Intracranial pressure, mean arterial pressure and heart rate after rapid paralysis with atracurium in cats

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The effect of atracurium on intracranial pressure (ICP) was investigated in six cats with normal and increased ICP. The cats were anaesthetized with intraperitoneal pentobarbitone (33 mg·kg^{-1}), acepromazine (0.6 mg·kg^{-1}) and incremental fentanyl (p.r.n. ≅ 20 μg·kg^{-1}), intubated, and ventilated with nitrous oxide in oxygen. Mean arterial pressure (MAP), heart rate (HR), twitch response and ICP were continuously recorded. After the effect of atracurium had been ascertained under the condition of normal ICP, and after full recovery of twitch response, pH-adjusted Ringer's lactate solution was infused into the cisterna magna until an ICP baseline of 26 ± 2 mmHg was established and stabilized. Atracurium was then administered again to determine its effect under the condition of elevated ICP.

Complete ablation of twitch response was obtained in 68 ± 15 sec with 0.4 mg·kg^{-1} atracurium, and there was no significant change in ICP, MAP, HR or cerebral perfusion pressure (CPP) whether initial ICP was normal or elevated.

Key words
NEUROMUSCULAR RELAXANT: atracurium; BRAIN: intracranial pressure, cerebral perfusion pressure.

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The ideal muscle relaxant for neurosurgical anaesthesia should be non-depolarizing and reversible, should not affect systemic or central variables, and should not alter intracranial pressure (ICP).[1] Atracurium is currently challenging pancuronium's position as the most widely used non-depolarizing muscle relaxant.[2,3] Atracurium has considerably shorter onset of action[3,4] and maintains haemodynamic stability at dosages adequate for complete paralysis.[5–11,12] If, like pancuronium[13] but unlike succinylcholine[14] and curare,[15] atracurium does not entail the risk of increased ICP, it may be especially appropriate for neurosurgical procedures.

Using dosages adequate in cats to cause complete ablation of twitch response within 70 seconds, we tested the effect on atracurium on both normal and artificially elevated ICP.

Methods

After obtaining approval of our institution's Animal Care Committee, six male cats weighing 4–5 kg were anaesthetized with pentobarbitone (33 mg·kg^{-1}, IP) and acepromazine (0.6 mg·kg^{-1}, IP), followed by incremental fentanyl (p.r.n. ≅ 20 μg·kg^{-1}, IV). The animals were intubated without inducing paralysis and ventilated with nitrous oxide (N_2O) in oxygen (O_2) to maintain arterial oxygen tension (PaO_2) at 90–110 mmHg and arterial carbon dioxide tension ($PaCO_2$) at 36 ± 4 mmHg. Temperature was kept at 36 ± 0.5° C with a heating blanket. A femoral arterial catheter was used to sample blood gases and continuously record MAP and HR. Dextrose five per cent in normal saline, (4–5 ml·kg^{-1}·hr^{-1}) and drugs were administered through a catheter placed in the cephalic vein.

TABLE I Results (Mean ± SEM)

	Normal ICP		*Elevated ICP*	
	Control	*Atracurium**	*Control*	*Atracurium**
ICP (mmHg)	4.7 ± 0.6	4.9 ± 0.8	27.6 ± 1.3	26.6 ± 1.2
MAP (mmHg)	87 ± 4	91 ± 5	102 ± 6	105 ± 5
HR (beats/min)	178 ± 5	182 ± 5	179 ± 6	183 ± 8
CPP (mmHg)	75 ± 6	76 ± 6	75 ± 6	76 ± 6

*Maximum change subsequent to administration of muscle relaxant and prior to recovery of twitch response (n = 6).

Sciatic nerve twitch response was continuously recorded with a Grass Instruments force-displacement transducer.

A single 19-gauge curved needle was inserted into the cisterna magna and secured with cyanoacrylate tissue adhesive (Krazy Glue). Intracranial pressure was monitored continuously and readings were accepted if the pressure tracing changed 1–3 mmHg with respiration.

With haemodynamic values stabilized and ICP within normal range, a bolus of atracurium ($0.4\ mg \cdot kg^{-1}$) was administered intravenously. After recovery of twitch response and reestablishment of haemodynamic controls, pH-adjusted Ringer's lactate solution was infused over a 10–20 min period into the cisterna magna. Pulsation of ICP with respiration was not disturbed by fluid infusion (our method for increasing ICP has been more fully explained elsewhere).[16] With ICP stabilized at an elevated baseline of 26 ± 2 mmHg, the same dose of atracurium was again administered in each cat. Total elapsed time between atracurium doses was approximately one hour.

