THE EFFECT OF NITROUS OXIDE AND HALOTHANE UPON THE INTRACRANIAL PRESSURE IN HYPOCAPNIC PATIENTS WITH INTRACRANIAL DISORDERS

BENT B. MISFELDT, P. BALSLEV JÖRGENSEN AND M. RISHÖJ

SUMMARY

In nine patients with severe intracranial disease causing increased intracranial pressure (ICP), the effects on ICP and cerebral perfusion pressure (CPP) of the following manoeuvres were studied: (1) endotracheal intubation, (2) addition of 50% nitrous oxide to the inspired gas after hyperventilation with oxygen and thereafter (3) addition of halothane to the nitrous oxide/oxygen mixture. The mean “peak” increase in ICP during endotracheal intubation was 16.6 mm Hg. Critically small CPP values were prevented by an increase in arterial pressure. Nitrous oxide caused only a minor increase in ICP. Halothane caused a mean increase in ICP of 7.6 mm Hg and critically small CPP values in three patients.

Any significant increase in intracranial pressure (ICP) may be dangerous in patients with intracranial disorders, because of local or global ischaemia resulting from a decrease in tissue perfusion pressure.

The effects of many anaesthetics upon ICP has been investigated both experimentally and clinically. While the neuroleptanalgesia techniques seem to produce a decrease in ICP (Fitch et al., 1969) all volatile agents studied so far cause an increase in intracranial pressure, as a result of cerebral vasodilatation and an increase in cerebral blood volume. The resulting intracranial hypertension may be completely or partially counteracted by hyperventilation (Jennett, McDowall and Barker, 1967; Adams et al., 1972; Henriksen and Jørgensen, 1973; Jørgensen and Henriksen, 1973).

Halothane is considered a valuable drug for many reasons and is widely used also in neuroanaesthesia. However, some controversy exists about how safely it may be applied in patients with intracranial diseases. Jennett et al. (1969) found that the resulting increase in intracranial pressure depends upon the halothane concentration and was greatest in patients with intracranial space-occupying lesions. They found that hyperventilation could not be relied upon to counteract this effect. The risk of using halothane in neuroanaesthesia was stressed in an Editorial (Br. J. Anaesth. (1969), 41, 277). To the contrary, Adams et al. (1972) showed that hyperventilation, applied for 10 min before the addition of halothane abolished any serious increase in the intracranial pressure.

Because of this controversy we have performed further studies of the effects of halothane and hypocapnia. We selected a series of patients with severe intracranial disorders and an increased intracranial pressure, patients who must be considered close to decompensation of intracranial pressure regulation, and therefore very sensitive to the cerebral vasodilating effect of halothane.

MATERIAL AND METHODS

Nine patients were studied.

Pre-study procedures and measuring techniques.

Under local anesthesia, a catheter was placed in the lateral ventricle opposite the intracranial lesion through a frontal burr-hole. Intracranial pressure was measured continuously for at least 24 hours before the study.

Premedication with diazepam 5–10 mg and atropine 0.5 mg was given i.m. 1 hour before induction of anaesthesia. The radial artery opposite the dominant side was cannulated after performing Allen's test (Allen, 1929). The arterial catheter was used for continuous monitoring of arterial pressure and for sampling of blood for gas analysis.

In 6 patients the superior vena cava was catheterized through a medial cubital vein for measurement of central venous pressure (CVP).
Systemic arterial pressure and intracranial (ventricular) pressure were measured using Statham P23Db transducers and recorded on a two-channel Servogor potentiometric recorder. CVP was measured using a water column. All measurements were performed with the patient in the supine position. The forehead was the reference point for pressure measurements. The mean pressures (MABP, MICP) were calculated as diastolic pressure plus one third of the pulse amplitude. Arterial samples for determination of $P_2O_2$, $P_CO_2$ and pH were taken at selected times. Radiometer equipment was used for the pH and blood gas analysis.

**Anaesthesia.**

After making control measurements, atropine 0.5 mg was given i.v. Anaesthesia was induced with enbomal-sodium 200-400 mg i.v., followed by suxamethonium 75–125 mg i.v. to facilitate endotracheal intubation. One patient (No. 9) already had a tracheostomy and received no suxamethonium. Measurements were noted when the ICP had reached the maximum value.

