Intracranial Pressure - Basic Concepts and Management

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Abstract

The basic concept of Intracranial Pressure and its elivation in pathological conditions is discussed. The e&ects of Barbiturates, Corticosteroids, Furosamide, man-nitol, urea hyperventilation and hypothermia are mentioned. Experimental data from the published literature are reported.

The brain, by virtue of the fact that it is encased in a container with rigid walls, is unique among the organs of the human body. The resultant restricted ability of the intracranial contents to expand implies that the intracranial pressure (ICP) is a parameter of great importance for intracranial hemodynamics (Krayenbuhl, 1974).

This inter-relation between ICP and intracranial hemodynamics is directly related to the cerebral (blood flow (CBF), as expressed in this equation:

$$CBF = K \frac{SAP\text{-}ICP}{CVR}\text{(Krayenbuhl, 1974)}$$

SAP-Systemic Arterial Pressure

CVR.-Cerebral Vascular Resistance

CPP=SAP-ICP

Autoregulation of the CBF, i.e., the vasomotor mechanism which maintains an adequate CBF in spite of variations of cerebral perfusion pressure may thus become manifest not only when systemic blood pressure falls, as in other organs, but also in the fact of increase in intracranial pressure.

The craniospinal intradural space (is, it should be emphasized, almost constant in volume, and its contents are nearly uncomprehensable. Any local increase of pressure leads to a compensatory evacuation of CSF into another area. The inter-relationships between factors such as these are expressed by the Monroe-Kelly Doctrine, whose essential features may briefly be portraryed in this manner:

^{V}Brain+^{V}Blood+^{V}CSF+^{V}Expanding

Lesion = ^{V}intracranial Space.

Finally, the compensations that occur in the craniospinal space to maintain a normal intracranial pressure can be represented by Lanffit's Curve.

Control of Increased Intracranial Pressure Osmotic Diuretics

Osmotic diuretics have been described by Mudge (Goodman and Gillman, 1971) as those electrolytes which: (1) are freely filterable at the glomerulus, (2) undergo limited reabsorption by renal tubules, and (3) are pharmacologycally intert.

Given in large doses they contribute significantly to the osmolarity of plasma, glomerular filtrate and the tubular fluid. The reduction in intracranial pressure attendant on their use is due to withdrawal of water from the intracranial contents by osmosis.(Thus, these agents increase the osmotic activity of blood above that of brain fluid will subsequently itself increase slowly as a result of influx of the compound and an out-flux of water. In fact, when the infusion is stopped, the osmotic pressure of blood may actually fall below that of brain. The flux of water is than reversed, and the intracranial pressure starts rising once more, at times exceeding pretreatment levels (Krayenbuhl, 1974).

Following the discovery by Weed and McKillen in 1919 that intravenous hypertonic sodium chloride was followed by a fall in ICP and a reduction in brain bulk, the principle of therapeutic osmotic manipulation was exhibited. Not until Javid are Settlage in (1957) introduced intravenous urea,

however, did this principle become accepted practice. It is now widely recognized that Hypertonic solutions given intravenously produce cerebral decompression yb altering osmotic gradient between blood and brain. A number of agents may be used for this purpose.

Urea

Urea is a non-polar unionised water soluble material that penetrates most cell membranes.It penetrates slowly into the brain and CSP sufficiently to create an osmotic gradient (Goodman and Gillman, 1971). Its differential uptake into various compartments of brain is based upon a "fast" and complete penetration of grey matter as contrasted with a "slower" and less complete entrance into white matter (Shenkin et al., 1965). It penetrates more slowly into Myelin than into other tissue constituents. As a result, the water is functionally compartmentalized into intracellular, interstitial and Myelin comporents.

The initial response to a high osmotic gradient between the water in plasma and water in brain is movement of water out of all compartments of brain, predominantly from the(grey matter. The release of water at different rates appears to be the explanation for the biexpon-ential fall in CSF pressure observed following the infusion of urea (Shenkin et al.,(1965).

Urea is usually given at 2 grams per kg body weight. (When prompt effect is needed 20 mg of 30% urea is given at 3 cc per minute. The effect starts as early as 2 minutes and lowest pressures are reached after 18.4 minutes. Mannitol in an equivalent dosage takes 43.9 minutes for the same pressure end-points. Such low pressures persist longer than with urea (Shenkin et al., 1969, 1970).

Amongst the side effects of urea usage one may enumerate;

(1) Infiltration in subcutaneous [issue, causing necrosis and slowing.
(2) Dehydration.
(3) Hemoglobinuria (Prevented by mixing urea with 10% intert sugar).
(4) Abnormality of prothrombin time.
(5) Rebound of CSF. A decrease in intracerebral water is compensated by an increase of blood and CSF volume. Increased bleeding may therefore (result in surgery.

