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Original Research Article

ASSESSING EFFICACY, SAFETY AND RECOVERY PROFILES OF ETOMIDATE VERSUS PROPOFOL FOR FIRST-TRIMESTER SURGICAL ABORTIONS: A COMPARATIVE STUDY

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Abstract

Even today, surgical abortions are generally very safe, but they are not entirely risk-free from either a surgical or anesthetic perspective. Patient safety has always been a major concern for practicing anaesthesiologists and ensure safety during abortion have great public health importance. Pregnant patients (6 to 8 weeks of gestation)aged 18 to 35 y, belonging to ASA Class I & II, weighing between 45 and 65 kg, and with specific height criteria. Exclusions included psychiatric diseases, uterine anomalies, previous cesarean sections, and drug abuse. EMF group: Injection of 0.1% midazolam at 0.02 mL/kg, followed by fentanyl 50 µg/mL at 0.01 mL/kg over 30 seconds. After 2 minutes, 0.2% etomidate was administered at 0.1 mL/kg (2 mg/mL) over 60 seconds. PMF group: Injection of 0.1% midazolam at 0.02 mL/kg, followed by fentanyl 50 µg/mL at 0.01 mL/kg over 30 seconds. After 2 minutes, 1% propofol was administered at 0.1 mL/kg (10 mg/mL) over 60 seconds as per group allocation. Various parameters were noted, including time to loss of consciousness, duration of surgery, time to return to consciousness, time to return to orientation, and recovery time for each patient in each group. We observed faster recovery with etomidate, with significantly shorter time to return to consciousness (44.32 ± 12.72 seconds) compared to propofol (59.52 ± 9.1 seconds). Etomidate consumption was lower (11.6 ± 1.77 mg) than propofol (73.75 ± 8.68 mg), with fewer supplemental doses in the EMF group. In the EMF group, the mean PADSS score at 30 minutes was 6.38 ± 0.67, significantly higher than the mean PADDS score of 5.45 ± 0.5, in the PMF group. At 60 minutes and 90 minutes, the difference in PADDS score was not significant between the two groups. The majority of patients in both groups achieved a mean PADSS score >9 within 120 minutes. Pain on injection was common but lower with etomidate, and myoclonus occurred only in the EMF group (10% incidence). Etomidate's advantages in induction speed, hemodynamic stability, and recovery make it favorable for first-trimester surgical abortions.

INTRODUCTION

First-trimester surgical abortion is the most commonly performed outpatient surgical procedure in women.[1] Even today, surgical abortions are generally very safe, but they are not entirely risk-free from either a surgical or anesthetic perspective. Major complications occur in <1% of cases, and the mortality rate is around 0.7 per 100,000 cases, with anesthesia-related events remaining the leading cause of morbidity for these procedures.[2-5] The decrease in legal abortion-related deaths can largely be attributed to an increase in the level of experience and skill of the providers.[2]

Anaesthetic strategies for first-trimester surgical abortion have been explored for decades and have been modified with the introduction of newer and safer agents.[1,6] Patient safety has always been a major concern for practicing anesthesiologists. Regarding general anesthesia for these procedures, the use of inhalational anesthetics has been replaced by intravenous anesthesia due to the numerous

drawbacks associated with inhalational anesthesia, such as increased procedure-related blood loss and the requirement of a vaporizer attached to the anesthesia machine.[7] Newer intravenous anesthetic induction agents with desirable effects and minimal side effects are available with variable degrees of acceptance.[8] An ideal intravenous anesthetic induction agent should produce minimal disturbance of cardiovascular and respiratory functions, induce sleep within one arm-brain circulation time, be chemically stable, nonirritating to the vein, nontoxic, nonallergenic, easy to administer, and have rapid recovery properties.[8]

Propofol is the most commonly used intravenous induction agent and has achieved widespread use in outpatient surgical procedures because of its rapid recovery profile. However, it is associated with marked respiratory depression and hemodynamic changes.[9,10]

Etomidate, an imidazole derivative used as an intravenous induction agent, is considered a safer alternative with regard to hemodynamic stability and minimum respiratory depression. However, due to side effects such as myoclonus and postoperative nausea and vomiting, it has not gained popularity as an induction agent during surgical abortion. Since these side effects can be reduced by using a combination of benzodiazepines (midazolam) and opioids (fentanyl), the use of etomidate in surgical abortions should be reassessed.[11]

Considering the large numbers of women who undergo first-trimester surgical abortion, studies designed to reduce abortion-related pain and ensure safety during abortion have great public health importance. The aim of the present study was to compare and evaluate the safety, efficacy, and recovery characteristics of propofol and etomidate used with adjunct agents in Indian patients undergoing first-trimester surgical abortion.

