INTRACRANIAL PRESSURE CHANGES IN NEUROSURGICAL PATIENTS DURING HYPOTENSION INDUCED WITH SODIUM NITROPRUSSIDE OR TRIMETAPHAN

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SUMMARY

Intracranial pressure has been measured in 45 patients undergoing neurosurgery during the induction of deliberate hypotension using either sodium nitroprusside or trimetaphan. A statistically significant increase in intracranial pressure (ICP) occurred during the early stages of the infusion of nitroprusside in normocapnic patients. A non-significant increase in ICP was obtained in hypocapnic patients. The mean ICP increased from 6.3 mm Hg to 11.7 mm Hg when the arterial pressure was reduced slightly, but the response in individual patients varied widely (range —1.6 mm Hg to +20.9 mm Hg). When the arterial pressure (BP) had decreased to 70% of the value existing before infusion of nitroprusside, mean ICP returned to control values and thereafter decreased with further reductions in BP. In patients rendered hypotensive with trimetaphan, there was no change in mean ICP but two patients showed moderate increases (+9.3 mm Hg and +5.7 mm Hg). The mechanism of the increase in ICP with nitroprusside is thought to be expansion of the intracranial blood volume as a result of cerebral vasodilatation. Trimetaphan does not usually produce ICP changes except when intracranial compression is severe, for in these circumstances a small change in intracranial blood volume consequent upon autoregulation may trigger an increase in ICP.

As a result of space-occupying pathology, the neurosurgical patient has often a diminished ability to accommodate increases in the volume of any one of the intracranial contents. For this reason, anaesthetic techniques are aimed at ensuring that, by avoiding hypoxia and hypercapnia, straining and venous obstruction, and those drugs which are known to increase cerebral blood flow (CBF) and cerebral blood volume (CBV), increases in the volume of any of the intracranial compartments do not occur. The effects of individual anaesthetic agents on intracranial pressure are well known and have been reviewed recently (McDowall, 1975). Some agents, such as halothane and ketamine, have been shown to produce significant increases in intracranial pressure (ICP) while others, such as thiopentone and Althesin, cause decreases.

The response of the cerebral circulation to agents used for inducing hypotension in neurosurgery is less well documented, and as moderate induced hypotension is used commonly in neurosurgical units, it appeared important to investigate the effects of hypotensive drugs on ICP.

METHODS

Forty-five patients, selected only in that hypotension was to be induced as part of their anaesthetic sequence, were admitted to the study. Clinical information on the patients is given in table I. Anaesthesia was induced in all patients with thiopentone and, after endotracheal intubation, all were ventilated artificially with nitrous oxide and oxygen using an East Freeman Ventilator. Tubocurarine was administered to produce muscular paralysis. Increments of fentanyl were given as required. In 35 patients the ventilation was adjusted to maintain $P_{\text{a}}^\text{CO}_2$ near normal. A further 10 patients were hyperventilated.

Arterial pressure (BP) was measured using a pressure transducer attached to a cannula placed in the radial artery, the trace being displayed on one channel of a heated stylus recorder (Devices). ICP was measured electronically via a ventricular catheter inserted through a burr hole. All measurements were taken before the bone flap was made, and referred to a zero point at the external auditory meatus. All values quoted are for mean BP and mean ICP; mean BP being calculated as diastolic + 1/3 pulse pressure, and mean ICP as diastolic + 1/3 pulsation.

Control measurements were taken of arterial pressure and ICP during stable conditions of nitrous oxide and oxygen anaesthesia, and then hypotension was induced, by the infusion of 0.01% sodium nitroprusside in 21 patients, and by the infusion of 0.05%
trimetaphan in 24 patients. Arterial samples for the estimation of pH, $P_{CO_2}$ and bicarbonate concentration were taken before and after the induction of hypotension.

**RESULTS**

The control data for BP, ICP and arterial blood acid-base state are shown in table II. Control BP was not significantly different between the groups, except between the hyperventilated sub-groups, in which the numbers were small. In the normocapnic group receiving sodium nitroprusside ICP was significantly less than that in the normocapnic trimetaphan group ($P<0.05$). This difference is discussed in detail later. There were no important differences in the acid-base data.

Hypotension was produced easily in all but two of the patients who received sodium nitroprusside, and three of those to whom trimetaphan was administered. The data from these five patients are not included in the mean results, since it was not possible to produce the BP values required for the ICP measurements.

