Changes in CSF pressure after mannitol in patients with and without elevated CSF pressure

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In view of the current concern that rapid infusion of mannitol might initially aggravate intracranial hypertension, the effects of a mannitol infusion on lumbar cerebrospinal fluid pressure (CSFP) were investigated in 49 patients. The studies were performed when the patients were under general anesthesia prior to elective craniotomy for tumor resection or intracerebral aneurysm clipping. The patients were divided into two groups: 24 patients with normal CSFP (Group I, mean CSFP 10.5 mm Hg) and 25 with raised CSFP (Group II, mean CSFP 20.8 mm Hg). Measurements of CSFP, mean arterial blood pressure (MABP), and central venous pressure (CVP) were made serially during and after the infusion of 20% mannitol (1 gm/kg infused over a 10-minute interval). In both groups, mannitol infusion provoked a fall in MABP and an increase in CVP. An immediate increase in CSFP was observed in Group II, whereas CSFP increased transiently but significantly in Group I. Analysis of the arterial and venous driving pressures which contribute to CSFP suggests that the transient increase in CSFP after mannitol in Group I was partly due to the increase in CVP. The presence of intracranial hypertension may thus alter the CSFP response to arterial and venous pressure changes.

Cerebral blood volume (CBV) was measured in dogs in a separate study analogous to the human protocol. The CBV increased approximately 25% over control values after mannitol infusion both in the normal animals and in those with CSFP raised by an epidural balloon. The response of the CSFP to mannitol infusion differed between both groups in a fashion similar to that observed in the human subjects. Thus, differences in CBV changes after mannitol do not account for the difference in CSFP response between normal subjects and those with raised CSFP.

KEY WORDS: cerebrospinal fluid pressure, cerebral perfusion pressure, mannitol, intraoperative monitoring

Mannitol is an osmotic diuretic widely used during neurosurgery and neuroanaesthesia to decrease brain bulk and intracranial pressure (ICP). It increases brain compliance, thereby reducing the degree of tissue retraction required during surgery. Paradoxically, ICP increases transiently after mannitol infusion in brain-tumor patients with normal ICP. Since infusion of mannitol increases cerebral blood flow (CBF) and cerebral blood volume (CBV), it has been suggested that these vascular effects are responsible for the rise in ICP immediately following rapid mannitol administration.

It remains to be determined whether these effects of mannitol are observed under conditions of increased ICP. A recent study demonstrated that, while mannitol administration raised ICP in normal dogs, no increase occurred in dogs with intracranial hypertension. The present study was undertaken to determine whether patients with elevated ICP respond to a mannitol infusion in the same fashion as patients with similar intracranial pathology but normal ICP. The results were confirmed in a separate CBV study in dogs with intracranial hypertension.

Clinical Material and Methods

The protocol was approved by the Ethics Committee of the Centre Hospitalier Universitaire Vaudois, and informed consent was obtained from each patient. Our current neurosurgical practice is to facilitate surgical exposure with intravenous mannitol administration and lumbar drainage of cerebrospinal fluid (CSF) in
patients undergoing supratentorial tumor resection or cerebral aneurysm clipping. Excluded from the present study were patients with a history of cardiac or renal failure, those with internal ventricular drains in place, and those whose intracranial pathology could obstruct the CSF pathway between the lateral ventricles and the lumbar cistern. None of the patients had an external ventricular drain. Based on these selection criteria, 49 consecutive adult patients about to undergo elective intracranial surgery for tumor resection (36 patients) or aneurysm clipping (13 patients in Hunt and Hess Grade I or II) were studied.

General Procedure and Mannitol Infusion Protocol

The patients were premedicated with midazolam (0.1 mg · kg⁻¹) given intramuscularly 1 hour before induction of anesthesia. Anesthesia was induced with midazolam, 0.1 to 0.4 mg · kg⁻¹, and fentanyl citrate, 1 to 8 µg · kg⁻¹, and was maintained with midazolam, 0.1 to 0.3 mg · kg⁻¹ · hr⁻¹, nitrous oxide 66% in oxygen, and fentanyl supplements as required. Muscle relaxation was provided with pancuronium, 0.08 mg · kg⁻¹, at induction and additional doses as required. Controlled ventilation was adjusted to provide slight hypocapnia (mean ± standard error of the mean (SEM): PaCO₂ 36 ± 0.3 mm Hg). Patients were maintained at normal temperature. Tactile and auditory stimulations were minimized during the study. Fluid requirements were provided by an infusion of normal saline (2 ml · kg⁻¹ · hr⁻¹).

