A randomized controlled double blind study on quick intubation regimen using vecuronium priming infusion technique with the use of patient controlled analgesia pump vs bolus priming technique

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Received September 8, 2005

Background & objectives: Priming principle is implied to hasten intubation with the use of vecuronium. Priming dose is usually injected by bolus and certain side effects have been observed due to acute rise in plasma levels after bolus injection. In the present study priming infusion regimen of vecuronium using patient controlled analgesia (PCA) pump was compared for the intubation dose onset, intubation, and the side effects with the usual bolus priming.

Methods: Adult ASA grade 1 patients of both sexes (n=112) were randomized into four groups of 28 patients each. In group 1 patients, vecuronium (10μg/kg) was given bolus (30sec). In group 2, priming infusion (5μg/kg/min) regimen for vecuronium (1200μg/kg) was used by setting up the background infusion rate (ml/h) at 1/4th of the patient body weight on PCA pump. Priming infusion for 3min delivered the priming dose (15μg/kg). In group 3, higher priming infusion (10μg/kg/min) was given by setting up the PCA pump at the ½ the patient body weight for 1.5 min, to deliver same dose (15μg/kg). In group 4, the priming infusion (10μg/kg/min) for 2min delivered higher priming dose (20μg/kg). After induction of anaesthesia with fentanyl, propofol, the intubating dose of vecuronium (0.06mg/kg) was injected by activating patient demand button and grading laryngoscopy/intubation after 1 min in each group.

Results: In demographically similar patients, the laryngoscopy/intubation was excellent in 53 per cent (group 3) and in 64 per cent patients (group 4) after 1 min of the intubation dose. While in bolus priming (group 1), 50 per cent patients developed ocular side-effects, none had it on priming infusion in groups 2 or 3. Only 2 patients complained of diplopia at the higher priming dose (20μg/kg) (group 4).

Interpretation & conclusion: PCA pump regimen for vecuronium priming infusion significantly shortened the onset of intubation. Side effects from the smaller priming dose by bolus were not seen in priming infusion regimen.

Key words Intubation - PCA pump - priming infusion - priming principle - vecuronium

Priming principle has been implied to hasten the onset of nondepolarizing neuromuscular blocking agents (NMBA)\(^1,2\). It includes injection of subclinical dose of vecuronium 3-4 min prior to injection of intubation dose
for its quick onset and intubation. Later on, the clinical utility of priming for rapid intubation sequence was questioned due to higher incidence of side effects, and the potential risk of aspiration in full stomach patients in emergency. All studies done so far injected priming dose by bolus and recommended a dose of 10 per cent the drug's effective dose (ED₉₅) and the priming interval not less than 5 min. Since, some of the side effects like histamine release after atracurium injection have been correlated with the acute rise in plasma levels after bolus injection, and slow rate of injection was recommended to avoid this side effect, we hypothesized that the priming dose administration by infusion might also decrease the potential side effects of the bolus priming dose. The present study was therefore undertaken to evaluate the use of priming of vecuronium by infusion with the use of patient controlled analgesia (PCA) pump and compare it with the bolus priming dose administration.

Material & Methods

The study was performed at Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow in operation theatre during 2002. Following institute's ethics committee approval, 112 consecutive American Society of Anaesthesiologists (ASA) grade 1 patients aged 34 to 54 yr, posted for cholecystectomy, and abdominal operations were included. The number of patients to be studied was calculated using power analysis considering 20 sec difference in between mean onset time of intubating dose effect significant at standard deviation of 20 in each population, at alpha (two sided) the confidence interval of 95 per cent and the beta (type II error) value of 0.05. The number of patients to be studied was calculated using power analysis considering 20 sec difference in between mean onset time of intubating dose effect significant at standard deviation of 20 in each population, at alpha (two sided) the confidence interval of 95 per cent and the beta (type II error) value of 0.05. The number of patients to be studied in each group was calculated to be 27. Thus, we decided to study 28 patients in each group to make total number of 112. The written informed consent was obtained from all patients after explaining the nature of study. Patients with neuromuscular disorder or taking medicines to interact with muscle relaxants like calcium channel blocker, antiepileptics, aminoglycosides known to interact with NMBA and the anticipated difficult intubation were excluded from the study at the time of pre-anaesthetic evaluation.

All patients received fentanyl 2μg/kg intravenously before the study to assist neuromuscular junction (NMJ) monitoring. NMJ monitoring was started using Accelograph (Biometer, Denmark). Ulnar nerve was stimulated at the wrist using surface electrodes. Initially supramaximal stimuli were titrated and then train-of-four (four stimuli at 2 Hz) were given at 15 sec interval to monitor the vecuronium effect.

