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Brain death and intraocular pressure

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Abstract

The authors report on the behavior of the intraocular pressure of 20 patients who had sustained severe head injury. The 8 patients who retained normal intraocular pressure all survived. The 12 patients who developed intraocular hypotony all suffered brain death. Although optic disc edema was not noted in any brain-dead patients, we did find signs of fundus ischemia in most.

Keywords: Brain death, head injury, intraocular pressure, ophthalmoscopy.

1 Introduction

Declaration of brain death is normally established by clinical criteria [4] whereby the demonstration of isoelectric electroencephalograms (EEG's) is helpful. Early diagnosis of brain death is especially important in cases who are potential organ donors.

Because in patients treated with barbiturates an isoelectric EEG only mimicks brain death, in these cases it can not be used as a brain death criteria. The measurement of the intraocular pressure (IOP) is a simple method to plan cerebral angiography as in indication of the time of brain death. Serial measurements of IOP thus provide a simple indication for the usefulness of angiographic demonstration of lack of intracranial flow.

2 Material und methods

This study includes 20 patients with severe head injury who underwent serial measurements of IOP. Of these patients 13 had a closed head injury (3 acute subdural hematomas, left hemisphere; 1 intracerebral hematoma, right frontal; 9 diffuse severe brain edema) and 7 an open head trauma (1 acute epidural hematoma, large bifrontal; 2 acute subdural hematomas, right hemisphere; 2 depressed skull factures; 2 diffuse severe brain edema).

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Management included intubation and controlled ventilation, computerized tomography, and early surgery for hematomas. Treatment for intracranial hypertension included hyperventilation, barbiturate coma (2–5 gm/kg body weight/hour sodium thiopentone), steroid administration (dexamethasone, 6×8 gm, i.v.), and administration of mannitol for intracranial pressure (ICP) elevation uncontrolled by barbiturate coma. In the intensive care unit, ICP monitoring by means of the Gaeltec epidural pressure transducer was performed with treatment of pressure values higher than 20 mm Hg. Normal ICP was defined as below 15 mm Hg. Systemic blood pressure was measured with a radial artery cannula. The cannula was connected to a pressure transducer and recorder. All patients underwent continous EEG monitoring via scalp electrodes using a four channel Rikadenki recorder.

The IOP was measured three times daily with a Schioetz tonometer with the patient in lying position. IOP values between 10 and 20 mm Hg were considered normal. Eyes were controlled serially using direct ophthalmoscopy for changes of the fundus, in particular swelling of the optic disc. In addition, in some patients color photographs of the fundus were taken. Possible effects of barbiturates on IOP were studied in so-called normal subjects, i.e., patients who had undergone a lumbar disc operation. Baseline IOP's were measured before the operation. Immediately after the operation the measurements were repeated. Statistical analysis was performed with the WILCOXON test for comparison of paired and unpaired samples. P values of < 0.05 were considered significant. All summary data are expressed as means $\pm$ standard error of the mean.

3 Results

The age of the patients ranged from 4 to 79 years (mean age 32,2 years). Of the 20 patients, 15 were

males. The 20 patients were divided into two groups according to their outcome (Group I: survivors with post-traumatic acute midbrain syndrome and normal IOP. Group II: nonsurvivors with post-traumatic acute midbrain syndrome and intraocular hypotony).

3.1 Group I: Survivors with post-traumatic acute midbrain syndrome and normal IOP

There were 8 patients (7 males, 1 female) in the survivor group, ranging in age from 7 to 79 years (mean age 27 years). The mean IOP (± standard error of the mean) for the series during the observation period of 6.4 days was 15.1 ± 0.6 mm Hg (Figure 1) (range 12.4 ± 0.4 to 17.3 ± 1.1 mm Hg; Table I). ICP was monitored in all patients but not in one whose bifrontal extradural hematoma had been removed so that immediate results of the acute operation were clear. The mean ICP during the observation period of 4.9 days was 9.9 ± 1.9 mm Hg (Figure 1), range 5.3 ± 0.8 to 19.8 ± 1.9 mm Hg (Table I). In all these patients, continous EEG monitoring always revealed an unequivocally positive EEG.
Figure 2 shows the course of the mean IOP and ICP values between day 1 and 8.

