THE EFFECT OF FLUROXENE ON INTRACRANIAL PRESSURE IN PATIENTS WITH INTRACRANIAL SPACE-OCCUPYING LESIONS

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SUMMARY

The intracranial pressure was studied in nine patients with space-occupying lesions before and after addition of 4% fluroxene to a nitrous oxide-oxygen mixture at normocapnia and hypocapnia. At normocapnia (PaCO₂ 38 mm Hg) fluroxene produced a 16 mm Hg (range 1-59 mm Hg) increase in intracranial pressure leading to a decrease in cerebral perfusion pressure, in three cases to critically low values. Hypocapnia (PaCO₂ 28 mm Hg) resulted in all cases in a rapid fall in intracranial pressure to near normal values and restoration of satisfactory cerebral perfusion pressure. It is concluded that fluroxene can be used in neuroanaesthesia, provided hyperventilation is applied and non-flammable concentrations are used.

Any significant increase in intracranial pressure may be damaging to patients with intracranial disorders because of resulting decrease of regional cerebral blood flow to diseased areas (Paulson, 1972). Also intracranial pressure gradients may develop with subsequent distortion and compression of the brain stem (Fitch and McDowall, 1971).

Therefore, any drug considered for use in neuroanaesthesia should be investigated in respect to its influence on intracranial pressure, especially in patients with intracranial space-occupying lesions. This has been done for halothane (Jennett, McDowall, and Barker, 1967; Jennett, et al., 1969; Gordon 1970), trichloroethylene (Jennett et al., 1969), methoxyfluorane (Fitch, et al., 1969a), nitrous oxide (Henriksen and Jørgensen, 1973) and neuroleptanalgesic drugs (Fitch et al., 1969b). Since fluroxene (Fluoromar*) has some advantages over other volatile agents, such as minimal cardiovascular depression (Cullen, et al., 1970) and low incidence of cardiac arrhythmias (Price and Dornette, 1965), we have studied its effect on intracranial pressure in a series of patients with intracranial space-occupying lesions.

MATERIAL AND METHODS

Nine patients were examined during nine anaesthetic procedures. The series is presented in table I. The selection of patients was determined by the need for continuous monitoring of intracranial pressure over a 24-48-hour period. Eight patients had identified brain tumours; one patient had "encephalitis" as clinical diagnosis, but was suspected to have an unidentified mass lesion.

Intracranial pressure was recorded continuously for 24-48 hours prior to the study and throughout the study. The pressure in one of the lateral ventricles was registered via a catheter inserted through a frontal burr-hole and connected to a Swema Sp 6-3 transducer and a Speedomax potentiometer recorder, as described by Lundberg (1960). The forehead was chosen as reference level. The preanaesthetic values are shown in table I. In three patients severe intracranial hypertension, occurring as pressure waves, necessitated intermittent drainage of ventricular fluid. Mean intracranial pressure was calculated as diastolic intracranial pressure plus one-third of the intracranial pulse pressure.

Before induction a radial artery cannula was inserted for measurement of arterial blood gases (Radiometer standard equipment) and for continuous recording of mean arterial blood pressure with a Statham P23 Db transducer.

In six cases central venous pressure was measured from a superior vena cava catheter inserted through a medial cubital vein and connected to a water column.

The mean arterial blood pressure and central venous pressure values were referred to the level of the intracranial pressure measurement. Cerebral perfusion pressure was thus obtained as the difference between mean intracranial pressure and mean arterial blood pressure.

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The patients were premedicated with diazepam 2.5–10 mg and atropine 0.2–0.6 mg, both drugs given intramuscularly 1 hour before induction of anaesthesia.

