ISSN: 2581 – 3633
PubMed - National Library of Medicine - ID: 101745081

International Journal of Medical Science and Advanced Clinical Research (IJMACR)

Available Online at:www.ijmacr.com

Volume – 8, Issue – 4, July - 2025, Page No.: 01 – 08

Effect of Priming on Intubating Conditions Produced By Atracurium - Comparative Study

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How to citation this article: Dr Burhan Ul Khursheed, Dr Shikha Sharma, Dr Nandita Mehta, Dr Sheikh Tabeen, "Effect of Priming on Intubating Conditions Produced By Atracurium - Comparative Study", IJMACR- July - 2025, Volume – 8, Issue - 4, P. No. 01 – 08.

Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

Background: The study was done to see how priming affects the intubating conditions caused by Atracurium.

Material and methods: Patients were distributed into 3 groups by random. The subjects in each group were 40 patients. Group A- Priming with 0.1mg/kg Atracurium followed by intubation at 90 second after intubating dose of 0.6mg/kg Atracurium. Group B -0.1mg/kg Atracurium i.v. + Intubation at 120 sec after 2nd dose of 0.6mg/kg Atracurium. Group C- Placebo & Normal saline with intubation at 90 sec post single intubating dose (0.7 mg/kg) of Atracurium. Pre-anaesthetic check-up was performed before surgery, which comprised a detailed history, general physical and systemic examination, and airway evaluation, for every patient. All standard investigations and any other special investigations as might have been required for the patient were performed. The demographic profile i.e. age, sex, weight, height and BMI. Pre- anaesthetic examination was conducted with written informed consent of all patients. The statistical analyses were performed with special care to guarantee the robustness and validity of the findings using different R (v4. 4. 0; R Core Team, 2022). Statistical Description Descriptive statistics were used in this study. The mean ± SD and (Min-Max) were used to describe continuous variables and Number (%) was used to report categorical variables. $P < 0.05$ was considered statistically significant. Means across groups were compared by ANOVA test. The chi-square (χ^2) test was used to test

the association of categorical variables. The ggplot2 package was used to create a variety visualisations like heat maps, bar charts and violin plots which enabled a full and detailed understanding of the data.

Results: There was no significant difference in gender ratio between the two groups; 42 males and 35 females in Group A and 47 males and 35 females in Group B. Group B had more of the female contestants, a quarter of them were females and rest were males, about15 Contestants. In contrast, the same split as Group A held in Group C, 21 males and 19 females. The Vocal cord positions were divided into three categories: Closed, Semi-closed and Open. The results in terms of the group-A (Table 3).Open vocal cords were commonest on Group B (57.5%), compared to Group A (25%) and Group C (30%). This may mean that Group B had probably been in the most optimal conditions for intubation in which open vocal cords is usual predictor of better visualisation of glottis and easier intubation. Furthermore, of the three groups, Group B had the fewest number of those whose vocal cords were half-closed (20%) while Groups A and C presented an equivalent proportion of 40%.The neuromuscular blockade was monitored using TOF monitoring in which Group B has the highest proportion (52.5%) of patients with only 1 twitch, indicating the deepest neuromuscular blockade. Compared with Group A (30%) and Group C (35%). Lowest % of Partial Blockade (1,2,3 Twitches = 75% Strength): Group B has the lowest proportion (22.5%) of patients in this category, suggesting fewer patients had lighter blockade. *Comparison*: Group A (25%), Group C (30%). Intermediate Blockade (1,2 Twitches = 80% Strength): Group A has the highest proportion (45%), implying more patients in this group had *moderate blockade*. Group B (25%) shows the lowest in this category, reinforcing its trend toward deeper blockade.

Conclusion: Priming is a valuable technique for achieving rapid muscle relaxation, especially when depolarizing agents like succinylcholine are contraindicated. In this study, a priming dose of 0.1 mg/kg atracurium followed by 0.7 mg/kg after 3 minutes (Group B) resulted in superior intubating conditions compared to other groups. Group B demonstrated, optimal vocal cord positioning, deeper neuromuscular blockade (as indicated by TOF), and more stable hemodynamics. These findings suggest that atracurium priming is an effective and safe alternative for intubation, particularly in high-risk patients or settings where hemodynamic stability is essential.

