Midazolam or mini-dose succinylcholine as a co-induction agent to aid Laryngeal mask airway insertion during propofol Anaesthesia

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ABSTRACT
BACKGROUND: Laryngeal Mask Airway (LMA) fills a niche between the facemask and endotracheal tube. For LMA insertion, use of only propofol as sole induction agent has less success rate. So many co-induction agents had been tried to get better success rate. Aim: To evaluate whether midazolam or mini-dose succinylcholine eases LMA insertion during propofol anaesthesia. MATERIALS AND METHOD: 75 adult patients of ASA grade I & II were divided in three groups (n=25) for surgery of up to one hour duration. Group-P was Propofol group (2.5mg/kg), Group-PM was propofol (2.5mg/kg) & midazolam (.04mg/kg) & Group-PS was Propofol (2.5mg/kg) & succinylcholine (0.25mg/kg). RESULTS: Parameters observed were jaw relaxation, airway reflexes & successful insertion at first attempt, overall insertion conditions & any other side effects. Hemodynamic changes during LMA insertion were found to be stable in groups PM & PS than group P. Dose of propofol required for LMA insertion was less in PM (2.52mg/kg) & PS (2.66mg/kg) groups than group P (3.1mg). Success rate at first attempt was significantly high in PM (88%) & PS (84%) groups compared to group P (56%). Overall excellent to acceptable conditions for LMA insertion were observed in PM (92%) & PS groups (88%) than group P(52%). CONCLUSION: propofol as a sole agent did not produce satisfactory conditions for LMA insertion with normal dose. This can be improved by addition of midazolam or low dose succinylcholine providing haemodynamic stability and minimum side effects.

Key words: Propofol, Midazolam, Succinylcholine, Laryngeal Mask Airway.

INTRODUCTION
Maintenance of airway is of prime importance during any anaesthetic procedure. The quest for finding an ideal device for the maintenance of unobstructed airway is on since the inception of general anaesthesia. Looking to the existing airway devices like facemask or endotracheal tube, LMA can be called “the missing link” between the Face Mask & Endotracheal tube. First described by Dr. Archie Brain in 1981 at Royal London hospital, White chapel, LMA is a new device to assist in the management of pediatric & adult airway3. LMA is reusable, cost effective, simple to use, atraumatic to insert, helpful in overcoming an obstructed airway & life saving in the management of airway crisis. Insertion of LMA requires the airway reflexes to be obtunded by general/topical anaesthesia or muscle relaxants. Intact airway reflexes may cause gagging, coughing or laryngospasm. If general anaesthesia is used, LMA insertion requires a depth almost similar or more to that necessary for insertion of an oropharyngeal airway but not as deep as is needed for tracheal intubation4. The most popular induction agent for LMA insertion continues to be propofol as this agent best obtunds oropharyngeal reflexes, suppresses cough reflex & decreases the sensitivity of upper airway. When used alone in unpremedicated patients, propofol requirements for uncomplicated LMA insertion often exceed 2.5 mg/kg, which may lead to hypotension & prolonged apnea and has cost implications. In day-care surgery, the anaesthetic techniques should be tailored to allow early patient recovery with minimal side effects. Much research has therefore been conducted using a variety of supplementary drugs to find a compound which eases LMA insertion e.g. midazolam, lignocaine, fentanyl & recently succinylcholine3,4,5,6.
Benzodiazepines like midazolam when given intravenously produce significant depression of upper airway sensitivity. Midazolam is found to act synergistically with propofol & improve LMA insertion condition. Mini-dose succinylcholine has also been added to propofol for good LMA insertion condition while its standard dose may preclude its use because of high incidence of myalgia. We have conducted this study to observe the ease of LMA insertion using midazolam or mini-dose succinylcholine as a co-induction agent to propofol with haemodynamic changes & side effects.

MATERIALS AND METHODS
After ethical committee’s approval & written informed consent, this prospective, randomized clinical trial was performed in 75 American society anaesthesiology (ASA) risk I & II adult patients aged 18 to 65 years having 40 to 80 kg weight (Body Mass Index<35) undergoing elective uro-gynecological procedures having < one hour duration. Patients who had contraindications to use propofol, midazolam or succinylcholine & to LMA placement were excluded from the study. Patients having abnormal airway anatomy or mouth opening <2.5 cm, risk of gastric regurgitation & >2 attempts during LMA insertion were excluded from the study. Other cases which could have made insertion of LMA difficult such as limited neck extension, prominent incisors and large tongue excluded.