Anaesthesia was induced by inhalation of 66% nitrous oxide followed by suxamethonium and endotracheal intubation. Anaesthesia was maintained with 66% nitrous oxide and relaxation with gallamine. Ventilation was controlled with an Engström ventilator (non-rebreathing circuit). A few minutes of hyperventilation was applied in order to study the effect of hypocapnia on intracranial pressure elevation produced by nitrous oxide. Normocapnia was then established. When stable levels of intracranial pressure, mean arterial blood pressure and central venous pressure were obtained (control values, table II), 4% fluroxene (administered from a Fluoromartec vaporizer) was added to the anaesthetic mixture, and pressures were followed and read after 10 min. This period of time was dictated by the practical circumstances. Finally hypocapnia was induced by increasing tidal volume and all pressures were read again. After the end of the study the scheduled surgical procedure, in most cases craniotomy, was performed.

RESULTS
As seen in table I all patients except one had varying degrees of intracranial hypertension preoperatively, in three cases necessitating drainage of ventricular fluid. In five of the patients the level of consciousness was reduced.

As previously reported (Henriksen and Jørgensen, 1973) inhalation of 66% nitrous oxide produced elevation of intracranial pressure, which could in all cases be efficiently counteracted by hyperventilation.

Intracranial pressure, mean arterial blood pressure, central venous pressure, arterial carbon dioxide tension and cerebral perfusion pressure measurements before and after addition of 4% fluroxene to the nitrous oxide-oxygen mixture at normocapnia are given in table II and figure 1. Intracranial pressure rose from 21.8 mm Hg (range 10–48) to 37.8 mm Hg (range 11–72), a mean increase of 16.0 mm Hg (range 1–59). The rise occurred gradually over 8 minutes (range 6–9), after which the pressure stabilized at the new level. Mean arterial and central venous pressures were essentially unchanged. The changes in arterial carbon dioxide tension were small (39.6 to 37.9 mm Hg); only patient No. 1 had a major unintended fall (41 to 31 mm Hg). Arterial pH and oxygen tension were unremarkable and did not change significantly.

Cerebral perfusion pressure decreased from 71.4 mm Hg (range 22–100) to 51.2 mm Hg (range 1–87), mean change 20.2 mm Hg.

Hyperventilation with 4% fluroxene in nitrous oxide-oxygen (Paco₂ 28 mm Hg), studied in all cases except No. 6, produced a rapid and immediate reduction of intracranial pressure to 11 mm Hg (range 2–22 mm Hg) and a rise in cerebral perfusion pressure to 74 mm Hg (range 57–88 mm Hg).

DISCUSSION
The changes in intracranial pressure produced by 4% fluroxene at normocapnia in this series are non-uniform. In all cases an acute rise was seen, and a stable level of pressure was established after 6–9 minutes, although full equilibrium was not achieved.
TABLE II. Intracranial pressure, mean arterial blood pressure, $P_{\text{a}CO_2}$, central venous pressure and cerebral perfusion pressure in nine patients before and after addition of 4% fluroxene to a nitrous oxide-oxygen mixture (controlled ventilation). Figures in brackets are values obtained during hyperventilation.

<table>
<thead>
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<th>Patient no.</th>
<th>Intracranial pressure (mm Hg)</th>
<th>Mean arterial blood pressure (mm Hg)</th>
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<th>Central venous pressure (mm Hg)</th>
<th>Cerebral perfusion pressure (mm Hg)</th>
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Mean change: Intracranial pressure 21.8 (11.0), Mean arterial blood pressure 37.8 (84.6), $P_{\text{a}CO_2}$ 16.0, Central venous pressure 4% fluroxene 0.2, Cerebral perfusion pressure 51.2 (73.6).

Fig. 1. The effect of 4% fluroxene on intracranial pressure in nine patients with intracranial space-occupying lesions. First measurement:

$N_2O-O_2$—gallamine, normocapnia

Second measurement:

$N_2O-O_2$—gallamine + fluroxene, normocapnia

Third measurement:

$N_2O-O_2$—gallamine + fluroxene, hypocapnia

However, the magnitude of the elevation was varying and could not be predicted from the preoperative intracranial pressure values. In seven of nine cases the increases were indeed small. The major contribution to the average pressure elevation of 16 mm Hg originated from cases Nos. 8 and 9 (46 and 59 mm Hg respectively). Correspondingly the changes in cerebral perfusion pressure varied from minor to catastrophic reductions. Three patients had cerebral perfusion pressures far below 40 mm Hg, which in animal experiments has been found to be the critical limit for maintaining adequate cerebral oxygenation (Håggendal et al., 1970).

