Clinical applications of the pressure-volume index in treatment of pediatric head injuries

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The pressure-volume index (PVI) technique of assessing neural axis pressure-volume relationships was used as an adjunct to managing 22 children with severe head injuries and a Glasgow Coma Scale score of 8 or less. Ventricular cannulation was used to continuously monitor intracranial pressure (ICP). Actual PVI was measured by bolus injection of fluid and compared with predicted values determined from head circumference and spinal axis length in each patient. In 55% of the children, ICP was below 20 mm Hg at initial monitoring. During the course of monitoring, 86% of the children had ICP's exceeding 20 mm Hg. Reduced PVI (less than 80% of predicted normal) proved to be an accurate indicator of impending intracranial hypertension. The PVI proved to be a useful test for assessing the response to therapies for lowering ICP. This study demonstrates that reduced neural axis compliance accompanies intracranial hypertension following severe head injury in children, and that treatment of reduced neural axis compliance may prevent refractory intracranial hypertension.

KEY WORDS □9 intracranial pressure □9 pediatric head injury □9 barbiturate coma □9 pressure-volume relationship

RECENT studies in the care of severely head-injured children have demonstrated that both morbidity and mortality can be reduced by effective monitoring and control of intracranial hypertension. Standard techniques for monitoring intracranial pressure (ICP) include the use of subarachnoid bolts and intraventricular catheters coupled to electrical recording systems for simultaneous and continuous recording. Although these methods accurately record the absolute level of ICP, the inability of these techniques to anticipate changes in ICP prior to abrupt, and often fatal, rises in pressure represents a critical shortcoming. To circumvent this deficiency, techniques using bolus manipulation of fluid and, more recently, pulse wave analysis have been developed. These techniques can be used to assess neural axis compliance in order to identify patients at risk of sudden increases of ICP. One of these techniques, the pressure-volume index (PVI), which utilizes bolus manipulation of cerebrospinal fluid (CSF), has been developed in this laboratory. The application of PVI testing to the care of head-injured children will be discussed in this paper.

In the range of ICP's encountered in clinical practice, the relationship between ICP and volume added to the neural axis describes an exponential intracranial pressure-volume (ICPV) curve. Viewed in another way, as pressure increases the ability to buffer successive additions of volume diminishes, so that equal increments of volume introduced on the steeper portion of this ICPV curve will produce disproportionately higher elevations of ICP. One way to assess the steepness of the ICPV curve is to measure compliance or its reciprocal, elastance. Compliance is defined as the rate of change in pressure produced by a bolus increment added to the CSF compartment. More compliant systems are characterized by smaller changes in CSF pressure induced by equal bolus increments. However, the exponential shape of the ICPV curve dictates that compliance is greater on the more horizontal portion of this curve than on the vertical segment of the same ICPV curve. For this reason, compliance or elastance determined at one portion of the ICPV curve cannot be applied to other portions of the same curve, because compliance changes are, in part, a function of ICP. In order to overcome this restriction, Marmarou transformed the exponential curve into a linear plot by graphing pres-
sure on a logarithmic scale against volume. The slope of the resulting straight line was defined as the "pressure volume index" (PVI) which quantified the steepness of the exponential curve and provided a measure of neural axis compliance which was independent of ICP. In contrast to compliance, which describes a point on the ICPV curve, the PVI describes the entire curve. In earlier work from this laboratory, we reported that the PVI is dependent on neural axis volume, so that in smaller normal children, PVI is less than in larger children. A nomogram was constructed for predicting the normal PVI based on external measurements of head circumference and spinal length. This technique enabled us to predict the PVI for any child with intracranial pathology and then to measure the PVI in the pathological setting to determine how the disease process had influenced neural axis pressure-volume relationships.

The present study is an attempt to apply these techniques to a group of severely head-injured children who were undergoing continuous ICP monitoring. The objectives of this study were to determine 1) the PVI in head-injured children and compare this with the expected normal plot; 2) the relationship between measured PVI and ICP in pediatric head injury; and 3) whether reduced PVI can identify impending intracranial hypertension.