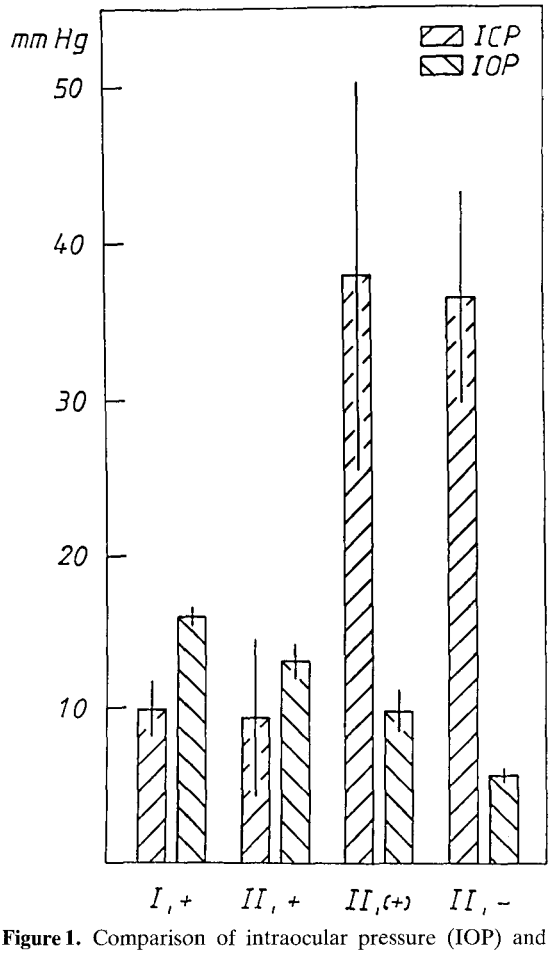

Figure 1. Comparison of intraocular pressure (IOP) and intracranial pressure (ICP) (Means ± SEM) in head-injured patients with various EEG patterns. Group I: N = 8, survivors. Group II: N = 12, nonsurvivors. EEG + = positive, EEG (+) = reduced positive, EEG – = isoelectric electroencephalogram.

3.2 Group II: Nonsurvivors with post-traumatic acute midbrain syndrome and intraocular hypotony

All of the 12 fatally brain-injured patients died. Out of these (8 males, 4 females), the youngest was 4 and the oldest 74 years of age (mean 37.6 years). The mean observation and monitoring period for IOP and ICP measurements was 5.7 and 6.0 days, respectively. At the time of unequivocally positive EEG activity, the values for IOP and ICP were 13.1 ± 1.1 mm Hg (N=6) and 9.3 ± 5.2 mm Hg (N=2), respectively. In the state of reduced EEG activity, the mean IOP decreased to 9.8 ± 1.4 mm Hg (N=8), but there was also an increase in ICP values to 37.8 ± 12.4 mm Hg (N=3). A marked fall in mean IOP to 5.6 ± 0.5 mm Hg (N=12) was found when the EEG was isoelectric; the mean ICP was 36.4 ± 6.7 mm Hg (N=6) (Figure 1 and Table II).

Figure 3 shows the course of mean IOP and ICP values between day 1 and 8.

