Effect of priming Principle on the induction dose Requirement of Propofol

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ABSTRACT
BACKGROUND: Priming principle can be applied for induction agent like Propofol to reduce induction dose requirement. We performed this study to know its effect on the induction dose requirement of Propofol and to observe associated peri-intubation hemodynamic alterations and complications if any.

MATERIALS & METHODS: A prospective randomized study of 60 patients of either sex, 18-55 years and of ASA I-II category was performed. All patients were divided into group S(n=30) and group C(n=30). All the patients were premedicated with Inj.Glycopyrrolate and Inj.Midazolam and given general anaesthesia with Inj.Fentanyl and Inj.Propofol in which patients in group S were primed with 20% of the total dose requirement of Propofol(2 mg/kg) 2 minutes before giving rest of the dose till loss of eyelash reflex while patients in group C were induced routinely. RESULTS: We observed mean reduction of 27.69% in the induction dose requirement of Propofol in group S compared to group C. There was a highly significant rise in mean pulse rate and highly significant fall in mean systolic, diastolic and mean arterial pressure in group C compared to group S. Incidence of post-suxamethonium fasciculation was more in group S while hypotension was more in group C. CONCLUSION: Thus application of priming principle for the induction agent like Propofol is associated with significant reduction in the induction dose requirement with better peri-intubation hemodynamic stability.

Keywords: Priming principle, propofol, induction dose requirement.

INTRODUCTION
Induction can be considered as one of the most crucial events in Anaesthesiology as it is associated with number of alternations in hemodynamic and physiology of various body systems. This is an era of day care surgery and anaesthesia. Unusual and prolong hospital stay due to anaesthetic drugs definitely increases economic burden and risk of hospital acquired complications. Propofol, therefore, is preferred induction agent nowadays due to its properties of smoother and more rapid induction, rapid awakening & orientation times, clear headed recovery, decreased incidence of post-operative nausea vomiting better intubating conditions & upper airwayintegrity compared to Thiopentone sodium. However, major disadvantage of rapid induction with Propofol is the considerable dose dependent decrement in the systemic arterial pressure, primarily due to reduction in cardiac output & systemic vascular resistance. Priming principle, also known as 'auto-coinduction', in relation to induction agents, aims at utilizing the sedative, anxiolytic& amnestic properties.

By applying priming principle in relation to Propofol, we can significantly reduce the dose requirement and thus the consequent dose-dependent hemodynamics alterations.

MATERIALS AND METHODS
After local research ethical committee approval & obtaining an informed consent, A prospective randomized study of 60 patients of age between18-55 years, come under ASA-I or ASA-II category undergoing surgery which requires general anaesthesia as a mode of anaesthesia chosen to determine effect of priming principle in relation to Propofol in SSG Hospital Vadodara from December 2011 to March 2013. Sample size is estimated using MedCalc software considering Type I alpha error as 0.05 and Type II beta error as 0.20 and mean difference in reduction in dose requirement between control and study group 30 mg SD for control & study group 23.89 and 20.28 respectively.

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Inclusion criteria:
1. Adult patients of both sexes between 18-55 years of age
2. Patients undergoing elective surgeries undergoing general anaesthesia
3. Patients of ASA status I & II.

Exclusion criteria:
1. Unwillingness of the patient,
2. History of allergy to opioids, eggs
3. History of opioid abuse,
4. Patient is on opioid analgesic, phenothiazine, tranquilizer, sedatives, hypnotics or any other CNS depressants.
5. Patient with impaired respiration (bronchial asthma, Chronic Obstructive Pulmonary Disease), severe infection or uraemia
6. History of severe cardiac disease, renal/hepatic/cerebrovascular disease.
7. Anticipated difficult intubation.
8. Pregnant & lactating women.

Explanation & consent:
All the selected patients were explained about the purpose, procedure & side effects of the study. After this a written & informed consent was taken. Tab. ranitidine 150 mg & Tab, diazepam 10 mg was given to all patients the night before the surgery.

Group of patients:
Patients were randomly allocated into 2 groups of 30 patients each.

Group S (study) (n=30): Induction using priming principle (20% of the total calculated dose of Propofol - 2 mg/kg followed by rest of the required dose after 2 minutes till loss of eyelash reflex).