The principal measurements made during this study were lumbar CSF pressure (CSFP), central venous pressure (CVP), mean arterial blood pressure (MABP), heart rate, and urinary output. A No. 20 malleable spinal needle placed into the lumbar subarachnoid space permitted measurement of CSFP, while No. 20 and 16 catheters inserted into the femoral artery and superior vena cava (internal jugular route) provided measurements of the MABP and CVP, respectively. Arterial, venous, and CSF pressures were measured with the patient in the supine position using g calibrated strain-gauge transducers* referenced to the external auditory meatus. Mean pressures were determined by electronic integration of the respective transducer signals using a two-channel Hewlett-Packard system† from which the heart rate could be measured and cerebral perfusion pressure (CPP) calculated (CPP = MABP - ICP). A bladder catheter was inserted and urine output measured. Arterial blood gas tensions were measured with a Radiometer device‡.

During the period of stable anesthesia prior to surgery, cardiovascular variables, urinary output, and CSFP were recorded serially before, during, and after the rapid infusion of 20% mannitol (1 gm · kg⁻¹ infused through the central venous line over a 10-minute period). Specific times for data recording were: immediately before the start of the mannitol infusion (control value), and 2, 5, 10, 15, 20, 30, and 45 minutes thereafter. The CSFP was considered to be elevated at values exceeding 15 mm Hg. On the basis of lumbar CSFP determined prior to mannitol administration, the 49 patients were assigned to either Group I with CSFP 15 mm Hg or less (24 cases) or Group II with CSFP greater than 15 mm Hg (25 cases).

Data Analysis

Within each group of patients, values of the cardiovascular variables, urinary output, and CSFP were averaged at each of the data recording times. The mean values for cardiovascular variables and CSFP during and following mannitol administration were compared with control values using repeated-measures analysis of variance. When the analysis of variance was significant (p < 0.05), individual values were compared to control levels using a paired t-test with the Bonferroni correction for multiple comparisons. At each of the data-recording times, mean values of the above parameters for Groups I and II were compared using an unpaired t-test.

To evaluate the putative association between the change in CSFP during the first 5 minutes of mannitol administration and control CSFP, a linear regression line was constructed from the individual values in all patients and the Pearson's correlation coefficient was calculated using the least-squares method. All values are expressed as means ± SEM (p < 0.05 was used to designate statistical significance).

Results in Clinical Series

The two patient groups were similar with respect to weight, sex, medications administered, and concomitant medical conditions (Table 1). Group II patients were on the average 10 years older than those in Group I. Values of the measured cardiovascular variables prior to mannitol infusion were similar in the two groups. Mean values of CSFP differed by 10 mm Hg (10.5 ± 0.53 mm Hg in Group I versus 20.8 ± 1.1 mm Hg in Group II, p < 0.001). The study was completed in all patients and no complications from lumbar needle insertion or mannitol infusion were encountered. After 45 minutes, the mean urinary output was 230 ml in Group I and 270 ml in Group II. In both groups, PaCO₂ did not vary by more than 3 mm Hg during the study; PaO₂ was always higher than 90 mm Hg and pH was stable at 7.38 ± 0.02. Heart rate did not change during or after mannitol infusion in either patient group. All CSFP and hemodynamic data are summarized in Table 2.

Effect of Mannitol Infusion on CSFP

During the mannitol infusion CSFP increased from 10.5 ± 0.53 mm Hg to 13.5 ± 0.78 mm Hg (p < 0.001).

* Strain-gauge transducer, Model 800, manufactured by Bentley Laboratory, Inc., Irvine, California.
† Hewlett-Packard system, Model 78342A, manufactured by Hewlett-Packard, Inc., Palo Alto, California.
‡ Gas analyzer, Model ABL3, manufactured by Radiometer, Copenhagen, Denmark.
Effect of mannitol on CSF pressure

