THE EFFECT OF NITROUS OXIDE ON THE CEREBROSPINAL FLUID PRESSURE DURING ENCEPHALOGRAPHY

BY

E. GORDON AND T. GREITZ

SUMMARY

Cerebrospinal fluid pressure was measured in twenty-three patients undergoing encephalography. Three different programmes were followed to determine the effect of nitrous oxide on intracranial pressure with and without injection of air and nitrous oxide into the theca. In every case the initial c.s.f. pressure remained unchanged when nitrous oxide was used for encephalography, while it increased significantly after the inhalation of nitrous oxide with air encephalography. However, this increase always remained within the normal range of c.s.f. pressure and therefore the conclusion is drawn that the use of nitrous oxide in the anaesthetic mixture during encephalography could be followed without any risk in cases of normal intracranial pressure. In cases of high intracranial pressure, and in the presence of nitrous oxide in the anaesthetic gas mixture, the intrathecal use of nitrous oxide instead of air is probably a safer method.

Patients undergoing neuroradiological investigations often have an elevated intracranial pressure and are extremely sensitive even to the slightest pressure change in the cranial cavity. Any method of pre-operative examination which tends to elevate intracranial pressure is liable to precipitate a serious crisis which can result in irreversible brain damage. It is therefore of great clinical importance to avoid such precipitating factors not only during operative treatment of neurological diseases but also during the pre-operative diagnostic investigations.

Nitrous oxide is the basic agent in nearly every anaesthetic technique and is widely used in neuroradiological practice. The knowledge of the presence and magnitude of the elevation of intracranial pressure caused by nitrous oxide is therefore of primary importance.

Saidman and Eger (1965) have reported an increase of intracranial pressure during pneumo-encephalography in patients anaesthetized with nitrous oxide. They explained this by showing that nitrous oxide is carried to a closed air-containing space within the body in greater quantity and at more rapid rate than nitrogen can be carried away, resulting finally in an increased number of gas molecules within the space.

The validity of this hypothesis was confirmed both by animal experiments (Saidman and Eger, 1965) and in clinical practice (Philippart, Thibaut and Bonnal, 1968) but these data are rather limited and a more precise knowledge of pressure changes in various clinical conditions is still lacking. It was therefore decided to study the exact effect on intracranial pressure of nitrous oxide in the anaesthetic gas mixture during the various phases of encephalography.

MATERIAL AND METHODS

Twenty-three patients with differing pathology undergoing encephalography were studied. All patients were premedicated with atropine 0.5 mg and droperidol 0.1 mg/kg, and induction carried out with an ultra rapid-acting barbiturate followed by suxamethonium and endotracheal intubation. Ventilation was controlled and normal alveolar ventilatory volumes were calculated with the help of the Engström-Herzog nomogram (1959). Anaesthesia was maintained either by 0.5-1 per cent halothane or a combination of phenoperidine or fentanyl and droperidol. Thereafter three different procedures were followed.

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EFFECT OF NITROUS OXIDE ON CEREBROSPINAL FLUID PRESSURE

(1) Programme A. The anaesthetic gas mixture used consisted of 50 per cent oxygen and 50 per cent air. Lumbar puncture was performed at one vertebral interspace and another needle was inserted into the subarachnoid space at the intervertebral space above, and a pressure transducer connected through a polyethylene catheter. The transducer was always adjusted to the level of the patient's external auditory meatus. Air was then injected through the first needle according to a fixed schedule (5 ml at zero time, 5 ml at 5 min, 5 ml at 10 min, 15 ml at 15 min, and sometimes another 15 ml at 25 min). The injection rate was about 10 ml/min. Only one or two drops of c.s.f. were allowed to escape during this procedure. Patients from whom more c.s.f. was lost were excluded from the series. The variations in c.s.f. pressure were recorded with Elema-Schönander low-pressure transducers, amplifiers and ink-jet recorder (Mingograph type 81). When c.s.f. pressure was stabilized after the last injection, the air in the inhalation gas mixture was replaced by 50 per cent nitrous oxide; c.s.f. pressure was then monitored until stabilized for at least 10 minutes. During this recording no other parameters were changed and the patient was not moved from the sitting position. Recording was then ended and encephalography completed.

(2) Programme B. The gas mixture used consisted of 50 per cent oxygen and 50 per cent air. After positioning of the two lumbar needles and pressure-recording for at least 5 minutes the air was replaced by 50 per cent nitrous oxide and the c.s.f. pressure monitored for another 10 minutes before anything was injected. Intrathecal injection of air was then begun according to the schedule described above, with continuous pressure recordings. After this procedure encephalography was completed.