The relationship between the mean values for ICP and BP for the normocapnic patients is shown in figures 1A and 1B for the period of the induction of hypotension with nitroprusside or trimetaphan respectively. To demonstrate this relationship at equivalent levels of hypotension in different patients with varying starting arterial pressures, the results have been expressed in terms of ICP at 90, 80 and 70% of the starting BP calculated for each individual patient. The starting value used was that present immediately before the induction of hypotension, that is during anaesthesia with nitrous oxide/oxygen, supplemented where necessary with fentanyl. Significance values are based on paired $t$ tests and refer to each percentage level of BP to the change in ICP from the control starting value. The drugs were infused at a rate designed to induce hypotension at the same rate in both groups; thus BP was decreased to 70% of the control value in 78.2 s (SEM 8.3) with nitroprusside and 83.1 s (SEM 10.5) with trimetaphan.

Figures 2 and 3 show the BP : ICP relationship in each individual patient during the induction of hypo-

### Table I. Main surgical pathology and procedure in those patients in whom induced hypotension was produced satisfactorily, 40 of the 45 cases admitted to the study (see results)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Sodium nitroprusside infusion</th>
<th>Trimetaphan infusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>$P_{ACO_2}$ (kPa)</td>
<td>$n$</td>
<td>$n$</td>
</tr>
<tr>
<td></td>
<td>5.37 ± 0.11</td>
<td>4.96 ± 0.2</td>
</tr>
<tr>
<td>Tumour</td>
<td>14</td>
<td>16</td>
</tr>
<tr>
<td>Aneurysm</td>
<td>8</td>
<td>7</td>
</tr>
<tr>
<td>Pituitary tumour</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Leucotomy</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

$*1$ kPa = 7.5 mm Hg.
EFFECTS OF NITROPRUSSIDE AND TRIMETAPHAN ON ICP

**Sodium nitroprusside hypotension**
- CBP = 94 ± 3.28 (mm Hg)  
- PaCO₂ = 5.37 ± 0.11 (kPa)  
- \( n = 14 \)

**Trimetaphan hypotension**
- CBP = 99 ± 3.10 (mm Hg)  
- PaCO₂ = 4.96 ± 0.2 (kPa)  
- \( n = 16 \)

**FIG. 1.** The relationship between ICP and BP during hypotension induced by sodium nitroprusside (A) and trimetaphan (B) in normocapnic and hypocapnic groups. BP is expressed as percentage of control value obtained during nitrous oxide in oxygen anaesthesia, supplemented where necessary with fentanyl. Significant increases in ICP occurred when nitroprusside reduced BP to 90 and 80% of control in the normocapnic group. The results appear similar in the hypocapnic group, but do not reach statistical significance. Unlike nitroprusside, trimetaphan produced no change in ICP as BP decreased to 70% of control in either the normocapnic or the hypocapnic group.

Individual results in hyperventilated patients are indicated by short horizontal lines at the right-hand side of each diagram.

It will be seen from these figures that, during the induction of hypotension with nitroprusside, ICP increased significantly but returned to its starting value when BP reached 70% of control. A similar, although not statistically significant, increase was seen in the hyperventilated group of patients receiving nitroprusside. With trimetaphan there was no such increase in ICP at any stage during the induction of hypotension, either at normocapnia or at hypocapnia. Table III shows the starting ICP value and the greatest ICP value measured during the induction of hypotension with nitroprusside or trimetaphan respectively.

**FIG. 2.** Results in individual patients for the relationship between ICP and BP during hypotension induced with sodium nitroprusside. The hypocapnic patients are denoted by short horizontal bars at the right-hand side of each diagram. The left-hand y axis in each diagram shows the starting value of ICP during nitrous oxide/oxygen/fentanyl anaesthesia, before the start of nitroprusside infusion. The changes shown are those that occurred at 90, 80 and 70% of control BP.

**FIG. 3.** Results in individual patients for the relationship between ICP and BP during hypotension induced with trimetaphan. The hypocapnic patients are denoted by short horizontal bars at the right-hand side of each diagram. The left-hand y axis in each diagram shows the starting value of ICP during nitrous oxide/oxygen/fentanyl anaesthesia, before the start of trimetaphan infusion. The changes shown are those that occurred at 90, 80 and 70% of control BP.
hypotension, together with $P_{CO_2}$ existing at the time of the measurements for each individual patient.