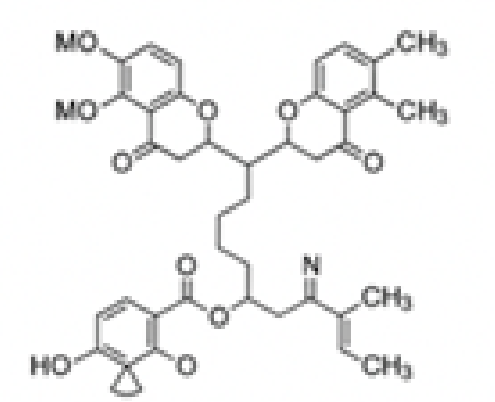
Keywords: Priming, Atracurium, Intubation, Train of Four

Introduction

Endotracheal intubation is an essential intervention in anaesthesia, intensive care, and emergency medicine to secure the airway, to enable mechanical ventilation, and to protect against aspiration. The effectiveness of intubation relies on the degree of laryngeal visualisation, the inhibition of airway reflexes, and a good level of neuromuscular blockade. Suboptimal intubating conditions can result in airway trauma, haemodynamic instability, hypoxia, and increased risk of aspiration, thus the selection of NMBAs and the manner of their administration are extremely important. Neuromuscular blockade plays an important role in the safe management of patient's airway, surgical field improvement and respiratory care during general anesthesia.[1]

It is obtained through depolarizing and non-depolarizing muscle relaxants. Depolarizing agents like

succinylcholine have been previously preferred due to fast onset and ultra-short duration of action, but are related with complications including hyperkalemia, malignant hyperthermia, and hemodynamic instability. Therefore, non-depolarizing agents, such as rocuronium, vecuronium, and atracurium, have become increasingly common, and provide a safe option with use-dependent effect even though intubation conditions are less satisfactory than those with succinylcholine. Nevertheless, these agents 99 tend to have a slower onset, and intubation may be delayed until the onset is optimal. [2]



Atracurium

Atracurium is a benzylisoquinolinium NMBA commonly employed second to its intermediate duration of action and liver-independent clearance through Hofmann degradation and ester hydrolysis. Thus, it is especially beneficial in patients with renal or hepatic disease. Its onset time, however, is relatively slow compared with that of succinylcholine, limiting its use in conditions with urgent tracheal intubation. Various techniques to accelerate the onset and facilitate intubation conditions such as priming principle have been devised to overcome this. [3,4]

This study was conducted to assess the effect of priming on intubating conditions produced by Atracurium.

Material and methods

40 patients were randomized in 3 groups. Group A - Priming with 0.1mg/kg Atracurium and intubation at 90 sec after giving intubating dose of 0.6mg/kg Atracurium. Group B - priming with 0.1mg/kg Atracurium and intubation at 120 sec after second dose of 0.6mg/kg Atracurium. Group C - Placebo with Normal saline and intubation at 90 second after single intubating dose of 0.7mg/kg Atracurium. Pre-anaesthetic check-up was performed before surgery. This involved detailed history, general physical examination and systemic examination and airway assessment of all patients. Routine investigations and any other relevant specific investigations were performed on each patient. Basic demographic profile like: age, sex, weight, height and BMI was noted. Informed written consent was obtained from all patients at the pre- anaesthetic examination. All patients were kept fasting for 8 hours before surgery. Prior to surgery, all patients were given dose of Tab Pantoprazole 40mg and Tab Alprazolam 0.5mg orally the night prior to surgery. On the morning of surgery intravenous line secured with 20G venous cannula. Patients received Inj pantoprazole 40mg I/V and Inj Ondansetron 0.1mg/kg I/V. The standard monitor were attached to all patients to monitor (NIBP, Pulse rate, Spo2, ECG) upon arrival to the operating theatre. Baseline Blood pressure, MAP, Pulse, peripheral oxygen saturation (Spo2) was recorded. All surgeries proceeded under general anaesthesia. After giving a priming dose of atracurium (only in a group A and group B), Inj Propofol 2mg/kg IV was given. Patients in group A and group B got a intubating dose of 0.6mg/kg Atracurium and patients in group C got 0.7mg/kg of atracurium intubating dose after 3 minutes of priming. Intubating conditions were assessed by position of vocal cords,