Group C (Control) (n=30): Induction with total calculated dose of Inj. Propofol - 2 mg/kg till loss of eyelash reflex.

Anaesthetic procedure:
Premedication: Inj. Glycopyrolate 0.004mg/kg IV and Inj.Midazolam 0.03 mg/kg IV 15 minutes before induction.
Induction: (Anaesthetic technique) Preoxygenation with 100% O2 for 3 min.

Group S- Inj. Fentanyl 1 µg/kg over 30 seconds followed by priming with 20% of the total calculated dose of Propofol-2 mg/kg followed by rest of the required dose after 2 minutes till loss of eyelash reflex.

Analysis of results:
Two groups were comparable to each other with respect to age, weight, ASA physical status. There was no significant difference in baseline pulse rate & baseline SBP, DBP & MAP, oxygen saturation between group S & Grou C (p value > 0.05).

A. Induction Dose Requirement
The mean induction dose in group S was 81.37 ± 15.82 and in group C it was...
113.27 ± 18.68. Thus we observed a 27.69% reduction in induction dose requirement in group S. (table1)

Table: 1 Mean Induction dose Requirement of Propofol

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean Induction dose(mgms)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group S</td>
<td>81.37±15.82</td>
<td>&lt;0.001[HS]</td>
</tr>
<tr>
<td>Group C</td>
<td>113.27±18.68</td>
<td></td>
</tr>
</tbody>
</table>

Table: 2 Changes in the Mean Pulse Rate (BPM)

<table>
<thead>
<tr>
<th>Time</th>
<th>Group S</th>
<th>Intragroup p value</th>
<th>Group C</th>
<th>Intragroup p value</th>
<th>Inter group p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>90.53±13.26</td>
<td>&gt;0.05[NS]</td>
<td>88.17±12.43</td>
<td>&gt;0.05[NS]</td>
<td>&gt;0.05[NS]</td>
</tr>
<tr>
<td>Just before induction</td>
<td>88.93±14.53</td>
<td>&gt;0.05[NS]</td>
<td>87.16±12.97</td>
<td>&gt;0.05[NS]</td>
<td>&gt;0.05[NS]</td>
</tr>
<tr>
<td>One minute after induction</td>
<td>88.56±15.21</td>
<td>&gt;0.05[NS]</td>
<td>99.46±12.1</td>
<td>&lt;0.001[HS]</td>
<td>&lt;0.001[HS]</td>
</tr>
<tr>
<td>During intubation</td>
<td>90.13±13.57</td>
<td>&gt;0.05[NS]</td>
<td>103.4±12.38</td>
<td>&lt;0.001[HS]</td>
<td>&lt;0.001[HS]</td>
</tr>
<tr>
<td>Immediately after intubation</td>
<td>94.06±13.88</td>
<td>&gt;0.05[NS]</td>
<td>108.3±10.6</td>
<td>&lt;0.001[HS]</td>
<td>&lt;0.001[HS]</td>
</tr>
<tr>
<td>5 minutes later</td>
<td>92.53±13.24</td>
<td>&gt;0.05[NS]</td>
<td>104.76±10.4</td>
<td>&lt;0.001[HS]</td>
<td>&lt;0.001[HS]</td>
</tr>
</tbody>
</table>

Table: 3 Changes in Mean Arterial Pressure (Mm of Hg)

<table>
<thead>
<tr>
<th>Time</th>
<th>Group S</th>
<th>Intragroup p value</th>
<th>Group C</th>
<th>Intragroup p value</th>
<th>Inter group p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>100.97±9.49</td>
<td>p&gt;0.05</td>
<td>97.7±21.65</td>
<td>p&gt;0.05</td>
<td>&gt;0.05[NS]</td>
</tr>
<tr>
<td>Just before induction</td>
<td>97.13±11.6</td>
<td>p&gt;0.05</td>
<td>99.16±12.16</td>
<td>p&gt;0.05</td>
<td>&gt;0.05[NS]</td>
</tr>
<tr>
<td>One minute after induction</td>
<td>94.6±10.2</td>
<td>p&gt;0.05</td>
<td>83.0±11.9</td>
<td>&lt;0.001[HS]</td>
<td>&lt;0.001[HS]</td>
</tr>
<tr>
<td>During intubation</td>
<td>96.86±8.46</td>
<td>p&gt;0.05</td>
<td>82.66±11.5</td>
<td>&lt;0.001[HS]</td>
<td>&lt;0.001[HS]</td>
</tr>
<tr>
<td>Immediately after intubation</td>
<td>98.8±9.15</td>
<td>p&gt;0.05</td>
<td>84.4±10.4</td>
<td>&lt;0.001[HS]</td>
<td>&lt;0.001[HS]</td>
</tr>
<tr>
<td>5 minutes later</td>
<td>95.23±9.77</td>
<td>p&gt;0.05</td>
<td>85.23±11.9</td>
<td>&lt;0.001[HS]</td>
<td>&lt;0.001[HS]</td>
</tr>
</tbody>
</table>

