EFFECT OF KETAMINE VS FENTANYL ON RECOVERY TIME AS AN ADJUVANT TO PROPOFOL IN DILATATION AND CURETTAGE CASES: A RANDOMISED DOUBLE BLIND INTERVENTIONAL STUDY.

ABSTRACT

Background: The aim of this study is to compare the clinical efficacy of combination of propofol-ketamine and propofol-fentanyl in terms of recovery time, haemodynamic variables and side effects.

Methods: The study was done on 60 patients of (age 18-35 years, weight 40-70 kilograms) ASA grade I&II. These were randomly allocated in 2 groups of 30 each. They were undergoing Dilation and Curettage procedures lasting up to 30 minutes. Group A received Inj. Ketamine 0.75 mg/kg body weight IV slowly over 2 minutes, after 5 minutes Inj. Propofol given at rate of 1ml/3 seconds till loss of consciousness. Group B received Inj. Fentanyl 2 mcg/kg body weight as slow IV injection, after 5 minutes Inj. Propofol given at rate of 1ml/3 seconds till loss of consciousness. Hemodynamic variables were recorded intra and post-operatively at regular intervals. Recovery time, use of rescue analgesia and side effects were assessed. The results were tabulated and analysed statistically.

Conclusion: Propofol-ketamine compared to propofol-fentanyl causes delayed recovery and took longer time to reach Modified Aldrete's score of >9 but is more efficacious and provides better peri-operative hemodynamic stability during anaesthesia and produces good analgesia with less requirement of rescue drug in post-operative period with fewer peri-operative complications.

KEYWORDS

Propofol, Ketamine, Fentanyl, Hemodynamic variables, Recovery time.

INTRODUCTION

Dilatation and Curettage (D&C), is a short surgical procedure, performed for the diagnosis and treatment of endometrial and intrauterine disorders. It causes significant pain due to cervical dilatation with dilators and tissue extraction. Drugs to be used for this procedure should ensure fast onset of action, rapid recovery and adequate level of sedation and good analgesia. The most important objective in the intra-operative period is to observe maintenance of the hemodynamic-respiratory stability and minimising the side effects of the drug. Propofol is a widely used sedative agent due to its rapid onset of action and fast recovery time, but it causes cardiovascular and respiratory depression in a dose dependent manner but it lacks analgesic properties. Combining propofol with other drugs such as opioids or ketamine is recommended for improving the sedation, analgesia and minimising the potential adverse effects with maintenance of a stable cardiovascular and respiratory status in the peri-operative period.

Ketamine, a NMDA receptor agonist, in sub-anesthetic doses with propofol has gained attention in total intravenous anaesthesia because of its powerful analgesic action without causing myocardial and respiratory depression. Ketamine also causes some degree of sympathetic stimulation, which tends to counter-balance the cardiovascular side-effects of propofol.

Fentanyl on the other hand is opioid analgesic which has rapid onset and short duration of action and can be used in combination with propofol satisfactorily.

The present study is designed to assess the intra-operative hemodynamics, post-operative recovery profile and stability of hemodynamics in both the propofol-ketamine and propofol-fentanyl groups. Overall recovery and the benefits were assessed by discharge criteria and which group offers more advantage will be evaluated.

METHODS

The present study was carried out in the Department of Anaesthesiology at SMS Medical College and Hospital, Jaipur, Rajasthan. After obtaining institutional ethical committee approval and patients written informed consent, the study was conducted in 60 patients, aged 18-35 years of ASA Grade I&II scheduled for Dilatation and Curettage lasting up to 30 minutes. The patients were randomly allocated using sealed envelope method in 2 groups (30 of each). Patients with cardiovascular, respiratory, neurological and liver diseases, patients who are on narcotic therapy were excluded from study. A detailed pre-anæsthetic evaluation including history and a thorough general and systemic examination and all relevant investigations were done for all the patients.

