Effects of Flunitrazepam – Atracurium Administration on the Pressor Response to Laryngoscopy and Tracheal Intubation

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Introduction

The pressor response to direct laryngoscopy and endotracheal intubation was recognized by many investigators (Burstein et al.)[1], (Stoelting et al.)[2]. The transitory nature of hypertension and tachycardia are probably of no consequence in healthy individuals, but may be hazardous in those patients suffering from cardiovascular diseases (Katz and Brigger)[3]. Attempts to attenuate this pressor response were not satisfactory either because the reflex was incompletely blocked or the agent used may be too long acting and sometimes causes undesirable side effects (King et al.)[4].

The aim of the present study is to evaluate the pressor response to laryngoscopy and tracheal intubation following anaesthetic induction using Flunitrazipam Atracurium sequence and comparing the results with the commonly used Thiopentone-Suxamethonium one.

Material and Methods

After obtaining hospital authorities permission a study was performed on 23 informed and consenting ASA class I patients. The pulse rate and arterial blood pressure were measured while the patients were breathing oxygen via a face mask. Through an intracath all patients received Atropine 0.01 mg/kg b.w. just before the inducing agent.

In the first group of 10 patients (7 males and 3 females) repeated readings were performed: –

a. one minute following the injection of Thiopentone sodium 5 mg/kg b.w.
b. one minute after Suxamethonium 1 mg/kg b.w.
c. during laryngoscopy and tracheal intubation and then
d. 1, 3, 5 and ten minutes afterwards.

The second group comprising 13 patients (7 males and 7 females) had the pulse rate and arterial blood pressure measured and then anaesthesia induced. The pulse rate and arterial blood pressure were measured: –

a. one minute after Flunitrazepam 0.02 mg/kg b.w.
b. one minute after Atracurium 0.5 mg/kg b.w.
c. during laryngoscopy and tracheal intubation
d. 1, 3, 5 and ten minutes later.

Anaesthesia was maintained by N_2O : O_2 (6 : 3 L/min) and Halothane 0.5% and the respiration controlled mechanically using Manley Pulmovent Model MPT.

As a muscle relaxant both groups had Atracurium 0.5 mg/kg b.w. given at 20 minutes intervals.

Results

The demographic data of both groups of patients are shown in *table 1*. In the first group the mean basal pulse rate was insignificantly altered following Thiopentone and Suxamethonium administration while it was significantly increased during laryngoscopy and tracheal intubation (P less than 0.001). This significant increase was recorded also one and three minutes after tracheal intubation (P less than 0.001 and P less than 0.01 respectively) but it returned to the basal rate (*table 2*). The systolic arterial blood pressure was significantly increased during laryngoscopy and tracheal intubation (P less than 0.001), at one minute (P less than 0.001) and three minutes (P less than 0.01) after intubation (*table 3*).

The diastolic arterial blood pressure was significantly increased during endotracheal intubation (P less than 0.001) one minute (P less than 0.001), three minutes (P less than 0.01) and at 5 minutes (P less than 0.05) from intubation (*table 4*).

In the second group of patients there was an insignificant alteration in the pulse rate following the administration of Flunitrazepam, Atracurium or during laryngoscopy and tracheal intubation (*table 5*). An insignificant alteration in the arterial blood pressure was found during the administration of Flunitrazepam and Atracurium while a significant increase in the systolic blood pressure was measured during tracheal intubation (P less than 0.001) and one minute later (P less than 0.01). The

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diastolic blood pressure was significantly increased during laryngoscopy and tracheal intubation (P less than 0.001) and after one minute (P less than 0.05). However, both the systolic and diastolic arterial pressures returned to the basal levels (*table 6 and 7* respectively). It is to be noted that quicker return to basal levels occured in group one compared to group two.

TABLE 1:

	Thiopentone – Suxamethonium		Flunitrazepam – Atracurium	
	Age / Years	Weight / kg	Age / Years	Weight / kg
Range	18 – 60	60 – 70	16 – 63	55 – 75
Mean ±	35	63.5	27.5	65.1
S.D.	14.1	4.1	8.8	6.1

Demographic data of the patients of the Thiopentone – Suxamethonium group (10 patients) and the Flunitrazepam – Atracurium group (13 patients)

TABLE 2:

	Basal pulse rate/ min.	1 min. after Thiopen-entone Atropine	1 min. after Suxame-thonium	During Laryn-goscopy and intub.	1 min. after intuba-ation	3 min. after intuba-ation	5 min. after ibtuba-ation	10 min. after intuba-ation
Mean	94.4	101.8	100.6	129	127.8	111.8	104	97
Range	80-100	90-120	82-124	100-150	110-150	100-128	90-120	88-112
S.D. ±	7.088	11.173	14.485	15.699	12.090	11.013	11.738	7.071
t. value		1.678	1.153	6.026	7.150	3.986	2.100	0.779
P.				(0.001	(0.001	(0.005		
		Insig.	Insig.	Sig.	Sig.	Sig.	Insig.	Insig.

