THIOPENTONE SUPPLEMENTED ANAESTHESIA FOR NEUROSURGERY

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SUMMARY

A technique of anaesthesia for intracranial surgery involving the use of a thiopentone drip as a supplement to nitrous oxide and oxygen was used in 166 patients who were curarized and artificially ventilated. Maintenance of immobility and unconsciousness during the operation was satisfactory. The degree of recovery at the end of operation was acceptable in that nearly 90 per cent were awake and talking, or responding to speech at the conclusion of the procedure. There was an undefined period of amnesia after the patient had apparently regained full consciousness. A few patients were restless in the postoperative period. There were no difficulties with the airway. The intracranial tension during operation was acceptably low.

It has been known since the 1930s that barbiturates reduce cerebral metabolic rate (Quastel and Wheatley, 1932) and it has more recently been shown that they reduce cerebral blood flow (Landau et al., 1955). Barbiturates on their own produce anaesthesia which is too prolonged to make it acceptable for neurosurgical work. They can, however, be utilized as supplements to nitrous oxide. Such supplements are needed because there is a possibility that the inadequately anaesthetized patient under nitrous oxide and oxygen alone may remember something of what has happened to him during operation. Even when memory is abolished the patient may still be responsive to sensory stimulation at times when anaesthesia is insufficient. This will be troublesome mainly during the extracranial part of the operation especially as it is this part of the procedure during which painful stimuli are likely to arise. This can also cause difficulty later during the intracranial part of the operation because diseased brain contains large areas in which autoregulation is already so disturbed by the disease process that the local cerebral blood flow becomes blood pressure dependent. Blood flow will therefore increase should surgical stimulation cause a rise in blood pressure and local wound bleeding will be troublesome.

Barbiturates therefore seem to offer the prospect of adequate supplementation of nitrous oxide and oxygen anaesthesia with, at the same time, a reduction in cerebral blood flow and therefore of brain bulk. A trial of a thiopentone drip was therefore initiated.

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Anaesthesia was induced with a sleep dose of thiopentone, that is to say the amount which abolished the eyelash reflex. Intubation was achieved with the aid of suxamethonium or, if the patient had bled recently from an intracranial aneurysm or angioma, alcuronium or tubocurarine. The dose of suxamethonium for intubation was 5 mg/6.35 kg (= 1 stone) body weight; that of alcuronium 2 mg/6.35 kg, and that of tubocurarine 4 mg/6.35 kg. The patient’s lungs were inflated with oxygen before intubation and the inside of the trachea sprayed with 4% lignocaine solution. Those who had already received a non-depolarizing relaxant were thereafter ventilated artificially for the remainder of the operation. Those who had been intubated with the aid of suxamethonium were subsequently paralysed, usually immediately after the skin incision had been made. The amount of relaxant given was that which was sufficient to produce manifest respiratory depression. It usually amounted to 1 mg/6.35 kg body weight of alcuronium or 2 mg/6.35 kg of tubocurarine. Thereafter tubocurarine 10 mg per hour, or alcuronium 5 mg every 45 minutes, was given to maintain relaxation. No attempt was made to preserve spontaneous respiration in patients undergoing operations in the posterior fossa. The extent of the artificial ventilation was such as to produce a minute volume of 1 litre/6.35 kg body weight, the rate being set to 10 per min.

**Thiopentone drip.**

As soon as anaesthesia had been induced, and before the patient was put into position for the operation, the thiopentone drip was begun. This was prepared by putting 500, 1000 or, in very resistant cases, 1500 mg of thiopentone into a 500 ml drip bottle containing 5% dextrose in 0.18% saline. The initial dosage of thiopentone was determined by the patient’s resistance to the induction dose of the drug. If the patient required 25–30 mg/6.35 kg for induction and his total weight was above 55 kg, thiopentone 1000 mg was put in the drip bottle. If the patient was very small, very frail or more sensitive to thiopentone, only 500 mg was put in the drip bottle. If the induction dose of thiopentone substantially exceeded 300 mg, or the patient’s weight was over 70 kg then 1500 mg of thiopentone was put in the drip bottle. The drip rate was set initially at 80 drops/min. At the time at which the skin flap was marked out (with a knife), the drip rate was so adjusted that the rate of administration of thiopentone would control the minor movements of face or fingers which were produced by skin stimula-

**Assessment of intracranial tension.**

The intracranial tension was assessed as follows. The intracranial pressure was described as “excellent” when the exposed dura, before any cerebrospinal fluid had escaped, was visibly concave in any part of its surface at some phase of the respiratory cycle; “good” when the brain was very readily depressed by the palpat ing finger of the surgeon; “fair” when the dura could be opened only with difficulty but without recourse to adjuvants to reduce intracranial pressure; and “poor” when recourse had to be made to ventricular tap or to the administration of mannitol 20% in a dose of 1 g/kg in order to make safe dural opening possible.