Patients were kept fasting for at least 8 hours prior to anaesthesia. Preoperative baseline heart rate, blood pressure (systolic, diastolic and mean), spo2 was recorded. A peripheral intra-venous line was established. All patients were pre-medicated with Inj. Glycopyrrolate 0.004 mg/kg and Inj. Midazolam 0.02 mg/kg. Group A received Inj. Ketamine 0.75 mg/kg body weight IV slowly over 2 minutes, after 5 minutes Inj. Propofol given at rate of 1ml/3 seconds till loss of consciousness. Group B received Inj. Fentanyl 2 mcg/kg body weight as slow IV injection, after 5 minutes Inj. Propofol given at rate of 1ml/3 seconds till loss of consciousness.

Intra-operatively heart rate, blood pressure, oxygen saturation were recorded at different time intervals of 5, 10, 15, 20, 25, 30 minutes following induction of anaesthesia in both groups. Throughout the procedure patients were allowed to breathe spontaneously on room air and oxygen supplementation was given to some patients during anaesthesia. Top-up dose of Inj. Propofol 0.5 mg/kg was given when patient became light during anaesthesia as indicated by rise in heart rate, blood pressure or any other movement to surgical stimulus. Total dose of propofol required for the patients was noted.

Post-operatively all vital parameters like heart rate, blood pressure, oxygen saturation, visual analogue score and Modified Aldrete's score was recorded every 30 minutes for first 2 hours then every 2 hours till 12 hours. Any complication like nausea, vomiting, delirium, pain was noted. The patients were discharged accordingly to Modified Aldrete's score.

STATISTICAL ANALYSIS

Continuous variables like age, heart rate, systolic blood pressure, diastolic blood pressure, spo2, total dose of propofol, recovery time etc were presented as Mean ± SD. Continuous variables were compared at different time intervals between ketamine and fentanyl groups by performing unpaired t-test, p<0.05 was considered as statistically significant.

Observations

A total of 60 patients who underwent Dilation and Curettage lasting up to 30 minutes were enrolled for the study and were randomly divided into 2 groups. The demographic profiles with regard to age and weight was comparable. The distribution as per ASA status was similar.

Pre-induction heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, spo2 were comparable in both the groups with a statistically no significant difference between them (p>0.05).
In the present study, Group A received ketamine 0.75 mg/kg as well as propofol as an inducing agent for short surgical procedures like D&C. Hence whether pre-induction with ketamine 0.75 mg/kg or fentanyl 2 mcg/kg in combination with propofol was given at the rate of 1ml/3 seconds till loss of consciousness. The rate of injection of propofol was kept constant at approximately 1ml/3 second.

In our study that intra-operative period in Group B there was fall in HR at all times except at 25 and 30 min as compared to A group, which was statistically significant. The decrease in the HR in Group B can be attributed to the action of fentanyl on the cardiovascular system. Similar findings were found in Brajesh K and M. Arikan\textsuperscript{et al} study they found significant fall in HR in fentanyl group as compared to ketamine group at all times intra-operatively.

The fall in SBP, DBP, MBP was statistically significantly higher in Group B than Group A. There was minimal fall in SBP, DBP and MBP in Group A as compared to Group B in intra-operative period, due to good sedation, maintaining hemodynamic and respiratory stability and good analgesic management while minimizing the side effects of drugs.

Propofol, when introduced shown to have many of these properties. Many studies have been performed to assess propofol both as a sole anaesthetic agent and in combination with fentanyl and ketamine in different doses. But there are no studies about comparisons with the combinations of propofol-fentanyl infusion with propofol-ketamine combination infusion in paediatric short term procedure. Similar findings like our study were noted, that is more hypotension was found in B group (38.6%) as compared to A group (14.6%).

In our study there was no significant difference in fall in SPO\textsubscript{2} in both the group. The change in SPO\textsubscript{2} was found to be in the range of 98.1 ± 0.96 % to 99.41 ± 0.90 % whereas in Group B SpO\textsubscript{2} was 97.21 ± 1.50 % to 98.18 ± 1.44 %.

