7.6</td>
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<td>101.6±5.2</td>
<td>101.8±5.2</td>
<td>90.8±5.6</td>
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</tbody>
</table>

(*p value<0.05=significant)

**Table 2. Clinical variable mean±SD in propofol group at different time intervals**

<table>
<thead>
<tr>
<th>Clinical variables</th>
<th>1st min</th>
<th>2nd min</th>
<th>3rd min</th>
<th>4th min</th>
<th>5th min</th>
<th>10th min</th>
<th>15th min</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate</td>
<td>86.6±11.1</td>
<td>*81.7±11.7</td>
<td>*75.7±10.5</td>
<td>71.8±9.3</td>
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<tr>
<td>Systolic blood pressur e</td>
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<td>*126.1±11.2</td>
<td>106.6±11.4</td>
<td>100.6±11.2</td>
<td>102.3±8.2</td>
<td>*106.1±7.6</td>
<td>*117.5±8.1</td>
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<tr>
<td>Diastolic blood pressur e</td>
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<td>*81.7±7.0</td>
<td>*75.4±6.8</td>
<td>70.9±6.5</td>
<td>*69.9±5.6</td>
<td>*74.8±6.5</td>
<td>*78.8±6.6</td>
</tr>
</tbody>
</table>

**Mean blood pressure**

|          | 100.1±7.3 | *96.6±7.5 | *88.7±7.7 | 82.8±7.6 | 78.4±6.5 | 80.7±6.5 | 85.2±5.8 |

(*p value<0.05=significant)

**Table 3. Side effects of drugs**

<table>
<thead>
<tr>
<th>Side effects of drugs</th>
<th>Nausea and vomiting</th>
<th>Myoclonus</th>
<th>Thrombophlebitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Etomidate(n=40)number of patients</td>
<td>4</td>
<td>2</td>
<td>4</td>
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<tr>
<td>Propofol(n=40)number of patients</td>
<td>0</td>
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<td>0</td>
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**References**

4. Purcell-Jones and James JG. The characteristics of Propofol (diprivan) for induction of general anaesthesia in paediatric surgery. Postgraduate medical journal. 1985;61(suppl. 3):115.