<table>
<thead>
<tr>
<th>Assessment of intracranial pressure after turning the bone flap (before giving mannitol or tapping the ventricle).</th>
<th>Excellent</th>
<th>Good</th>
<th>Fair</th>
<th>Poor</th>
<th>Not seen because of nature of operation</th>
<th>Not recorded</th>
<th>Total</th>
</tr>
</thead>
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<tr>
<td>Excellent</td>
<td>31 cases</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Good</td>
<td>78</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fair</td>
<td>12</td>
<td></td>
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<td></td>
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<tr>
<td>Poor</td>
<td>21</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Not seen because of nature of operation</td>
<td>13</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not recorded</td>
<td>11</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>166</td>
<td></td>
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</tbody>
</table>

The state of the patients on return to bed immediately after operation was assessed as follows: (1) awake and talking; (2) responding to simple verbal commands such as “Open your eyes” or “Squeeze my hand” but not speaking spontaneously or answering questions in words, i.e. responding to speech; (3) responding to painful stimuli but not responding to verbal commands (these patients usually required an oropharyngeal airway in order to ensure the patency of the upper respiratory passages after extubation).

**RESULTS**

**Dosage of thiopentone.**

The mean induction dose of thiopentone was 280 mg (range 150–500). During maintenance a mean total dose of 953 mg was required. This represented a total dosage varying from 100 to 2500 mg. During
the period of thiopentone drip administration the average rate was 300 mg/hour. The range of dosage per hour, however, varied from 28 to 800 mg. There was little relationship between duration of operation and total dosage.

The intracranial pressure at the time of exposure of the brain was shown in table II. It will be noted that this was “excellent” in 31 and “good” in 78 of the 166 cases. In only 21 was intracranial pressure “poor” to the extent of requiring a ventricular tap or the administration of mannitol.

There were no blood pressure changes which could be specifically related to the administration of thiopentone. The mean minimum blood pressure in the cases was substantially identical with that in a group of cases in whom analgesic drugs together with small doses of droperidol had been used to produce anaesthesia. The minimum blood pressure recording usually coincided with the administration of the relaxant to permit the taking over of respiration.

Respiratory depression was not noted except for short periods when an inadvertent overdose had been given. The PaO₂ was measured in 29 spontaneously breathing patients in whom the thiopentone drip was in progress. The mean figure was found to be 44.2 mm Hg (range 38–55). There was no depression of respiratory rate (to less than 16/min) in the post-operative period.

Blood thiopentone levels were measured in 7 patients. Values ranging from 0.5 to 0.76 mg/100 ml were obtained. These measurements were all carried out during the period of drip administration, at least 1 hour after the drip had been started and more often after 2 or more hours.

The dilute solution of thiopentone used in the drip did not appear to have any tendency to produce venous thrombosis. The same cannula was used for the postoperative fluid infusion and the interval until the drip stopped after the patient’s return to bed, as a result of local venous thrombosis, was usually of the order of 24 hours or more. In general, the cannulae were put into the internal saphenous vein at the ankle or into a vein on the dorsum of the foot.

Postoperative state.

Details of the postoperative state of all the patients are not available. The state of a representative sample of 47 unselected cases was as follows. All but 6 of these patients were able to communicate with the anaesthetist as they were being removed from the operating table; of these, 25 were actually awake and talking. Four of 41 patients for whom information was available were restless in the immediate postoperative period. Bedside were, however, sufficient to restrain them and there was no need to give sedative drugs.

One patient developed an intracranial clot in the immediate postoperative period. He had, however, recovered sufficiently from the hypnotic action of the thiopentone for the appearance of the complication to be recognized. He was returned to the operating theatre and the clot was removed without difficulty. No other patient of the 166 was drowsy for a long period after the use of a thiopentone drip.