The change in peripheral oxygen saturation at different time interval were statistically not significant (p > 0.05). In M. Arikan\textsuperscript{study} there was no significant difference in fall in SPO\textsubscript{2} in both the group.

The mean total dose of propofol required in Group B (113.8 ± 11.09mg) was higher than that in Group A (104.3 ± 15.43) which was statistically significant (P value < 0.05). The change in peripheral oxygen saturation at different time interval were statistically not significant (p > 0.05). In M. Arikan\textsuperscript{study} the mean consumption of propofol was higher in fentanyl group as compared to ketamine group.

We have noted in our study that intra-operative complications (desaturation, hypotension) were significantly higher in Group B than in Group A (P value < 0.05). In Group A out of 30 patients, 3 had episodes of desaturation and 4 had hypotension, whereas, in Group B out of 30 patients, 7 had episodes of desaturation and 7 had hypotension. In study of Khutia SK \textsuperscript{et al} more hypotension was found in Group B compared to Group A at all times intra-operatively.

At 15, 20, 25, 30 min the DBP of Group A and that of Group B was statistically significant (P<0.05).

The fall in SBP, DBP, MBP was statistically significantly higher in Group B than Group A. There was minimal fall in SBP, DBP and MBP in Group A as compared to Group B in intra-operative period, due to the sympathetic-mimetic activity of ketamine which counteracts with the cardiovascular depressant action of propofol thus maintaining a stable hemodynamic profile as compared to fentanyl. Khutia SK \textsuperscript{et al}, compared combination of propofol-fentanyl infusion with propofol-ketamine infusion in paediatric short term procedure. Similar findings like our study were noted, that is more hypotension was found in B group (38.6%) as compared to A group (14.6%).

At 10 and 15 mins the DBP of Group A and that of Group B was statistically significant (P<0.05).

At 10, 15 , 20, 25 min MBP of Group A and that of Group B was statistically significant. (P<0.05).

<table>
<thead>
<tr>
<th>Heart rate</th>
<th>Baseline</th>
<th>1 min</th>
<th>5 min</th>
<th>10 min</th>
<th>15 min</th>
<th>20 min</th>
<th>25 min</th>
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</thead>
<tbody>
<tr>
<td>Group A Mean ± SD</td>
<td>84.46±3.34</td>
<td>81.10±4.93</td>
<td>87.82±5.2</td>
<td>83.03±6.33</td>
<td>83.0±5.58</td>
<td>80.25±6.02</td>
<td>80.32±6.2</td>
<td>80.8±6.1</td>
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<tr>
<td>Group B Mean ± SD</td>
<td>86.96±3.86</td>
<td>88.25±6.04</td>
<td>82.46±6.00</td>
<td>77.21±5.27</td>
<td>78.14±4.85</td>
<td>76.75±6.63</td>
<td>80.85±6.16</td>
<td>79.75±6.31</td>
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<td>P-value</td>
<td>0.01</td>
<td>0.0001</td>
<td>0.0005</td>
<td>0.0003</td>
<td>0.0007</td>
<td>0.03</td>
<td>0.741</td>
<td>0.497</td>
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<th>SBP</th>
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<th>25 min</th>
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<tbody>
<tr>
<td>Group A Mean ± SD</td>
<td>123.64±5.48</td>
<td>119.14±12.17</td>
<td>120.60±11.30</td>
<td>119.14±9.90</td>
<td>116.35±10.97</td>
<td>114.10±11.87</td>
<td>114.78±10.56</td>
<td>115.07±10.23</td>
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<td>Group B Mean ± SD</td>
<td>123.35±5.42</td>
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<td>0.030</td>
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<table>
<thead>
<tr>
<th>Mean BP</th>
<th>Baseline</th>
<th>1 min</th>
<th>5 min</th>
<th>10 min</th>
<th>15 min</th>
<th>20 min</th>
<th>25 min</th>
<th>30 min</th>
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</thead>
<tbody>
<tr>
<td>Group A Mean ± SD</td>
<td>89.59±3.69</td>
<td>89.59±3.69</td>
<td>86.39±4.46</td>
<td>85.3±6.69</td>
<td>84.07±6.22</td>
<td>83.2±6.53</td>
<td>83.30±4.70</td>
<td>84.52±5.13</td>
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<tr>
<td>Group B Mean ± SD</td>
<td>90.23±3.64</td>
<td>86.33±5.56</td>
<td>85.11±3.60</td>
<td>82.09±3.80</td>
<td>80.04±4.60</td>
<td>79.60±4.09</td>
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<td>P-value</td>
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<td>0.01</td>
<td>0.11</td>
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At 10, 15, 20, 25, 30 min MBP of Group A and that of Group B was statistically significant. (P<0.05).