Data are expressed as mean±standard deviation. HS=Highly significant NS=Not significant

C. Mean Arterial Pressure (MAP)

There was highly significant fall in MAP at one minute after induction, during intubation, immediately after intubation and 5 minutes later. (Table3)

Table: 4 Side Effects or Complications

<table>
<thead>
<tr>
<th>Side effects Or Complications</th>
<th>Group S</th>
<th>Group C</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain on injecting Propofol</td>
<td>07</td>
<td>09</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>Respiratory depression</td>
<td>08</td>
<td>12</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>Postsuxamethonium fasciculations</td>
<td>19</td>
<td>08</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Hypotension</td>
<td>03</td>
<td>21</td>
<td>p&lt;0.001</td>
</tr>
</tbody>
</table>

DISCUSSION

1. Induction dose requirement

“Priming principle” is a technique of giving a pre-calculated dose of induction agent prior to giving the full dose of same induction agent; this technique is also known as “the auto co-induction”.

Propofol is known to produce sedation and anxiolysis at low doses. Initial administration of low dose (priming dose) of propofol (20% of the total dose requirement) is thought to produce anxiolysis and thereby reduces the associated sympathetic drive and the induction dose to produce hypnosis.

Thus we observed a 27.69% reduction in the induction dose requirement of propofol by applying priming principle, which is statistically highly significant.(p<0.001)

2. Hemodynamic Parameters

The application of priming principle is associated with the stability in the pulse rate during peri-intubation period compared to control group.

Also there was a lesser fall in SBP, DBP & MAP at one minute after induction, during intubation, immediately after intubation and 5 minutes later.
Propofol is known to have a biphasic effect on the cardiovascular system. Firstly, immediately after injection, decrease in the systemic vascular resistance and mean arterial pressure predominate. This decrease in the systemic vascular resistance causes reflex increase in the sympathetic activity, which is mediated by the baroreceptors present in the carotid sinus and aortic arch, thereby causing an increase in the heart rate. Secondly, from 2 minutes after injection, despite less than normal systemic vascular resistance, the heart rate and stroke volume are decreased to less than baseline. This is attributed to ‘resetting’ of the baroreceptor reflex to a smaller pressure value than normal by propofol.

The lesser fall blood pressure in propofol group was probably because of reduction in total induction dose of propofol after its autoco-induction. We looked for various side effects and complications during our study like pain on injecting propofol, respiratory depression, hypotension and post-suxamethonium fasciculations. The lower incidence of pain on injection of propofol in our study could be attributed to injecting propofol in the larger peripheral vein and prior administration fentanyl.

Hypotension was seen in group C compared to group S because of the greater amount of dose requirement of propofol and consequent dose dependent fall in blood pressure. But this seemed to be transient and within physiological limit and didn’t require any intervention. Post-suxamethonium fasciculations was found more in group S compared to group C. It has been documented through several studies that the incidence of fasciculations varies with the depth of anaesthesia at the time of administration of suxamethonium. The lesser incidence of fasciculations in group C of our study can be attributed to the adequate depth offered by bolus dose of propofol. Logical thinking implies that the patients of group S in our study received only about 70 % of the bolus dose of propofol, which obviously could not offer protection against occurrence of fasciculations. Anil kumar et al observed the same pattern of side effects as in our study.

CONCLUSION
Hence, Priming principle when applied for the induction agent like Propofol is associated with significant reduction in total induction dose requirement of Propofol and improved peri-intubation hemodynamic stability.

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Conflicts of interest-Non declared

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