Clinical monitoring of intracranial pressure in fulminant hepatic failure

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SUMMARY   Cerebral oedema is the commonest immediate cause of death in fulminant hepatic failure and an investigation was carried out to determine the value of monitoring intracranial pressure (ICP) and to examine the effects on ICP of dexamethasone therapy and mannitol administration. ICP values in 10 patients at the time of insertion of a subdural pressure transducer (grade IV encephalopathy) averaged $15 \cdot 5 \pm SD$ $14 \cdot 8$ mmHg. Despite dexamethansone therapy, which had been started on admission, rises in ICP were subsequently observed in seven of the eight patients who died. In the two patients who survived, the highest readings were 47 and 35 mmHg. Mannitol consistently reversed or arrested ICP rises when pressure was < 60 mmHg. ICP monitoring provides additional information in the management of patients and is essential if mannitol therapy is to be used.

The frequency of cerebral oedema in patients who die of fulminant hepatic failure has always been disturbingly high.[1][2] Since the introduction of better therapy for the management of certain complications of this failure, particularly prophylactic cimetidine therapy for gastrointestinal haemorrhage, it has become the most frequent cause of death and in the last series of patients analysed from this Unit, cerebral oedema was found at necropsy in over 80% of those patients who died as a result of fulminant hepatic failure.[3]

In the earlier experimental studies to elucidate the mechanism involved, we used a subdural pressure transducer to monitor intracranial pressure (ICP) in an animal model with surgically induced liver failure.[4] From the onset of liver failure, there was a progressive rise in ICP which could be prevented by early high-dose corticosteroid therapy. In the present study a similar technique was used to monitor the changes in ICP in a group of patients with FHF who received prophylactic dexamethasone therapy from the time of their admission.

Methods

PATIENTS
Ten patients (age-range 14–56 years) were investiga-

ted. Six had fulminant hepatic failure caused by paracetamol overdose, in two it was due to non-B viral hepatitis and in two it was presumed to be drug hypersensitivity reaction. Shortly after their admission, or when the patient went into grade IV coma, a stable drift-free intracranial pressure transducer (Gaeltec Ltd, Waternish, Isle of Skye, Scotland) was inserted through either a right parietal or temporal burr hole and attached to a flat-bed recording system. The procedure was carried out in an operating theatre and anaesthesia was maintained with either a mixture of nitrous oxide and oxygen or halothane. Two units of fresh frozen plasma were infused during the procedure to minimise peroperative haemorrhage.

As both hypoxia and hypercapnia can influence ICP, arterial blood gases were measured at least twice daily.[5][6] Dexamethasone was given on admission (32 mg intravenously) and four-hourly thereafter (8 mg) and intravenous mannitol was given in bolus doses (40–100 g) when sustained rises in ICP exceeded 50 mmHg (three patients) or 30 mmHg (five patients). All patients were treated in the Liver Failure Unit with full supportive measures and in eight patients polyacrylonitrile (PAN) membrane dialysis was used as a means of temporary liver support.

When the transducer was removed, superficial and dural wound swabs were taken for bacterio-

logical culture. Brains were examined macroscopically at necropsy in seven of the eight who died.

Informed consent was obtained from the relatives of all the patients and permission was granted by the local Ethical Committee to carry out this study.

Results

At the time of the insertion of the transducer, levels of ICP ranged widely from 3 to 45 mmHg (mean 15.5 ± 14.8) compared with an upper limit of normal range of 15 mmHg. Fluctuations in ICP exceeding 15 mmHg were seen in all patients, despite the high doses of dexamethasone. In the two patients who survived to leave hospital the maximum recorded ICP was less than 50 mmHg (35 and 47 mmHg), whereas six of the eight patients who died had values of 100 mmHg or more at some time during their illness. It was notable that, in these six patients, the rises in ICP occurred precipitously (to more than 110 mmHg over six to nine hours) (Fig. 3). In the other two who died, the maximum recorded ICP was 31 and 45 mmHg.