**Nitrous oxide and hypocapnia.**

The patients were ventilated with an Engström ventilator immediately after endotracheal intubation and controlled hyperventilation was established with 100% oxygen as the inspired gas, to achieve $P_CO_2$ values between 20 and 30 mm Hg. Anaesthesia and muscle relaxation were maintained with one or more additional doses of enbomal-sodium 50 mg, a total of 50–300 mg, and gallamine 80–120 mg. Stable values for ICP were reached after 2–11 min, but hyperventilation was continued for at least 10 min before making a new set of control measurements. The inspired gas was then changed to 50% nitrous oxide in oxygen with unchanged tidal and minute volumes. Stable measurements were restored 1–8 min after the start of nitrous oxide inhalation. In 2 patients (Nos. 3 and 6) nitrous oxide and halothane were commenced simultaneously.

**Halothane and hypocapnia.**

After 10 min of continued hyperventilation with nitrous oxide in oxygen, measurements were noted and 0.5–1.0% halothane was added to the anaesthetic gas mixture with unchanged ventilator settings. Pressures were recorded for at least 10 min, and a plateau was reached after 4–15 min. In one patient (No. 6) a rapid reduction in arterial pressure to 40 mm Hg necessitated interruption of the halothane administration. Otherwise the surgical procedure was performed under these conditions of anaesthesia.

**RESULTS**

Table I shows the preoperative data. All the patients had some degree of intracranial hypertension during the period of observation. Two patients (Nos. 4 and 5) exhibited fluctuations in ICP. Patient No. 9 was stuporous with signs of brain stem damage, being in the 20th day after haemorrhage from an arteriovenous aneurysm in the right cerebral hemisphere. A tracheostomy had been performed 14 days before the study. This patient had only a mild intermittent increase of ICP. Papilloedema was present in 7 patients. The 5 patients with supratentorial tumours were treated with dexamethasone after operation, while intermittent ventricular drainage was necessary in the one patient with an infratentorial space-occupying lesion. All patients had adequate spontaneous

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Sex</th>
<th>Age</th>
<th>Diagnosis</th>
<th>Intracranial pressure during 24 hours prior to study (mm Hg)</th>
<th>Plateau waves</th>
<th>Clinical state</th>
<th>Treatment during observation period</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>52</td>
<td>Cerebral metastasis</td>
<td>30–40</td>
<td>Somnolent/papilloedema</td>
<td>Dexamethasone</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>61</td>
<td>Cerebral glioblastoma</td>
<td>25–40</td>
<td>Alert/papilloedema</td>
<td>Dexamethasone</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>38</td>
<td>Hydrocephalus</td>
<td>20–30</td>
<td>Alert/papilloedema</td>
<td>Dexamethasone</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>23</td>
<td>Cerebral astrocytoma</td>
<td>10–60</td>
<td>Alert/papilloedema</td>
<td>Dexamethasone</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>33</td>
<td>Temporal glioblastoma</td>
<td>20–60</td>
<td>Alert/papilloedema</td>
<td>Dexamethasone</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>60</td>
<td>Acoustic neurinoma</td>
<td>10–20</td>
<td>Alert/papilloedema</td>
<td>Dexamethasone</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>F</td>
<td>21</td>
<td>Cerebellar angioma</td>
<td>25–35</td>
<td>Alert/papilloedema</td>
<td>Intermittent drainage of ventricular fluid</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>F</td>
<td>57</td>
<td>Cerebral metastasis</td>
<td>15–20</td>
<td>Alert/papilloedema</td>
<td>Dexamethasone</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>M</td>
<td>36</td>
<td>Aneurysm</td>
<td>5–15</td>
<td>Stuporous</td>
<td>Dexamethasone</td>
<td></td>
</tr>
</tbody>
</table>
respiration and did not require respiratory assistance. The mean ICP before anaesthesia in the 9 patients was 26.9 mm Hg (range 7–48 mm Hg), at a mean \( P_{\text{aco}} \) of 36.7 mm Hg (range 28–44 mm Hg), indicating some degree of spontaneous hyperventilation in some of the patients.

**Endotracheal intubation.**

The initial dose of barbiturate reduced ICP in 7 patients (range of decrease 5–17 mm Hg) with concomitant minor reductions in arterial pressure. No changes were seen in 2 patients. The effects of barbiturates were not analysed further. The maximum values of ICP during intubation varied from 12 to 87 mm Hg with changes in \( P_{\text{aco}} \) ranging from −2 to 10 mm Hg. However, the increases in MICP did not cause any critical reduction in CPP since there was simultaneous increase in MABP (table II). These pressure changes were of very brief duration (1–3 min). CVP was virtually unchanged.