Clinical Material and Methods

Twenty-two children, aged 3 months to 15 years, were included in this study. The majority were evaluated within 2 hours of head injury. All children with surgical mass lesions were excluded from this study. All patients were classified by the Glasgow Coma Scale (GCS); preverbal children were awarded the maximum of 5 points for the verbal response if they uttered any sound; those without verbal output scored only 1 point for verbal response. Following emergency room resuscitation and the administration of dexamethasone (0.4 mg/kg), computerized tomography (CT) or cerebral angiography was performed. Following the neuroradiological procedure, patients again underwent GCS scoring.

Ventricular catheterization was performed in all whose GCS score was 8 or less with ventricles discernible on CT scan. Most patients required intubation and sedation or paralysis in order to maintain PaO2 values greater than 90 torr and PaCO2 values of 28 to 32 torr. Intracranial pressure was monitored by low-volume displacement electrical transducers* connected to the ventricular catheter by saline-filled tubing. The output of the transducer was displayed digitally; the wave form was displayed on an oscilloscope; ICP was recorded continuously on a slow-speed (1 cm/hr) trend recorder.† When bolus manipulation (see below) was performed, transducer output was recorded directly on strip charts recording at 1 mm/sec.

The PVI determinations were performed according to the previously published protocol demonstrated in Fig. 4 upper. After a stable baseline ICP had been obtained, a bolus of 1 to 2 ml was withdrawn at a rate of 1 ml/sec. The drop in ICP following bolus withdrawal was used to calculate the PVI using the equation: PVI = ΔV/log (Pp/P0), where ΔV is the volume (ml) withdrawn, Pp the baseline ICP, and Pm the trough ICP produced by bolus withdrawal. Diastolic pressure of the ICP was used for all calculations, with all pressures taken from the same phase of the cardiac and respiratory cycles. Since bolus withdrawal has been shown to be equivalent to bolus injection for calculation of the PVI, the bolus withdrawal was used to predict the responses to bolus injection, allowing insertion of safe volumes for later manipulation. The maximum volume injected (Vlimit) was computed from the equation: Vlimit = (PVI) log (Plimit/P0), where PVI is the value obtained from the withdrawal sequence; Plimit is the maximum ICP considered safe for an individual patient and was never allowed to exceed 25 to 30 mm Hg; and P0 the initial baseline ICP. Following return of the ICP to baseline, a suitable bolus was injected in all patients whose ICP was less than 30 mm Hg. When the initial ICP exceeded 30 mm Hg, bolus injection was only carried out after ICP had been reduced below this level. The PVI was calculated from the peak pressure generated by bolus injection, using the equation: PVI = ΔV/log (Pp/P0), where Pp is the peak pressure produced by bolus injection and P0 the baseline ICP preceding injection (Fig. 4 upper). At least four determinations were made at each test session. These manipulations were repeated daily for each patient and after therapeutic interventions.

The actual values of PVI measured in each patient were compared to predicted normal values determined from measurements of head circumference and spinal length. The quotient of Actual PVI/Predicted PVI × 100 was recorded as the percent predicted PVI.

Intracranial hypertension was defined as: 1) ICP above 20 mm Hg lasting 10 minutes or more; 2) plateau waves or spontaneous elevations of pressure exceeding 30 mm Hg without associated noxious stimuli; and 3) progressive increases in ICP exceeding 20 mm Hg. When these events occurred, mannitol (1 mg/kg) or ventricular drainage was instituted. Barbi-

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* Low-volume displacement electrical transducer, Model P23 DB, manufactured by Statham Instruments, 2230 Statham Boulevard, Oxnard, California.
† Trend recorder, Model HP-7825A, manufactured by Hewlett-Packard, 16399 West Bernardo Drive, San Diego, California.
turate coma was induced when osmotic diuretics were used more often than every 4th hour.

Monitoring was continued as long as intracranial hypertension persisted. After ICP was maintained below 20 mm Hg for 24 hours, medical therapy was withdrawn, usually over 24 to 96 hours. Intraventricular catheters were removed after all medical therapy had been withdrawn and ICP remained below 20 mm Hg.