### TABLE 1
Demographic data, anesthetic medication, and intracranial pathology in 49 patients*

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group I</th>
<th>Group II</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>no. of cases</td>
<td>24</td>
<td>25</td>
<td>NS</td>
</tr>
<tr>
<td>demographic data</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>age (yrs)</td>
<td>47.4 ± 2.4</td>
<td>57.3 ± 2.7</td>
<td>p &lt; 0.05</td>
</tr>
<tr>
<td>sex (M/F)</td>
<td>14/10</td>
<td>13/12</td>
<td>NS</td>
</tr>
<tr>
<td>body weight (kg)</td>
<td>65.7 ± 2.6</td>
<td>66.7 ± 2.3</td>
<td>NS</td>
</tr>
<tr>
<td>induction of anesthesia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>midazolam (mg·kg⁻¹)</td>
<td>0.31 ± 0.06</td>
<td>0.29 ± 0.07</td>
<td>NS</td>
</tr>
<tr>
<td>fentanyl (µg·kg⁻¹·hr⁻¹)</td>
<td>3.9 ± 2.5</td>
<td>4.0 ± 3.6</td>
<td>NS</td>
</tr>
<tr>
<td>maintenance of anesthesia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>midazolam (mg·kg⁻¹·hr⁻¹)</td>
<td>0.2 ± 0.08</td>
<td>0.21 ± 0.07</td>
<td>NS</td>
</tr>
<tr>
<td>fentanyl (µg·kg⁻¹·hr⁻¹)</td>
<td>1.9 ± 0.9</td>
<td>2.0 ± 0.9</td>
<td>NS</td>
</tr>
<tr>
<td>intracranial pathology</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>brain tumors</td>
<td>19 (79%)</td>
<td>17 (68%)</td>
<td>NS</td>
</tr>
<tr>
<td>ruptured aneurysms</td>
<td>5 (21%)</td>
<td>8 (32%)</td>
<td>NS</td>
</tr>
</tbody>
</table>

* Group I patients had cerebrospinal fluid pressures (CSFP) of 15 mm Hg or less; Group II patients had CSFP greater than 15 mm Hg. Means are given ± standard error of the mean. NS = not significant.

FIG. 1. Cerebrospinal fluid pressure (CSFP) values at baseline (0 min) and at various times following the start of mannitol infusion (1 gm · kg⁻¹) in Groups I and II. Values are means ± standard error of the means.

in patients with normal CSFP (Group I). This increase in CSFP was observed at 2 minutes after the start of the infusion, peaked at 5 minutes, and persisted until the end of the infusion (Fig. 1). It was followed by the expected decrease to values below control levels at 20 minutes. No such increase in CSFP was noted during mannitol administration in the patients with raised CSFP; instead, a rapid and immediate decrease was recorded. Mean CSFP values between Groups I and II were significantly different at baseline and at 2 (p < 0.001) and 5 (p < 0.05) minutes after the start of mannitol infusion; however, statistical significance was lost by 10 minutes of infusion. In all patients the decline in CSFP preceded the onset of diuresis.

### Effect of Mannitol Infusion on MABP

Mean arterial blood pressure fell 7% (p < 0.001) during the mannitol infusion in both groups of patients (Fig. 2). This decrease was maximal 2 minutes after the start of the infusion but had returned to control levels by the end of the 10-minute infusion.

### TABLE 2
Summary of data from the human study*

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Patient Group</th>
<th>Baseline</th>
<th>Measurements at Various Times After Start of Mannitol Infusion</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>2 Min</td>
</tr>
<tr>
<td>CSFP (mm Hg)</td>
<td>I</td>
<td>10.5 ± 0.53†</td>
<td>12.8 ± 0.67‡</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>20.8 ± 1.1†</td>
<td>18.6 ± 0.89‡</td>
</tr>
<tr>
<td>CSFP, (mm Hg)</td>
<td>I</td>
<td>10.5 ± 0.53†</td>
<td>10.9 ± 0.6†</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>20.8 ± 1.1†</td>
<td>18.4 ± 1.0‡</td>
</tr>
<tr>
<td>MABP (mm Hg)</td>
<td>I</td>
<td>89.0 ± 2.8</td>
<td>83.0 ± 2.6‡</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>90.0 ± 2.7</td>
<td>84.0 ± 2.6‡</td>
</tr>
<tr>
<td>CVP (mm Hg)</td>
<td>I</td>
<td>3.9 ± 0.53†</td>
<td>6.6 ± 0.52‡</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>5.1 ± 0.78</td>
<td>6.9 ± 0.76‡</td>
</tr>
<tr>
<td>CPP (mm Hg)</td>
<td>I</td>
<td>78.0 ± 2.8</td>
<td>70.0 ± 2.6‡</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>70.0 ± 2.7</td>
<td>65.0 ± 2.7‡</td>
</tr>
<tr>
<td>HR (min)</td>
<td>I</td>
<td>66.0 ± 2.5</td>
<td>67.0 ± 2.7</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>71.0 ± 3.2</td>
<td>74.0 ± 2.9</td>
</tr>
<tr>
<td>n§</td>
<td>I</td>
<td>0.081 ± 0.009†</td>
<td>0.083 ± 0.009†</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>0.185 ± 0.015†</td>
<td>0.155 ± 0.014‡</td>
</tr>
</tbody>
</table>