On the day of operation, patients were taken in operation theatre after confirming preoperative fasting & a brief pre-operative review examination. Routine pre-induction monitors- NIBP(non-invasive blood pressure), ECG, Pulse Oxymeter were attached and baseline vitals were recorded. Intravenous line was secured with 18 G needle & 0.9% normal saline infusion was started. Intraoperative line was secured with 18 G needle & 0.9% normal saline infusion was started. This was a double blind study in which patients were randomly allocated with and compared between three groups, each having 25 patients. For induction of anaesthesia, Group P patients received intravenous propofol 2.5 mg/kg, Group PM patients received intravenous midazolam 0.04mg/kg. 3 minutes before intravenous propofol 2.5 mg/kg and Group PS patients received IV succinylcholine 0.25 mg/kg (minidose) immediately after intravenous propofol 2.5 mg/kg. The size of LMA was selected according to manufacturer’s guidelines. LMA classic™ was used in all patients of either group. All patients were preoxygenated with 100% oxygen for 3 min. The adequacy of anaesthesia was assessed by loss of response to verbal command plus loss of eyelash reflex. If inadequate, further boluses of propofol 0.25 mg/kg every 15sec. were given as required. Total dose of propofol required for LMA insertion was recorded. LMA insertion was attempted 30 seconds after loss of eyelash reflex in all groups by same experienced anaesthetist. The position of LMA was verified by capnography, chest movement & the absence of gas leak around the cuff. Duration of apnea was recorded. Ventilation was not assisted unless the patient’s oxygen saturation fell below 90%. If more than two insertion attempts were required, patients were excluded from the study. Condition during insertion of LMA was assessed & graded as shown in table 1.

Jaw relaxation was graded as I - good, II – incomplete & III – poor (7). Patient’s reaction to LMA insertion in the form of airway reflex (gagging/coughing) & head or limb movement was assessed & graded. Grade I means none, II means mild but transient, III means moderate which lasted for few seconds (<10 sec.) & IV means severe & sustained which required interventions. Incidence of Laryngospasm (none-partial-severe) during LMA insertion was recorded. Total dose of propofol, fasciculations (in group PS), duration of apnoea & the number of insertion attempts were recorded. The overall insertion condition was assessed as shown in table 1.

After confirming the proper LMA position, intravenous fentanyl 1µg/kg was given & anaesthesia was maintained with sevoflurane 2-3% and O2/N2O 50:50. Mean arterial blood pressure, oxygen saturation and heart rate were recorded before & after induction of anaesthesia, one minute & five minute after LMA insertion. At the end of procedure, all
anaesthetics were discontinued except 100% oxygen. LMA was removed after patients followed the verbal commands. After removal, the surface of the LMA was checked for the presence of blood. In post anaesthetic care unit (PACU), patients were followed up for the presence of sore throat & regarding the experience of anaesthesia. Myalgia (in PS group) was assessed by telephonic interview after discharge from the hospital.

**Statistical Analysis:** Sample size was decided on the basis of power analysis. A minimum sample of 25 patients would be required in each group to provide 80% power to detect a statistical significance difference of (α=0.05). Hence a sample size of 25 patients was selected to each group. Statistical Analysis was performed using SPSS version 12. Data were expressed as mean±SD for continuous variable. Comparisons of Continuous variables were compared using analysis of variance (ANOVA). Categorical variables were compared using chi-square tests. ‘p’ value <0.05 is considered to be statistically significant.