The fact that the elevation of intracranial pressure was not associated with elevation of systemic arterial pressure, central venous pressure or arterial carbon dioxide tension makes a direct cerebral vasodilator effect of fluroxene likely, leading to increased cerebral blood volume. The marked differences in the magnitude of intracranial pressure elevation are best explained by varying degrees of exhaustion of the mechanisms which normally compensate for expansion of the intracranial contents. The intracranial reserve-space, containing cerebrospinal fluid, is reduced and the cerebrospinal fluid pathways possibly blocked by the space-occupying lesions.

In one patient (No. 9) the extremely low cerebral perfusion pressure resulted from a simultaneous marked rise in intracranial pressure and a considerable fall in mean arterial pressure.

In all patients satisfactory cerebral perfusion pressure could immediately be established by hyperventilation.

All volatile anaesthetic agents hitherto studied, have been shown to cause increases in intracranial pressure, particularly in patients with intracranial...
space-occupying lesions, (Jennett McDowall and Barker, 1967; Jennett et al., 1969; Fitch et al., 1969a). The present study demonstrates that fluroxene is no exception. Since our method is similar to the one employed by Jennett and associates (1969), a comparison with their findings on halothane seems justified although the heterogeneity in our results tends to make comparison of average figures less valid. These authors also examined a group of patients with intracranial disorders requiring neurosurgical intervention. The control conditions (i.e. controlled ventilation with nitrous oxide-oxygen in the relaxed normocapnic patient) as well as the control level of intracranial pressure were almost identical to those in the present study. Halothane 1% (approximately equipotent to fluroxene 4%) caused a 20 mm Hg increase in pressure and a 41 mm Hg drop in cerebral perfusion pressure, as compared to a 16 mm Hg increase in intracranial pressure and a 20 mm Hg drop in cerebral perfusion pressure following 4% fluroxene. It was also shown that hypocapnia could not always be relied upon to counteract the effect of halothane on intracranial pressure. The average figures suggest that fluroxene interferes less with cerebral haemodynamics than does halothane. However, two patients in the present study developed severe intracranial hypertension during fluroxene anaesthesia.

Neither halothane nor fluroxene are ideal anaesthetic agents for patients with intracranial disorders because both these agents may result in dramatic rises in intracranial pressure when the intracranial reserve space is very limited. For these patients neuroleptanalgesic drugs, which have been shown by Fitch and associates (1969b) to reduce intracranial pressure, also in the presence of space-occupying lesions, may be preferable.

Fluroxene is a flammable agent, but the lower limit of flammability is between 4.0 and 4.5% (Lawrence and Bastress, 1959; Miller and Dornette, 1961; Patterson, Adams and Johnson, 1965). Since minimum alveolar concentration of fluroxene is 3.4% (0.8% for fluroxene in 77% nitrous oxide; Munson, Saidman and Eger, 1965), this agent can provide useful supplementary anaesthesia in non-flammable concentrations.

The present data do not provide conclusive evidence that fluroxene is better for neuroanaesthesia than halothane. The advantage of fluroxene is that mean arterial pressure is better preserved than with halothane and that hyperventilation efficiently counteracts the induced intracranial hypertension.

It is concluded that fluroxene in low, non-flammable concentrations can be used with relative safety for patients with intracranial disorders, provided hyperventilation is applied.