* Values are means ± standard error of the means for the 49 patients. Groups I and II are described in Table 1. CSFP = CSF pressure; CSFPc = corrected CSF (see Discussion); MABP = mean arterial blood pressure; CPP = central venous pressure; CPP = cerebral perfusion pressure; HR = heart rate. ANOVA (analysis of variance) = p < 0.0001 for all parameters except HR, for which it was not significant.
† Significant at p < 0.05 between Groups I and II.
‡ Significant at p < 0.05 within Groups I and II.
§ n = (CSFP - CVP)/(MABP - CVP) = transmission rate of arterial and venous pressures to CSFP (see text for explanation).
Effect of Mannitol Infusion on CVP

There was a significant increase in CVP in both groups (p < 0.001), observed 2 minutes after the start of the mannitol infusion and persisting until 20 minutes thereafter (Fig. 3). No significant difference was detected between the groups in the amount or duration of the CVP rise.

Effect of Mannitol Infusion on CPP

Cerebral perfusion pressure (Fig. 4) decreased within 2 minutes after the start of mannitol infusion in both Groups I and II (mean decrease 8 and 5 mm Hg, respectively; p < 0.001). By 10 minutes, with the return of MABP to baseline levels (before mannitol infusion), CPP surpassed control values in both groups and continued to increase during the last 35 minutes of the protocol. This increase paralleled the decline in CSFP.

Initial CSFP Response to Mannitol Infusion

In Fig. 5, the initial change in CSFP during the first 5 minutes of infusion in all patients is shown graphically in relation to the control CSFP. Regression analysis revealed a highly significant association (r = 0.79, p < 0.0001) between these two parameters. The even distribution of data points along the regression line suggests that these two parameters are correlated in a continuous fashion. The regression line crosses the x-axis line at a control CSFP value of 14.4 mm Hg.

CSFP Response to Mannitol Infusion in SAH Versus Tumor Patients

There were 13 patients (five in Group I and eight in Group II) with subarachnoid hemorrhage (SAH) under-
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going craniotomy for aneurysm clipping. Their CSFP response to mannitol did not differ from the CSFP response to mannitol of the brain-tumor patients, nor did their hemodynamic response to mannitol infusion. For that reason, no special SAH subgroup was considered.

Experimental Material and Methods

The differences in the CSFP response to rapid mannitol infusion between subjects with normal ICP and those with intracranial hypertension that were found in the present study could be due to differences in the effects of mannitol on cerebrovascular volume between the two groups. This hypothesis was tested in a canine model. The responses of CSFP, MABP, and CBV to rapid mannitol infusion in the dog have been previously characterized under conditions of normal ICP. For the present experimental study, elevation of CSFP was produced in dogs by inflating an intracranial epidural balloon.

General Procedure

The experimental protocol was approved by the Montreal Neurological Institute Animal Care Committee. Eight male mongrel dogs, each weighing 18 to 24 kg, were studied under general anesthesia (pentobarbital, 30 mg·kg$^{-1}$, and morphine, 0.3 mg·kg$^{-1}$, intravenously). Spontaneous respiration was abolished with pancuronium, 0.1 mg·kg$^{-1}$, and controlled ventilation through an oral tracheal tube was adjusted to produce normocapnia and normoxemia (PaCO$_2$ 37 ± 0.6 mm Hg, PaO$_2$ > 85 mm Hg) as determined by blood gas analysis. Rectal temperature was maintained at 38° ± 1°C. Vascular catheters included a venous line, a right atrial line, and an arterial line, all inserted surgically via the femoral vessels. Local anesthesia to the cutdown site was provided by infiltration of 5 ml of 0.125% bupivacaine. A No. 20 cannula was inserted into the cisterna magna posteriorly between the occiput and the arch of the first cervical vertebrae for the measurement of CSFP. Central venous pressure was measured with a water monometer. All other pressures were measured with calibrated transducers, and all pressures were referenced to the external auditory meatus. For the remainder of the surgical preparation and the CBV study, the animals were positioned prone with the head fixed in the sphinx position in a stereotaxic frame. The scalp was then incised along the midline and the soft tissues from the posterior aspect of the orbits to the external occipital protuberation were reflected laterally down to the level of the zygoma. Local anesthesia was provided by infiltration of 20 ml of 0.125% bupivacaine. This completed the surgical preparation for the five animals with normal CSFP (Group A). In three animals (Group B), a No. 7 French Fogarty venous embolectomy catheter was inserted into the epidural space through a 3-mm hole drilled in the right parietal region 1 cm from the midline. In these animals, intracranial hypertension was induced by inflation of the embolization balloon with saline; a target level of 15 to 20 mm Hg CSFP was selected and the balloon volume was adjusted until this level remained stable for 15 minutes without a change in balloon volume.