**OBSERVATION & RESULTS**

**Table: 1 Overall insertion condition**

<table>
<thead>
<tr>
<th>Condition</th>
<th>PM (N=25)</th>
<th>PS (N=25)</th>
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<tr>
<td>Excellent</td>
<td>Good jaw relaxation, no reflex, No movement, no laryngospasm.</td>
<td></td>
</tr>
<tr>
<td>Acceptable</td>
<td>Good/ incomplete jaw relaxation, and/or mild reflex and/or moderate movement and no laryngospasm.</td>
<td></td>
</tr>
<tr>
<td>Unacceptable</td>
<td>Poor jaw relaxation and/or moderate/severe reflex and/or severe movement or laryngospasm.</td>
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**Table: 2 Side Effects**

<table>
<thead>
<tr>
<th>Side Effects</th>
<th>PM</th>
<th>PM</th>
<th>PS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laryngospasm</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Blood on LMA</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Sore throat</td>
<td>2</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Myalgia</td>
<td>0</td>
<td>0</td>
<td>5</td>
</tr>
</tbody>
</table>

All three groups were comparable & no statistical difference was found among three groups with respect to demographics. There was a significant reduction in the dose of propofol required for successful LMA insertion in PM (2.52mg/kg) & PS (2.66mg/kg), (p<0.01) compared to group P (3.1mg/kg) (Figure 1). Also propofol dose requirement in group PM was significantly low than group PS (p<0.05) (Table 1).
Apnoea was observed in 80%, 48% and 84% patients in group P, PM & PS respectively. Duration of apnea was significantly higher (p<0.05) in groups P (43.15 ± 4.65 seconds) and PS (97.71 ± 5.50 seconds) as compared to group PM (20.33 ± 4.05 seconds). Even Group PS had significantly higher duration of apnea compared to group P (p<0.05). First time successful LMA insertion rate was significantly high in PM (88%) & PS (84%) groups compared to group P (56%) (p<0.05) (Figure 2).

Jaw relaxation in PM & PS groups was found to be better over control group P in which further boluses of propofol were required for successful LMA insertion (Figure 3). 36% patients had poor jaw relaxation in group P as compared to 4% in group PM and none in group PS. Patients with no coughing/gagging were significantly higher (p<0.05) in group PM (76%) and group PS (72%) compared to group P (28%) (Figure 4). 60% patients had head or limb movement during LMA insertion in group P in which 15% patients had severe movement requiring further boluses of propofol (Figure 5). Overall conditions for LMA insertion was either excellent or acceptable with no statistically significant difference between group PM (92%) & group PS (88%) (Figure 6). This was significantly higher (p<0.05) over group P (52%).

In hemodynamic changes, decrease in MAP from pre-induction value was seen in all the three groups but it was significant (p<0.05) only in group P not requiring any medication (Figure 7). Heart rate fluctuations were observed more in group P as compared to group PM & PS. Initially there was bradycardia followed by tachycardia after LMA insertion in group P. No significant changes were seen in PM & PS groups. The arterial oxygenation (SPO2) did not show significant changes in any group.

No significant difference was seen in all groups in view of side effects like laryngospasm, blood on LMA & sore throat. Myalgia was recorded in 20% of patients in group PS only (Table 2).

**DISCUSSION**

The LMA has gained popularity as a general purpose airway device and is currently used as frequently as the endotracheal tube. Once patient is adequately anaesthetized, it can be inserted blindly, without recourse to laryngoscopy. Endotracheal intubation but not laryngeal mask airway insertion may be associated with narrowing of the glottic aperture postoperatively. The LMA is tolerated at lower anesthetic concentration than the tracheal tube which allows earlier emergence from anesthesia.

A variety of induction and co-induction agents have been used for the placement of LMA. Such an agent should have the following characteristics.

- **Fast induction**
  - Adequate relaxation and reflex suppression
  - Easy insertion
  - Cardio respiratory stability
  - Minimal side effects and contraindications
  - Good patient acceptance
Depression of pharyngeal and laryngeal reflexes is crucial for successful LMA insertion. Different intravenous induction agents have been tried for LMA insertion. Scanlon et al found propofol as better choice than thiopentone for LMA insertion. Studies show an incidence of poor insertion ranging from 38-60% with standard induction doses (2-3mg/kg) of propofol associated with side effects like swallowing, gagging, coughing, limb movement etc. In the present study, average dose of propofol required for successful LMA insertion in unpremedicated patients was found to be 3.1 mg/kg, still the incidence of successful insertion at first attempt was only 56% with side effects like coughing, gagging, head/limb movement, hypotension & prolonged apnea. Similarly according to Waffa T. S., successful insertion at first attempt was seen in 60% patients along with significant fall in mean arterial pressure and increase in heart rate seen in post induction period with a dose of 3.0 mg/kg of propofol. K.M.Ho found correct LMA positioning after first attempt in 67% patients but having significant reduction in mean arterial pressure with a dose of 3.0mg/kg of propofol.

