

Original Research Article

Frequency of occurrence of urticaria after the administration of atracurium

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ABSTRACT

Background: Atracurium is a non-depolarizing neuromuscular blocking agent generally used for short and intermediate duration surgical procedures. Atracurium may cause urticaria due to direct, non-immunological release of histamine from mast cells. Though cutaneous changes due to histamine release by atracurium have been reported in various studies these changes were not clinically evaluated by dermatologists. The aim of the study was to assess the frequency of occurrence of urticaria after the administration of atracurium in the conventional dose schedule. Haemodynamic changes in pulse rate and mean arterial pressure (MAP) were also evaluated.

Methods: 60 patients aged 12 years and above, undergoing various elective surgical procedures were enrolled in the study. Atracurium was administered in a dose of 0.6 mg/kg body weight after induction. Cutaneous changes if any including erythema and urticarial weals were observed during the intraoperative phase and images recorded for further evaluation by the investigators including dermatologists. Baseline values of pulse rate and MAP as well as values 1 min, 3 min and 5 min after the administration of atracurium were recorded.

Results: None of the patients developed urticarial weals after the administration of atracurium. Five patients (8.33%) developed erythema during the intraoperative period. Changes in pulse rate and MAP were found to be significant.

Conclusions: Atracurium in conventional dosage is not associated with urticaria. Haemodynamic changes after the administration of atracurium are significant.

Keywords: Atracurium, Urticaria, Haemodynamic changes

INTRODUCTION

Atracurium is an intermediate duration, non-depolarizing benzyloquinolinium skeletal muscle relaxant. It may cause urticaria due to direct, non-immunological release of histamine from mast cells.¹⁻³ It is used as an adjunct to general anaesthesia to facilitate mechanical ventilation and provide muscle relaxation during surgery. Non-depolarizing agents antagonize the neurotransmitter action of acetylcholine by binding competitively with cholinergic receptor sites on the motor end plate. The benzylquinolinium muscle relaxants have retained a distinct edge due to unique degradation by Hofmann

elimination and ester hydrolysis resulting in short half-lives with rapid termination of effect and recovery.^{4,5} Due to their rapid degradation in plasma and tissues these muscle relaxants are given precedence in patients with impaired hepatic and/or renal parameters. Atracurium is a less potent releaser of histamine than d-tubocurarine.

The aim of the study was to assess the relative frequency of urticaria due to the administration of atracurium. The primary objective was to assess the occurrence of urticaria reviewed clinically by dermatologists after administration of 0.6 mg/kg body weight of atracurium in patients undergoing surgical procedures. Hemodynamic

changes in mean arterial pressure (MAP) and pulse rate due to the release of histamine by atracurium were assessed as the secondary objective.

METHODS

An observational cross sectional study was carried out on 60 patients aged 12 years or above with ASA grades I and II, undergoing elective surgical procedures under general anesthesia, with atracurium as the non-depolarizing muscle relaxant at Maharishi Markendeshwar Institute of Medical Sciences and Research, Mullana, Ambala, India. Patients with a personal history of urticaria, allergic rhinitis, bronchial asthma, mastocytosis or neuromuscular disease and those with a history of hypersensitivity to drugs were excluded. Those who had received H1 or H2 blockers or systemic corticosteroids within a week prior to surgery were also excluded from the study.

The study was approved by the institutional ethics committee (IEC) and written informed consent was obtained from all patients or their parents/guardians. All patients were administered a benzodiazepine anxiolytic medication and a proton pump inhibitor orally on the night prior to surgery. Premedication was carried out with intravenous administration of 4 mcg/kg of glycopyrrolate and 0.2 mg/kg of nalbuphine.

Baseline values of pulse and mean arterial pressure (MAP) were recorded and induction of anesthesia was carried out by intravenous administration of 2 mg/kg of propofol.

Recording of pulse rate and MAP was then carried out 1 min, 3 min and 5 min after intravenous administration of 0.6 mg/kg of atracurium. Cutaneous changes if any including erythema and urticarial weals after the administration of atracurium were observed throughout the intraoperative phase and the images recorded with a 16 megapixel camera. The images were clinically evaluated and reviewed by the investigators including dermatologists. The results were evaluated and compared. The data was entered in excel database and statistical analysis carried out.

RESULTS

The study included 60 patients undergoing elective surgical procedures. Out of this 28 patients were males while 32 were females. The age of the patients ranged from 12 to 58 years, the highest frequency being in the 12 to 21 years age group as given in Table 1. Erythema was observed in a total of 5 patients (8.33%) after the administration of atracurium. Out of this 4 patients had transient mild to moderate erythema in localized areas while 1 patient had marked erythema extensively on the face neck and upper trunk during the intraoperative period. Urticarial weals were not observed in any patient as in Table 2.

Table 1: Sample characteristics.

Age in years	Number of patients		Total
	Male	Female	
12 – 21	15	12	27
22 – 31	6	9	15
32 – 41	4	8	12
42 – 51	2	2	4
52-61	1	1	2
Total	28	32	60

Table 2: Cutaneous changes after the administration of atracurium.

Age in years	Cutaneous changes		Total
	Erythema	Urticaria	
12 – 21	2	0	2
22 – 31	0	0	0
32 – 41	0	0	0
42 – 51	2	0	2
52-61	1	0	1
Total	5	0	5

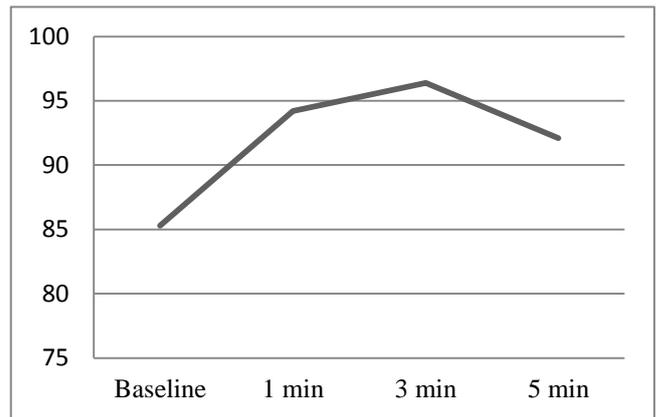


Figure 1: Rise in pulse rate after the administration of atracurium.

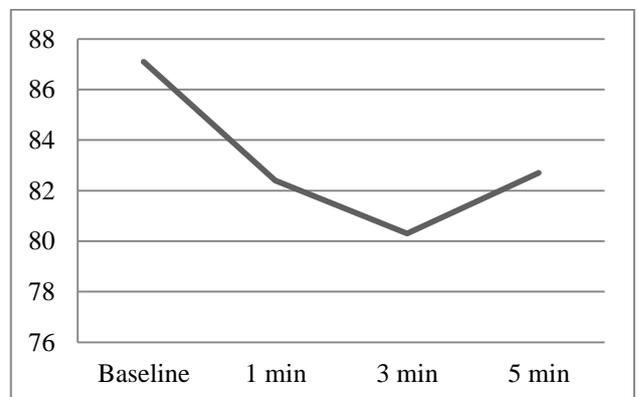


Figure 2: Fall in mean arterial pressure (MAP) after the administration of atracurium.

Table 3: Changes in pulse rate after the administration of atracurium.

Paired sample	Mean	Mean difference	p-value	
Pair 1	Baseline pulse	85.30	- 8.933	0.000
	Pulse 1 min after atracurium	94.23		
Pair 2	Baseline pulse	85.30	- 11.117	0.000
	Pulse 3 min after atracurium	96.42		
Pair 3	Baseline pulse	85.30	-6.783	0.001
	Pulse 5 min after atracurium	92.08		

Table 4: Changes in mean arterial pressure (MAP) after the administration of atracurium.

Paired sample	Mean	Mean Difference	p-value	
Pair 1	Baseline MAP	87.12	4.633	0.000
	MAP 1 min after atracurium	82.48		
Pair 2	Baseline MAP	87.12	6.783	0.000
	MAP 3 min after atracurium	80.33		
Pair 3	Baseline MAP	87.12	4.350	0.000
	MAP 5 min after atracurium	82.77		

A rise in pulse rate and a fall in MAP occurred after the administration of atracurium, peak changes being observed at 3 min as shown in Figures 1 and 2. The mean difference between baseline values of pulse rate and MAP paired with values 1 min, 3 min and 5 min after the administration of atracurium was determined by the paired samples t-test as presented in Tables 3 and 4. The mean difference in paired data for pulse rate and MAP in each pair was significant ($p < 0.01$).

DISCUSSION

Histamine release is a major drawback with benzylquinolinium muscle relaxants.⁴ The peak increase in plasma histamine concentration is observed at 1 min and returns to control value within 5 min of the administration of atracurium.⁶ Urticaria due to direct, non-immunological histamine release from mast cells may be caused by morphine, codeine, atracurium, radiocontrast media, dextran, polymyxin and

vancomycin.² Though a large number of studies have reported transient flushing and erythema after the administration of atracurium, few studies have reported urticarial weals due to atracurium.^{1,6-10,12,13}

In a study comparing adverse drug reactions due to neuromuscular blocking agents Movafegh et al reported urticaria due to atracurium in 6 out of 50 patients whereas erythema was observed in 9 patients.⁷ In another study carried out in children aged between 2 and 12 years, Voss et al reported urticaria as a side effect in 6 out of 42 children after receiving 0.5 mg/kg of atracurium.⁸ Flushing occurred much less frequently.

Though mild to moderate erythema was reported by Elbradie in 62% of patients who received atracurium, no case of urticaria was reported.¹ In another study flushing, erythema or constant redness after atracurium was observed in 7 out of 40 patients by Doenicke et al, but urticaria was not reported.⁹ Mild to moderate erythema after administration of atracurium in 9 out of 15 patients was reported by Naguib et al, but urticaria was not observed in any patient.⁶ In a study of histamine release following atracurium in the elderly by Shorten et al, skin flushing was observed in 7 out of 15 patients aged above 65 years but urticaria was not reported.¹⁰ Flushing and erythema were observed in 2 out of 16 patients who received atracurium by El-Kasaby et al, but urticaria was not reported.¹² In another study Loan et al have reported that 2 out of 10 patients who received atracurium developed erythema over the face and upper trunk but urticaria was not observed.¹³

In our study cutaneous changes were evaluated by dermatologists after the administration of 0.6 mg/kg body weight of atracurium and it was observed that erythema occurred in 8.33% of patients. Though atracurium is known to induce urticaria due to histamine release by direct mast cell degranulation none of our patients developed urticarial weals as seen in Table 2.²

Various studies have reported hypotension and tachycardia after the administration of atracurium that may correlate with increased histamine levels.^{1,6,7,11} A few studies have refuted this and reported minimal haemodynamic changes with atracurium.⁹

The inducing agent propofol has been associated with a significant drop in blood pressure.¹¹ Hence the temporal proximity of the inducing agent with atracurium may make interpretation of haemodynamic changes difficult.⁹ In the present study a rise in pulse rate and a fall in MAP was observed after the administration of atracurium as shown in Figures 1 and 2. These haemodynamic changes were found to be significant ($p < 0.01$).

CONCLUSION

Although it is a known non-immunological mast cell liberator, atracurium in conventional doses is not

associated with urticaria. However haemodynamic changes in pulse rate and MAP after the administration of atracurium are significant.

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Conflict of interest: None declared

Ethical approval: The study was approved by the institutional ethics committee

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