Decerebrate and decorticate posturing with or without central neurogenic hyperventilation was observed in four patients. On occasions these epi-
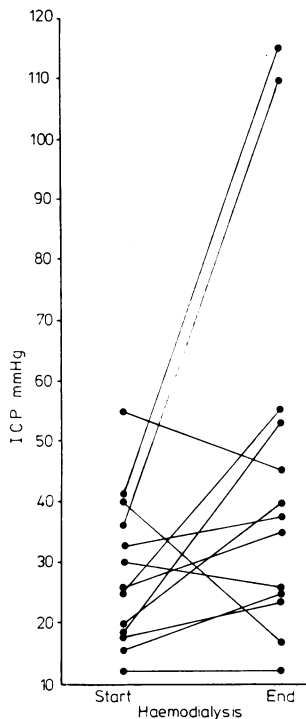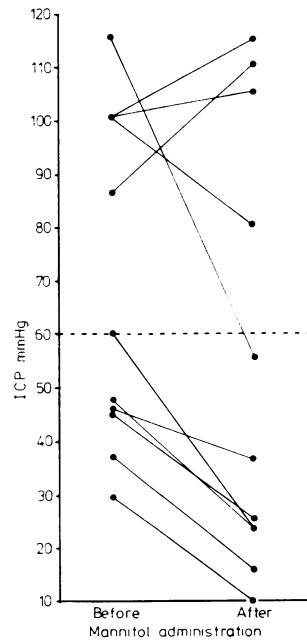

Fig. 2 *ICP before and one hour after a bolus dose of mannitol, showing difference in response with level of above and below 60 mmHg.*

sodes were associated with transitory rises in ICP. In six of the eight who died, however, the main rise in ICP was associated with deterioration in the clinical condition of the patient, with respiratory arrest, hypotension, and loss of brainstem reflexes (Fig. 3). One of the survivors, however, had decerebrate posturing throughout the period of grade IV coma which ceased as the coma lightened.

Analysis of the continuous EEG monitoring carried out in all patients showed that delta-wave activity was already present by the time of admission. In the six patients who developed ICP of more than 100 mmHg a sudden deterioration in clinical condition and in the isoelectric pattern coincided with the rise in ICP. In the other two who died, there was a gradual decrease in EEG activity.

At necropsy, cerebral oedema with evidence of either tentorial or cerebellar herniation was seen in all seven patients examined. In two of the cases oedema was unilateral and found on the left side only.

EFFECTS OF MANNITOL THERAPY AND PAN MEMBRANE HAEMODIALYSIS

Six patients were treated with intravenous mannitol (40–100 g) on 11 occasions. ICP fell when the manni-
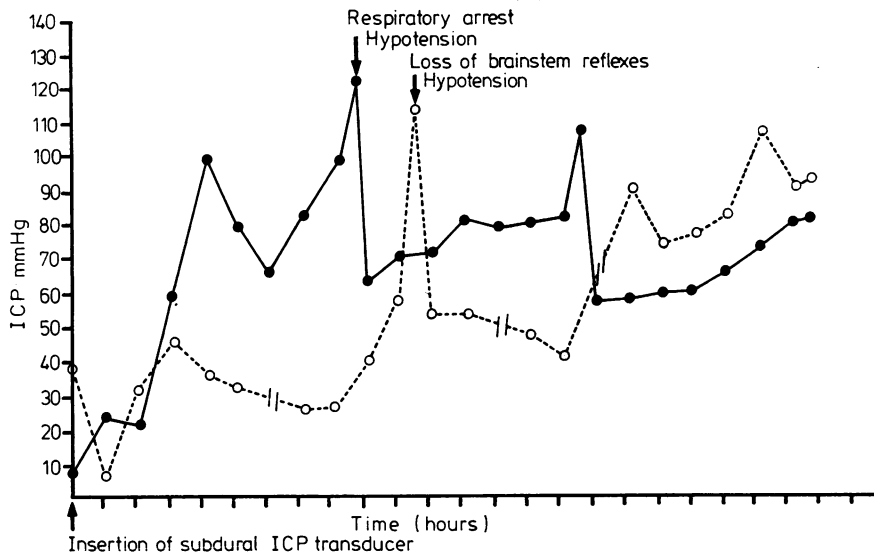

Fig. 1 *ICP at the start and end of PAN haemodialysis.*

Fig. 3 *Changes in ICP in two patients, showing the precipitous rises in ICP associated with clinical deterioration.*

tol was administered before the pressure had risen to above 60 mmHg (Fig. 2). The response was variable when mannitol was administered with an ICP of more than 60 mmHg, and on three occasions the ICP increased after therapy.