**Nitrous oxide.**

When plateau values were reached during hyperventilation with 100% oxygen after 2–11 min, in all patients MICP had decreased to values below 20 mm Hg (table III). MICP was now 9.7 mm Hg compared with 26.9 mm Hg before induction of

![Table II. Mean intracranial pressure (MICP), mean arterial pressure (MAP), arterial carbon dioxide tension (\( P_{\text{aco}} \)), central venous pressure (CVP) and cerebral perfusion pressure (CPP) in nine patients before anaesthesia (control) and at maximum values of MICP during endotracheal intubation after induction of anaesthesia with a barbiturate–oxygen–suxamethonium sequence ("peak"). Patient No. 9 already had a tracheostomy.](image)

![Table III. Mean intracranial pressure (MICP), mean arterial pressure (MAP), arterial carbon dioxide tension (\( P_{\text{aco}} \)), central venous pressure (CVP) and cerebral perfusion pressure (CPP) at the plateau values after endotracheal intubation and hyperventilation with 100% oxygen and the injection of gallamine and barbiturate (control), and at the plateau values after changing to 50% nitrous oxide in oxygen with continued hyperventilation. Figures in brackets indicate time (min) before stable values were reached. Seven patients were studied.](image)
Measurement of intracranial pressure has become an important tool in the management of patients with intracranial diseases. Preoperative monitoring of ICP facilitates rational therapy of intracranial hypertension, thus creating the best possible conditions for surgical procedures. In patients with tumours the treatment of choice will usually be dexamethasone administered for one to several days before operation. If the cerebrospinal fluid pathways are obstructed, intermittent or continuous ventricular drainage is of the utmost importance to minimize the risks of anaesthesia and surgical trauma to the brain.

The consequences of a significant increase in intracranial pressure are:

1. **Global ischaemia** resulting from a reduction in CPP to values below those values necessary for adequate cerebral blood flow and metabolism. The critical lower limit of cerebral perfusion pressure was determined by Häggendahl et al. (1970) as 40 mm Hg in normal dog brain.

2. **Local ischaemia.** This critical lower limit found in normal dog brain cannot be regarded as applicable to diseased areas of human brain in which impaired autoregulation and possible local increases in tissue pressure may exist. In such areas the local tissue perfusion pressure cannot be calculated as the difference between systemic arterial pressure and ventricular pressure. Local ischaemia may develop before global ischaemia.

3. **Obstruction of the cerebrospinal fluid pathways** from mass shift may result in development of pressure gradients and possible subsequent distortion of the brain and internal herniation with compression of the brain stem.

An increase in intracranial pressure during anaesthesia. The small supplemental doses of barbiturates did not alter ICP during this period of hyperventilation. MABP had also stabilized at slightly lower values than before induction. A new steady state was reached 1–8 min after changing to 50% nitrous oxide in oxygen. A small but significant reduction in CPP to 71.0 mm Hg occurred as a result of the combination of a slight increase in MICP and a minor decrease in MABP. Critically low values of CPP were not observed. Changes in CVP were negligible. The mean \( P_{\text{aco}_2} \) had decreased from 27.9 to 24.9 mm Hg despite unchanged ventilation.

**Halothane.**

Addition of halothane to the anaesthetic gas mixture resulted in an increase in MICP from 12.9 to 19.3 mm Hg. In only 2 patients was MICP higher than before anaesthesia. The highest MICP was 43 mm Hg. The plateau occurred after 4–15 min (table IV). The reduction in mean CPP to 52.4 mm Hg was, in all patients, mainly the result of a reduction in MABP. One patient (No. 6) had a marked reduction in MABP to 40 mm Hg, associated with a reduction in CPP to 20 mm Hg. Patients Nos. 1 and 7 developed CPP values below 40 mm Hg. In the remaining patients satisfactory CPP values were maintained. During the entire study changes in CVP were very small. The compiled data are graphed in figure 1.