MATERIALSANDMETHODS

Study Design

A randomized comparative single blind trial.

Study Location

The research is conducted at the Department of Anaesthesiology and Critical Care, NDMC Medical College, and affiliated Hindu Rao Hospital, Delhi.

Ethics Approval

The study received approval from the Institutional Review Committee, and informed consent was obtained from all patients following a detailed explanation of the study procedures.

Study Duration

The study spanned duration of two years.

Sample Size

The anticipate a difference of 10% in efficacy between the two groups, alpha level (α) at 0.05. (Type I error), statistical power of 80% to achieve the desired power level and detect the assumed difference in efficacy in each group. The formula commonly used for sample size calculation in this scenario is based on comparing two independent proportions:

$n=2\cdot(Z\alpha/2+Z\beta)^2\cdot p\cdot(1-p)/(P_1-P_2)^2$

Zα/2 corresponding to α=0.05 is approximately 1.96

Zβcorresponding to a power of 80% is approximately 0.84P is the assumed average proportion of efficacy across both groups (which would be (p1 + p2)/2)

p1-p2is the assumed difference in efficacy

Therefore, they require a total sample size of **80 patients (**40 patients per group).

Inclusion Criteria

Pregnant patients (6 to 8 weeks of gestation confirmed by ultrasound examination). Age between 18 and 35 years. Patients belonging to ASA Class I and II.[12] Patients weighing between 45and 65 kg. Patients with height between 150 and 170 cm.[6]

Exclusion Criteria

Patients with a history of psychiatric diseases, uterine anomalies, previous cesarean section, emergency abortion, and drug abuse, known hypersensitivity to any anesthetics or adjuvants, and any other severe medical conditions were excluded. Additionally, any patients developing any type of surgical complication at any time during the procedure were also excluded from the study.

Group Allocation

Forty patients each were randomly allocated to one of the following groups:

Group EMF

etomidate, midazolam, fentanyl): etomidate 0.2% administered at 0.1 mL/kg over 60 seconds.

Group PMF

Propofol, midazolam, fentanyl): 1% propofol administered at 0.1 mL/kg over 60 seconds.

Preoperative Preparation

Patients underwent a detailed history, complete physical examination, and routine investigations (including complete blood count, urine analysis, and special investigations as indicated). The anesthetic procedure, as well as the visual analogue scale for nausea and vomiting and visual analogue scale (VAS) of pain, were explained to the patients. All patients were kept nil per orally since the night before the procedure. In the operation theater, patients were placed in the supine position, and baseline parameters (Pulse Rate, Blood pressure, Oxygen saturation, and Electrocardiograph) were recorded before starting the induction. All patients received injection prostaglandin F2α ($PGF_{2\alpha}$) 250-µg IM half an hour before the procedure. Subsequently, all patients were given 100% oxygen via a face mask for 3 minutes prior to the induction of general anesthesia.

Drug Doses and Administration

The study drug solution was prepared by an anesthesiologist not participating in the study to maintain randomization. Observations were conducted by a blinded anesthesiologist. General anesthesia was administered to patients according to the randomization schedule:

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In Group EMF

Intravenous induction was conducted as follows – injection of 0.1% midazolam at 0.02 mL/kg, followed by fentanyl 50 µg/mL at 0.01 mL/kg over 30 seconds. After 2 minutes, 0.2% etomidate was administered at 0.1 mL/kg (2 mg/mL) over 60 seconds as per group allocation.[6]

In Group PMF

Intravenous induction was performed as follows – injection of 0.1% midazolam at 0.02 mL/kg, followed by fentanyl 50 µg/mL at 0.01 mL/kg over 30 seconds. After 2 minutes, 1% propofol was administered at 0.1 mL/kg (10 mg/mL) over 60 seconds as per group allocation.[6]

Parameters Studied: Efficac

Demographic data were recorded, and induction doses, as well as any supplemental bolus doses of propofol or etomidate, were noted. The total dose of propofol or etomidate administered was calculated by adding these values.

Various parameters were noted, including time to loss of consciousness in seconds, duration of surgery in minutes, time to return to consciousness, time to return to orientation, and recovery time (defined as the time in minutes from the end of anesthesia to achieving adequate recovery as denoted by PADDS ≥ 9),[14] for each patient in each group.

Safety Parameters

Side effects during induction and maintenance, such as injection-induced pain, and myoclonus (assessed on a scale of 0 to 3),[15] were noted. The incidence of adverse effects during the intraoperative and postoperative periods was recorded.[16]

Statistical Analysis

Categorical variables were presented in numbers and percentages, while continuous variables were presented as mean ± SD and median. Normality of data was tested using the Kolmogorov-Smirnov test. If normality was rejected, nonparametric tests were utilized. Quantitative variables were compared using unpaired t-tests/Mann-Whitney tests (for non-normally distributed data) between the two groups, and paired t-tests/Wilcoxon rank sum tests were employed for comparison within groups across follow-up. Qualitative variables were correlated using chi-square tests/Fisher's exact tests.*significant **highly significant ***very highly significant.