Various studies have been conducted by adding various drug combinations like opioids, benzodiazepines, muscle relaxants & other volatile anesthetic adjuvants to propofol for ease of LMA insertion (excellent to acceptable). Benzodiazepines are well known to reduce upper airway reflexes. Propofol and midazolam co-induction also results in significant reduction of total dose of propofol. The purpose of the present study was to compare the ease of LMA insertion using propofol alone & in combination with midazolam or low dose succinylcholine. Salem found successful LMA insertion after first attempt in 95% patients and excellent to good insertion conditions in 100% patients in propofol & midazolam group. In the present study, addition of midazolam to propofol attenuated the physical responses to LMA insertion, providing excellent to acceptable conditions in 92% of patients & successful insertion at first attempt in 88% patients. This finding is consistent with previous studies where midazolam has been shown to improve conditions for LMA insertion. Midazolam when used with propofol was found to provide haemodynamic stability which may be useful in elderly patients. There was a transient nonsignificant hypotension (P>0.05). Changes in HR were also not significant.

However the use of midazolam in short term surgery may be controversial as its duration of action is long. So short acting muscle relaxants have been used as adjuvants. Although rapid onset, short acting, non-depolarising neuromuscular blocking agents are available, they have yet to completely replace succinylcholine. Succinylcholine suppresses laryngeal reflexes by depolarisation of motor neurone end-plates. The usual dose of succinylcholine required for intubation is 1-2 mg/kg. Side effects which limit its usefulness include prolonged apnoea, true anaphylaxis and the most frequent is myalgia, occurring in up to 60% of patients. A reduction in postoperative myalgia using a reduced dose of succinylcholine (0.5 mg/kg) for nasal intubation has been demonstrated with satisfactory insertion conditions by Nimmo and colleagues. Yoshino et al found excellent to good LMA insertion conditions with succinylcholine 0.5 mg/kg (95%) compared to dose 0.25 mg/kg (60%) but with more side effects like prolonged apnoea duration (234 sec Vs 194 sec), fasciculations & myalgia. In the present study, the duration of apnea was higher in PS group compared to PM and P. However there was no clinical problem. However in patients with cholinesterase deficiency, it could be much longer and should be avoided in these patients. Ho.K.M.(1999) found improved LMA insertion condition in 93% patients with succinylcholine 0.1 mg/kg & propofol 2.5 mg/kg compared to 60% patients with propofol alone. The total dose of propofol was lower in succinylcholine group than propofol alone & was associated with less hypotension (p<0.05) but having myalgia in 23% patients.
In our study, addition of minidose of succinylcholine to propofol facilitated LMA insertion, by improving mouth opening, relaxing pharyngeal muscles and abolishing the gagging and coughing responses with less limb movements. It gave us ability to rapidly & reliably secure patient’s airway with LMA resulting in excellent/acceptable conditions for LMA insertion. The improvements in overall conditions were comparable in both groups PS & PM with hemodynamic stability. The propofol group had a greater fall in mean blood pressure and heart rate after induction and changes were significant at all intervals without any complication but it may mandate a reduction in dosage of propofol in old frail patients and those with cardiovascular diseases as seen in other study. In our study, because of low dosage, myalgia was observed in 20% patients in PS group after 24 hours of surgery which was invariably mild allowing the routine work. However potential problems such as masseter spasm, prolonged apnoea, myalgia may be seen in patients with pseudocholinesterage defficiency and succinylcholine should be avoided in such cases.

Although there is an improvement in the overall ease of LMA insertion, there is no significant difference in postoperative complications like sore throat & blood on LMA. Other factors like cuff pressure & lubricant may be more important than trauma at insertion in determining incidence of these complications.

CONCLUSION

Midazolam & succinylcholine both facilitated LMA insertion producing excellent to acceptable conditions during propofol anaesthesia and provided almost similar conditions for LMA insertion. Both caused a reduction in dose of propofol required for LMA insertion and maintained haemodynamic stability with minimum side effects. However, mini-dose succinylcholine is not recommended in patients prone to myalgia.

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Midazolam or mini-dose succinylcholine as a co-induction

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