No case of optic disc edema (ODE) could be identified, but in 10 brain-dead patients peripapillary ex-

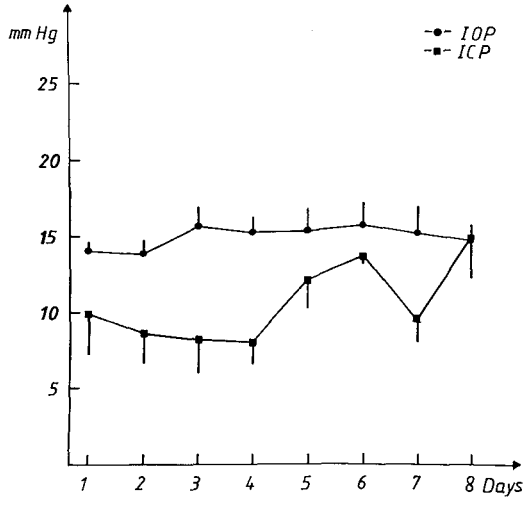

Figure 2. Intraocular pressure (IOP) and intracranial pressure (ICP) in head-injured patients, Group I (N = 8, no brain death) during the observation period of 8 days (Means ± SEM).

Table I. Group I (no brain death). Results of 8 patients with acute midbrain syndrome after severe head injury. Age and sex distribution. Relationship of intraocular pressure (IOP), intracranial pressure (ICP) and electroencephalogram (EEG) activity during the mean observation period of 6.4 and 4.9 days for IOP and ICP, respectively. Ophthalmoscopy.

Patient	Age/Sex	IOP[a] (mm Hg)	ICP (mm Hg)	EEG	Fundus
1	22 / M	16.7 ± 0.7	9.0 ± 1.4	+	Ø ODE
2	19 / M	13.2 ± 0.1	6.9 ± 1.5	+	Ø ODE
3	25 / M	17.3 ± 1.1	7.6 ± 1.8	+	Ø ODE
4	79 / M	15.5 ± 1.8	19.8 ± 0.2	+	Ø ODE
5	22 / F	12.4 ± 0.4	12.1 ± 0.9	+	Ø ODE
6	7 / M	15.2 ± 0.9	8.3 ± 1.7	+	Ø ODE
7	23 / M	16.6 ± 0.9	——[b]	+	Ø ODE
8	19 / M	13.6 ± 0.6	5.3 ± 0.8	+	Ø ODE
Total	27 / 7 M, 1 F	15.1 ± 0.6	9.9 ± 1.9	+	Ø ODE

[a] Each patient contributes one value, representing the average of the two eyes. [b] No epidural pressure tranducer. + = Unequivocally positive electroencephalogram. ODE = Optic disc edema. Data or IOP and ICP are arithmetic means ± SEM for 8 and 7 patients, respectively.

Table II. Group II (brain-dead patients). Results of 12 patients with an acute midbrain syndrome after severe head injury. Age and sex distribution. Relationship of intraocular pressure (IOP), intracranial pressure (ICP) and electroencephalogram (EEG) activity during the mean observation period of 5.7 and 6.0 days for IOP and ICP, respectively. Ophthalmoscopy.