RESULTS

Patients aged between 18 and 35 years were included in this study. In the EMF group, the mean age was 29.55 ± 4.47 years, and in the PMF group, it was 29.12 ± 4.44years. The age distribution between the two groups was statistically comparable, with a p-value of 0.671. [Table 1]

In our study, early recovery characteristics, including time to return to consciousness and time to return to orientation (the ability to state one's name, age, and place), were significantly faster with etomidate compared to propofol. The time to return to consciousness was notably shorter with etomidate (44.32 ± 12.72 seconds) compared to propofol (59.52 ± 9.1 seconds) (p-value 0.0001). [Table 2]

The total amount of drug consumed during the procedure, including bolus and supplementary doses, was11.6 ± 1.77 mg for etomidate and 73.75 ± 8.68 mg for propofol. Furthermore, the mean number of supplemental doses of propofol in the PMF group (1.72 ± 0.51 times) during the procedure was significantly higher (p-value < 0.0001) than that in the EMF group (0.95 ± 0.75 times). [Table 3]

In the EMF group, the mean PADSS score at 30 minutes was 6.38 ± 0.67, significantly higher than the mean PADDS score of 5.45 ± 0.5, in the PMF group (p-value < 0.0001).At 60 minutes and 90 minutes in the recovery room, the difference in PADDS score was not significant between the two groups (p > 0.05). The majority of patients in both the PMF and EMF groups achieved a mean PADSS score>9 within 120 minutes. [Table 4]

High incidence of pain on injection for both drugs, although it was lower with etomidate. The incidence of myoclonus following drug administration was noted only in EMF group. Out of 40 patients, 4 patients (10%) had myoclonus after receiving etomidate. None of the patient had myoclonus after propofol administration. Incidence of myoclonus in etomidate group versus propofol group was statistically comparable with p value of 0.096. In present study, out of 40 patients 20 (50%) developed apnea for more than 60 seconds and required manual ventilation in PMF group while in EMF group, 7 patients(17.5%) out of 40 developed apnea for more than 60 seconds and required manual ventilation.

Table 1: Demographic distribution

Parameters (mean)	Group EMF	Group PMF	P value
Age (years	29.55± 4.47	29.12± 4.44	0.671
Height (cm)	156.38± 4.71	157.7 ± 3.01	0.062
Weight (kg)	55.35 ± 8	56.15 ± 6.84	0.632

Table 2: Surgery duration, loss of consciousness and recovery Characteristics

Parameters (mean)	Group EMF	Group PMF	P value
Surgery duration (min)	6.75 ± 1.61	6.95 ± 1.48	0.420
Time to loss of consciousness (Sec)	22.5 ± 9.45	26.38 ± 7.59	0.030*
Timeto return to	44.32±12.72	59.52 ± 9.1	<0.0001***
Time to return to orientation(Sec)	93.7 ± 21.38	108.8±17.01	0.002**
Amount of drug (mg)	73.75±8.68	11.6± 1.77	-

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No. of supplementary doses	0.95 ± 0.75	1.72 ± 0.51	<0.0001***

Table 3: Amount of drug, and number of times requiring supplemental doses

Number of Supplementary	No of Pt requiring supplemental doses		P value
	Group EMF	Group PMF	
0	13	0	<0.0001***
1	17	12	0.0001***
2	10	27	<0.0001***
3	0	1	0.001**

Table 4: Recovery time: Time to achieve PADSS score ≥9

Time in minutes	Mean PADSS score		P value
	Group EMF	Group PMF	
30	6.38±0.67	5.45 ± 0.5	<0.0001***
60	7.05 ±0.6	6.85 ± 0.66	0.125
90	7.82± 0.45	7.68 ± 0.57	0.156
120	9.18± 0.59	9.35 ± 0.66	0.174
150	9.48± 0.64	9.65 ± 0.53	0.124

Table 5: Mean VAS score for pain

VAS for pain	Mean VAS score		P value
	Group EMF	Group PMF	
0 min	4.06 ± 0.32	4.09 ± 0.44	0.155
15 min	3.95 ± 0.33	4.08 ± 0.44	0.234
30 min	3.8 ± 0.41	3.85 ± 0.43	0.618
60 min	3.12 ± 0.52	3.08 ± 0.53	0.671
90 min	2.33 ± 0.62	2.33 ± 0.62	1.000
120 min	1.48 ± 0.51	1.4 ± 0.5	0.502
150 min	1 ± 0	1 ± 0	1.000