For each experimental condition in each animal (normal or increased ICP), control values for MAP, ICP, HR and cerebral perfusion pressure (CPP = MAP − ICP) were compared with their values at the point of maximum change subsequent to administration of muscle relaxant and prior to recovery of twitch response. Each animal served as its own control and maximum change for all variables was analyzed for statistical significance by the two-tail paired t test. All intervals reported with mean values are mean ± SEM.

Results

Complete ablation of twitch response was obtained in 68 ± 15 sec and this onset of action was unaffected by the baseline level of ICP. There was no significant change in ICP, MAP, HR or CPP whether initial ICP was normal or elevated (see Table).

Discussion

Previous investigations indicate that atracurium is an improvement over pancuronium[2–11] and our investigation indicates that, unlike succinylcholine[14] and curare,[15] atracurium does not entail the risk of increased ICP. Evidence that succinylcholine increases ICP is not unequivocal in the sense of significantly increasing ICP across a sample of subjects. Nevertheless, all but the smallest studies indicate that some individuals in each sample do suffer significant increases (see 14 and references therein). Although a serious detrimental effect in one or two out of ten or 20 patients may not significantly alter a group's mean value, in such cases the mean is meaningless as a parameter for making clinical judgements. As indicated by the small SEM's reported with mean values in the Table, in this study no individual subject suffered a significant increase in ICP after administration of atracurium. Our largest single observed change was an increase of 2.5 mmHg, which occurred when the cat's baseline ICP was normal (4.5 mmHg). This result complements the recent report of a 72-hour infusion of atracurium to successfully control the ICP of a severely head injured 7-year-old patient.[17]

We also found that atracurium failed to produce a statistically or clinically significant change in MAP or HR. This finding is especially noteworthy since atracurium, like curare and metubine,[7] is suspected of causing histamine release at dosages adequate to induce rapid paralysis.[12] Our results with atracurium concur with those that indicate no histamine release and/or no cardiac instability within the clinical dose range.[3-11]

In conclusion, we found atracurium to be capable of inducing rapid paralysis in cats without causing the decrease in MAP that often characterizes high dose curare and metubine.[7] We also failed to detect changes in HR that would indicate ablation of the vagolytic response, as sometimes accompanies paralysis with pancuronium.[18] In addition, we did not detect a single case of significantly increased ICP whether ICP before paralysis was normal or artifically elevated. Since cats are an especially sensitive animal model for detecting effects on ICP, our observed ICP stability marks a significant improvement over succinylcholine[14,16] and curare.[15] When considered together with observed haemodynamic stability at dosages adequate to induce rapid paralysis, to the extent that our model can be used to make inferences about humans, our ICP result suggests that atracurium is an especially appropriate muscle relaxant for neurosurgical procedures.

Acknowledgements

We thank Dr. Christopher Stein and George McCoy for assistance in the laboratory, Bartol Matanic, DVM for professional courtesies, and Ms. Ellen L. Jackson for manuscript preparation.

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Résumé

Les effets de l'atracurium sur la pression intracrânienne (ICP) ont été investigués sur six chats présentant une pression intracrânienne normale ou élevée. Les chats ont été anesthésié avec du pentobarbitone (33 $mg \cdot kg^{-1}$) administré par voie péritoniale, l'acepromazine (0.6 $mg \cdot kg^{-1}$) et des doses additionnelles de fentanyl (p.r.n. $\cong 20\ \mu g \cdot kg^{-1}$), intubés et ventilés avec le protoxide d'azote dans l'oxygène. La pression artérielle moyenne (MAP) fréquence cardiaque (HR), réponse neuromusculaire, et la pression intracrânienne ont été enregistrés d'une façon continue. Après l'établissement des effets de l'atracurium lors d'une pression intracrânienne normale ainsi qu'après le rétablissement de la fonction neuromusculaire, les solutions de lactate Ringer's à pH-ajusté a été injectés dans la grande citerne jusqu'à l'obtention de la pression intracrânienne de base de 26 ± 2 mmHg. L'atracurium a été ensuite administré afin de déterminer son effet dans des conditions d'une pression intracrânienne élevée.

L'abolition complète des contractions a été obtenu après 68 ± 15 sec avec 0.4 $mg \cdot kg^{-1}$ d'atracurium. Aucun changement significatif n'a été observé dans la pression intracrânienne, la pression artérielle moyenne à fréquence cardiaque ou la pression de perfusion cérébrale (CPP) lorsque la pression intracrânienne était normale ou élevé.