Reye's syndrome: assessment of intracranial monitoring

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Abstract

Direct measurements of arterial blood pressure and intracranial pressure were recorded in 39 patients aged 3.6 months to 5 years 11 months with Reye's syndrome judged to be stage 2 or beyond. Of 33 patients who survived, 27 made a full recovery and six were severely handicapped. Measurement of cerebral perfusion pressure, which is greatly reduced in the more severe forms of Reye's syndrome, was a better guide to prognosis and management than intracranial pressure alone.

The findings emphasise that maintenance of cerebral perfusion pressure is essential if mortality and morbidity are to be reduced. Intracranial monitoring is mandatory in all but the mildest cases of Reye's syndrome.

Introduction

Reye's syndrome is a serious acute childhood encephalopathy of uncertain cause associated with acute hepatic failure.¹ After a trivial presumed viral infection there is an abrupt onset of vomiting, possibly accompanied by hypoglycaemic seizures, and variable reduction in the level of consciousness. The underlying pathophysiology is cerebral oedema. As this progresses there is an exponential increase in intracranial pressure. It is the degree to which brain swelling has occurred and the extent to which it can be controlled therapeutically that largely determine the outcome.² Hence current management consists of aggressive measures to reduce cerebral swelling combined with direct intracranial monitoring.³ Nevertheless, some patients in whom intracranial pressure has been strikingly raised may recover fully, whereas others with a less obvious increase may die or be left with permanent neurological damage.⁴ A more appropriate parameter may therefore be the cerebral perfusion pressure, which is the difference between mean arterial blood pressure and intracranial pressure.^{2,4} We have extended our previous studies^{5,6} to see whether values of intracranial and cerebral perfusion pressure might be used as pointers to prognosis or guides to management.

Patients and methods

Simultaneous recordings of arterial blood pressure and intracranial pressure suitable for analysis were available in 39 of 53 patients with Reye's syndrome aged 3.6 months to 5 years 11 months (median 9.0 months)

between 1979 and 1985. All patients met widely accepted diagnostic criteria.^{1,5,7} Each had been managed by a multidisciplinary team in the regional paediatric intensive care unit. Patients' level of consciousness and neurological state were assessed according to a modification of the scheme outlined by Lovejoy and colleagues.⁷ Those judged to be Lovejoy stage 1 (drowsy) did not have intracranial pressure monitored, but only those thought to be stage 2 (restless and hyperventilating) or beyond³ (coma). Intracranial pressure was monitored by a Ladd epidural fibreoptic sensor in 24 patients, a Richmond bolt in 12, and a ventricular catheter in three. Arterial blood pressure was displayed in digital form using an intra-arterial cannula. In each case values of blood pressure and intracranial pressure had been charted hourly from the recording equipment and it was from these hourly data that initial and maximum intracranial pressures were extracted. Initial and minimum cerebral perfusion pressures were then calculated by subtraction.

Outcome was assessed by a paediatrician or paediatric neurologist a median of 13.2 months after the initial illness. Of 33 patients who survived, 27 made a complete developmental and neurological recovery. Six had sustained a severe degree of mental and physical handicap. Statistical analysis was by the χ^2 or Mann-Whitney U test.

FIG 1—Maximum intracranial pressures in 39 patients with Reye's syndrome showing lack of statistical relation with outcome.

Results

Mean intracranial pressure increased from an initial 9.4 (SD 10.4) mm Hg to a maximum of 22.6 (20.2) mm Hg, this difference being significant ($p < 0.001$). Initial intracranial pressure in patients who subsequently had a poor outcome (died or handicapped) did not differ significantly from that in those who recovered completely (10.7 (9.6) v 9.0 (11.0) mm Hg). Similarly, maximum values of intracranial pressure did not differ significantly between these groups (33.6 (37.6) v 18.4 (12.4) mm Hg) (fig 1). There was no difference in the mean duration of monitoring between those with a poor outcome and those who recovered fully (115 (48) v 95 (29) hours). Initial intracranial pressure did not correlate well with Lovejoy stage nor with initial glucose concentrations in blood or cerebrospinal fluid.⁵ Increases in maximum intracranial pressure were most pronounced, however, in those in

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whom the first recorded blood ammonia concentrations were substantially above normal ($r=0.4$; $p<0.01$).