(3) Programme C. The gas mixture used consisted of 50 per cent oxygen and 50 per cent air. After positioning of the two lumbar needles and the beginning of pressure-recording, intrathecal injection of nitrous oxide was made according to the same time schedule as for air injection. When this schedule was completed and c.s.f. pressure stabilized after the last injection the air in the inhaled mixture was replaced by nitrous oxide and c.s.f. pressure monitored for at least 10 minutes. Encephalography was then completed.

During each procedure systolic blood pressure was followed throughout by palpation of the radial artery and measured by a sphygmomanometer. Arterial, or in a few cases capillary, blood samples were collected soon after the recording of the c.s.f. pressure and analyzed by the Astrup micro-technique (Siggaard-Andersen et al., 1960).

RESULTS

Programme A was carried out in 11 cases (table I and fig. 1). Initial cerebrospinal fluid pressure (c.s.f.p.) varied between —16 and +34 cm H₂O (mean value 5.0 cm H₂O). After injection of air the c.s.f.p. was increased every time but within a few minutes returned to the initial value. However, when nitrous oxide was introduced the c.s.f.p. was again increased (except in two cases, where it remained virtually unchanged) but did not return to the initial values after an observation time of at least 10 minutes. This increase varied between 0 and 35.6 cm H₂O (mean value 16.5 cm H₂O).

![Diagram of CSFP and BP](image)

Fig. 1
A typical curve of pressure changes during encephalography carried out according to Programme A, patient No. 7 (for further explanation see text).
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**TABLE I**

*Cerebrospinal fluid pressure values and means during encephalography in eleven patients carried out according to Programme A.*

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Age</th>
<th>Clinical diagnosis</th>
<th>Encephalographic diagnosis</th>
<th>Anaesthetic agent</th>
<th>Cerebrospinal fluid pressure (cm H₂O)</th>
<th>Initial</th>
<th>After injection of 30 ml air</th>
<th>Change</th>
<th>After injection of 45 ml air</th>
<th>Change</th>
<th>Inhalation of nitrous oxide</th>
<th>Before</th>
<th>After</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7</td>
<td>Cerebral contusion</td>
<td>Normal</td>
<td>Halothane</td>
<td>34</td>
<td>73</td>
<td>−18</td>
<td>12</td>
<td>38</td>
<td>50</td>
<td>12</td>
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<tr>
<td>2</td>
<td>60</td>
<td>Senile dementia</td>
<td>Cortical atrophy</td>
<td>NLA</td>
<td>0</td>
<td>61</td>
<td>52</td>
<td>13.6</td>
<td>30</td>
<td>16.4</td>
<td></td>
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</tr>
<tr>
<td>3</td>
<td>60</td>
<td>Brainstem glioma</td>
<td>Brainstem glioma</td>
<td>NLA</td>
<td>−4</td>
<td>71</td>
<td>−7</td>
<td>2.7</td>
<td>22</td>
<td>19.3</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>4</td>
<td>31</td>
<td>Epilepsy</td>
<td>Ventricular dilatation</td>
<td>Halothane</td>
<td>0</td>
<td>24</td>
<td>26</td>
<td>6.8</td>
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<td></td>
<td></td>
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</tr>
<tr>
<td>5</td>
<td>54</td>
<td>Glioma corp. callosum</td>
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<td>Halothane</td>
<td>13.6</td>
<td>170</td>
<td>−156</td>
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<td></td>
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<tr>
<td>6</td>
<td>60</td>
<td>Meningiitis?</td>
<td>Ventricular dilatation</td>
<td>Halothane</td>
<td>0</td>
<td>20</td>
<td>75</td>
<td>6.8</td>
<td>37</td>
<td>30.2</td>
<td></td>
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<tr>
<td>7</td>
<td>60</td>
<td>Acromegaly</td>
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<td>81</td>
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<td>8</td>
<td>66</td>
<td>Post-traumatic encephalopathy</td>
<td>Communicating hydrocephalus</td>
<td>NLA</td>
<td>2.7</td>
<td>20</td>
<td>16</td>
<td>13.3</td>
<td>0</td>
<td>0</td>
<td></td>
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<tr>
<td>9</td>
<td>54</td>
<td>Cushings disease</td>
<td>Intracerebral tumour</td>
<td>NLA</td>
<td>0</td>
<td>102</td>
<td>81.5</td>
<td>6.8</td>
<td>24.5</td>
<td>17.7</td>
<td></td>
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<tr>
<td>10</td>
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<td>Menigioma op.</td>
<td>Cortical atrophy</td>
<td>Halothane</td>
<td>−16</td>
<td>−2.7</td>
<td>13.5</td>
<td>29.5</td>
<td>−10.8</td>
<td>16.8</td>
<td></td>
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<tr>
<td>11</td>
<td>47</td>
<td>Epilepsy</td>
<td>Communicating hydrocephalus</td>
<td>Halothane</td>
<td>24.5</td>
<td>54</td>
<td>75</td>
<td>50.5</td>
<td>16</td>
<td>30</td>
<td>14</td>
<td></td>
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</tr>
</tbody>
</table>