Results

Intracranial Pressure

Table 1 provides an overview of the children reported in this series. In 55% of the children, the initial ICP was less than 20 mm Hg. In the remaining 45%, initial ICP ranged between 21 and 40 mm Hg. The distribution of GCS scores for this group is shown in Fig. 1 left. Scattergrams showed no correlation between GCS score and either initial ICP or peak ICP during the course of monitoring (Fig. 1 center and right). Although initial ICP was below 20 mm Hg in over half the patients, 86% of the patients developed elevated ICP which required treatment. The distribution of peak ICP is also shown in Table 1; 31% of patients had maximum pressures between 21 and 40 mm Hg and, in an additional 55%, ICP exceeded 40 mm Hg. The mean initial ICP was 22.4 ± 8.3 (SD) mm Hg for the entire group. The mean peak pressure for all patients was 41.1 ± 16.2 mm Hg.

Pressure-Volume Analysis

In order to analyze the data obtained when the PVI was used to characterize neural axis pressure-volume

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(mean ± SD) 59 ± 14 22.4 ± 8.3 41.1 ± 16.2

* GCS = Glasgow Coma Scale; PVI = pressure-volume index; ICP = intracranial pressure; SD = standard deviation. Outcome: 1 = good recovery, returning to pre-morbid activities; 2 = moderate disability, but independent function; 3 = severe disability, requiring intensive support.

† Predicted PVI was calculated using nomograms based on head circumference and spinal axis length. Percent predicted PVI was computed from the formula: % Predicted PVI = Measured PVI/Predicted PVI × 100.

| FIG. 1. Left: Bar histogram showing the distribution of Glasgow Coma Scale (GCS) scores for the 22 severely head-injured children included in this study. Center and Right: Scattergrams showing the relationships between GCS score and initial intracranial pressure (ICP) (center) and peak ICP encountered during monitoring (right).
buffering capacity, PVI was expressed as a percentage of predicted PVI (Table 1). This ranged from 33% to 89% of predicted PVI for the entire series. The mean for the series was 59 ± 14%, indicating marked compromise of volume-buffering reserves in these children. Figure 2 shows the relationship between predicted PVI and actual PVI for this group of severely head-injured children as contrasted with the same relationship found in an earlier study of normal children.¹⁴

In order to analyze the relationship between ICP and PVI, scattergrams were constructed comparing initial ICP to the percent of predicted PVI (Fig. 3). There was no statistically significant correlation between percent predicted PVI and initial ICP (p = 0.029, Student's t-test). However, the relationship between percent predicted PVI and the peak ICP observed in these children was highly significant (p < 0.001). The initial PVI identified prospectively children at risk of developing intracranial hypertension.

This relationship is further illustrated in Table 2, which relates percent predicted PVI and categorization of ICP. Children whose measured PVI was 80% or more of their predicted PVI had peak ICP's that remained below 20 mm Hg without treatment. In those children with measured PVI 60% to 80% of predicted PVI, ICP ranged between 21 and 40 mm Hg. Of the 14 patients whose measured PVI was less than 60% of the predicted normal level, two had ICP between 21 and 40 mm Hg and the remaining 12 had ICP elevations that exceeded 40 mm Hg. Thus, the more the measured PVI deviated from the predicted normal, the greater the risk of ICP elevation. In addition, the children with severely reduced PVI had the highest ICP's.

Changes in PVI occurred during the course of monitoring. Although many of these changes were spontaneous, the majority were associated with ther-
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Therapeutic maneuvers of CSF drainage, osmotic diuresis, and iatrogenic barbiturate coma. All of these maneuvers increased PVI. In 16 patients in whom PVI was measured before and after therapy, 14 had a mean increase of PVI of 16.6 ± 4.8%. The ICP could be managed by medical means in all of these patients. In two patients with severely compromised PVI (33% and 35% of predicted normal), there was no change of PVI following mannitol administration. Both of these patients died from uncontrolled intracranial hypertension. Among the 14 patients whose PVI improved after treatment, five patients showed rapid return of their PVI to pretreatment levels within 1 to 2 hours after osmotherapy. This was followed invariably by a rapid return of ICP to pretreatment levels.