**DISCUSSION**

Figures 1A and 1B show the difference between the two agents in their effect on ICP. Mean ICP in the patients receiving sodium nitroprusside almost doubled from the control value of 6.3 mm Hg, to a new value of 11.7 mm Hg with BP only slightly reduced. There was no similar change in ICP in the patients who received trimetaphan. Under the controlled conditions of this study, the increase in ICP can presumably be ascribed to cerebral vasodilatation, sodium nitroprusside having a direct action on arteriolar smooth muscle. Such a direct vasodilatory action on cerebral vessels, with consequent increases in CBF, has been demonstrated by Ivankowitch and colleagues (1976). Interpretation of this difference between the two drugs is complicated by the different control ICP values between the two groups (control ICP for the trimetaphan group was 4.6 mm Hg, greater than for the nitroprusside group ($P < 0.05$)). Examination of all the clinical data leads us to believe that in all respects they form comparable groups. Five of the sodium nitroprusside patients had papilloedema, as did five in the trimetaphan group. Furthermore, the anaesthetic and surgical management of the cases did not change during the 15 months occupied by this study and the investigation protocol was adhered to strictly throughout. In retrospect, a randomized comparison would have been better, but the study was designed initially only to investigate sodium nitroprusside in neurosurgery.

Despite this inability to define any clinical difference between the two groups of patients, one must assume that the greater ICP in the trimetaphan group indicates that these patients had more advanced space-occupation as a group. Fortunately, instead of negating the value of this study, this difference in control ICP accentuates the difference observed because the greater starting ICP value in the trimetaphan groups would tend to accentuate any increase produced by this drug. In spite of this greater starting ICP, trimetaphan produced no mean change in ICP, while nitroprusside caused an increase from a smaller starting value.

Mean changes are of importance, of course, to the statistical assessment of any drug effect, but the clinician is interested also in the action of drugs in individual patients. From this standpoint it is relevant to point out that, despite the absence of a mean change in ICP in the trimetaphan group, two patients in this group exhibited major increases in ICP when the drug was infused (patients 30 and 37 in table III).
Both these patients had papilloedema, and in one the increase in ICP continued for some time after the cessation of trimetaphan infusion. In this latter patient, ICP increased to 45 mm Hg and aspiration of cerebrospinal fluid (c.s.f.) was deemed necessary. In view of this we suggest that the infusion of trimetaphan may have initiated a plateau wave in this patient. It is possible that the ganglionic blockade produced by trimetaphan could cause such a pressure wave by altering neurogenic control of CBV (Harper et al., 1972).

Another difference existed between the results in the two groups. The comparatively slow onset of hypotension with trimetaphan produced a steady level of reduced BP during induced hypotension but the evanescent action of nitroprusside often produced sudden variations in BP. The rapidity of these BP changes appeared to outstrip the capacity of the cerebral circulation to autoregulate its flow so that ICP and BP moved together during rapid changes in BP; these rapid variations were superimposed on a mean overall increase in ICP produced by the nitroprusside itself. One record is included to illustrate this point (fig. 4), which might be particularly important when nitroprusside infusion is stopped at the end of a period of induced hypotension.

The observed increases in ICP produced by nitroprusside occurred only when the degree of hypotension was modest, for, once the BP had decreased to less than 70% of the starting value, ICP was less than the initial level.

The sodium nitroprusside-induced increase in ICP was reflected in greater difficulty in performing intracranial surgery as compared with the trimetaphan group, and in five patients during nitroprusside infusion the dura was judged to be so tight as to make surgery impossible. All five patients were then hyperventilated and received hyperosmolar therapy, but three patients required, in addition, c.s.f. aspiration before surgery was possible. In only one patient in the trimetaphan group was the dura so tense as to interfere with surgery, and this patient has been discussed above.

The response of ICP to sodium nitroprusside infusion at normocapnia made it important to assess ICP response to the drug during hypocapnia. The increase in ICP in the small group of patients hyperventilated before the infusion of sodium nitroprusside was started is shown in figures 1A and 2 and appears to be similar to that in the larger normocapnic group, but the change does not reach statistical significance.

In a comparison of the effects of sodium nitroprusside and trimetaphan on ICP in the cat, Stullken and Sokoll (1975) obtained opposite results, that is trimetaphan increased ICP and nitroprusside produced no change. However, in this quoted study the hypotensive agents appear to have been given by bolus injection, resulting in a rapid reduction of BP to mean values of 35–40 mm Hg. From our records we would not expect to see ICP increases at such hypotensive values, so that the results of the two studies are not necessarily discordant in relation to nitroprusside. Stullken and Sokoll's finding of ICP increase with trimetaphan is ascribed by them to possible increases in intracranial volume resulting from the sympathetic blockade, and this finding resembles our results in the two patients who showed major ICP increases with this drug. It may be that there is a species difference in the degree of cerebrovascular control exerted by the sympathetic nervous system, such that alterations in intracranial blood volume produced by sympathetic blockade are

![Fig. 4. The BP and ICP records in one individual patient. The increase in ICP with the onset of nitroprusside-induced hypotension can be seen, but note also that a subsequent inadvertent recovery of BP led to a further marked increase in ICP. The gaps in the time trace indicate 1-min intervals.](https://academic.oup.com/bja/article-abstract/49/5/419/280365)
relatively much greater in the cat than in man, except when patients with critical intracranial compression are studied (for example, cases 30 and 37).