Measurement of Relative CBV

Cerebral blood volume was measured by the radioisotope indicator-dilution technique first described by Risberg, et al., and modified for this study only by using chromium-51 ($^{51}$Cr)-labeled red blood cells as the indicator instead of radioiodinated serum albumin. This technique has been described in detail previously, and the CBV results agree with those obtained with positron emission tomography. The method calculates the relative CBV at any time (t) as the ratio of the tissue radioactivity counts (head counts, HC) per minute (cpm) to the radioactivity cpm of a peripheral arterial sample drawn simultaneously (blood counts, BC) and normalized to the baseline ratio (b = HC/BC at control time), as follows:

$$\text{relative CBV (% of baseline)} = \frac{HC(t)/BC(t)}{b} \times 100.$$
FIG. 6. Cerebrospinal fluid pressure (CSFP) and relative changes in cerebral blood volume (CBV) at baseline (control) and at various times following the start of mannitol infusion (2 gm · kg⁻¹) in Group A and B dogs. Values are means ± standard error of the means.

FIG. 7. Mean arterial blood pressure and central venous pressure (CVP) values at baseline (control) and at various times following the start of mannitol infusion (2 gm · kg⁻¹) in Group A and B dogs. Values are means ± standard error of the means.

Discussion

The clinical study demonstrates that a rapid infusion of mannitol did not raise CSFP in patients with intracranial hypertension as it did in patients with normal CSFP, thus confirming in humans what had previously been demonstrated in canine models of intracranial hypertension. This is clinically significant because the safety of rapid mannitol administration is controversial. Several authors have advised against giving mannitol rapidly because it may initially increase CBV and CSFP. Others have suggested that the initial effects of mannitol on CSFP are not related to cerebral dehydration but to effects of decreased blood viscosity, and that CBV may decrease during and after rapid mannitol administration.

The rapid infusion of mannitol may affect CSFP by at least four different mechanisms. 1) Hemodynamically, mannitol is a vasodilator and may cause both direct and indirect (autoregulation-mediated) changes in CBV. 2) The vascular pressures in both the cerebral arteries and veins are altered, and this may affect CSFP independently. 3) Brain dehydration may play a role since the osmotic effects of mannitol can be observed even 2 minutes after administration. 4) Finally, mannitol may have effects on CSF formation and reabsorption.

A major limitation of this study is the lack of information about CBV during and immediately after mannitol administration. Since CBV is technically difficult to measure in humans, a separate study analogous to the human protocol was undertaken in dogs. The results showed that CBV increased approximately 25% of control values after mannitol infusion both in the normal animals (Group A) and in those with CSFP raised by an epidural balloon (Group B). The response of the CSF to mannitol infusion differed between Groups A and B in a fashion similar to that observed in the human subjects. These data therefore do not support the hypothesis that the differences in CBV changes observed
Effect of mannitol on CSF pressure

after mannitol infusion account for the difference in CSF response between normal subjects and those with raised CSF; they tend to indicate that autoregulation, although not tested in the present study, was still intact in Group II patients and in Group B dogs.

Ideally, a control group composed of patients to whom mannitol was administered but who did not experience a fall in MABP and a rise in CVP would help to clarify the effect of these vascular pressure changes on the CSF. Such a group was not practically feasible in this study. However, the direct effect of changes in arterial and venous pressures on the CSF may be estimated from the measurements of MABP, CVP, and CSF using a theoretical model. An analysis of this kind essentially treats the skull as a "black box" and attempts to evaluate the effects of changes in the vascular pressures on CSF without specifying the mechanisms of what is happening inside the skull. Theoretical models describing the static and transient behavior of the CSF have been developed and were recently summarized by Marmarou. Among the CSF models that are based on the transmission of intravascular pressure to the surrounding CSF, the proposal of Ikeyama, et al.,2 addresses the transmission of arterial and venous pressures to the CSF and was therefore applied in this study. Their proposal was based upon the observation that, in physical terms, the ICP must derive from the vascular pressures (MABP and CVP) since, in the absence of vascular pressures, ICP is atmospheric.