**Barbiturate Therapy**

Among the group discussed above, four patients required barbiturate therapy to maintain ICP below 20 mm Hg. In one patient the addition of barbiturate therapy produced no change in PVI or in ICP. In the other three patients receiving barbiturates in addition to osmotic diuretics, PVI improvement paralleled that found in the group discussed above (Fig. 4). Since this group was receiving both barbiturates and mannitol, it was difficult to attribute the improved PVI solely to barbiturates. However, these children had shown minimal improvement in PVI with mannitol alone, but, within hours after barbiturate coma was induced, PVI increased by a mean of 21%.

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**Fig. 4.** Upper: Strip chart recording showing changes in intracranial pressure (ICP) and pressure-volume (PVI) following barbiturate coma in an 11-year-old boy with closed-head injury. His Glasgow Coma Scale score was 8, the predicted PVI 23 ml, and the initial PVI 11 ml. Both tracings show the ICP response to two bolus manipulations of cerebrospinal fluid (ΔV), a withdrawal and an injection. The immediate ICP response (P_m for withdrawal and P_p for injection) was used to calculate PVI. I_f is the calculated rate of cerebrospinal fluid formation extracted from the response of ICP to bolus withdrawal. Lower: Trend recording from the same child shows the response of ICP to various therapeutic modalities. Following induction of barbiturate coma, ICP peaks have become less frequent and more easily managed. After many medical complications, this child survived without detectable deficit. Broken vertical line = mannitol administration, solid vertical line = cerebrospinal fluid drainage.
Computerized Tomography Findings

The anatomic diagnosis, usually based on CT scans, was as follows: 12 patients had diffuse cerebral swelling,17 three had cerebral contusions, and four had diffuse cerebral swelling accompanied by brain contusion; two had brain-stem contusions (based on radiological or clinical findings); and one had a normal CT scan. Although diffuse cerebral swelling was useful in identifying patients at risk of developing intracranial hypertension, in 25% of patients with this diagnosis ICP remained below 20 mm Hg without therapy. All patients with contusion or contusion plus diffuse cerebral swelling developed intracranial hypertension requiring treatment.

Outcome

Five of the patients in this series died. Two of the deaths were due to uncontrolled intracranial hypertension. In both children, ICP rose rapidly within the first 6 hours after injury and was refractory to both mannitol and barbiturate therapy. Another death was caused by the medical complications of management; the other two deaths were caused by injuries outside the central nervous system (CNS). Of the survivors, 76% had good outcomes or were moderately disabled, but the remaining four, or 24% of survivors, were severely disabled.

Discussion

In contrast to adult head-injury victims in whom control of intracranial hypertension may not significantly affect outcome, control of ICP in pediatric head injury clearly influences survival and functional outcome.3,4 However, with conventional techniques of ICP monitoring, at least 50% of children with GCS scores of less than 8 will have normal ICP at the outset, as shown in this study. Further, our experience shows that clinical signs of impending intracranial hypertension may not be apparent in the stuporous or comatose head-injured child. Although the technique of continuous monitoring of ICP is useful in documenting intracranial hypertension as it occurs, it does not identify children likely to experience abrupt and life-threatening elevations of ICP.

Using the norms derived from an earlier study,14 we have shown in this communication that severely head-injured children do have reductions in their ideal PVI or neural axis volume-buffering capacity. This occurs independently from the absolute ICP. Furthermore, reduced PVI is an accurate predictor of impending intracranial hypertension. In analyzing the data presented in this paper, it is important to remember that these patients were also undergoing treatment for intracranial hypertension. Many of the children studied did not develop sustained elevations of intracranial hypertension because treatment to reverse the trend was already underway. In some of the patients treated earlier in this series, before it was apparent that a markedly reduced PVI was predictive of incipient pressure elevations, patients succumbed to abrupt elevations of ICP. Later in this series, four patients were treated earlier for intracranial hypertension, so that some patients who had markedly reduced PVI did not develop unmanageable intracranial hypertension. Only one of these children developed markedly elevated ICP, and this occurred only in small peaks. All of these children have done well, with total recovery, and have returned to their school environments.

