ABSTRACT

OBJECTIVE: To assess the applicability of priming technique in case of anesthetic agents propofol and midazolam.

STUDY DESIGN: A Randomized controlled trial.

PLACE AND DURATION: Department of Anaesthesiology and Intensive Care, Holy Family Hospital, Rawalpindi from 1st of January 2016 to 30th June 2016.

METHODOLOGY: Current study had ninety participants divided equally in 3 groups with equal number of patients. Group I was given 0.5 mg/kg propofol intravenously which was about twenty percent of the worked out dose of propofol for anesthesia induction. Group II was injected 0.05 mg/kg intravenous midazolam while Group III was injected 3 ml 0.9 % saline, which was succeeded two min afterwards in all the groups with intravenous propofol injection till the loss of corneal reflex. Hemodynamic variables systolic blood pressure, diastolic blood pressure and mean arterial blood pressure were noted.

RESULTS: The results showed a statistically significant reduction in the dosage requirement of induction agents. Induction dosage worked out to be 23.65% lower in the Group I (propofol auto-coinduction group) and 12.87% lesser in the Group II (midazolam co-induction group) in comparison to the control. The hemodynamics remained more stable in Group II (midazolam propofol co-induction group) during per intubation period.

CONCLUSIONS: The principal of co-induction was found to be efficacious in terms of anesthesia induction agents propofol and midazolam.

KEYWORDS: Priming principal, coinduction, auto-coinduction, propofol, midazolam.

HOW TO CITE THIS:

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INTRODUCTION

The approach of infusing a pre-worked out dose of induction drug before injecting the complete dose of the same drug is termed as “priming technique”1-3 “Auto-coinduction”4. This method has been used extensively in case of neuromuscular blocking agents. In the priming methods a small dosage of non-depolarizing muscle relaxants (20% of the ED95 or 10% of the intubating dose) two to four minutes before injecting the full dose for endotracheal intubation.

Coinduction5 may be defined as the simultaneous infusion of more than one drugs that expedite start of anesthesia indicating synergism6. So far there is scarcity of studies performed to check the priming principal in induction agents1. In terms of the induction agents the aim is to utilize sedative, anxiolytics and amnestic affects, at sub hypnotic doses of anesthesia induction drugs by giving them some time before the induction agents. Propofol is now the agent most frequently used for induction of anesthesia because of its quick onset of action and a short duration of action7. There is no hang over effect after surgery, good conditions for endotracheal tube placement. But quick intravenous injection of the conventional doses leads to a fall in blood pressure which is dose dependent8. Propofol and midazolam are often used in conjunction for induction of anesthesia as they show synergism hypnotics and sympathetic suppression9-12. We also used these drugs in our study to check the effectiveness of priming principal.

This study was performed to find out if the priming technique decreases the effective anesthesia dosage requirements for induction drug and also if it improves stability in the per intubation hemodynamics.

METHODOLOGY

This randomized control trial was conducted in Department of Anesthesiology Holy Family Hospital Rawalpindi from 1st of...
January 2016 to 30th June 2016 after getting the approval of Institutional Ethical Committee. 90 patients ASA Grade I and ASA Grade II, of either sex without any history of anesthetic complication were included in the study. Patients with obesity, expected difficult intubation were excluded from the study. Selected patients were randomly divided into 3 groups with equal number of patients: Group 1 got propofol, Group 2 got midazolam and Group 3 was injected normal saline. All 3 groups had 30 patients. In the OT, monitoring as per ASA guidelines, i.e., blood pressure, pulse oximetry and ECG, were attached. Baseline readings of heart rate and blood pressure were measured five minutes apart prior to the start of anesthesia. An intravenous access was placed on the left arm.

Patients in all the groups (1, 2, 3) were injected with the priming medicine 0.5 mg/kg intravenous propofol, midazolam intravenous 0.05 mg/kg and normal saline in equal volume (3 ml), respectively, trailed by IV induction with propofol one hundred twenty seconds later in all the entire study groups until corneal eye reflex was lost. The speed of injection of propofol was kept at the rate of thirty mg in ten seconds. Occurrence of any problem amid intubation course, i.e., apnea (cessation of respiration), vomiting (regurgitation), laryngospasm, non-purposeful movements, coughing, was recorded.

Muscle relaxation and endotracheal tube was placed by Injecting atracurium 1 mg/kg given intravenously and maintenance of anesthesia was done on isoflurane, Oxygen and atracurium. Surgical stimuli was avoided for five minutes after intubation.

The variables recorded included total dosage of propofol needed for reaching absence of corneal reflex. $\text{SpO}_2$, heart rate and non-invasive blood pressure (systolic, diastolic and mean blood pressure) were measured preceding induction, afterwards of induction, forthwith endotracheal tube placement, and 5 min afterwards endotracheal tube placement. All intervention by done by the registrar.

The sample volume of this investigation was worked out placed on considering a power of 80% and $\alpha$ (alpha) value of 0.05 as significant working with SPSS version 10.0. Data was presented as mean value ±2SD.

**DATA ANALYSIS:** Statistics were worked out with use of the SPSS version 10.0. Analogy amongst the three batches for the anesthetic requirement and hemodynamic stability variables done by use of analysis of variance (ANOVA) with Tukey’s post-hoc test. $P$ value of <0.05 decided to be significant and $P<0.001$ was decided to be highly significant.

**RESULTS**

90 patient were included. Demographic data for weight, age, ASA Grade and gender as indicated in Table I and were almost the same in all the groups. Statistically significant variation ($P<0.001$) is noted in dosage need of propofol in Group 1 and Group 2 in contrast with control. Propofol dosage noted as 23.65% lower in the propofol auto-coinduction group and 12.87% lesser in Group II in relation to the control. Results tabulated as under in Table - II.