In steady-state conditions, CSF is then expressed as:

\[ \text{CSFP} = n \text{MABP} + (1 - n) \text{VP}. \]  

Thus,

\[ n = \frac{\text{CSFP} - \text{VP}}{\text{MABP} - \text{VP}}. \]  

where VP is the venous pressure (CVP) and n is defined as the transmission rate of arterial and venous pressures to the CSF. It can be seen from Equation 2 that, when CSF is normal, n is small. Conversely, when CSF is high, n is larger (Table 2). At the limit of extreme intracranial hypertension (CSFP = MABP), n equals 1. From Equation 1, we may postulate that the change in CSF which results from a change in MABP will be greater when n is large (high CSFP) than when n is small (normal CSFP). Concerning changes in venous pressure, the converse would be true since \((1 - n)\) would be larger when CSF is normal than when CSF is high. Therefore, the effect of changes in arterial and venous pressures on CSF may be estimated by calculating the change in CSF (CSFP) due to changes in vascular pressure which occurred during the interval under consideration, t. Thus, Equation 1 becomes:

\[ \text{CSFP}_t = n_0 (\text{MABP}_0 - \text{MABP}) + (1 - n_0) (\text{CVP}_0 - \text{CVP}). \]  

Applying this analysis to the patients in our study, we can calculate the effect of the observed changes in MABP and CVP on the CSF for each patient at any given level of CSF and so "correct" the observed CSF for the hemodynamically related changes by subtracting CSFP; from the observed values. The results of such calculations (Fig. 8 and Table 2) show what we speculate that the CSFP values would have been if vascular pressures had not changed to arrive at the corrected CSFP (CSFPc). These findings suggest that most of the transient rise in CSFP in Group I patients can be accounted for by the effects of arterial and venous pressure changes. In Group II patients CSFPc appears to decrease faster (Fig. 8 and Table 2) than in the original observations (Fig. 1) because the effect of the early vascular pressure changes on CSFP may have resulted in a positive change in both groups; however, the change was less in Group 2 and was obscured by the rapid decline of CSFP in that group.

Brain water was not measured in this study; we can only comment that if the rates of brain dehydration were the same in both groups of patients, then a more rapid fall in CSFP would be anticipated in Group 2, since that group would likely have increased intracranial elastance (change in CSFP for a given change in intracranial volume). No measurements of CSF dynamics were made in either the human or the canine portion of the present study, so no comments are offered as to the role of this mechanism in the results.

The decrease in MABP observed in this and other studies is likely to be multifactorial. Mannitol has been shown to dilate blood vessels directly and by histamine release. Moreover, acute hemodilution causes a decrease in blood viscosity and systemic vascular resistance. The decrease in MABP observed in our patients persisted for a longer time than was documented in a previous report. In the present study, general anesthesia is likely to have obtunded the sympathetic response which was evident following a mannitol bolus in unanesthetized subjects. The magnitude

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**Fig. 8.** Corrected values of cerebrospinal fluid pressure (CSFPc) for mean arterial blood pressure and central venous pressure changes at baseline (0 min) and at various times following the start of mannitol infusion (1 gm ∙ kg−1) in Groups I and II. Values are means ± standard error of the means.
and duration of the CVP increase observed were similar to those reported in the same study.12

An important assumption in this investigation is that the lumbar CSFP reflects ICP in patients with intracranial hypertension. The patients studied were clinically free of pathology likely to obstruct CSF pathways between the intracranial and lumbar CSF spaces. Experimental analysis of the volume-pressure relationships at various locations in the neuraxis of dogs during inflation of an epidural balloon13 has revealed that an intracranial-cisterna magna pressure gradient develops when the lateral ventricular pressure is approximately 20 mm Hg. If these data can be extrapolated to human subjects, then our Group II patients would have had at the most a small intracranial-lumbar CSFP gradient, and the CSFP measured at that point should accurately reflect ICP.

In conclusion, in a series of patients with either a brain tumor or SAH, infusion of mannitol did not cause CSFP to increase in patients with raised CSFP as it did in patients with normal ICP. These different reactions to mannitol infusion may be due to a difference in CSFP responsiveness to changes in arterial and venous pressures between subjects with and those without intracranial hypertension, rather than to differences of cerebrovascular volume changes between those two categories of subjects.

References