### DISCUSSION

Measurement of intracranial pressure has become an important tool in the management of patients...
NITROUS OXIDE, HALOTHANE AND INTRACRANIAL PRESSURE

CPP (mm Hg)

1 2 3 4 5

160-
140-
120-
100-
80-
60-
40-
20-

CPP = cerebral perfusion pressure.
MICP = mean intracranial pressure.
MABP = mean arterial pressure.
CVP = central venous pressure.
P_{Aco2} = arterial carbon dioxide tension.

1. Preanaesthetic values, spontaneous respiration.
2. Intubation after barbiturate, oxygen, suxamethonium.
3. Controlled hyperventilation, 100% oxygen, barbiturate, gallamine.
4. Controlled hyperventilation, 50% nitrous oxide in oxygen, gallamine.
5. Controlled hyperventilation, 50% nitrous oxide in oxygen, gallamine halothane.

The interrupted lines represent the two patients in whom the separate effect of nitrous oxide was not measured.

anaesthesia is considered to be the result of an increase in cerebral blood volume caused by an increase in arterial pressure in patients with impaired autoregulation, hypercapnia, the vasodilator effect of the anaesthetic agent, or high venous pressure from compression of jugular veins or inappropriate positioning. Furthermore, when the skull is open, brain swelling may cause external herniation, increase bleeding and make surgery difficult.

The present study of the effect of endotracheal intubation in patients following a barbiturate-oxygen-muscle-relaxant-anaesthesia sequence showed an increase in ICP in most patients, presumably as a result of an increase in arterial pressure, hypercapnia or jugular vein compression. On the other hand, the simultaneous increase in arterial pressure compensated for this, preventing a reduction in cerebral perfusion pressure.

In a previous study of the use of nitrous oxide as the sole agent for induction of anaesthesia (Henriksen and Jørgensen, 1973) it was suggested that the combined effect of nitrous oxide and endotracheal intubation on ICP may result in a severe reduction in CPP. In this investigation nitrous oxide caused only minor changes in ICP, probably because its effect was separated from that of endotracheal intubation by 10 min of hyperventilation (fig. 1). However, the supplementary doses of barbiturate may have had modifying effect upon changes in ICP (Sönnergard, 1961).

In a study by Jennett et al. (1969) halothane was found to cause an increase in ICP in patients with space-occupying lesions. The effect could not be controlled by hyperventilation. In contrast, Adams et al. (1972) showed that if the addition of halothane to the anaesthetic gas mixture was preceded by 10 min of hyperventilation, intracranial hypertension did not develop. These investigators further demonstrated that if hyperventilation and halothane administration were started simultaneously ICP did increase but returned to control values after 10-30 min.

Using the same anaesthetic procedure as Adams et al. (1972) this investigation showed that adding halothane after 20 min of hyperventilation, including the 10 min of nitrous oxide administration, resulted in only minor increases in ICP in most patients, although 1 patient developed an ICP of 43 mm Hg (table IV). However, cerebral perfusion pressure decreased in 3 patients to values below 40 mm Hg. This was mainly the result of the systemic hypotensive effect of the combination of halothane and hyperventilation. Arterial pressure decreased in 1 patient to 40 mm Hg. The magnitude of the changes in ICP could not be predicted from preoperative values, whereas cardiovascular depression by halothane may be expected in debilitated and hypovolaemic patients. Because of the possibility of a reduction in cerebral perfusion...
pressure we do not consider it safe to wait for a spontaneous return to normal intracranial pressure as suggested by Adams et al. (1972).

Although Adams et al. (1972) did not give information about preoperative condition and treatment and although they recorded lumbar and not ventricular pressure, we consider that our studies are in agreement with their finding that if the administration of halothane is preceded by a period of hyperventilation the increase in ICP is not serious.

It is concluded that the effect upon ICP and CPP of endotracheal intubation is harmless after induction of anaesthesia with barbiturate–oxygen–muscle-relaxant sequence, that administration of nitrous oxide is not dangerous in the presence of hypocapnia and, finally, that the increase in ICP, caused by halothane after a period of hyperventilation, is small. However, the combined effect of an increase in ICP and a reduction in arterial pressure from hyperventilation with halothane may contraindicate the use of this anaesthetic agent in some patients with intracranial diseases and a labile circulation. Other anaesthetics may be preferable if dangerous cardiac depression is suspected, for example fluroxene (Jørgensen and Henriksen, 1973), or neuroleptanalgesic drugs which seem to cause a reduction in ICP (Fitch et al., 1969).

REFERENCES