No variation was found in mean $\text{SpO}_2$ value at any time during the course of this study amongst the three groups. A statistically significant ($P<0.001$) decrease in heart rate was observed in Group I after priming. Increase in Heart rate was seen in all groups but minimum rise was noted in Group 1.

Mean systolic blood pressure was observed to have a slight fall at induction in the propofol and saline group but maintained in the midazolam. Post intubation rise in SBP was found to be increased in all three groups with highest rise in propofol group. 5 minutes post intubation the hemodynamics were back to baseline levels in all groups.

Mean DBP was registered to be stable in normal saline group and midazolam group with a minimal decrease in the propofol group. Post intubation rise in DBP was in the propofol followed by the midazolam group. DBP remained stable in the control group.

**TABLE - I: DEMOGRAPHIC DATA AGE, WEIGHT, GENDER AND ASA GRADING. (N=30)**

<table>
<thead>
<tr>
<th></th>
<th>ASA Grade</th>
<th>Sex</th>
<th>Weight</th>
<th>Age</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>2</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>Propofol</td>
<td>26(86.7%)</td>
<td>4(13.3%)</td>
<td>23(76.7%)</td>
<td>7(23.3%)</td>
</tr>
<tr>
<td>Midazolam</td>
<td>25(83.3%)</td>
<td>5(16.7%)</td>
<td>21(70.0%)</td>
<td>9(30.0%)</td>
</tr>
<tr>
<td>Normal Saline</td>
<td>21(70.0%)</td>
<td>9(30.0%)</td>
<td>29(96.7%)</td>
<td>1(3.3%)</td>
</tr>
<tr>
<td>Total</td>
<td>72(80.0%)</td>
<td>18(20.0%)</td>
<td>73(81.1%)</td>
<td>17(18.9%)</td>
</tr>
<tr>
<td>P-Value</td>
<td>0.233</td>
<td>0.049</td>
<td>0.124</td>
<td>0.149</td>
</tr>
</tbody>
</table>

**TABLE - II: DOSE OF PROPOFOL IN THE THREE GROUPS. (N=30)**

<table>
<thead>
<tr>
<th></th>
<th>Dose</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean+SD</td>
<td></td>
</tr>
<tr>
<td>Group I</td>
<td>91.4+24.8</td>
<td></td>
</tr>
<tr>
<td>Group II</td>
<td>104.3+24.5</td>
<td>0.0001</td>
</tr>
<tr>
<td>Group III</td>
<td>119.7+16.7</td>
<td></td>
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</table>
DISCUSSION

This inquiry was undertaken to compare the effectiveness of auto co-induction of propofol in comparison to combination of propofol and midazolam co-induction, for lowering the induction dosage requirement of propofol as well as hemodynamic balance during the peri-intubation time.

Amongst group I patients, post priming propofol induction dosage of propofol as shown in Table II is 91.4 milligram in contrast to propofol requirement of 119.7 mg in Group III. It was found by applying auto-co-induction 23.65% reduction in induction dosage of propofol. In the past studies have also showed similar observations that propofol priming significantly brings down the induction dosage requirement. Anil Kumar and associates stated 27.48% less propofol dose with propofol auto-co-induction. Sedative and amnesia result at sub-anesthetic dose of propofol may have through synergism reduced the requirement of propofol. In group 2, after co-induction along midazolam, dosage of propofol as shown in Table II is 104.3 milligram in contrast to the dose of 119.7 milligram in Group I patients. 12.87% lowering in requirement of propofol was found in combination midazolam co-induction.

Older studies also show the decrease in the induction dosage of propofol after an earlier intravenous dose of midazolam. There was a statistically significant decrease in the heart rate after priming in propofol group in comparison to midazolam and normal saline. Increase in heart rate post intubation was registered in all patients with the increase least in Group I. Systolic BP found to rise post intubation in all groups with the rise least in the normal saline. DBP was found to increase in all groups with more stability seen in normal saline, but statistically considering rise in DBP was not significant in midazolam and propofol group.

Diastolic blood pressure post priming decreased significantly in propofol group post priming. Propofol caused a decrease in BP by reducing tone of the smooth muscles in blood vessels and total peripheral resistance at the same time by reducing sympathetic activity. The reduction SBP in Group I may perhaps be secondary to lowering in dosage of propofol post its self-co-induction. Similar findings were also claimed by Djaiani et al. The rise in heart rate after intubation (Table III) was registered in all three groups but it was convincingly lowered in Group I of patients. Increase in Systolic BP and Diastolic BP as shown in Table III after endotracheal intubation was observed in all the three groups. Five minutes post-intubation the hemodynamics returned to baseline levels in all groups. Propofol pre-treatment failed to blunt the reflex sympathetic stimulation after intubation and the hemodynamic stability in SBP and DBP according to our study results was more in the normal saline group.

The findings that despite midazolam co-induction compellingly lowers the requirement of propofol, it lacks the hemodynamic stability. Such findings were reported by Cressy et al. in which compelling lowering in requirement of propofol was noted in Group II but hemodynamic variations could not be avoided.

CONCLUSIONS

The principal of co-induction was found to be efficacious in terms of anesthesia induction agents.

Contribution of authors:
Shah AA: Conceived Idea, Designed methodology, Manuscript Writing, Data Collection
Abid L: Designed Research Study, Manuscript Writing
Nazir A: Data Collection, Manuscript writing
Tariq Z: Data Collection, Manuscript writing
Naz F: Data Collection, Manuscript writing

Disclaimer: None.
Conflict of Interest: None.
Source of Funding: None.

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2. Kumar AA, Sanikop CS, Kotur PF. Effect of priming principle on the induction dose requirements of propofol-A