Mannitol

Mannitol is the alcohol of 6-carbon sugar mannose. In molecular configuration it is similar to glucose, but is not metabolized and remains entirely in an extracellular distribution. It was introduced into Neurosurgery by Wise and Chater in 1961 who demonstrated that in comparison with uea. Mannitol reduces tha CSF pressure for a longer period of time and with little if any rebound effect (Shenkin et al., 1969 and 1969). Since Mannitol does not enter the intracellular compartment as does Urea, the creation of a reverse osmotic gradient on excretion of the substance aftr the cessation of infusion would tend to be minimal.

Wise (1961) employed a dose of 2.5-4.25 grams per kilogram given intravenously over a period of 30-90 minutes. Shenkin et al. (1965, 1969, 1970) found that 30% Urea and 20% Mannitol delivered rapidly (10-20 minutes, intravenously) resulted in a satisfactory control of CSF pressure. As with other osmetic diuretics, the time and rate of infusion appear as important as the total dose in producing the desired therapeutic effects.

The expansion of the plasma volume which occurs with the intravenous infusions of hypertonic solutions can cause circulatory overload and pulmonary edema, especially in elderly patients with heart diseases. The abnormality of prothrombin time does not occur after Mannitol treatment.

Sucrose

It was reported by Bullock et al (1935) that Sucrose, an agent which does not diffuse into brain or CSF, causes and osmotic diuresis in dogs. Indeed it appeared to induce a substantial reduction in ICP for an extended period and without a rebound effect. However Patterson (1942) reported no consistant reduction in spinal fluid pressure in normal humans, or in patients with increased intracranial pressure.

Non-Osmotic Diuretics

Furosemide

Furosemide or 4-Chloro-N-Furfuryl-5-Su!-famoylanthranilic acid, inhibits primarily reab-sorption of sodium and Chloride in the proximal and distal tubules as well as in the loop of Henle. The action at the distal tubule is independent of any inhibitiory effect on carbonic anhy-drase and aldosterone. Additionally it decreased cerebral spinal fluid production, thereby decreasing cerebral elastance (Polly, 1975). It also causes marked diuresis; given intravenously the onset of diuresis is as early as 5 minutes, the peak effect occurring within half an hour and the duration of its effect lasting approximately 2 hours.

There is substantial evidence both clinically (Bergland, 1975; Meing, 1976) and in experimental animals (James, 1978; Baethmann, 1975, Clasen, 1974) that furosemide reduces increased intracranial pressure. James et al. (1978) compared the effects of furosemide, Dexamethasonc, and Mannitol in experimental animals by producing cytotoxic edema, by administering 6-amino-nicotinamide intrapeiitonially in rats and by following the parameters of E.E.C., intracranial pressure, elastance measurements, the brain peptides in which the furosemide treated animals had significant (P<0.001) benelits. However, the reduction in the water content of the brain in furosemide treated animals was only second to that of Mannitol.

Corticosteroids

Corticosteroids have recently enjoyed great popularity in the management of increased ICP. It has long been known that ACTH and adrenal cortical extracts have an influence on capillary permeability. Prados et al. (1945) found that such agents counteract experimental brain swelling produced by exposure to air. Since then, there has been extensive clinical experience attesting to the clinical applicability of agents of this sort in reducing edema, seen perhaps most strikingly in patients with metastatic brain tumors. Kullberg and West (1965) reported a decrease in number and frequency of Traube Herring-Mayer waves in patients with increased intracranial pressure treated with steroids.

The precise mode, or modes, of action of corticosteroids remain unclear. The improvement in the neurological status of the patients (French et al., 1964) is in all likelihood an expression of reduction of edema ,perhaps by virtue of a stabilizing effect on cell membranes with a redistribution of water and electrolytes in situations of edema characterized by changes in cell membrane permeability while their anti-inflammatory effect may be helpful in conditions where necrosis excites inflammation. There is also some evidence that steroids may reduce CSF production (Reulen and Schuman, 1972).

The dose of steroid varies according to the indications. According to Kullberg's experiment (Kullberg et al., 1965) Dexamethason 16-24 mg., daily shewed a definite decrease in 24 hours mean ventricular fluid pressure. Out of five patients, 2 had a decrease on the first day while others had a delay of 2 to 8 days. However, I patient showed dramatic improvement within 24 hours without any change in pressure.

Withdrawal is performed over weeks to permit restoration of normal adrenal cortical functions and to diminish the risk of recurring edema. In long term treatment steroids are reduced to the lowest levels that maintain symptomatic control.

