The treatment of raised intracranial pressure following aneurysm surgery*

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SUMMARY The effect of intravenous mannitol infusion and withdrawal of cerebrospinal fluid on the intracranial pressure and clinical state was studied in 26 patients with raised intracranial pressure after direct surgery for ruptured aneurysm. Each method decreased the mean intracranial pressure by about 60% of the pre-treatment level. The maximal decrease following mannitol occurred after 60–90 minutes and generally lasted between three and four hours. The effects of mannitol did not decrease when repeated infusions were necessary. Rebound increases in the intracranial pressure following infusion were not observed. Withdrawal of cerebrospinal fluid lowered the intracranial pressure immediately and the effect persisted for approximately 60 minutes. This could be repeated as often as necessary and was without systemic disturbance, although a patent intraventricular catheter was necessary. The two methods could be used simultaneously.

Raised intracranial pressure (ICP) following aneurysm surgery is associated with neurological deterioration and affects the outcome when assessed three months after operation.1 Control of the ICP therefore, is an important part of the postoperative management. We report a study of two methods used to treat 26 patients with raised ICP and neurological deterioration following a direct operation for ruptured intracranial aneurysm. A comparison was made between the effects of mannitol infusion and cerebrospinal fluid (CSF) withdrawal on the ICP. The effects of repeated infusions of mannitol also were studied.

Patients and methods

The patients underwent craniotomy and clipping of the aneurysm using microneurosurgical techniques and controlled hypotension. They comprised part of a larger, previously reported group1 but who required treatment for postoperative raised ICP. The neurological level was assessed using a score scaled from 20 to 0, indicating a progressively deteriorating level of response.2

Continuous ICP monitoring was performed using an intraventricular catheter which was inserted at operation. This was connected by a saline-filled column to an externally mounted Hewlett-Packard 1280C strain-gauge transducer. A permanent paper record was obtained with a Devices M4 heated stylus recorder (Devices Instruments Ltd, Welwyn Garden City, Herts, UK). The postoperative ICP patterns were divided into three groups based on the level of the mean intracranial pressure (MICP). In group 1, the MICP was less than 15 mmHg for most of the postoperative course, in group 2 between 15 mmHg and 25 mmHg, while in group 3, the MICP exceeded 25 mmHg.

The MICP was calculated as the diastolic pressure plus one-third of the pulse pressure3 and the following observations were extracted from the paper record: (1) The pre-treatment level of ICP. (2) The ICP at five minute intervals for the 60 minutes following treatment and again at 90 minutes. (3) The lowest ICP reached and the time taken to reach that level. (4) The time for the MICP to reach 25 mmHg following treatment. (5) The percentage change from the pre-treatment level of ICP. (6) The neurological score.

Treatment was commenced when the ICP exceeded 25 mmHg regardless of whether a worsening in the neurological level was associated with the increase in the ICP, or whether deterioration had occurred previously. We also treated the patient if deterioration occurred and the ICP was rising toward 25 mmHg.

Mannitol infusion Mannitol 20% was infused intravenously over 30 minutes in a dose of 1.5 g/kg. This dose was approximately 500 ml of 20% mannitol in a 70 kg adult. Serum electrolytes and serum osmolality were monitored when repeated infusions were given.

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A maximum of three infusions were given in any 24 hour period

CSF withdrawal Ten ml of ventricular CSF was withdrawn on each occasion. A trial 0·5 ml was first withdrawn to ensure that the system was patent. A further 9·5 ml was then removed over 60 seconds. Strict asepsis was observed and CSF was sent daily for culture.

Effects of treatment The effects of treatment were assessed as either an improvement, no change or worsening in the neurological level after treatment. Patients were subdivided into those who deteriorated clinically with raised ICP ("deteriorated+RICP"), or those in whom the ICP had risen and required treatment in a patient who had deteriorated previously (RICP only).