An interval of some hours elapsed between the recovery of the power of coherent speech and recovery of memory. The exact duration of this interval could not be defined because only a few patients could state what was the time of the first remembered postoperative event. All that could be established was that the visits by the anaesthetist were not remembered by patients who at the time had apparently conversed quite coherently.

DISCUSSION

The essential factors which determine the intracranial pressure and the bulk of the brain at operation have by now been more or less completely defined. The first factor is the amount of fluid within the ventricles and the substance of the brain. In a normal brain this should not present any serious obstacle to the safe opening of the dura mater and procedures aimed at reducing this, such as lumbar puncture, ventricular tap or the administration of dehydrating agents, should not be required. The cerebrospinal fluid is, however, perhaps the most readily alterable part of the intracranial mechanics and much has been written already about the various methods of affecting the brain bulk at operation by removal of cerebrospinal fluid. It should be stressed, however, that extreme drainage of all the intracranial fluid, however effective in lowering the intracranial pressure it may be, inevitably leaves the patient with a very severe headache for some days after operation. It is also true that the use of dehydrating agents, and indeed of tapping the contralateral ventricle, inevitably involve an increase in the shift produced by a large intracranial mass and that this is by no means always to the patient’s advantage, for it adds to the shift produced by a space-occupying lesion and shift is in some ways as lethal as generalized rise in intracranial pressure. Techniques of anaesthesia for intracranial surgery which depend on the modification of this factor are therefore by no means ideal.
The second factor which is of importance in relation to intracranial pressure is the amount of blood in the cerebral veins. This is to a large extent under the control of the anaesthetist and the author has pointed out the importance of curarization in reducing the intracranial venous pressure by means of reducing the abdominal straining which is almost invariably present in the spontaneously breathing patient under light anaesthesia with an endotracheal tube in situ (Hunter, 1960). The brain bulk can also be modified by altering the cerebral blood flow and in this way the anaesthetist can do much to facilitate anaesthesia for intracranial surgery and it is probably because of their effect on this that barbiturates are so satisfactory.

Barbiturates, however, are not the only drugs which will reduce cerebral blood flow. It has also been shown that the administration of droperidol and fentanyl will also substantially reduce cerebral blood flow (Miller and Barker, 1969). It is not entirely clear whether this effect is mediated through a reduction in cerebral metabolic rate as Kreuscher (1965) suggests, or whether the droperidol/fentanyl simply acts as a cerebral vasoconstrictor in its own right. It is interesting that the very early work on the effects of fentanyl on the cerebral circulation suggested that in fact it produced cerebral vasodilatation by excitation of the reticular activating system (Nilsson and Ingvar, 1965). But this was a cat response and the cat responds to opiate drugs in a very different way from man and other species.

There is, however, a more serious problem in relation to the use of droperidol and fentanyl. The author has occasionally seen patients with persistent bradypnoea lasting several hours at the end of operations when appreciable quantities of fentanyl have been given, usually for procedures on the spine. These were patients whose respiratory apparatus was, as far as could be determined, normal. Patients with posterior fossa tumours which are invading or pressing on the respiratory centre, and some with tumours even higher in the brain stem, are extremely sensitive to the depressant effects of opiate drugs. The author therefore fears that the use of droperidol and fentanyl in such cases might lead, in occasional instances at least, to persistent respiratory depression in the postoperative period. Further, there is at least an element of doubt as to whether this depression is reversible by nalorphine. The author has certainly seen a case in which phenoperidine was used to supplement nitrous oxide and oxygen anaesthesia for intracranial surgery and where the patient had profound respiratory depression after operation in spite of the administration of nalorphine.

The question arises whether the rate of awakening after operation which was noted in the patients of this series is acceptable in those who have undergone neurosurgical procedures involving intracranial manipulation. It does seem, however, that a technique which results in all the patients being at least responsive to the spoken word within 1 hour of discontinuing the anaesthetic is acceptable. It is extremely rare for serious intracranial bleeding to occur within 1 hour of the end of the surgical procedure. Even should it occur it is still possible to recognize the deepening coma, even if the patient is only responding to pain as he comes off the operating table. Major intracranial bleeding should not, therefore, pass unnoticed because this particular technique of anaesthesia has been used.