Clearly, the use of sodium nitroprusside after the dura has been opened will not be associated with increases in ICP, but the increases in pressure recorded here in the closed skull are indicative of increasing brain bulk, which is likely to make neurosurgery difficult even after opening the dura. It would appear that hyperventilation in these circumstances may not restore adequate operating conditions in patients receiving sodium nitroprusside, since increases in ICP occurred during hypocapnia also.

We would suggest that the use of sodium nitroprusside in neurosurgery should involve particular attention to the production of a stable reduced BP, and that minor degrees of hypotension produced by the drug may impair neurosurgical operating conditions. If nitroprusside is given to a patient before the dura is opened, ICP increases which result might lead to brain shift.

REFERENCES


VARIATIONS DANS LA PRESSION INTRACRANIENNE CHEZ LES MALADES NEUROCHIRURGICAUX PENDANT L'HYPOTENSION PROVOQUEE PAR LE NITROPRUSSIATE DE SOUDE OU LE TRIMETAPHAN

RESUME

On a mesuré la pression intracrânienne de 45 malades subissant une intervention neurochirurgicale pendant l’induction d’une hypotension délibérée à l’aide de nitroprussiate de soude ou de triméthaphan. Il s’est produit une augmentation de la pression intracrânienne (ICP) d’une importance statistique au cours des premiers stades de l’infusion de nitroprussiate sur les malades normocapniques. On a obtenu une augmentation sans importance de l’ICP sur les malades hypocapniques. L’ICP moyenne est passée de 6,3 mm Hg à 11,7 mm Hg lorsqu’on a légèrement réduit la tension artérielle, mais la réaction sur chacun des malades a varié très largement (plage —1,6 mm Hg à + 20,9 mm Hg).

Lorsque la tension artérielle (BP) était tombée à 70% de la valeur existant avant l’infusion de nitroprussiate, l’ICP moyenne est retournée aux valeurs témoins et a, par la suite, baissé lorsqu’on a effectué d’autres réductions dans la BP. Chez les malades rendus hypotensifs à l’aide de triméthaphan, il n’y a eu aucun changement dans l’ICP moyenne, mais deux malades ont accusé des augmentations modérées (+9,3 mm Hg et +5,7 mm Hg). On pense que le mécanisme de l’augmentation de l’ICP à l’aide de nitroprussiate est dû à une expansion du volume sanguin intracranien résultant d’une vasodilatation cérébrale. Le triméthaphan ne produit pas habituellement de variations dans l’ICP sauf lorsque la compression intracrânienne est grave, car dans ces circonstances, toute petite variation du volume sanguin intracranien découtant de l’autorégulation peut déclencher une augmentation de l’ICP.

CAMBIOS EN LA PRESION INTRACRANIANAL EN PACIENTES NEURO QUIRURGICAS DURANTE HIPOTENSION INDUCIDA CON NITROPRUSSIATO SODICO O TRIMETAFAN

SUMARIO

Se ha medido la presión intracraneal en 45 pacientes sometidos a neurocirugía durante la inducción de hipoten- sión deliberada empleando o bien nitroprussuro sódico o trimetafán. Se produjo un aumento estadísticamente significativo de la presión intracraneal (PIC) durante las primeras etapas de la infusión del nitroprussuro en pacientes
EFFECTS OF NITROPRUSSIDE AND TRIMETAPHAN ON ICP

normocápicnicos. Un aumento no significativo de PIC fue obtenido en pacientes hipocápicinos. La PIC media aumentó desde 6,3 mm Hg hasta 11,7 mm Hg cuando la presión arterial estaba reducida ligeramente, pero la respuesta en los pacientes individuales varió ampliamente (límites –1,6 mm Hg hasta +20,9 mm Hg). Cuando la presión arterial (PA) había descendido al 70% del valor existente antes de la infusión de nitroprusuro, la PIC media retornó al valor testigo y luego descendió con nuevas reducciones de la PA. En pacientes con hipotensión deliberada mediante trimetofán, no hubo cambio en la PIC media pero dos pacientes mostraron aumentos moderados (+9,3 mm Hg y +5,7 mm Hg). Se cree que el mecanismo del aumento de PIC con nitroprusuro se debe a la expansión del volumen hemático intracraneal como resultado de vasodilatación cerebral. Trimetofán no suele producir cambios en PIC excepto cuando la compresión intracraneal es severa, ya que en estas circunstancias un pequeño cambio en la volemia intracraneal consecutivo a la autorregulación pudiera provocar un aumento de la PIC.