PAN haemodialysis was carried out on 13 occasions in eight patients (Fig. 1). Although overall this was associated with a small but significant rise in ICP during the four-hour period of dialysis (mean 18·38%±SD 31·23, P <0·05, paired *t* test), in most instances the rises in ICP were minor. The two occasions when ICP rose precipitously during dialysis, may have been coincidental rather than the direct result of haemodialysis.

COMPLICATIONS

All dural swabs taken on removal of the transducer were sterile on culture and local haemorrhage was not a problem. In one of the seven who died examined at necropsy, some blood clotting was seen around the burr hole and extended along the subdural space to cover the right occipital lobe.

Discussion

The present study shows that cerebral oedema may be preceded by marked and precipitous rises in ICP. The pattern of the rises appears to be very similar to the changes described in Reyes' syndrome[7-9] and is quite unlike the progressive, almost linear rate of rise in ICP seen in the experimental animal model.[4] Even with the knowledge of the ICP readings, few clinical correlations were apparent

and none of the patients developed papilloedema. An exception to this, however, was the oculovestibular reflex which disappeared at a pressure close to 100 mmHg, suggesting that probably this is the critical level for tentorial or cerebellar herniation in fulminant hepatic failure.

ICP can be influenced by changes in arterial blood gases and blood pressure, by altering cerebral blood flow. Arterial blood gases were estimated at least twice daily and p_aO_2 was maintained above 12 kPa and p_aCO_2 below 6·1 kPa. Assisted ventilation was instituted when necessary. Blood pressure was routinely measured at hourly intervals or more frequently if there was a sudden increase or decrease in the recording, and remedial steps were taken. Spontaneous rises in ICP occur normally[10] and these might become exaggerated as cerebral oedema develops.

The rises in ICP occurred despite the high doses of dexamethasone started on admission. Possibly the results would have been different if the drug had been started much earlier in the course of liver failure, as in the animal model. As seen consistently in patients with a moderately raised ICP (<60 mmHg) mannitol appears to act by increasing plasma osmolarity, promoting a fluid shift from the brain to the intravascular compartment and thereby reversing the rise in ICP. Experimental studies have recently shown that the permeability of the blood-brain barrier is increased in an anhepatic model of acute liver failure[11] and this may also be the case in man when ICP levels exceed 60 mmHg. The increases in ICP seen after mannitol administration

in these cases would be consistent with a mannitol and concomitant water flux into the brain. In view of the deleterious effects of mannitol in these patients its administration cannot be routinely recommended in fulminant hepatic failure without prior knowledge of the ICP reading.

Although the rises in ICP during PAN haemodialysis were generally minor, in two cases the increase was more marked and gave rise to concern. The mechanism of these changes has to remain speculative, but an obvious possibility lies in the rapid removal of solute from the intravascular pool by haemodialysis, leading to a state in which the brain tissue is hyperosmolar relative to the intravascular pool with subsequent fluid shift into the brain.

The present results suggest that, as long as the subdural pressure transducer is inserted by experienced operators, monitoring of ICP is a safe procedure in fulminant hepatic failure. Indeed, on present findings a case could be made for routinely monitoring ICP in patients with this condition as rises in ICP to over 60 mmHg are associated with a poor prognosis. If survival figures in fulminant hepatic failure are to be improved further, measures to prevent the particular complications of cerebral oedema will have to be instituted much earlier. By the time grade IV coma has ensued, the situation in many cases is already irreversible.

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