Mean values: 5.0 58.7 52.5 61.5 12.9 27.4 16.5

**TABLE II**

*Cerebrospinal fluid pressure values and means during encephalography in seven patients carried out according to Programme B.*

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Age</th>
<th>Clinical diagnosis</th>
<th>Encephalographic diagnosis</th>
<th>Anaesthetic agent</th>
<th>Cerebrospinal fluid pressure (cm H₂O)</th>
<th>Initial</th>
<th>After 10 min inhalation of nitrous oxide</th>
<th>Change</th>
<th>After inj. of 45 ml air</th>
<th>Final</th>
<th>Initial-final difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>18</td>
<td>Cerebral contusion</td>
<td>Normal</td>
<td>Halothane</td>
<td>−6.8</td>
<td>−13.6</td>
<td>−6.8</td>
<td>12</td>
<td>0</td>
<td>6.8</td>
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<tr>
<td>2</td>
<td>28</td>
<td>Epilepsy</td>
<td>Normal</td>
<td>Halothane</td>
<td>−5.4</td>
<td>−5.4</td>
<td>0</td>
<td>47.5</td>
<td>0</td>
<td>5.4</td>
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</tr>
<tr>
<td>3</td>
<td>48</td>
<td>Intracerebral abscess</td>
<td>Intracerebral expansion</td>
<td>Halothane</td>
<td>−6.8</td>
<td>27</td>
<td>33.8</td>
<td>75</td>
<td>24.5</td>
<td>31.3</td>
<td></td>
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<td>4</td>
<td>17</td>
<td>Pituitary adenoma</td>
<td>Normal</td>
<td>Halothane</td>
<td>0</td>
<td>2.7</td>
<td>2.7</td>
<td>65</td>
<td>26</td>
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</tr>
<tr>
<td>5</td>
<td>15</td>
<td>Hydrocephalus?</td>
<td>Ventricular dilatation</td>
<td>Halothane</td>
<td>−13.6</td>
<td>−12.2</td>
<td>1.4</td>
<td>13.6</td>
<td>2.7</td>
<td>16.3</td>
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<tr>
<td>6</td>
<td>25</td>
<td>Hydrocephalus Arachnoiditis</td>
<td>Non-communic. hydrocephalus</td>
<td>NLA</td>
<td>−5.4</td>
<td>−5.4</td>
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<td>136</td>
<td>13.6</td>
<td>19</td>
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</tr>
<tr>
<td>7</td>
<td>16</td>
<td>Epilepsy</td>
<td>Normal</td>
<td>NLA</td>
<td>−11</td>
<td>−11</td>
<td>0</td>
<td>62</td>
<td>3</td>
<td>14</td>
<td></td>
</tr>
</tbody>
</table>

Mean values: −7.0 −2.57 4.4 58.7 10.0 17.0

Mean values without patient No. 3: −7.0 −7.5 −0.45 56.0 7.5 14.6
Programme B was followed in seven cases. In all these patients except one c.s.f.p. remained unchanged 10 minutes after the introduction of nitrous oxide into the inhalation gas mixture, but became elevated shortly after the introduction of air into the ventricles. One patient (Case no. 3) began to cough shortly after the introduction of nitrous oxide into the gas mixture so that it was necessary to increase the concentration of halothane. In this case c.s.f.p. increased during nitrous oxide inhalation from an initial value of —6.8 to 27 cm H2O after 10 minutes. However, this increase of c.s.f.p. was probably due to halothane, rather than to nitrous oxide (see Discussion). Therefore, it was considered justifiable to omit this case when calculating mean pressure values in this group of patients. However, in table II mean values are given with and without the values of this patient.