**Priming by infusion protocol:** Graseby PCA pump-3300 (Graseby Ltd., UK) syringe infusion pump is designed to deliver background infusion of the drug and can also deliver the same drug as bolus in 20 to 30 sec by activating the patient demand button at any point of time. This property of the equipment was used to develop vecuronium priming infusion regimen. The background infusion rate was set to deliver priming dose at two infusion rates (5 and 10 μg/kg/min). Intubation dose was injected by activating the patient demand button at the end of 3 min. Priming dose infusion period was used to pre-oxygenate patients. Vecuronium bromide (1200 μg/ml) solution was prepared in 50 ml syringe up to 10 ml volume. At this concentration of the vecuronium, by setting up the background infusion rate (ml/h) at 1/4th body weight of the patient, the desired infusion rate of 5 μg/kg/min was delivered and by setting at 1/2 the body weight (ml/h) vecuronium (10 μg/kg/min) was infused at a higher rate. The PCA pump was programmed to inject bolus intubating dose of vecuronium (0.06 mg/kg) on pressing demand button and setting the bolus dose (ml) as follows: Bolus dose (ml) = [0.06×body wt. (kg)/1.2] ml in 20 to 30 sec.

All patients were randomly assigned into the four study groups on the basis of the random number generation on computer. In group 1-(control) smaller priming dose of vecuronium (10 μg/kg) was given intravenously as bolus (in 30 sec) and then intubating dose (0.06 mg/kg) after 3 min and the laryngoscopy-intubation was graded 1 min after intubating dose injection. In group 2, vecuronium priming infusion rate was 5 μg/kg/min for 3 min i.e. total priming dose (15 μg/kg) followed by intubating dose (0.06 mg/kg) by pressing patient demand button and the laryngoscopy-intubation after 1 min of intubating dose. In group 3, higher vecuronium priming infusion rate (10 μg/kg/min) was used by setting up the background infusion rate (ml/h) at half of the body weight of patient for 1 min 30 sec, i.e., total priming dose (15 μg/kg) was the same as in group 2. Intubation dose (0.06 mg/kg) was again given
in same fashion as in group 2 by PCA pump and laryngoscopy-intubation 1 min after intubation dose. In group 4 patients priming infusion rate (10µg/kg/min) was the same as in group 3 given for 2 min i.e., higher priming dose (20µg/kg) with the same intubating dose as in groups 2 and 3. Again laryngoscopy-intubation was performed 1 min after the intubation dose.

All patients were awake during priming and oxygenated for 3min by loosely fitting facemask. Anaesthesia was induced with another dose of fentanyl (1µg/kg) and propofol (1-2 mg/kg) titrated till the loss of eyelash reflex at the end of preoxygenation. The patient demand button was activated at the end of 3 min preoxygenation time to inject intubating dose of vecuronium (0.06 mg/kg). Experienced anaesthetist graded laryngoscopy and intubation as modified by the Lund and Stovener12 and used by Mirakhur et al13, at the end of 1 min of intubation dose injection and he was blinded for the priming regimen (Table I).

Besides neuromuscular junction monitoring, ECG lead-II, heart rate, non-invasive arterial blood pressure, and pulse oximetry were also continuously monitored in all patients. Patients were observed for the priming dose side effects like blurring of vision, difficulty in eye opening or swallowing or head lift, heaviness over chest or any evidence of hypoventilation by using Wright's spirometer (Ohmeda, Japan).

Statistical analysis: All proportions were analysed using Chi-square test and Student's t-test to compare mean values. *P*<0.05 was considered as statistically significant at 95 per cent confidence.

### Table I. Grades of direct laryngoscopy and intubation

<table>
<thead>
<tr>
<th>Grades</th>
<th>Description</th>
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<tbody>
<tr>
<td>Excellent</td>
<td>Good jaw relaxation</td>
</tr>
<tr>
<td></td>
<td>Vocal cords open</td>
</tr>
<tr>
<td></td>
<td>No response to intubation</td>
</tr>
<tr>
<td>Satisfactory</td>
<td>Good jaw relaxation</td>
</tr>
<tr>
<td></td>
<td>Vocal cords open</td>
</tr>
<tr>
<td></td>
<td>Minimal coughing on intubation</td>
</tr>
<tr>
<td>Fair</td>
<td>Jaw relaxed</td>
</tr>
<tr>
<td></td>
<td>Vocal cords moving</td>
</tr>
<tr>
<td></td>
<td>Intubation requires firm pressure</td>
</tr>
<tr>
<td></td>
<td>Marked coughing on endotracheal tube</td>
</tr>
<tr>
<td>Poor</td>
<td>Intubation impossible due to poor jaw relaxation</td>
</tr>
<tr>
<td></td>
<td>And/or closed vocal cords</td>
</tr>
</tbody>
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### Results

Physical characteristics of the patients like age, sex, weight, and height were similar in all the study groups (Table II). Intubating conditions were comparable between groups 1 and 2 and in majority of patients (22/28) in both groups, fair to satisfactory intubating conditions were achieved after 1 min. However, in 2(7%) patients in group 1 intubation was rated poor due to poor jaw relaxation and the cord movement Fig. In groups 3 and 4, intubation was rated excellent (*P*<0.05) compared to group 1 in 53 and 64 per cent patients respectively (Table III; Fig).