Patient	Age/Sex	IOP[a] (mm Hg)	ICP (mm Hg)	EEG	Fundus
1	63 / M	15.1 ± 1.4	4.1 ± 0.9	+	Ø ODE, H, E
		7.5 ± 0.4	5.0 ± 1.0	−	
2	34 / M	4.6 ± 0.2	——[b]	−	Ø ODE, H, E
3	4 / F	5.2 ± 0.1	——[b]	(+)	Ø ODE
		4.5 ± 0.1	39.3 ± 19.0	−	
4	36 / M	13.0 ± 1.8	14.5 ± 1.8	+	Ø ODE, H, E
		7.9 ± 0.6	38.0 ± 12.0	−	
5	74 / M	17.8 ± 4.0	——[b]	(+)	Ø ODE, H, E
		5.9 ± 0.2	——[b]	−	
6	45 / F	9.4 ± 1.5	41.2 ± 23.7	(+)	Ø ODE, H, E
		4.6 ± 0.4	51.6 ± 4.2	−	
7	53 / F	10.9 ± 0.5	——[b]	+	Ø ODE
		5.9 ± 1.2	——[b]	−	
8	18 / M	17.6 ± 0.9	——[b]	+	Ø ODE, H, E
		11.3 ± 0.4	——[b]	(+)	
		8.5 ± 1.1	——[b]	−	
9	47 / F	11.3 ± 7.1	——[b]	(+)	Ø ODE, H, E
		5.3 ± 0.5	——[b]	−	
10	25 / M	6.1 ± 0.9	57.3 ± 3.0	(+)	Ø ODE, H, E
		6.0 ± 0.9	46.5 ± 1.5	−	
11	36 / M	12.0 ± 1.0	——[b]	+	Ø ODE, H, E
		10.5 ± 0.4	——[b]	(+)	
		2.3 ± 1.6	——[b]	−	
12	16 / M	10.1 ± 0.8	——[b]	+	Ø ODE, H, E
		7.0 ± 1.3	15.0 ± 1.0	(+)	
		4.2 ± 0.1	38.0 ± 7.6	−	
Total	37.6 / 8 M, 4 F	13.1 ± 1.1	9.3 ± 5.2	+	Ø ODE, H, E
		9.8 ± 1.4	37.8 ± 12.4	(+)	
		5.6 ± 0.5	36.4 ± 6.7	−	

[a,b] See notes in Table I. H = Hemorrhage, E = Exudate, ODE = Optic disc edema. + = Unequivocally positive, (+) = reduced positive, − = isoelectric encephalogram. Data for IOP and ICP are arithmetic means ± SEM for 12 and 6 patients, respectively.

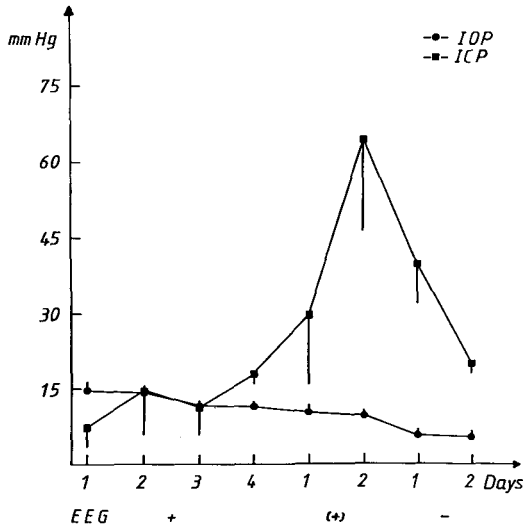

Figure 3. Intraocular pressure (IOP) and intracranial pressure (ICP) in head-injured patients, Group II (N = 12, nonsurvivors) during the observation period of 8 days (Means ± SEM). EEG + = positive, EEG (+) = reduced positive, EEG − = isoelectric electroencephalogram.

udates, narrow arterial vessels, and retinal hemorrhage could be seen (Figure 4).

4 Evaluation of the results

Initially all patients had an acute midbrain syndrome with disturbance of the pupillary light response, abnormal extensor posturing, and reduced respiratory effort. Patients who survived had constantly normal IOP's and unequivocally positive EEG activity (Group I). In contrast, those patients who developed brain death following head injury revealed a quite different IOP behavior (Group II). No correlation could be detected between normal IOP or ICP with development of brain death. The state of isoelectric EEG was related to a substantial fall in IOP to below 10 mm Hg; this phenomenon was significant ($p < 0.01$) compared with Group I. We also observed that the IOP was inversely proportional to the ICP in the state of reduced EEG activity (decrease in IOP, increase of ICP) and besides in the isoelectric state with significant ocular hypotony we observed a gradual decrease of ICP. In the controls, no ocular hypotony followed anesthesia with barbiturates, pre- and postoperative measurements of the IOP were normal (pre-operative: 15.3 ± 0.6 mm Hg; post-operative: 14.4 ± 1.0 mm Hg).