Initial c.s.f.p. varied in this group between —13.6 and 0 cm H2O (mean value —7.0 cm H2O). Values after 10 minutes of nitrous oxide inhalation were between —13.6 and 2.7 cm H2O (mean value —7.5 cm H2O). After the injection of 45 ml air c.s.f.p. increased to between 12 and 136 cm H2O (mean value 56 cm H2O). Cerebrospinal fluid pressure stabilized finally at levels varying between 0 and 26 cm H2O (mean value 7.5 cm H2O), thus the difference between initial and final c.s.f.p. showed values between 5.4 and 26 cm H2O (mean value 14.6 cm H2O).

Programme C was followed in five patients. In these cases the c.s.f.p. increased from an initial value of between —8 and +4 cm H2O (mean value —0.26 cm H2O) to values between —3 and 13.6 cm H2O (mean value 9.75 cm H2O) after the intrathecal injection of nitrous oxide but returned within some minutes to initial levels. The c.s.f.p. increase after nitrous oxide injection was much less than the increase after air injection (mean value 9.75 cm H2O against 52.5 cm H2O) which is probably due to a very rapid absorption of nitrous oxide from the subarachnoid space. Moreover, in some of these cases it was
necessary to introduce a quantity of air into the ventricles after the pressure monitoring was finished, to be able to complete encephalography. After the introduction of nitrous oxide to the inhalation gas mixture the c.s.f.p. remained practically unchanged in all cases.

**Blood pressure** changes were small except in two cases in whom systolic pressure fell to about 70 mm Hg during halothane administration, but returned rapidly to normal levels without any medication. Also in other cases when halothane was used, the blood pressure fell always below induction levels although it remained within the normal range. Another characteristic change was a rapid elevation of blood pressure usually observed when c.s.f.p. increased to high levels after air injection. This increase varied between 20 and 60 mm Hg and remained at these higher levels long after the c.s.f.p. returned to normal values.

**Blood gas analysis** was done once during anaesthesia in a steady respiratory state, mostly to control the Pco₂ level, as Pco₂ changes are liable to influence c.s.f.p. The analyses were usually made on arterial blood, but in a few cases capillary blood was used. Pco₂ values were usually within normal levels (35–40 mm Hg for arterial and 40–45 mm Hg for capillary samples). In some cases a lower Pco₂ value was found but the normal levels quoted were never exceeded.

In each case the patients awoke from anaesthesia without any complication. The postanaesthetic course was uneventful. There was no difference between the clinical course of the patients examined with air and those with nitrous oxide in this series of patients.

**DISCUSSION**

The investigation of cerebrospinal fluid pressure during encephalography in this series of twenty-three patients confirms the findings of several authors (Saidman and Eger, 1965; Philippart and Thibaut, 1967; Philippart, Thibaut and Bonnal, 1968) that the addition of nitrous oxide into the anaesthetic gas mixture during air encephalography elevates c.s.f. pressure. It was clear from the cases studied with programme B that nitrous oxide by itself does not elevate intracranial pressure, which is in contradiction to the findings of Laitinen, Johansson and Tarkkanen (1967) but in agreement with the findings of Stephen and associates (1953), Søndergard (1961) and Gordon (1969). With the use of nitrous oxide instead of air for encephalography the increase in c.s.f. pressure could be avoided. On the other hand, the measurements showed that the elevation of c.s.f. pressure during nitrous oxide inhalation was moderate and never attained dangerously high levels. These findings are in agreement with those of Philippart, Thibaut and Bonnal (1968) who furthermore recorded a slow return of pressure to normal levels after the initial rise. They offered no explanation for this phenomenon, but speculated about the possibility of diffusion of nitrous oxide into the blood or a decrease of cerebral blood flow. The intact brain certainly...
has different ways of compensating rapidly for a slow moderate increase in the volume of intracranial contents. One of the most effective of these mechanisms is probably that provided by the unidirectional valves between arachnoid villi and venous channels described by Welch and Friedman (1960). It is reasonable to suppose that these compensatory mechanisms in cases with high initial intracranial pressure are more or less exhausted and here the effect of nitrous oxide in increasing c.s.f. pressure is more significant. In such cases, of course, other precautions have to be carried out, such as a preliminary burr-hole and ventricle drainage to allow prevention of coning by a release of c.s.f. Moreover, as shown in many investigations (Stephen et al., 1953; Søndergård, 1961; McDowall, Barker and Jennett, 1966; Jennett, McDowall and Barker, 1967) most of the other inhalation anaesthetic agents have a significantly higher pressure-elevating effect than that of nitrous oxide. The death during pneumoencephalography reported by Saidman and Eger (1965) was therefore probably not primarily due to nitrous oxide but to a combination of halothane and hypercarbia. It is well known to those familiar with treating neurosurgical patients, that halothane causes a respiratory depression sufficient to raise arterial carbon dioxide tension to levels which cause cerebral vasodilatation and elevated intracranial pressure. As shown by Gordon (1969) and Jennett and associates (1969) halothane increases intracranial pressure even in the presence of hyperventilation. A combination of halothane and hypercarbia certainly has a far more significant intracranial pressure-elevating effect than nitrous oxide during pneumoencephalography. This, of course, does not exclude the possibility that nitrous oxide could have played some role in the fatal outcome described by Saidman and Eger (1965).