The degree of compromise of PVI bore a direct relationship to the ability to control ICP. Patients with PVI less than 60% of the predicted normal invariably experienced elevated ICP that required vigorous treatment (barbiturates, osmotherapy, and CSF drainage). When PVI was less than 50% of the predicted normal, ICP management was usually unsuccessful. In these settings pressure-volume relationships are characterized by steep ICPV curves, with marked depletion of volume-buffering reserves. The addition of small increments of volume created by the pathophysiological imbalances within the cranium are probably enough to create refractory intracranial hypertension and, ultimately, poor outcome.

Perhaps the most important finding in this study was the identification of eight children with reduced PVI and initial ICP below 20 mm Hg who later developed intracranial hypertension. Not only did the PVI identify those at risk of developing high ICP, but it shed light on the mechanism operative within the neural axis to accommodate mass. All of these children were able to maintain relatively normal ICP by progressively depleting volume-buffering reserves. As volume accumulates within the cranium, ICP is maintained at relatively normal levels either by expressing blood volume from the venous side of the cerebral vasculature,8 or by compression of the CSF spaces.8 The activation of these mechanisms leads to a decrease in PVI so that pressure-volume relationships are now described by steeper ICPV curves. As shown by Miller, et al.,10 the identification of depletion of volume-buffering reserves signifies a potentially unstable situation with respect to ICP. The rapidity with which ICP can change in this setting reaffirms the need for identifying these high-risk patients.

This study has shown a method for identifying this high-risk group; however, the mechanism responsible for the derangement in volume distribution and pressure regulation within the neural axis has not been delineated. Brain edema was conspicuously absent from the early CT scans of these patients, so that we infer, as have others,2 that alterations in vascular volume are partly responsible for the early intracranial hypertension. It is hoped that studies correlating cerebral blood flow abnormalities with PVI changes might unravel the pathophysiological sequence leading to intracranial hypertension in head-injured children. This may be especially important in the patients treated with barbiturates, for we found that the PVI
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improved within hours after inducing barbiturate coma.

The incidence of intracranial hypertension in severe pediatric head injury is higher than that found in adults. In our study we encountered ICP of greater than 20 mm Hg in 86% of our patients, similar to the 81% reported by others. However, in contrast to Bruce, et al., who encountered few children with elevated ICP when their GCS score was greater than 5, our experience leads us to believe that any child with GCS scores of 8 or less may have raised ICP. Other risk factors along with GCS scores include CT evidence of cerebral contusion and diffuse cerebral swelling.

At first glance, our mortality rate of 23% appears higher than that reported by others for severely head-injured children. If the two deaths unrelated to the CNS are excluded, severe head injury alone accounts for a 14% mortality rate, similar to the 10% reported by Bruce, et al. However, quality of survival does not approach that experience. Only 59% of patients had good recovery or moderate disability, whereas four patients (18%) had severe disability or a persistent vegetative state. In contrast to other series showing a relatively low incidence of brain contusions in head-injured children, 41% of severely injured children in this study had cerebral contusions. Even though focal anatomic injury of the brain did not invariably prejudice outcome, the majority of the children with contusions had moderate or severe deficits. Despite the differences in quality of survival, both studies clearly document that the severely head-injured child has a better chance of meaningful survival than does an adult with a similar GCS score.

Based on our experience, we advocate aggressive ICP monitoring of all head-injured children with GCS scores of 8 or less. The high incidence of ICP elevations reported herein leads us to conclude that tests of neural axis compliance, such as the PVI technique, should be used to identify the patients who will invariably develop intracranial hypertension. Since ICP peaks can develop abruptly without warning, and can be uncontrollable, we also advocate treatment of severely compromised neural axis compliance in an anticipatory fashion, to prevent the development of refractory intracranial hypertension. We believe that this aggressive approach is justified by the high salvage rate demonstrated by this and other studies.

References