Results

The effects of mannitol infusion and CSF withdrawal on the ICP was studied in 26 patients. Six patients had both forms of treatment during the post-operative period. Eight patients had a group 2 pattern and 18 had a group 3 ICP pattern post-operatively. Although a variety of factors were associated with the raised ICP (table 1), it was generally possible to implicate only one factor as responsible in each patient. These factors have been analysed previously.1

Table 1 Factors associated with raised ICP in 26 patients who required treatment

<table>
<thead>
<tr>
<th>Factor</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early onset cerebral arterial spasm</td>
<td>14</td>
</tr>
<tr>
<td>Raised ICP without arterial spasm</td>
<td>7</td>
</tr>
<tr>
<td>Hydrocephalus</td>
<td>4</td>
</tr>
<tr>
<td>Operative misadventure</td>
<td>1</td>
</tr>
</tbody>
</table>

Cerebral arterial spasm occurring within hours of surgery and which was followed shortly after by profound neurological deterioration was most commonly associated with raised ICP. Seven patients in whom the ventricles remained small, developed raised ICP without evidence of cerebral arterial spasm. All four patients with hydrocephalus were treated with CSF withdrawal only. One patient in whom premature intra-operative aneurysm rupture occurred developed raised ICP which required treatment.

Mannitol infusion The effect on the ICP of the infusion of 1·5 g/kg of 20% mannitol was studied on 57 occasions in 21 patients. The average level of MICP at which treatment commenced was 33·4±5·6 mmHg (mean±ISD). The mean maximum decrease in the ICP from the pre-treatment level (ΔPmax) was 23·6±6·3 mmHg (mean±ISD), which was reached in 73·3±37·6 minutes (mean±1SD). The mean time taken to reach an MICP of 25 mmHg following infusion was 189·2±116·9 minutes (mean±ISD). These values are compared with those for CSF withdrawal in table 2. Infusion of mannitol resulted in a smooth decrease in the ICP (fig 1) with an onset of action some five to 10 minutes after infusion and maximal after approximately one hour.

Table 2 Comparison between the effects of infusion of mannitol and withdrawal of 10 ml of CSF (value±SD)

<table>
<thead>
<tr>
<th>Mannitol infusion</th>
<th>CSF withdrawal</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICP level at commencement of treatment (mmHg)</td>
<td>33·4±6·64</td>
</tr>
<tr>
<td>Maximum change in ICP (ΔPmax) (mmHg)</td>
<td>23·6±6·27</td>
</tr>
<tr>
<td>Mean time taken to reach P max (mins)</td>
<td>73·3±37·56</td>
</tr>
<tr>
<td>Mean time for ICP to reach 25 mmHg after treatment (mins)</td>
<td>189·2±116·90</td>
</tr>
</tbody>
</table>

Fig 1 Infusion of mannitol.

Effect of repeated mannitol infusions Twenty-one infusions were first treatments, 14 were second treatments, 11 were third and 6 were fourth. The effect of repeated infusions on the ΔPmax, the time taken to reach the ΔPmax and the time to reach an MICP of 25 mmHg after the treatment were studied (table 3). There was no difference between any ΔPmax when compared with the first infusion (first and fourth infusions, t=0·237, DF=25, p—not significant, NS). There was little variation in the time taken to reach the ΔPmax and these differences likewise were insignificant (first and fourth infusions, t=0·960, DF=25, p=NS). Similarly, there was no difference in the length of the effect of mannitol when the infusions were repeated as measured by the time taken for the ICP to reach 25 mmHg after the treatment (first and third infusions, t=1·250, DF=30, p=NS).
Table 3  Effect of repeated infusions of 20% mannitol (mean±SD)