On the basis of the present investigation it can be concluded that the use of nitrous oxide in the anaesthetic gas mixture during routine pneumoencephalographies when initial c.s.f. pressure is normal is certainly not a dangerous procedure. There is no reason to abandon the use of nitrous oxide in the anaesthetic nor is it necessary to replace air by nitrous oxide for visualizing the ventricles in these cases. On the basis of this series, it is not possible to draw any conclusions concerning the effect of nitrous oxide on c.s.f. pressure in cases of high intracranial pressure. It is reasonable to suppose that pressure changes in such cases will be more significant, and therefore the use of nitrous oxide in the anaesthetic gas mixture during air encephalography should be avoided.

In some clinics lumbar pneumoencephalography is not carried out on those with raised intracranial pressure. Ventriculography is performed instead, but wherever the contrast medium is air the same considerations apply as to lumbar encephalography.

REFERENCES


Correspondence

Sir,—Blood loss studies in patients anaesthetized by epidural block are scarce, and Dr. Bond is to be congratulated on his contribution to the literature (Brit. J. Anaesth. (1969), 41, 942).

He described an interesting clinical investigation in which 45 patients destined for vaginal surgery had a lumbar block induced. They were divided into two groups, the first sedated and the other anaesthetized by a conventional inhalational technique. A small, but statistically significant, difference in blood pressure was observed between these groups and a small, but statistically insignificant, fall of blood loss in the more hypotensive group. He concluded from this observation that lumbar epidural block had conferred an avascularity upon the operating site which was independent of the associated induced hypotension.

It may be maintained that this conclusion is not justified by the evidence presented. No data were recorded of blood loss from similar groups of patients anaesthetized without epidural block or from patients in whom hypotension was induced by other methods.

It could be concluded from this, and other studies (Loudon and Scott, 1960; Moir, 1968; Donald, 1969) that the relationship between blood loss and blood pressure was not linear. A steep fall of blood loss occurred until systolic blood pressure was about 90-100 mm Hg, and at lower levels of blood pressure only a small and clinically insignificant improvement in the operating field was observed. Since all but one of Dr. Bond's patients showed a substantial degree of hypotension, it may be that it was this small fall in blood loss at lower levels of blood pressure which was observed.

In a recent study (Donald, 1969), which would not be available to Dr. Bond, blood loss in patients during vaginal surgery was not significantly different when systolic blood pressure was reduced to 60–80 mm Hg, by ganglionic blockade or by epidural anaesthesia. This observation remains unconfirmed, and no data are available to suggest what is the optimum BP level for hypotension induced by ganglionic block but the inference is that so far as blood loss is concerned, epidural blockade is no more than a difficult and inconvenient method of inducing hypotension.

J. R. DONALD

Carlisle, Lanarkshire

References


Halothane and neurosurgery

Sir,—I feel I have to comment on the letter in the British Journal of Anaesthesia, 41, 1014 (Jennett and Barker).

The reply to the question about deterioration of patients under general anaesthesia is twofold. If the pressure is known to be raised beforehand, halothane is given in such a way, i.e. with controlled ventilation, that a significant rise does not occur. Secondly, if the surgical procedure is one which relieves the cause of the increase, any deterioration after the operation could well be due to the surgery.

We did not, it must be noted, comment on the article by the above-mentioned, only on the Editorial in the British Journal of Anaesthesia.

R. I. KEEN
Manchester