Neuromuscular blockade was assessed by train of four responses, using peripheral nerve stimulator to stimulate the ulnar nerve at wrist non-invasively, number of twitches and strength of contraction of adductor pollis muscle. Only those train of four (TOF) responses was seen just before intubation. Strength of twitch was seen as 1, 2, 3 twitches (75%) = Partial neuromuscular blockade. 1,2 twitches (80%) = Deeper blockade. 1 twitch (100%) = Near -complete blockade. Maintenance of anaesthesia was done with N20:O2 (60:40), intermittent positive pressure ventilation, isoflurane and additional doses of atracurium, until adequate surgery had taken place. At end of surgery neuromuscular blockade was antagonised with Inj Neostigmine (0.05mg/kg) and Inj Glycopyrrolate (0.1mg/kg). Tracheal extubation performed after appropriate suctioning.

The statistical methods were carried out with rigorous methodological detail to ensure the reliability and validity of the results, using different packages in R (v4.4.0; R Core Team, 2022). This study followed descriptive statistical approaches. Continuous variables are reported as Mean± SD (Min-Max) and categorical variables are reported as Number (%). An alpha level of 0.05 significance was used for all tests. An Analysis of Variance (ANOVA) test was used to compare means of those in each condition. The Chi-square (χ^2) test examined whether there were associations between qualitative variables. Heat maps, bar charts, and violin plots were made using the ggplot2 package. The reports were not only colourful but provided an extensive and detailed interpretation of the data.

Results

Table 1: Basic characteristics of patients studied between three groups

Basic Characteristics	Group A	Group B	Group C	P value
No. of patients	40	40	40	
Age (Mean ± SD)	38.7 ± 11.5	41.4 ± 11.5	42.5 ± 11.0	0.313
Weight (Mean ± SD)	69.4 ± 11.5	70.4 ± 12.8	67.0 ± 10.6	0.424
Male: No. (%)	21 (52.5)	15 (37.5)	21 (52.5)	0.532
Female: No. (%)	19 (47.5)	25 (62.5)	19 (47.5)	0.565
ASA Grade I: No. (%)	20 (50)	19 (47.5)	23 (57.5)	0.811
ASA Grade II: No. (%)	20 (50)	21 (52.5)	17 (42.5)	0.799

The baseline characteristics among Group A, Group B, and Group C revealed statistically insignificant differences, supporting the contention that groups were appropriately matched before any intervention. Each group included 40 patients, thus ensuring an equal sample size for comparison. The mean age was 38.7 ± 11.5 years in Group A, 41.4 ± 11.5 years in Group B, and 42.5 ± 11.0 years in Group C, with a p-value of 0.313, rendering this variable statistically insignificant among the groups. Likewise, body weight was similar and had mean values of 69.4 ± 11.5 kg, 70.4 ± 12.8 kg, and 67.0 ± 10.6 kg in Groups A, B, and C, respectively, with a p-value of 0.424. The distribution of gender was also balanced: Groups A and C had 52.5% males and 47.5% females, while Group B had 37.5% males and 62.5% females, with p-values of 0.532 and 0.565 among

males and females, respectively, confirming non-significance. Regarding the ASA physical status, it was evenly distributed among the groups for both Grade I and II, with p-values of 0.811 and 0.799, respectively. Group A had 50% of patients for both categories of ASA Grade I and II, whereas Group B had 47.5% in Grade I with a marginal increase to 52.5% in Grade II, while Group C had 57.5% in Grade I and 42.5% in Grade II. These findings collectively suggest that all three groups were demographically and clinically comparable at baseline. This homogeneity is crucial in clinical studies, as it reduces the potential for confounding variables and strengthens the validity of any observed differences in outcomes, allowing for a more accurate interpretation of the effects attributable to the interventions under investigation.