<table>
<thead>
<tr>
<th>Frequency</th>
<th>Mean ΔP max (mmHg)</th>
<th>Mean time to reach ΔP max (min)</th>
<th>Mean time for MICP to reach 25 mmHg after treatment (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infusion 1</td>
<td>21</td>
<td>23.0 ± 6.17</td>
<td>76.43 ± 39.57</td>
</tr>
<tr>
<td>Infusion 2</td>
<td>14</td>
<td>23.79 ± 7.36</td>
<td>63.36 ± 23.98</td>
</tr>
<tr>
<td>Infusion 3</td>
<td>11</td>
<td>22.91 ± 6.60</td>
<td>75.90 ± 41.15</td>
</tr>
<tr>
<td>Infusion 4</td>
<td>6</td>
<td>22.67 ± 5.28</td>
<td>60.90 ± 23.88</td>
</tr>
</tbody>
</table>

Table 4  The effects of treatment of raised ICP by mannitol infusion or by CSF withdrawal on the neurological level. The results are classed as where deterioration was associated with an acute rise in the ICP (deteriorated+RICP) or where the patient had deteriorated previously and the ICP was treated when it exceeded 25 mmHg (RICP only)

<table>
<thead>
<tr>
<th>Mannitol infusion</th>
<th>CSF withdrawal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deteriorated + RICP</td>
<td>RICP only</td>
</tr>
<tr>
<td>Improved</td>
<td>28 (75.7%)</td>
</tr>
<tr>
<td>No change</td>
<td>9 (24.3%)</td>
</tr>
<tr>
<td>Worse</td>
<td>0</td>
</tr>
</tbody>
</table>

Withdrawal of CSF  The effects of withdrawal of 10 ml of CSF were studied on 21 occasions in 11 patients. The mean level at which treatment commenced was 34.0 ± 5.7 mmHg (mean ± 1SD). The ΔPmax was 22.5 ± 8.8 mmHg (mean ± 1SD) and was reached in 7.6 ± 5.2 minutes (mean ± 1SD). The mean time taken for the MICP to reach 25 mmHg after treatment was 82.4 ± 82.0 minutes (mean ± 1SD). These results are compared with those following mannitol infusion in table 2. The mean changes in the ICP after CSF withdrawal are shown in fig 2. Initially, there was a large change in the ICP with a steady increase to pre-treatment levels over the next 60 to 90 minutes, although the time taken varied considerably.

Correlation between treatment and neurological level  Neurological improvement occurred after 34 (59.7%) of the mannitol infusions and no change was observed after 23 (40.3%). After CSF withdrawal, improvement was noted after 10 (47.6%) and no change in 11 (52.4%). No patient deteriorated following any treatment. Mannitol infusion resulted in an improved neurological level, more often when clinical deterioration was associated with the raised ICP. Improvement following CSF withdrawal in a patient who had already deteriorated was unusual.

Discussion  Following the demonstration by Weed and McBibben that intravenous infusion of hypertonic saline lowered lumbar CSF pressure, the use of hypervosmolar agents to control intracranial pressure by reduction in brain mass has found wide application in neurosurgical practice. Lundberg advocated removal of ventricular CSF in the control of raised ICP and considered that this ready access to the CSF space was an advantage of the intraventricular route when monitoring the ICP. Other methods, for example ventilation, frusemide and dexamethasone have been used to control raised ICP after aneurysm surgery. We found that neurological deterioration invariably followed when the MICP exceeded 25 mmHg and generally commenced treatment at this level. Neurological deterioration, however, occurred in some patients although the ICP never rose above 25 mmHg and we have shown that most of these patients have cerebral arterial spasm. This emphasises the value of continuous ICP monitoring which allows a rational treatment of ICP changes. We considered treatment in these patients with arterial spasm when the ICP was rising towards 25 mmHg and a worsening of the neurological level had occurred. It was our impression that those patients who deteriorated with lower ICP levels did not respond as well to mannitol or CSF.
Drainage as those patients in whom ICP exceeded 25 mmHg. However, a reduction in the ICP should improve cerebral perfusion and there is some evidence that mannitol itself increased the cerebral blood flow.\textsuperscript{13}

The level at which we commenced treatment was lower than that advocated by Johnston and Jennett\textsuperscript{14} in their discussion of the treatment of diffuse brain lesions which had caused a sustained increase in ICP, but Becker and Vries\textsuperscript{15} treated the ICP when it exceeded 25 mmHg in their patients with raised ICP due to differing diffuse cerebral disorders. Both mannitol infusion and CSF withdrawal provided an effective method of treating raised ICP, although the time courses differed (fig 3). The maximum decrease in the ICP was approximately 60\% from the pre-treatment level with each method.