REFERENCES


EFFET DU FLUROXENE SUR LA PRESSION INTRACRANIERNE CHEZ LES MALADES AFFECTES DE LESIONS DANS LES ESPACES INTRACRANIENS

SOMMAIRE

On a étudié la pression intracrânienne de neuf malades avec lésions dans les espaces avant et après l'addition de 4% de fluroxène à un mélange de protoxyde d'azote et d'oxygène en normocapnie et hypocapnie. En normocapnie (Paco2 38 mm Hg) le fluroxène a provoqué une augmentation de 16 mm Hg (domaine 1–59 mm Hg) de la pression intracrânienne, entrainant ainsi une chute de la
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pression de perfusion cérébrale dans trois cas où les valeurs étaient dangereusement abaissées. L'hypocapnie (PaCO₂ 28 mm Hg) a conduit dans tous les cas à une chute rapide de la pression intracrânienne voisine des valeurs normales et au rétablissement d'une pression de perfusion cérébrale satisfaisante. On conclut que le fluoxène peut être utilisé en neuro-anesthésie pourvu qu'on applique l'hyperventilation et que l'on utilise des concentrations non inflammables.

ÜBER DIE WIRKUNG VON FLUROXENE AUF DEN INTRACRANIELLEN DRUCK BEI PATIENTEN MIT INTRACRANIELLEN RAUMFORDERNDEN LÄSIONEN

ZUSAMMENFASSUNG

Bei 9 Patienten mit raumfordernden Läsionen wurde der intracranielle Druck vor und nach Zusatz von 4% Fluroxene zu einer Lachgas-Sauerstoffmischung bei Normokapnie und Hypokapnie untersucht. Bei Normokapnie (PaCO₂ 38 mm Hg) bewirkte Fluroxene eine Zunahme des intracraniellen Druckes um 16 mmHg (Schwankungsbreite von 1-59 mmHg) welcher zu einer Verminderung des cerebralen Perfusionsdruckes führte, und zwar in 3 Fällen auf kritisch niedrige Werte. Hypokapnie (PaCO₂ 28 mmHg) ergab in allen Fällen einen rapiden Abfall des intracraniellen Druckes auf nahezu normale Werte und eine Wiederherstellung eines zufriedenstellenden cerebralen Perfusionsdruckes. Es wird daraus die Folgerung gezogen, daß Fluroxene in der Neuroanaesthesie Verwendung finden kann, vorausgesetzt, daß eine Hyperventilation stattfindet und daß nicht brennbare Konzentrationen angewandt werden.

EL EFECTO DEL FLUROXENO SOBRE LA PRESION INTRACRANEAL EN ENFERMOS CON LESIONES QUE OCUPAN EL ESPACIO INTRACRANEAL

RESUMEN

Se estudió la presión intracraneal en nueve enfermos con lesiones que ocupan el espacio intracraneal, antes y después del suministro de 4% de fluoxeno añadido a la mezcla de óxido nitroso-oxígeno, en normocapnia e hipocapnia. En normocapnia (PaCO₂ de 38 mm Hg) el fluoxeno produjo un aumento de la presión intracraneal de 16 mm Hg (márgenes comprendidos entre 1 y 59 mm Hg), que condujo a una disminución de la presión de perfusión cerebral, llegando en tras casos a unos valores bajos críticos. La hipocapnia (PaCO₂ 28 mm Hg) provocó en todos los casos un descenso rápido de la presión intracraneal hasta alcanzar casi los valores normales, así como la restauración de una presión de perfusión cerebral satisfactoria. Se ha llegado a la conclusión de que el fluoxeno puede ser usado en neuro-anestesia, con la condición de que se aplique una hiperventilación y de que se empleen concentraciones no inflamables.

NEUROSURGICAL ANAESTHETISTS TRAVELLING CLUB

The next meeting of the Neurosurgical Anaesthetists Travelling Club will be held at the West Bromwich Postgraduate Medical Centre, Hallam Hospital, West Bromwich on Saturday, October 13, 1973. All interested in neuroanaesthesia, regardless of specialty are welcome to attend, and application forms for those not on the Club's mailing list can be obtained from Dr T. V. Campkin, Midland Centre for Neurosurgery and Neurology, Holly Lane, Smethwick, Warley, Worcs. B67 7JX.

Those wishing to present papers should send a summary (not exceeding 300 words) to Dr T. V. Campkin at the above address.