Table 2: Number and Strength of Twitches on TOF

Category	Group A	Group B	Group C
1,2,3 (75%)	10 (25%)	9 (22.5%)	12 (30%)
1,2 (80%)	18 (45%)	10 (25%)	14 (35%)
1 (100%)	12 (30%)	21 (52.5%)	35%)

The levels of neuromuscular blockade among the groups show that Group B had the strongest level of blockade among the groups studied, since the highest proportion of subjects in Group B (52.5%) showed only 1 twitch response as opposed to 30% in Group A and 35% in Group C. Supporting the observation of a stronger neuromuscular effect in Group B is the lower percentage of lighter partial blockade cases (75% strength), in which the subjects showed 1, 2, or 3 twitches, with only 22.5% of such cases, compared to Group A and C. On the other hand, Group A showed the highest proportion (45%) of patients with 1 or 2 twitches, demonstrating a likely trend toward moderate blockade, whereas Group B had the lowest proportion (25%) in this intermediate set of 1 to 2 twitches. Basing on these findings, one may assert that Group B demonstrates significantly deeper neuromuscular blockade relative to Groups A and C, which may imply the difference in potency or duration of neuromuscular blocking agents or intervention used.

Table 3: Vocal cord position

Category	Group A	Group B	Group C
Closed	14 (35%)	9 (22.5%)	12 (30%)
Semi-closed	16 (40%)	8 (20%)	16 (40%)
Open	10 (25%)	23 (57.5%)	12 (30%)

The vocal cord postures were separated into three categories: Closed, Semi-closed, Open. Each Group (A, B, and C) are listed in the results section of the Table 3. Group B had the greatest percentage of-open vocal cord postures (57.5%) compared to Group A (25%) and Group C (30%). This likely indicated Group B had the best intubation conditions, as aligned or open vocal cords typically correlate to improved visualization of the glottis for easier intubation. Furthermore, Group B also had the lowest percentage of semi-closed vocal cord postures (20%) when compared to Group A and C at 40% of patients with semi-closed vocal cords. The semi-closed postures likely presented less resistance during intubation in Group B than Groups A and C, both had

greater semi-closed vocal cord posture percentages. Group B also had the least occurrence of closed vocal cord postures (22.5%) compared to Group A (35%) and Group C (30%). Closed vocal cords are often associated as a clinical condition that leads to more difficult intubation conditions, the less frequency in Group B lends credence to the overall notion that intubation was less difficult in Group B.

Discussion

The introduction of neuromuscular blocking agents (NMBAs) has significantly advanced anesthetic practice by enabling controlled skeletal muscle relaxation and optimizing intubating conditions. These agents are broadly categorized into depolarizing and non-depolarizing neuromuscular blockers (NDMRs). Currently, succinylcholine remains the only clinically utilized depolarizing agent. It is favored for rapid sequence induction due to its rapid onset and short duration; however, its use is limited by a range of adverse effects and contraindications.[5] Among the NDMRs, commonly employed agents include atracurium, vecuronium, rocuronium, and cisatracurium. Despite their widespread use, these agents are generally avoided during rapid sequence intubation (RSI) due to their relatively longer onset times.[6] Atracurium is unique among these agents in that it undergoes organ-independent elimination through Hofmann degradation and non-specific ester hydrolysis, making it particularly useful in patients with compromised hepatic or renal function. To circumvent the delayed onset of NDMRs, the priming technique was developed. This technique involves the administration of a sub-paralyzing (priming) dose followed by the full intubating dose, thereby facilitating a more rapid onset of neuromuscular blockade. For atracurium, the recommended intubating dose using this approach is approximately 2–3 times the ED95, corresponding to a dose range of 0.46–0.69 mg/kg.[7,8] This study aimed to evaluate the effect of priming on intubating conditions achieved with atracurium. Participants were divided into three groups. Group A consisted of approximately 21 males and 19 females, reflecting near gender parity. Group B demonstrated a female predominance (25 females and 15 males), while Group C had a gender distribution nearly identical to Group A. Vocal cord position, a critical determinant of intubation ease, was categorized as closed, semi-closed, or open. According to Table 2, Group B exhibited the highest proportion of open vocal cords (57.5%), compared to 25% in Group A and 30% in Group C. This finding suggests that Group B achieved the most favorable intubating conditions, as open cords facilitate optimal visualization of the glottis and ease of endotracheal tube placement. Group B also demonstrated the lowest incidence of semi-closed cords (20%), compared to 40% in both Group A and Group C. The depth of neuromuscular blockade, as assessed by train-of-four (TOF) monitoring, further substantiates these findings. Group B demonstrated the deepest blockade, with 52.5% of patients exhibiting only a single twitch, corresponding to 90–100% neuromuscular blockade. In contrast, only 30% of patients in Group A and 35% in Group C reached this depth. Additionally, partial blockade (defined as 1–3 twitches or ≤75% block) was least common in Group B (22.5%), compared to 25% in Group A and 30% in Group C. Group A had the highest proportion of patients (45%) exhibiting intermediate blockade (1–2 twitches, approximately 80% block), further emphasizing the superior neuromuscular suppression achieved in Group B. These findings align with those of Birsinger et al. (1996), who reported that