One of the interesting features of the use of thiopentone as a supplement to nitrous oxide and oxygen was a prolonged period of loss, subsequent to anaesthesia, of memory of current events. This period extended usually for several hours after the patients were apparently awake and talking. It was, however, extremely difficult for the patients to recall the moment at which they thought their memory had returned and it was impossible to quantify this particular phenomenon. From the point of view of the patient who has had an intracranial operation, however, the absence of memory of the discomfort of the first few postoperative hours can only be a welcome result of the anaesthesia, particularly where this can be achieved without any danger of overlooking the deepening unconsciousness produced by accidental intracranial bleeding, and without the risk of respiratory obstruction inherent in prolonged narcosis.

Restlessness was noted in a number of patients and is indeed a possible disadvantage. This restlessness, however, disappeared spontaneously and required no more than a certain amount of restraint to the patient involving the application of bedsides and securing the patient’s wrists in order to avoid damage to the wound. Restlessness occurred only during the amnesic period and the necessary confining of activities was not remembered by the patient.

This restlessness could be a manifestation of the antianalgic effects of thiopentone but it will be remembered that these are not regarded particularly seriously any longer for they apply only to pain arising from deep pressure (Robson, Davenport and Sugiyama, 1965) and not to skin pain, and the bulk
of the discomfort of neurosurgical operation is skin pain. Antanalgesia would not be expected to cause difficulty during the operation itself, for it has been clearly shown that increasing depth of thiopentone anaesthesia obounds the response to surgical stimuli.

Finally, the question arises of the effect of the dose of thiopentone used on the cerebral blood flow. It has been established that it requires more than hypnotic doses of a barbiturate in order to produce substantial reduction of cerebral blood flow (Sokoloff, 1959). From a purely empirical point of view the doses were almost certainly adequate, for they fall within the range defined by Wollman, Alexander and Cohen (1967) as being effective in reducing cerebral blood flow, i.e. they amounted to approximately 1 g of thiopentone given over 4 hours. It would also seem that dosage would qualify as narcotic, for an appreciable proportion of the patients were still profoundly under the influence of the drug 1 hour after its administration had ceased.

REFERENCES

ANESTHESIE COMPORTANT L'ADITIONCTION DE THIOPENTONE, EN NEURO-CHIRURGIE

Chez 166 malades ayant fait l'objet d'une curarisation et d'une respiration assistée, on a eu recours à une technique d'anesthésie pour interventions de neuro-chirurgie intracérébralement, comportant l'administration de thiopentone en perfusions lentes, en plus de protoxyde d'azote et d'oxygène. Les malades ont ainsi été maintenus dans un état d'immobilité et d'inconscience satisfaisant au cours de l'opération. Le degré de récupération des malades à la fin de l'intervention a été acceptable, étant donné que près de 90% de ceux-ci étaient alors réveillés, causant ou participaient à la conversation. On a noté l'existence d'une période indéfinie d'amnésie, une fois que les malades eurent repris apparemment pleine conscience. Quelques malades ont présenté une agitation au cours de la période post-opératoire. Aucune complication en relation avec les voies respiratoires n'a été enregistrée. La pression intracrânienne mesurée pendant l'opération s'est maintenue à un taux bas, acceptable.

MIT THIOPENTAN ERGÄNZTE NARKOSE FÜR DIE NEUROCHIRURGIE

ZUSAMMENFASSUNG

ANESTESIA SUPLEMENTADA CON TIOPIENTONA EN NEUROCIRUGÍA

RESUMEN
Una técnica de anestesia para cirugía intracraneal utilizando un gota a gota de thiopentona como suplemento para el óxido nitroso y oxígeno fue aplicada en 166 pacientes que fueron curarizados y ventilados artificialmente. Fueron satisfactorios el mantenimiento de la inmovilización e inconsciencia durante la operación. El grado de restablecimiento al final de la operación fue aceptable ya que casi el 90 por ciento de los pacientes estaban despiertos y hablando, o contestando a preguntas, al concluir este procedimiento. Hubo un periodo indefinido de amnesia después de que el paciente había aparentemente recuperado su conciencia completa. Algunos pacientes estaban intranquillos durante el periodo posoperatorio. No hubo dificultades en las vías aéreas. La presión intracraneal durante la operación era suficientemente baja.