Mean cerebral perfusion pressure, which at insertion of the monitoring device was 66.6 (18.0) mm Hg, decreased during management to a minimum of 48.5 (15.4) mm Hg ($p<0.001$). Those in whom the outcome was satisfactory had a similar initial cerebral perfusion pressure compared with those whose outcome was poor (67.3 (18.3) v 62.9 (21.6) mm Hg). Minimum cerebral perfusion pressures, however, showed significant differences between these two groups of patients (56.0 (9.1) v 31.5 (13.2) mm Hg; $p<0.001$). There was a tendency for lower minimum cerebral perfusion pressures to be recorded in patients with more advanced Lovejoy stages on admission to intensive care—for example, stage 2, mean value 52.3 (11.0) mm Hg; stage 3, 47.2 (18.4) mm Hg; stage 4, 42.0 (13.1) mm Hg. There was no significant difference in the mean time interval between the onset of monitoring and the minimum recorded value of cerebral perfusion pressure (18 (23) v 43 (39) hours; $p=0.075$).

The relation between minimum cerebral perfusion pressure and outcome was particularly noteworthy (fig 2). All 10 patients with a value of less than

FIG 2—Relation between minimum cerebral perfusion pressure and outcome in 39 patients with Reye's syndrome.

40 mm Hg sustained severe neurological handicap or died compared with two of 29 whose minimum cerebral perfusion pressure was 40 mm Hg or greater ($p<0.001$). In neither of these two patients had maximum intracranial pressures been unduly high—namely, 11 and 19 mm Hg, respectively. One was severely handicapped after hypoglycaemic seizures for three hours before hospital referral and diagnosis, and the other died as a result of profound pulmonary complications. At necropsy the brain showed no evidence of raised intracranial pressure.

Discussion

These findings clearly show that values of intracranial and cerebral perfusion pressures recorded at the time of inserting an intracranial monitoring device are of no help in predicting outcome. The two children with highest initial intracranial pressures (40 and 42 mm Hg) each made a full recovery. It is also apparent that even the peak intracranial pressure in this acute illness is not of prognostic help, since four of the five children with a maximum intracranial pressure of greater than 35 mm Hg also recovered completely (fig 1).

The importance of maintaining a satisfactory cerebral perfusion pressure is evident. Two children with a minimum perfusion pressure of 40 mm Hg or greater who subsequently had a poor outcome each had other complications which may have been

clinically more relevant than the presence of cerebral oedema by itself. On the other hand, no child with a minimum cerebral perfusion pressure of less than 40 mm Hg made a full recovery.

Because our conclusions are based on values of intracranial pressure and arterial blood pressure which had been noted hourly from the original paper chart recordings, some made several years before and no longer in existence, we cannot comment on the time relation between outcome and the duration of cerebral perfusion pressure of less than 40 mm Hg. It seems likely that in this parlous setting an ischaemic or hypoxic insult develops rapidly. It is clear from these data, however, that our conclusions have not been biased by differences in the duration of monitoring between those who recovered and those who did badly.

Our data do not allow comment on the timing of lumbar puncture in conditions of potentially or actually raised intracranial pressure. None the less, we have had patients in whom this procedure may have precipitated deterioration in consciousness with a subsequent poor outcome. In a recent review of current management we have emphasised the wisdom of delaying cerebrospinal fluid examination until after initiation of measures to reduce a raised intracranial pressure and improve cerebral perfusion pressure.³

Our studies highlight the necessity of continuous intracranial monitoring in all but the mildest cases of this syndrome. This approach should be combined with optimal therapeutic endeavour to prevent cerebral perfusion pressure falling below a critical value, which in these young patients appears to be in the region of 40 mm Hg.

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(Accepted 18 November 1986)

100 YEARS AGO

The Peninsular and Oriental Company, we are glad to see, are increasing and multiplying facilities for holiday trips to India, the Mediterranean, and Australia. Their last new steamer, the *Victoria*, which is perhaps the finest model extant of an ocean steamer, replete with every comfort which ingenuity can suggest or a lavish expenditure supply, is about to start on an autumnal trip to India and back, than which it would be difficult to conceive a more delightful and healthful relaxation. Nor could a sea trip be undertaken under more favourable circumstances than in this magnificent boat. We had recently an opportunity of inspecting the *Victoria*, and of judging of her qualities as a sea-boat, and of the luxurious accommodation afforded on the occasion of a two days' cruise at the time of the Naval Review. She is lighted throughout with the electric light, and is provided with extensive refrigerating chambers. The ventilation and arrangement of the cabins are admirable, and a great improvement on the ordinary type. Her speed is great, and her stability in a heavy sea remarkable. Her burden is nearly 7,000 tons. Altogether she is a magnificent specimen of naval architecture, and in every respect well found. The P. and O. Company have decided to follow their fresh departure in the way of cheap trips to India by one to Australia. For 100 guineas they will take a passenger to Australia and back, accommodating him in the first saloon. The voyage is calculated to occupy about ninety days, and it will be possible to make a stay of ten or twelve days in the colonies, or the passenger can prolong his stay for six months without further charge. Some estimate may be made of the cheapness of the trip when it is borne in mind that living on board these steamers is equal to that at the best hotels. (*British Medical Journal* 1887;iii:479.)