Showing pulse rate changes before and after Atropine 0.01 mg/kg b.w. Thiopentone (5 mg/kg b.w.), 1 minute after Suxamethonium (1 mg/kg -1 b.w.) during laryngoscopy and endotracheal intubation and then 1, 3, 5 and 10 minutes after intubation.

TABLE 3:

	Basal systolic blood press-ure	1 min. after Thiopen-entone Atropine	1 min. after Suxame-thonium	During Laryn-goscopy and intub.	1 min. after intuba-ation	3 min. after intuba-ation	5 min. after ibtuba-ation	10 min. after intuba-ation
Mean	131.5	125	130.5	188	190	158	41	131.5
Range	110-150	110-140	115-150	170-220	170-220	140-180	120-150	120-150
S.D. ±	11.559	12.019	10.069	18.737	18.708	16.193	9.944	12.030
t. value		1.169	0.196	7.699	7.981	3.996	1.869	0
P.				(0.001	(0.001	(0.01		
		Insig.	Insig.	Sig.	Sig.	Sig.	Insig.	Insig.

Showing systolic blood changes before and after Atropine (0.01 mg/kg b.w.) Thiopentone (5 mg/kg b.w.), 1 min after Suxamethonium (1 mg/kg -1 b.w.) during laryngoscopy and endotracheal intubation and then 1, 3, 5 and ten minutes after intubation.

TABLE 4:

	Basal systolic blood pressure	1 min. after Thiopentone Atropine	1 min. after Suxamethonium	During Laryngoscopy and intub.	1 min. after intubation	3 min. after intubation	5 min. after ibtubation	10 min. after intubation
Mean	84	79.8	86.5	122.5	122	100	93	86
Range	70-95	70-95	80-100	100-180	95-180	90-120	80-100	80-100
S.D. ±	8.756	8.727	6.687	23.482	24.290	8.165	6.749	6.992
t. value		1.019	0.681	4.609	4.415	4.009	2.442	0.535
P.				(0.001	(0.001	(0.005	(0.05	
		Insig.	Insig.	Sig.	Sig.	Sig.	Sig.	Insig.

Showing diastolic blood changes before and after Atropine (0.01 mg/kg b.w.) and after Thiopentine (5 mg/kg b.w.), 1 min after Suxamethonium (1 mg/kg) during laryngoscopy and intubation then 1, 3, 5 and ten minutes after laryngoscopy and endotracheal intubation.

TABLE 5:

	Preanaesthetic. pulse/ minute	1 min. after Flunitrazepam	1 min. after Atracurium	During Laryngoscopy and intub.	1 min. after intubation	3 min. after intubation	5 min. after ibtubation	10 min. after intubation
Mean	111.38	109.23	103.15	119.92	112.77	110	103.92	99.69
Range	86-160	90-140	80-132	100-160	98-136	94-130	94-120	80-120
S.D. ±	18.350	18.647	16.842	16.148	11.649	12.936	10.004	12.486
t. value		0.285	1.145	1.210	0.222	0.213	1.237	1.825
P.								
		Insig.	Insig.	Insig.	Insig.	Insig.	Insig.	Insig.

Showing pulse rate changes before and after Flunitrazepam (0.02 mg/kg) one minute after Atracurium (0.5 mg/kg b.w.) during laryngoscopy and endotracheal intubation then 1, 3, 5 and 10 minutes after endotracheal intubation.

TABLE 6:

	Preanaesthetic. Systolic Blood Pressure	1 min. after Flunitrazepam	1 min. after Atracurium	During Laryngoscopy and intub.	1 min. after intubation	3 min. after intubation	5 min. after ibtubation	10 min. after intubation
Mean	128.85	123.85	123.5	155.38	143.46	125.38	122.69	121.92
Range	120-140	110-150	110-160	140-170	110-160	110-150	110-140	110-140
S.D. ±	7.403	9.608	12.647	10.500	13.751	10.500	8.807	9.903
t. value		1.428	1.265	7.153	3.241	0.936	1.855	1.942
P.				(0.001	(0.01			
		Insig.	Insig.	Sig.	Sig.	Insig.	Insig.	Insig.