Table 6: Incidence of Adverse effects during intraoperative period

Adverse effects	Group EMF	Group PMF	P value
Pain on injection	8	10	0.633
Hypotension	3	32	<0.0001***
Bradycardia	2	7	0.154
Myoclonus (grade 1)	4	0	0.096
Apnea≥60 seconds	7	20	0.002**

Table 7: Incidence of Adverse effects during Post-operative period

Adverse effects	Group EMF	Group PMF	P value
Hypotension	0	6	0.116
Bradycardia	0	0	-
Respiratory depression	0	0	-

DISCUSSION

In the study done by Jing Wu et al,[6] the total dose of propofol in group PMF (149.5 ± 30.0 mg) was significantly less than the total dose of etomidate in group EMF (15.8 ± 4.2 mg). The addition of midazolam and fentanyl with propofol or etomidate reduces total doses of these drugs in comparison to when used alone. The amount of total drug consumed during procedure in the study of Boysen, et al,[17] was 200 mg (143.0 to 337.5 mg) of propofol and 28.8 mg (19.9 to 45.1 mg) of etomidate. Our results are dissimilar to the above studies in reference to the total drug consumed during the procedure. This may be because we used propofol in the dose of 1.0 mg/kg and etomidate in the dose of 0.2 mg/kg in contrast to Boysen, et al (2.5 mg/kg propofol and etomidate 0.3 mg/kg) and Jing Wu et al,[6] used (2 mg/kg propofol and etomidate 0.2 mg/kg) and also supplemental doses used were less in our study (10 mg for propofol and 2 mg for etomidate) in respective groups versus 20-40 mg for propofol and 2-4 mg for etomidate.

Propofol, a potent cardiovascular depressant, often results in decreased blood pressure and a high incidence of apnea lasting more than 30 seconds, potentially leading to impaired SPO_2 levels.[18] Given that respiratory brain damage is a major cause of anesthesia-related morbidity, ensuring anesthesia safety is of paramount importance.[16] On the other hand, among rapid-acting induction agents, etomidate stands out for its minimal respiratory suppression and offers a greater margin of safety compared to propofol.[19]

Recovery times did not differ significantly between the two active ingredients. Injection site discomfort is often associated with the administration of propofol and etomidate.[20] In our study, propofol caused more injection-related pain compared with etomidate but stistically insignificant, which may be due to the higher concentration of propofol and differences in lipid emulsion. At elevated concentrations, both propofol and etomidate activate

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transient receptor potential cation channels of type A1, which can lead to discomfort at the injection site.[21]

As for other adverse effects, various studies have reported that administration of etomidate is associated with a higher incidence of nausea, vomiting (30% to 40%) and myoclonus (0% to 70%) compared to propofol.[22] Our study confirmed these results and showed that nausea, vomiting, and myoclonus were more common in the etomidate groups compared with the propofol groups.

Augmentation of general anesthesia with opioids has been shown to be beneficial in the treatment of postoperative pain and myoclonus.[6] However, the combination of opioids with propofol increases the risk of prolonged apnea and worsens hypotension.[23] In addition, it increases the frequency of nausea and vomiting associated with etomidate.[24] In present study, out of 40 patients 20 (50%) developed apnea for more than 60 seconds and required manual ventilation in PMF group while in EMF group 7 patients (17.5%) out of 40 developed apnea for more than 60 seconds and required manual ventilation. The difference in incidence of apnea was statistically significant with a p value of 0.002 between two groups. The episodes of apnea in our study were transient and were not associated with any fall in oxygen saturation.

The addition of midazolam has been suggested to relieve myoclonus and postoperative nausea and vomiting associated with intravenous anesthetics.[25] The past studies had shown that 50%-80% patients who do not receive any pre- treatment before etomidate develop myoclonus.[26-28] Most probable cause is that etomidate interacts with gamma amino butyric acid type A ($GABA_A$) receptors suppressing the central nervous reticular activating system.[28]

Our study provided similar results, showing a lower incidence of myoclonus and nausea/vomiting in the group receiving etomidate, fentanyl, and midazolam compared to the groups receiving etomidate alone.

CONCLUSION

Based on the observations and results, it can be inferred that the induction process with etomidate is quicker compared to propofol. Patients also tend to emerge from anesthesia earlier when induced with etomidate, leading to better recovery characteristics and earlier readiness for discharge home.Despite its benefits, etomidate is associated with an increase in postoperative nausea and vomiting. However, this increase in adverse effects does not significantly impact the overall time it takes for patients to be ready for discharge home. Therefore, despite the occurrence of postoperative nausea and vomiting, etomidate remains favorable due to its overall advantages in terms of induction speed, hemodynamic stability, and quicker recovery.

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