Amongst the side effects of steroid therapy under these circumstances, impairment in wound healing and an increased risk of infection must be considered. Gastrointestinal bleeding develops in some patients and the routine use of antacids or drugs like cimetidinc is recommended. Steroid induced psychosis may occur, although uncommonly, but should be kept in mind.

Hyperventilation

It has long been known that hyperventilation reduces increased intracranial pressure, presumably by virtue of its effect on the concentration of carbon dioxide in the blood. Since CO_2 rapidly diffuses through biological membranes, the PCO_2 in all fluid compartments is in equilibrium. An increase in extracellular pH results in constriction of cerebral arterioles with a consequent increase in peripheral vascular resistance and fall in cerebral blood flow. This in turn leads to a fall in the intracranial pressure; the reverse pertains when the pH falls. It is known, for example, that in regions of cerebral

contusion, tissue necrosis results in a local release of CO_2 and acidosis; that leading in turn to an increase in cerebral blood flow and thus in accordance with the relationship previously cited, a rise in intracranial pressure. Increase in PCO_2 to 50 mm Hg in a normal person can increase CBF by an average of 55%. Hyperventilation used in such circumstances rapidly lowers PCO_2 in the blood, and a striking reduction in brain congestion may be observed, along with marked reduction in pressure waves (Krayenbuhl et al., 1974).

Clinically, hyperventilation is most widely used during craniotomy under general anesthesia where a reduction in brain volume and decrease in intracranial pressure is desired to prevent respiratory embarrassment and herniation.

Hyperventilation if carried for an extended period of time may cause hypoxic damage to the brain as a result of hypocapnic cerebral vasoconstriction usually at PCO_2 below 20 mm Hg. (Bohr effect on the Haemoglobin Dissociation Curve). Hyperventilation with air reduces lactate/ pyruvate ratio, and cause changes in brain tissue, indicating tissue hypoxia (Plum and Posner, 1972).

Hyperberic Oxygen

Miller et al. (1970) showed that experimentally produced increased ICP in dogs can be reduced by 30% by increasing PCO_2 to above 1000 mm Hg. This is thought to be due to constriction of cerebral vessels in hypocap-nia with a consequent decrease in CBF.

Hypothermia

The application of hypothermia during neurosurgical procedures was initially based on the wish to protect the brain against ischemia in the course of temporary clamping of cerebral arteries during aneurysm surgery. Thus Bigelow et al. (1951) and Boereema et al. (1951), demonstrated that at body temperature of 20°C, dogs were able to tolerate total circulatory arrest for a period of 15 minutes. The explanation offered was one of slowing the brain metabolism and decrease in oxygen consumption. Consequent to the use of hypothermia, decrease in the intracranial pressure and brain bulk was elicited and confirmed by ventricular fluid pressure monitoring by Lundberg and Nielson (1959-1962).

Bloch (1967) using prolonged hypothermia in patients with malignant brain tumors found that although hypothermia temporarily alleviated the symptoms, they tend to recur on rewarm-ing. He also noted further risk of deterioration due to complications such as metabolic acidosis, hypothermia and an increase in intracranial pressure from cerebral edema and congestion due to a rebound effect. It however still remains a useful method in the hands of some neurosurgeons to reduce ICP due to head trauma.

Barbiturate-Augmented Hypothermia

It is well known that hypothermia reduces the intracranial pressure and can preserve the brain from anoxia by reducing the oxygen consumption. The reported reduction in the intracranial pressure by addition of barbiturates seems to have a promising future (Shapiro et al., 1974).

Thiopental has been reported to have reduced intracranial pressure within 0.5-3 minutes in craniotomy patients (Shapiro et al., 1974). Tshii (1959) has demonstrated a reduction in intracranial hypertension in brain damaged cats which was refractory to Urea. Since both barbiturates and hypothermia have similar effects on cerebral metabolism, it has been hypothesised that the therapy of barbiturate-augmented hypothermia would be more effective.

Shapiro (1974) reported such a therapy in five severely brain injured patients. There were three survivors and two deaths, one of which was upon rewarming. The patients were injected slowly with intravenous doses of Pentobarbital (adults 400 mg., children 15 mg.) and subsequent hourly doses were adjusted to maintain serum barbiturate levels between 2.7 mgs.-3.3 mgs.. During the therapy the patients were maintained on volume respirators, treated with steroids, osmotic diuretics, water restriction and hyperventilation; the rectal temperature was maintained at approximately 30°C.

It has been shown that barbiturates reduce cerebral blood volume and intracranial pressure. They

further reduce the intracranial pressure after it has been reduced by other effective modes of treatment like hyperventilation and osmotic diuretics.

However, it is not known whether the barbiturates act on the healthy brain with intact vasomotor control or upon damage tissues which has lost its ability to regulate its tone in response to changes in PCO2 and blood pressure.

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