Mannitol infusion provided a smooth decrease in the ICP which commenced shortly after the infusion began. The maximum decrease in ICP occurred 60 to 90 minutes later and, while there was a wide variation in the period of control of the ICP, the effect generally lasted for three to four hours. The potential disadvantage of mannitol is that of fluid and electrolyte disturbance but where the number of infusions was limited to three in any 24 hour period, this was not a problem. We found no evidence of a paradoxical rise in the ICP following mannitol infusion which, it had been suggested,\textsuperscript{16} may be due to a passive increase in cerebral blood volume, although there are theoretical objections to this hypothesis.\textsuperscript{13}

In this study we used higher doses of mannitol (1·5 g/kg) than reported previously. Following infusion of mannitol in a dose of 0·5 g/kg, Miller and Leech\textsuperscript{17} noted a maximal decrease in the ICP of 34\% from pre-treatment levels, occurring 15 minutes after infusion and persisting for 34 minutes. Similarly, Johnston \textit{et al}\textsuperscript{18} noted small, short-lasting decreases in the ICP in 21 patients who had undergone direct aneurysm surgery. Similar decreases were reported by Kullberg and Sundberg\textsuperscript{19} after reviewing 234 mannitol infusions in 41 patients with various neurological disorders. They concluded that effective control of raised intracranial pressure with mannitol would usually require larger doses than those used in their series, (0·5 g/kg). We agree with this conclusion and suggest that a dose of 1·5 g/kg is safe and effective provided that prolonged treatment is not necessary and that strict monitoring of fluid balance, serum electrolytes and serum osmolality be observed.

When repeated infusions of mannitol were necessary, we found no reduction in the effect on the ICP and this reduction persisted for similar periods. This data conflicts with that of Johnston \textit{et al}\textsuperscript{15} who reported that when low dose mannitol was given after aneurysm surgery, the effect on the ICP decreased with time. Osmotically active agents like mannitol are most effective in the presence of intact cell membranes,\textsuperscript{20} that is in a relatively undamaged brain. The patients in this study and in that of Johnston \textit{et al}\textsuperscript{17} were in this category, so we conclude that the differences between the findings are related to the doses of mannitol infused.

The maximal decrease after CSF withdrawal was immediate and pre-treatment levels were generally reached after about an hour, despite considerable variation in timing. Although control of the ICP was considerably shorter than with mannitol, the technique could be repeated without causing electrolyte disturbance. However, a patent ventricular catheter was necessary to remove CSF from the system.

These techniques could be used simultaneously. Immediate reduction in the level of ICP followed CSF withdrawal, while the effect of mannitol was maximal after 60 to 90 minutes and lasted between three and four hours. Most patients improved their neurological level following either type of treatment. Improvement was more likely where deterioration was associated with an acute rise in the ICP. Like Johnston and Jennett,\textsuperscript{14} we noted that the rise in the ICP preceded the decrease in neurological level. Those patients who had deteriorated previously and who were treated as the ICP exceeded 25 mmHg without any further clinical deterioration were less likely to show additional...
clinical improvement with subsequent therapy. However, 30% in this group did show some improvement after mannitol, perhaps related to an improvement in the cerebral perfusion and blood flow.

We have found that raised ICP due to brain swelling with or without cerebral arterial spasm occurs early in the post-operative period and we commence continuous ICP monitoring immediately following reversal of the anaesthesia. The period of brain swelling seldom persists after 60 hours and early, aggressive treatment of the intracranial hypertension during this critical period is necessary to avoid damage and to improve the neurological level and eventual outcome.

References

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