THE EFFECTS OF ALTHESIN ON CEREBRAL BLOOD FLOW AND INTRACRANIAL PRESSURE

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AS PART OF A CONTINUING SEARCH for suitable anaesthetic agents for use in neurosurgical and neuroradiological anaesthesia, we have studied the effects of Althesin (Glaxo CT1341) on cerebral blood flow (CBF) and cerebrospinal fluid (CSF) pressure in the dog.

Althesin is a mixture of two steroid compounds, both pregnanediones, dissolved in polyoxyethylated castor oil (Child *et al.*).¹ Clinical trials have shown that it rapidly induces anaesthesia adequate for various surgical operations (Campbell *et al.*).²

METHOD

Seven beagle dogs of 11 kg average weight were used in the experiment. Anaesthesia was induced with intravenous Althesin in an average dose of 4.8 mg/kg and 24 mg increments were given intravenously, as required to maintain surgical anaesthesia. A cuffed tracheal tube was inserted and the dog was ventilated with air by means of a Harvard pump to maintain an arterial P_{CO_2} of 34 to 37 mmHg, which is normal for dogs (Pickerell *et al.*).³ The dog was placed on a heating pad.

Catheters were inserted into the right atrium through the femoral vein and into the aorta through the femoral artery. The vertebral artery was cannulated through the other femoral artery using the Seldinger technique under roentgenographic control. Heart rate, blood pressure and temperature were monitored continuously.

When conditions were stable, 1 millicurie of Xenon¹³³ dissolved in 1 ml of saline was injected into the vertebral artery and the catheter was then immediately flushed with 2 ml of saline. The appearance and rate of clearance of the Xenon was recorded by a scintillation probe placed over the intact skull and positioned to exclude the airway from its field. A non-rebreathing circuit was used and the expired gases were vented outside the laboratory.

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The cerebral blood flows were calculated by stochastic analysis of the washout curves (Hoedt-Rasmussen *et al.*, Gray *et al.*).^{4,5}

Simultaneously with the cerebral blood flow measurements, arterial blood gases and cardiac output were measured. The cerebrospinal fluid pressure was measured through a 19-gauge needle inserted percutaneously into the cisterna magna and connected to a pressure transducer and to a continuous recorder.

RESULTS

Table I gives the mean value and standard deviation for each measurement.

TABLE I
EFFECTS OF ALTHESIN/AIR ANAESTHESIA
(7 Dogs)

Measurement	Mean	SD
CBF, ml/100 gm/min	37.9	7.6
CSF pressure, cm water	14.4	1.2
Pa CO ₂ , mmHg	35.7	2.9
Pa O ₂ , mmHg	93.0	6.8
pH, units	7.37	0.034
Cardiac output, L/min	2.3	0.45
MABP, mmHg	120.0	10.0
Temperature, °C	38.0	0.4

DISCUSSION

Since 1941 various steroids have been known to be capable of producing anaesthesia (Selye).⁶ In 1955 one of these, hydroxydione, was introduced into clinical practice (Taylor).⁷ We could find no reports of measurements of cerebro-spinal fluid pressure or cerebral blood flow during anaesthesia with hydroxydione. Usually steroid hormones reduce cerebrospinal fluid pressure slightly but the reduction is considerable in the presence of cerebral oedema (Hooshmand *et al.*).⁸

Cerebrospinal fluid pressure in the awake dog is reported to be 13.5 to 15.0 cm of water (Verdura).⁹ The mean value during anaesthesia with Althesin was within this range.

Cerebral blood flow in dogs anaesthetized with pentobarbitone was found to be 38.9 ml/100 gm/min (Gray *et al.*).⁵ The mean value during anaesthesia with Althesin was comparable to this.

These results indicate that Althesin does not increase cerebral blood flow or raise cerebrospinal fluid pressure and thus further investigation of its use in neurosurgery and neuroradiology is warranted.

SUMMARY

The effects of Althesin anaesthesia upon cerebral blood flow and cerebrospinal fluid pressure were studied in seven dogs. Althesin caused no increase of cerebral blood flow or elevation of cerebrospinal fluid pressure, suggesting that further

studies should be carried out on the use of Althesin anaesthesia for neurosurgery and neuroradiology.

RÉSUMÉ

Les effets de l'anesthésie à l'althésine sur le flot sanguin cérébral et la pression du liquide céphalo-rachidien furent étudiés chez sept chiens. L'althésine n'a pas causé d'élévation du flot sanguin cérébral ou de la pression du liquide céphalo-rachidien. Ceci suggère que des études plus poussées pourraient être entreprises sur l'usage de l'anesthésie à l'althésine particulièrement pour la neurochirurgie et la neuroradiologie.

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REFERENCES

1. CHILD, K.J., CURRIE, J.P., *et al.* The pharmacological properties in animals of CT1341: A new steroid anaesthetic agent. *Br. J. Anaesth.* 43: 2 (1971).
2. CAMPBELL, D., FORRESTER, A.C., *et al.* A preliminary study of CT1341: a steroid anaesthetic agent. *Br. J. Anaesth.* 43: 14 (1971).
3. PICKRELL, J.A., DUBIN, S.E., & ELLIOTT, J.C. Normal respiratory parameters of unanaesthetized Beagle dogs. *Lab. Anim. Sci.* 21: 677 (1971).
4. HOEDT-RASMUSSEN, K., SVEINSDOTTIR, E., & LASSEN, N.A. Regional cerebral blood flow in man determined by intra-arterial injection of radioactive inert gas. *Circ. Res.* 18: 237 (1966).
5. GRAY, I.G., MITRA, S.K., *et al.* The effect of methoxyflurane on cerebral blood flow in the dog. *Can. Anaesth. Soc. J.* 18: 408 (1971).
6. SELYE, H. Anaesthetic effect of steroid hormones. *Proc. Soc. Exp. Biol. (N.Y.)* 46: 116 (1941).
7. TAYLOR, N. & SHEARER, W.M. The anaesthetic properties of 21-hydroxypregnanedione sodium hemisuccinate (hydroxydione): a pharmacological and clinical study of 130 cases. *Br. J. Anaesth.* 28: 67 (1956).
8. HOOSHMAND, H., DOVE, J. *et al.* Effects of diuretics and steroids on CSF pressure: A comparative study. *Arch. Neurol.* 21: 499 (1969).
9. VERDURA, J., WHITE, R.J., & ALBIN, M. Chronic measurements of cerebrospinal-fluid pressure in the dog: A new method and results. *J. Neurosurg.* 21: 1047 (1964).