<table>
<thead>
<tr>
<th>Group A Mean ± SD</th>
<th>116 ± 38.38 mins</th>
<th>Time to reach MAS &gt;9</th>
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<tbody>
<tr>
<td>Group B Mean ± SD</td>
<td>75.83 ± 23.78 mins</td>
<td>0.0001</td>
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DISCUSSION

Over a period of years, the role of Total Intra-venous Anaesthesia (TIVA) in the short procedures like dilatation and curettage has increased the need for a technique with smooth induction, good intra-operative anaesthesia and analgesia and rapid recovery with minimal side effects so that early discharge is possible. Dilatation and curettage is a short procedure. It causes pain because of cervical dilatation and tissue extraction. Thus iv sedation techniques are widely used for D&C for good sedation, maintaining hemodynamic and respiratory stability and good analgesic management while minimizing the side effects of drugs.
which are important in pain processing and the modulation of pain. And hence the requirement of rescue analgesia was lower in Group A than in Group B (P value<0.05). In Yuce HH\textsuperscript{4}, they observed that Ketamine has been shown to decrease pain scores and reduce post-operative analgesic consumption by 35-40\%.

In our study the recovery time in terms of MAS was prolonged in ketamine group as compared to fentanyl group and it was statistically significant. Also time to reach MAS of >9 was statistically significant in both the groups. (P value >0.05). In study of M. Arikan\textsuperscript{5}, the mean recovery time was longer in Group A than that of Group B. Also in Pawar D\textsuperscript{5} recovery time was longer in ketamine than fentanyl group.

The post-operative complications like nausea- vomiting, desaturation, hypotension, post-operative pain were higher in Group B than in Group A (P value <0.05). There were no incidences of psychedelic effects of ketamine like hallucination, dysphoria. Similar findings in study of M. Arikan\textsuperscript{5} where prevalence of hypotension and apnoea found in Group B more than Group A. Also the occurrence of nausea and vomiting were higher in Group B. These findings correlate well with the study of Brajesh K\textsuperscript{2}, where there higher incidence of apnoea in Group B as compared to Group A.

CONCLUSION

It may be concluded from our present study that propofol with ketamine as an adjuvant in the dose of 0.75 mg/kg compared to propofol with fentanyl as adjuvant in the dose of 2 mcg/kg causes delayed recovery and took longer time to reach Modified Aldrete’s score of >9. But propofol-ketamine group is more efficacious and provides better peri-operative hemodynamic stability during anaesthesia as compared to propofol-fentanyl group. Also the propofol-ketamine combination produces good analgesia with less requirement of rescue drug in post-operative period with fewer peri-operative complications than propofol-fentanyl combination. We have not encountered any psychotomimetic effects of injection Ketamine in the 0.75mg/kg dose. Hence propofol-ketamine combination is a better choice especially when hemodynamic stability is of great importance in patients undergoing dilatation and curettage.

Acknowledgements

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Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES