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Original Article

Effect of cisatracurium versus atracurium on intraocular pressure in patients undergoing tracheal intubation for general anesthesia

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Abstract

BACKGROUND: Increase in intraocular pressure (IOP) following tracheal intubation during general anesthesia can be troublesome. We compared the influence of two muscle relaxants, cisatracurium and atracurium, on IOP in patients undergoing general anesthesia.

METHODS: This randomized, double-blind, comparative trial was conducted on 90 candidates for elective non-ophthalmic surgery under general anesthesia. Patients were 18 to 60 years old with the American Society of Anesthesiologists (ASA) class of I or II. Anesthesia was induced with fentanyl (1.5 mg/kg) and sodium thiopental (5 mg/kg). Patients received atracurium (0.5 mg/kg) or cisatracurium (0.15 mg/kg) two minutes prior to tracheal intubation. IOP, systolic (SBP) and diastolic blood pressure (DBP), and heart rate (HR) were measured at baseline (before medication), after medication (before intubation), and 2, 5, and 10 minutes after intubation.

RESULTS: In both groups IOP decreased after administration of muscle relaxants (-3.3 ± 3.6 mmHg), then increased 2 minutes after intubation (5.5 ± 4.4 mmHg), but decreased 5 (-3.3 ± 3.3 mmHg) and 10 (-0.5 ± 2.6 mmHg) minutes after intubation. IOP and SBP were significantly higher in the atracurium compared with the cisatracurium group after 2 ($p < 0.001$ and 0.002, respectively), 5 ($p < 0.001$ and 0.012, respectively), and 10 ($p = 0.02$ and 0.048, respectively) minutes after intubation.

CONCLUSIONS: Compared with atracurium, administration of cisatracurium can better prevent the increase of IOP following tracheal intubation in general anesthesia. The observed difference might be related to different effects on hemodynamic variables. Application of these results in patients under ophthalmic surgery is warranted.

KEYWORDS: Intraocular Pressure, Anesthesia, General, Intubation, Intratracheal, Neuromuscular Nondepolarizing Agents, Cisatracurium, Atracurium.

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Intraocular pressure (IOP), in normal conditions, ranges from 12 to 20 mmHg, which is influenced by several factors such as central venous pressure, choroidal blood volume changes, and extraocular muscle tonicity.[1] Sudden increase in blood pressure, as occurred after laryngoscopy and tracheal intubation during surgical practice, results in the choroidal blood volume increase and eventually a 10 to 20 mmHg increase in IOP.[2] This increase in IOP can be troublesome during ophthalmic surgeries, especially in the presence of glaucoma or open eye trauma. There is a concern about administration of succinylcholine for muscle relaxation in these conditions leading to the use of other muscle relaxants such as

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atracurium and vecuronium as a substitute for succinylcholine.[1,2]

The effect of atracurium as a non-depolarizing neuromuscular blocker on IOP has been evaluated by several studies, and the results indicated that it has no significant effect on IOP.[3-5] Cisatracurium, the stereoisomer of atracurium, has been recently used in surgical practices. Compared with atracurium, cisatracurium is three to four times more potent for muscle relaxation, but has less influence on autonomic and cardiovascular systems.[6,7] To the best of our knowledge, only one published report is available on the effect of cisatracurium on IOP. Sator-Katzenschlager et al conducted a randomized trial on postoperative intubated patients and found that IOP decreases after an intubation dose of either cisatracurium or atracurium with no difference between them.[4] However, this study did not investigate changes in IOP following tracheal intubation and preventive effects of muscle relaxants in this regard. Therefore, we evaluated and compared the influence of atracurium and cisatracurium on IOP in patients undergoing tracheal intubation for general anesthesia. Furthermore, we investigated if hemodynamic changes could be the underlying mechanisms of action in this regard.

Methods

Patients and Settings

This randomized, double-blind, comparative trial was conducted on consecutive adult patients candidated for elective non-ophthalmic surgery under general anesthesia from July 2005 to July 2008 in two university hospitals (Kashani and Al-Zahra), in Isfahan. Inclusion criteria were having the American Society of Anesthesiologists (ASA) class of I or II, baseline IOP of lower than 20 mmHg, stable hemodynamics, no history of ophthalmic diseases, not using drugs affecting IOP (e.g. anticholinergics, sympathomimetics), and no contraindication for atracurium or cisatracurium administration. Patients with difficulty in mask ventilation or in tracheal intubation, end expiratory carbon dioxide (CO_2) of below 35 mmHg or over 45 mmHg, or oxygen (O_2) saturation of below 90% were excluded from the study. Power analysis showed that a sample size of 45 participants in each group would have 80% power at the 5% significance level to detect a difference of 1 mmHg between the two groups in IOP. The study protocol was approved by the Ethics Committee of the Isfahan University of Medical Sciences and informed consent was obtained from all patients after explaining the study protocol and aims. The study protocol was also registered at clinicaltrials.org with registration number as NCT01273831.

Intervention

Patients were consecutively included to the study and then, using the Random Allocation Software[8] generated table list, were randomized into atracurium and cisatracurium groups. Pre-operation preparation and hydrotherapy and intra-operation hydrotherapy were performed equally for both groups. In the operation room, pre-oxygenation was done for three minutes and then 1.5 mg/kg of fentanyl and 5 mg/kg of sodium thiopental were administered intravenously for induction of anesthesia. In this phase 0.5 mg/kg of atracurium or 0.15 mg/kg of cisatracurium were administered two minutes prior to intubation. The anesthesiologist was unaware of the groups. Although halothane is not used in our centers now, at the time of the study, maintenance of anesthesia was conducted using N_2O-O_2 combination with 50% proportion and halothane (1-1.5 MAC).[9] Monitoring included SPO_2, arterial blood pressure and end expiratory CO_2.

Assessments

Using Schiotz Tonometer, IOP was measured at baseline, after medication (i.e. before intubation), and 2, 5, and 10 minutes after intubation. Systolic (SBP) and diastolic blood pressure (DBP) and heart rate (HR) were also recorded by an independent observer.

Statistical Analyses

The data were analyzed with SPSS software, version 16.0 (SPSS Inc., Chicago, IL), using independent sample t-test, repeated measures analysis of variance (ANOVA), and Pearson correlation. A p value of < 0.05 was considered statistically significance for analyses.

Results

All patients completed the study. There was no significant difference between the two groups in age (38.0 ± 11.9 vs. 36.7 ± 12.8, p = 0.6) or gender (Male/Female: 21/24 vs. 22/23, p = 0.5). Overall, a similar trend of changes in IOP was observed in both groups; IOP decreased after administration of muscle relaxants (-3.3 ± 3.6 mmHg), then increased 2 minutes after intubation (5.5 ± 4.4 mmHg), but again decreased 5 (-3.3 ± 3.3 mmHg) and 10 (-0.5 ± 2.6 mmHg) minutes after intubation (Figure 1). According to repeated measure analysis and test of between-subjects effects, there was a significant difference between the two groups regarding changes in IOP during the study (p = 0.046). IOP was significantly higher in the atracurium compared with

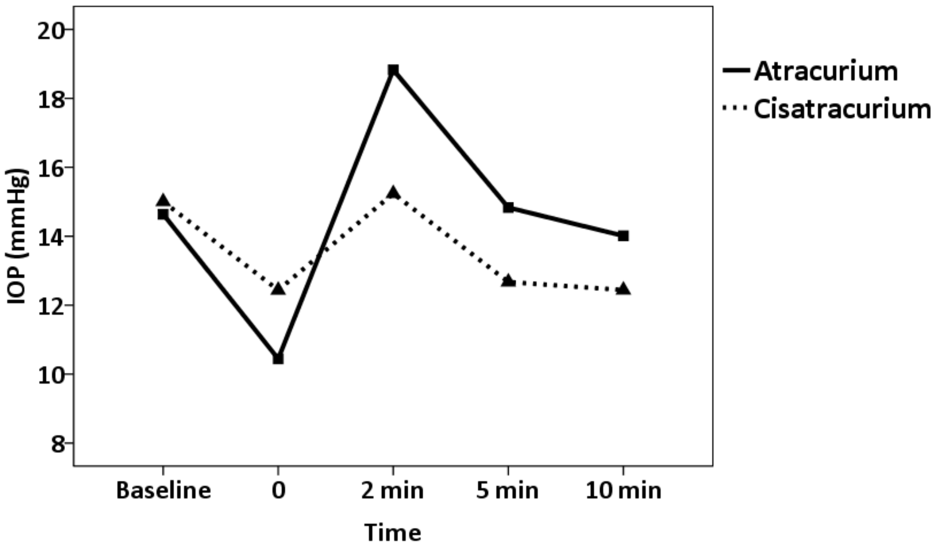

Figure 1. Trend of changes in intraocular pressure (IOP) in the two groups

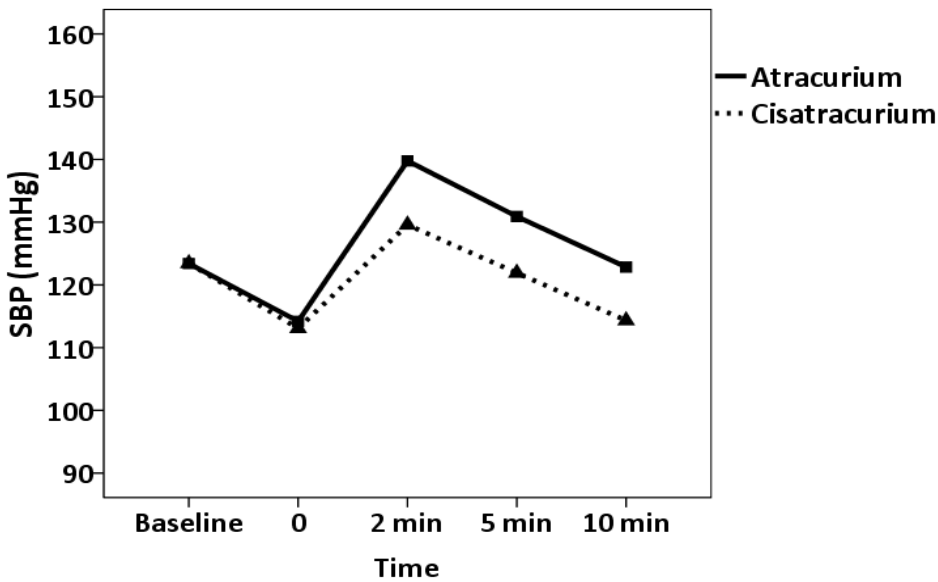

Figure 2. Trend of changes in systolic blood pressure (SBP) in the two groups

Table 1. Comparison of intraocular pressure (mmHg) between the two groups

	Baseline	0	Minute 2	Minute 5	Minute 10	P value*
Atracurium	14.8 ± 3.9	10.6 ± 3.3	19.0 ± 4.1	14.9 ± 2.8	14.0 ± 2.9	0.046
Cisatracurium	15.0 ± 3.6	12.4 ± 3.3	15.2 ± 3.1	12.6 ± 2.4	12.4 ± 3.4	
P value**	0.8	0.01	<0.001	<0.001	0.02	

Data are shown as mean ± SD
* Repeated measure; between subjects
** Independent sample t-test

cisatracurium group 2 ($p < 0.001$), 5 ($p < 0.001$), and 10 ($p = 0.02$) minutes after intubation. Two minutes after intubation, IOP higher than 20 mmHg was observed in 18 patients (40%) of the atracurium group compared with 5 patients (11.1%) in the cisatracurium ($p = 0.002$) (Table 1).

Trend of changes in SBP, DBP, and HR was also similar, in overall, in the both groups; there was a decrease in these variables after administration of muscle relaxants, then an increase 2 minutes after intubation, and again a decrease 5 and 10 minutes after intubation

Table 2. Comparison of systolic and diastolic blood pressures and heart rate between the two groups

		Atracurium	Cisatracurium	P value*
SBP (mmHg)	Baseline	121.0 ± 11.3	123.4 ± 14.6	0.379
	0	114.1 ± 12.1	113.0 ± 11.2	0.679
	Minute 2	139.1 ± 13.4	129.9 ± 13.8	0.002
	Minute 5	129.7 ± 15.8	121.9 ± 13.0	0.012
	Minute 10	119.8 ± 12.9	114.3 ± 13.3	0.048
P value**		0.014		
DBP (mmHg)	Baseline	72.2 ± 8.0	76.2 ± 12.2	0.071
	0	69.0 ± 7.0	70.8 ± 10.1	0.313
	Minute 2	80.8 ± 9.4	80.1 ± 9.2	0.711
	Minute 5	75.1 ± 8.8	73.7 ± 10.8	0.497
	Minute 10	70.7 ± 7.3	70.8 ± 9.6	0.951
P value**		0.745		
HR (beats/min)	Baseline	82.7 ± 10.8	85.0 ± 13.1	0.366
	0	77.5 ± 10.5	80.0 ± 12.5	0.295
	Minute 2	90.2 ± 10.6	89.9 ± 13.0	0.909
	Minute 5	82.5 ± 11.7	82.4 ± 12.4	0.965
	Minute 10	75.3 ± 9.6	75.4 ± 11.9	0.961
P value**		0.699		

Data are shown as mean ± SD
SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; HR: Heart Rate
* Independent sample t-test
** Repeated measure; between subjects

(Figure 2; Table 2). Repeated measure analysis and test of between-subjects effects revealed a significant difference between the two groups regarding changes in SBP ($p = 0.014$), but not DBP ($p = 0.745$) or HR ($p = 0.699$) during the study. SBP was significantly higher in the atracurium compared with cisatracurium group 2 ($p = 0.002$), 5 ($p = 0.012$), and 10 ($p = 0.048$) minutes after intubation, but there was no significant difference between the two groups in DBP or HR ($p > 0.05$) (Table 2).

The correlation between changes in IOP and changes in SBP was significant 2 ($r = 0.235$, $p = 0.026$) and 10 ($r = 0.223$, $p = 0.036$) minutes after intubation, but there was no correlation in this regard after medication or 5 minutes after intubation ($p > 0.05$).

Discussion

The aim of the present study was to evaluate and compare the influence of cisatracurium versus atracurium on IOP in patients undergoing tracheal intubation for general anesthesia. As the results showed, after laryngoscopy and tracheal intubation there was an increase in IOP in both groups of cisatracurium and atracurium, and this increase was in parallel with an increase in SBP, DBP, and HR. This increase in IOP after tracheal intubation, while using muscle relaxants, has been indicated by other studies. Igboko et al found that IOP increases, by about 5.9 mmHg, immediately after tracheal intubation in spite of the use of atracurium.[10] In another study, Vinik et al compared changes in IOP during rapid sequence induction and intubation following rocuronium, succinylcholine, and atracurium. Authors found an increase in IOP in all the three groups after intubation, but the increase was higher with atracurium (4 mmHg) compared with rocuronium or succinylcholine (2 mmHg).[5] As the results of our study showed, the increase in IOP was significantly higher in the atracurium compared with the cisatracurium group. These findings indicate that cisatracurium, compared with atracurium, can better prevent the increase of IOP following tracheal intubation.

The increase in IOP following intubation could be due to the reaction to laryngoscopy affecting sympathetic nervous system, catecholamine release, and increase in blood pressure.[11] As our study also indicated, change in IOP was correlated with blood pressure change and the increase in SBP following intubation was lower in the cisatracurium compared with the atracurium group. These finding indicate that preventing the increase of SBP might be a mechanism of action for preventive effect of cisatracurium in this regard.

Moreover, unlike cisatracurium, atracurium can induce histamine release [6,12] that in turn increases choroidal blood flow and lead to increase in IOP.[13] Histamine could also prevent aqueous fluid from the anterior chamber which could increase IOP, as well.[14] Therefore, higher IOP following atracurium compared with cisatracurium might be, to some extent, due to histamine release.

Conclusion

The results of this study showed that administration of cisatracurium, compared with atracurium, prior to tracheal intubation could effectively prevent the increase of IOP following tracheal intubation in patients undergoing general anesthesia. The observed effect might be related to higher SBP following atracurium compared with cisatracurium. Generalizing these findings to ophthalmic surgeries in which there is a high IOP, such as trabeculectomy in glaucoma, needs further studies.

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Conflict of Interests

Authors have no conflict of interests.

Authors' Contributions

All authors participated in generating the idea and designing and conducting the study. MJ managed the study and prepared the draft of the report. All authors studied and edited the draft, and approved the final version of the manuscript.

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