Showing systolic blood pressure changes before and after Flunitrazepam (0.02 mg/kg) one minute after Atracurium (0.5 mg/kg b.w.) during laryngoscopy and endotracheal intubation then 1, 3, 5 and 10 minutes after intubation.

TABLE 7:

	Preanaesthetic. Diastolic Blood Pressure	1 min. after Flunitrazepam	1 min. after Atracurium	During Laryngoscopy and intub.	1 min. after intubation	3 min. after intubation	5 min. after ibtubation	10 min. after intubation
Mean	86.15	81.92	82	102.69	93.85	83.38	83.08	81.769
Range	75-100	75-95	75-100	90-120	80-110	75-100	75-100	75-90
S.D. ±	7.946	6.262	7.937	7.804	8.454	7.292	7.511	6.379
t. value		1.414	1.280	5.145	2.299	0.247	0.973	1.489
P.				(0.001	(0.01			
		Insig.	Insig.	Sig.	Sig.	Insig.	Insig.	Insig.

Showing diastolic blood pressure changes before and after Flunitrazepam (0.02 mg/kg) one minute after Atracurium (5 mg/kg b.w.) during laryngoscopy and endotracheal intubation then 1, 3, 5 and 10 minutes after endotracheal intubation.

Discussion

The increase in the heart rate and arterial blood pressure during laryngoscopy and endotracheal intubation were probably due to reflex stimulation of the sympathoadrenal system and the consequent increase in the circulating catecholamine levels (Fox, et al., 1977) (5).

Flunitrazepam, a fluorinated benzodiazpine derivative is a new drug used for anaesthetic induction and it is less cardiovascular and respiratory depressant than Thiopentone sodium. The muscle relaxant requirement after both agents is not different.

Slowing of the heart rate is a common finding following induction of sleep with Flunitrazepam and this is probably related to its sedative and hypnotic effects together with an increase in the vagal tone (Stovner et al.)[6]. The moderate decrease in the systematic arterial blood pressure following the administration of Flunitrazepam is explained by (Haldemann et al.)[7] to be due to a decrease in the total peripheral resistance.

Most neuromuscular blocking agents cause haemodynamic changes. D-tubocurarine causes significant hypotension by stimulating histamine release or sympathetic ganglion blockade or both (Savarese)[8]. Gallamine (Thomas)[9] and Pancuronium (Stoelting)[10] may cause tachycardia and hypertension as a result of vagolytic or sympathomimetic effects. (Nigrovic et al.)[11].

Suxamethonium may interact with the nicotinic receptors releasing endogenous catecholamines which is responsible for the occasionally reported cardiovascular instability following its administration. Atracurium (Hughes and Chapple)[12] unlike many of the currently available muscle relaxants is devoid of any significant cardiovascular effects even at multiples of full neuromuscular blocking doses. However Basta et al.[13] demonstrated a transient significant decrease in the heart rate and arterial pressure, occuring 60 -90 seconds after the administration of Atracurium 0.6 mg/kg or more but these effects disappeared within 5 minutes.

In the present study a transient significant increase in the pulse rate, systolic and diastolic arterial blood pressure were recorded in the Thiopentone-Suxamethonium group of patients during laryngoscopy and tracheal intubation. These results agree with those reported by previous investigators and are associated with a significant increase in the plasma noradrenaline levels which lasted for 5 minutes before decreasing to the preanaesthetic values.

In the present study an insignificant alteration in the pulse rate was demonstrated during laryngoscopy and tracheal intubation in the Flunitrazepam Atracurium treated group of patients. In addition the systolic and diastolic arterial blood pressure although increased during laryngoscopy and tracheal intubation, returned to pre-aneasthesia levels quicker in this group.

Haigh et al[14] demonstrated a significant increase in the mean arterial pressure during laryngoscopy and intubation after Thiopentone – Suxamethonium as also after Thiopentone-atracurium sequences. It is quite possible that the use of Flunitrazepam and Atracurium through a combined enchantment of the cardiac vegal tone and the decreased total peripheral resistance modifies and attenuates the pressure response to laryngoscopy and intubation.

Conclusion

It is suggested from the present study that Flunitrazepam and Atracurium are worth using as an alternative to Thiopentone and Suxamethonium sequence in situations where these agents are contraindicated and when the pressor response to direct laryngoscopy is a real hazard.

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