On the basis of recorded myograph, lag time (from the time of priming dose injection to first sign of suppression in T1 amplitude) after bolus priming was 58±29.5 sec in group 1, and was significantly longer in groups 2, 3 and 4 patients (*P*<0.05), compared to group 1. Onset time [interval between the injection of intubating dose till the zero response to train of four (2Hz) stimuli] of the intubating dose effect was

![Fig. Bar diagram showing the distribution of grades of laryngoscopy and intubation amongst the studied patients in different priming regimens.](image-url)
comparable in similar priming dose groups 1 and 2 and significantly shorter in groups 3 (P<0.05) and 4 (P<0.01). The NMJ block recovery time (up to 10% of control twitch height) from the intubating dose was significantly (P<0.05) prolonged in group 4 (Table III).

In group 1 significantly higher number (50%) of patients developed blurring of vision and 9(33%) patients noticed difficulty in eye opening as well. These symptoms started 1 min after bolus priming dose administration. One patient also complained for heaviness over the chest and difficulty in head lift. Voluntary hyperventilation and oxygen by mask however helped allaying any incidence of desaturation. Symptoms improved in group 1 by the end of 3 min of priming interval. In groups 2 and 3, none of the patients developed the known side effects during priming (Table III). However, 2(7%) patients in group 4 complained of blurring of vision and diplopia by the end of 3 min. Nystagmus was also observed in these two patients.

In this study we have observed that with the help of PCA pump it was possible to inject priming dose by infusion utilizing 3 min preoxygenation period without producing side effects at the priming infusion rate of 5μg/kg/min. At the end of priming dose by infusion, the intubating dose of vecuronium injected by activating the patient demand button, had onset time well within 1 min (group 2). Even at higher priming infusion rate (10μg/kg/min) for same priming doses (15μg/kg; group 3), patients did not complain of side effects related to muscle weakness as reported after bolus priming.

In relation with NMBA, response variability is known for different groups of muscle in same patients14,15. In small doses of NMBA, diaphragm is the most resistant muscle of body16,17, while small rapidly moving muscles viz., ocular muscles18, glossal muscles of swallowing19 and genohyoid20 are affected earlier. It has also been reported that the side effects, which appear during bolus priming are short lasting and rather improve at the peak time of monitored effect of the priming dose at adductor pollicis21. This explains our observation of improvement in side effects by the end of 3 min in group 1 patients after bolus priming and no side effects on its infusions at 5 (group 2) and at 10μg/kg/min (group 3) for the same priming dose (15μg/kg).

It can be hypothesized that the acute rise in plasma levels of NMBA after priming bolus probably affected the small sensitive muscles earlier rather than the relatively resistant diaphragm, and presented the symptoms like diplopia, blurred vision, difficulty in eye opening (ocular muscle), difficulty in sustained head lift (neck muscles) and difficulty in breathing in supine position (genohyoid muscle). Genohyoid acts as the upper airway dilator during inspiration by displacing the hyoid bone anteriorly22. Its early paresis will lead to increase in upper airway resistance especially in supine position and the breathing difficulty18. Since the acute rise was not possible in priming by infusion, we could use higher priming dose (15μg/kg) without the side effects of smaller muscles paresis.

Laryngoscopy and intubation grades significantly improved in patients of identical priming dose infusion.
at higher infusion rate (group 3) compared to those with low infusion rate (group 2). The observed difference may be because the drug infused in the last one min of 3 min of infusion in group 2 patients was not able to show its effect while in group 3, the waiting period of 1 min 30 sec after priming dose infusion, allowed the last bit of priming dose to complete its effect by the time intubating dose was injected. However, the higher priming dose again showed ocular side effects in few patients in group 4, and may not be considered safe.

In summary, in spite of the availability of quick acting NMBA drugs, vecuronium is still very much in use in most of the places and to reduce the onset time of vecuronium within 1 min with good intubating conditions, priming infusion regimen in awake patients was effectively used for preoxygenation with the help of PCA pump. The priming dose infusion protocol for 10μg/kg/min for the priming dose of 15μg/kg did not show the side effect of muscle paresis seen after its bolus injection. Increase in priming dose from 15μg/kg to 20μg/kg did not improve further the intubation condition at 1 min but showed ocular side effect in few patients and prolonged recovery.

References


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