divided dosing of NMBAs significantly improved intubating conditions. Furthermore, Gomez-Ortiz et al.[9] conducted a randomized prospective study in 376 patients comparing intubating conditions at 1 minute using succinylcholine, rocuronium, and rocuronium with priming. Their results confirmed that priming rocuronium with vecuronium, atracurium, or cisatracurium is a safe and effective strategy in healthy patients without increasing the risk of pre-curarization. In another study, Alagha et al.[3] evaluated the efficacy of ephedrine administration following atracurium priming in a randomized clinical trial involving 64 elective surgery patients. Intubation conditions were assessed using Cooper's criteria. While a greater number of patients in the ephedrine group achieved acceptable intubation conditions (22 vs. 15), the difference was not statistically significant ($p = 0.13$). However, the ephedrine group exhibited a significantly elevated heart rate (>120 bpm, $p < 0.01$), suggesting increased cardiovascular risk without a clear benefit in intubation quality. Our study confirms that open vocal cord position, a key indicator of optimal intubation conditions, was most frequently observed in Group B (57.5%), which received priming with atracurium followed by intubation at 120 seconds. This was followed by Group C (30%) and Group A (25%). Group B also showed the lowest incidence of closed vocal cords (22.5%), reinforcing its superior efficacy in producing ideal intubating conditions. Supporting data from Phulkar et al. (2021)[10] reported that all patients receiving succinylcholine (2 mg/kg) and intubated at 90 seconds had open vocal cords, while 75% of patients in the primed atracurium group and only 23% in the non-primed atracurium group exhibited the same. These results underscore the rapid and reliable onset of succinylcholine, while also demonstrating that priming with atracurium offers a viable alternative for achieving favorable intubating conditions.

Conclusion

Priming can be strategically applied in circumstances that require rapid muscle relaxation, especially if depolarizing agents such as succinylcholine may not be appropriate. The priming method will not only improve intubating conditions but will also improve hemodynamic stability, thus providing a potentially useful plan in the induction phase of anaesthesia in both routine and high-risk situations. The safety profile and efficacy of intravenous 0.1 mg/kg atracurium priming dose and a subsequent intubating dose of 0.7 mg/kg after 3 minutes time (Group B) should provide anaesthesia providers with a reliable alternative to traditional intubation techniques used in the operating room. The findings of this study should be of particular interest to clinicians or facility where IV medications are administered for anaesthesia. The results very clearly illustrate the priming condition of a 0.1 mg/kg atracurium dose followed by an intubating dose of 0.7 mg/kg after a 3-minute time interval (Group B) provided the best intubating conditions when compared to Group A or Group C, including better jaw relaxation, a more open vocal cord position, limited or no coughing or straining, deeper substantial neuromuscular blockage showed by TOF at intubation and more stable blood pressures during intubation, which could have clinical implications in reducing cardiovascular effects during intubation.

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