# Shortening the onset time of atracurium for rapid tracheal intubation

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## Summary

The 'Priming principle' applied to non-depolarizing muscle relaxant atracurium was studied in 60 patients. This was a double blind study. The conditions observed for intubation were graded and the efficacy of priming dose of atracurium for shortening the onset time of intubation was studied. The patients were of ASA classification I and II and received standard premedication.

The purpose of the study was to use the priming dose of atracurium to shorten the onset time of intubating dose of atracurium. This would be desirable in conditions requiring rapid intubation and in situations when the depolarizing muscle relaxant suxamethonium is contra-indicated. The results were statistically significant.

*Key words*: Priming principle, atracurium, intubating dose.

## Introduction

One of the main differences between the depolarizing and the non-depolarizing muscle relaxant is the onset time. Suxamethonium can produce profound muscle relaxation suitable for endotracheal intubation from 45 seconds whereas the non-depolarizing muscle relaxants requires two minutes or more to produce adequate relaxation for intubation. The use of suxamethonium has been known to be accompanied by numerous side effects but is still recognised as the drug of choice for circumstances where rapid endotracheal intubation is desired.

With the emergence of 'intermediate' duration muscle relaxants like atracurium and vecuronium, the search is still on for an ideal muscle relaxant which can bridge the gap between the depolarizing and the non-depolarizing muscle relaxant, producing rapid onset of action with minimal side effects and yet providing moderate duration of action.

The priming principle refers to the administration of a small (subparalysing) dose of non-depolarizing neuromuscular blocking drug a few minutes before the intubating dose is given.[1,2] The rationale is based on the fact that the high margin of safety of neuromuscular transmission allows 70–75% occupancy of cholinergic receptors without any significant effect on neuromuscular activity. The administration of a second larger dose at the time of development of maximal effect of priming dose rapidly increases receptor occupancy to over 90% required for profound neuromuscular blockade.[3] It was suggested the priming dose be 15–20% of the customary intubating dose and priming time interval be 3–4 min.[4,5]

## Patients and methods

Sixty patients aged between 18–60 years ASA classification of I or II[6] were included in the study. The average weight of the patients was 56.7 kg with a standard deviation of 12.2. The average age of the patients was 36.7 years with a standard deviation of 11.9. Only cases undergoing elective surgery requiring intubation were included. Patients with known neuromuscular diseases, known hypersensitivity to atracurium and those where there was anticipated difficulty in intubation were excluded from the study. Those undergoing neurosurgical or cardiothoracic procedures were also excluded.

All patients were given premedication consisting of pethidine 1 mg/kg and promethazine 0.25 mg/kg intramuscularly 45 minutes to one hour before induction. The method of selection of patients for priming or non-priming was random.

Two sets of syringes were prepared by the trialist as shown in Table I. Each patient was given either set A or set B (control) at random. The contents of set A or set B were not known to the doctor administering the drug. The trialist was not told which set was given to the patient. After the first dose was given from the 2.5 ml syringe the patients were assessed for any associated problems attributed to priming i.e. difficulty in breathing, swallowing and drooping of eyelids. Three minutes later, the patient was induced by titrating 2.5% thiopentone sodium until loss of eyelids reflex was noted. The remaining dose of atracurium was given from the 5 ml syringe of the same set. The patient was then ventilated with 70% nitrous oxide and 30% oxygen. Sixty seconds after the administration of the contents of the 5 ml syringe, the patient was assessed for endotracheal intubation. The intubating conditions were assessed as stated in Table II.

**Table I**
**Sets of syringes prepared for trial**

| Sets | 2.5 ml syringe | 5.0 mil syringe | Total dose Atracurium (mg/kg) |
|---|---|---|---|
| Set A | 0.075 mg/kg Atracurium | 0.425 mg/kg Atracurium | 0.50 mg/kg |
| Set B | Equivalent volume of normal saline | 0.50 mg/kg Atracurium | 0.50 mg/kg |

**Table II**
**Grades of responses to intubation**

| | |
|---|---|
| Grade I: | Excellent. Jaws relaxed. Cords opened and no bucking response to intubation. |
| Grade II: | Good: Cords opened but minimal bucking to intubation. |
| Grade III: | Cords moving. Able to intubate with vigorous movement and bucking. |
| Grade IV: | Impossible to intubate due to poor jaw and cord relaxation. |

Grades I and II were classified as acceptable intubating conditions and grades III and IV as non-acceptable intubating conditions. Statistical significance of the acceptable and non-acceptable intubating conditions were tested using the chi-square tests.

## Results

The adverse effects were subjective patient feelings assessed two to three minutes after the priming dose. Chest discomfort was taken as feeling of tightness or heaviness over the chest. Clinically they were able to maintain a good tidal volume. As the diaphragm is known to have a higher margin of safety it is unlikely that the diaphragm is effected.[7] No patients developed feelings of suffocation. Swallowing difficulty was expressed by the patient on direct questioning. The dry mouth following premedication with promethazine could have some contribution. Ptosis was noted for significant eyelid droop.

The result showed that atracurium 0.075 mg/kg given three minutes before induction significantly ($P < 0.01$) shortens the onset time of atracurium to 60 seconds to achieve satisfactory intu-

**Table III**
**Response to endotracheal intubating conditions after priming or no-priming dose of atracurium**

| Response to intubation after 60 seconds | After a priming dose of atracurium | No priming dose |
|---|---|---|
| Grade I | 12 | 0 |
| Grade II | 18 | 6 |
| Grade III | 6 | 3 |
| Grade IV | 1 | 12 |
| Total | 37 | 21 |

$X_c^2 = 13.54$

$P < 0.01$ level

**Table IV**
**Adverse effects of priming with atracurium**

| | Problems | No. of patients | Percentage of total |
|---|---|---|---|
| 1. | Chest discomfort | 30 | 81.0 |
| 2. | Difficulty in swallowing | 10 | 27.0 |
| 3. | Eyelids droop | 13 | 31.1 |
| | Total | 37 | |

bating conditions. Out of the 60 patients studied, two patients had to be omitted from the study. One developed significant urticarial rashes on the skin over the venous injection line following the first dose (which contains atracurium). The other case was one of an unexpected difficult intubation with anterior larynx and two teeth in the way. The cords were not visualised at the time of intubation which took about two minutes to be accomplished.

## Discussion

A priming dose of atracurium does shorten the onset time of atracurium to factilate favourable intubating conditions at 60 seconds. Apart from a more rapid onset time observed, other desired effects are observed from the use of a priming dose. An unexpected hypersensitivity reaction can be alerted (as illustrated in one of the cases studied) and its use discontinued. As for atracurium, the incidence of cutaneous manifestation is high but generally harmless. The main intubating dose used is decreased and thus reducing the possibility of undesired effects like transient hypotension as compared to when a larger dose is used without a prior priming dose.[9]

In a clinical situation like a penetrating eye injury and a patient with a full stomach requiring urgent surgery, the use of suxamethonium to facilitate rapid endotracheal intubation is faced with problems of extrusion of eyeball contents and aspiration of gastric contents following fasciculations. The use of a non-depolarizing muscle relaxant requires a period of two to three minutes to achieve adequate relaxation to facilitate intubation. This long period requires assisted ventilation, which is undesired in an unprepared stomach, without the risk of developing hypoxia. With a priming dose, after a period of adequate pre oxygenation for about three minutes, assisted ventilation need not be performed after an intubating dose atracurium without the risk of developing hypoxia in 60 seconds. Intubation can satisfactorily be performed 60 seconds later.

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