5 Discussion and conclusions

Early diagnosis of brain death in potential organ donors is important. The evaluation of the clinical criteria used for the declaration of brain death is especially complicated in patients who are in a therapeutic barbiturate coma. In these cases the EEG cannot be used for determination of brain death. Uncertainties in diagnosis can be eliminated by angiographic demonstration of lack of intracranial flow, which is a definite indication of brain death. IOP measurements are thus a valuable and simple method of investigation of the potential usefulness of cerebral angiography in patients with barbiturate coma-induced isoelectric EEG's.

Until now there have been no systematic studies to evaluate the IOP in patients who had sustained a severe head injury with and without development of brain death. Decrease of the IOP below 10 mm Hg may be a sign of beginning development of brain

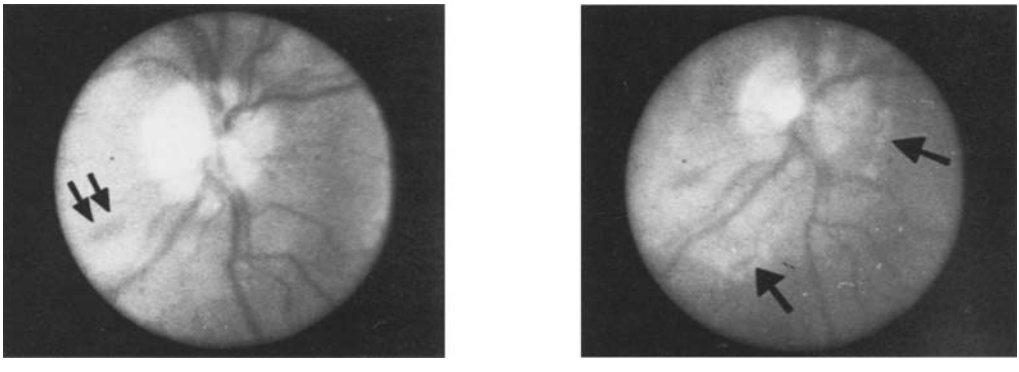

Figure 4. Photographs of the left ocular fundus in a patient before (1) and during (2) brain death after severe head injury. Compare ophthalmoscopic changes. Exudates (one arrow) and narrow arterial vessels as signs of reduced perfusion and ischemia, respectively (2). Note retinal hemorrhage (two arrows) near the temporal part of the optic disc (1 and 2). No optic disc edema.

death, but significant decreases in IOP can also be caused by a reduction of aqueous inflow after application of choleratoxin, forskolin, or isoproterenol [5]. Experimental and clinical investigations show the relationship between drug-induced blood acidosis and ocular hypotony [3]. The authors conclude that a marked reduction of bicarbonates in the aqueous humour because of a requirement by the enduvascular cumpartment corresponds to an increased flow of hydration water out of the ocular region.

Moreover it is known that adrenergic agents decrease IOP by modulating the sympathetic nervous system [2, 17]. As several authors [8] have reported, ventilation depends on parameters such as pCO_2 and pO_2, so that even anesthetics like barbiturates, can cause IOP changes. Previous studies have shown the large influence of pCO_2 on the circulation of the uveal tractus [1, 12, 14], whereby a slight hyperventilation ($pCO_2 \sim 35$ mm Hg) causes a decrease of IOP not above 5 cm of water column [1, 7, 11, 15]. Barbiturates, e.g., sodium thiopentone, are known to have a hypotensive effect on IOP [6, 13]. Pathogenesis of optic disc edema (ODE) due to increased ICP is explained by axoplasmic flow stasis in the nerve fibers of the optic nerve tip [10]. Experimental studies using rhesus monkeys established that it takes about 1 to 5 days for increased ICP to result in ODE [9].

ODE did not occur in our series. In another study of 426 patients, low grade ODE was identified after acute, severe head injury in 15 patients (3.5%). However, it is a well-known phenomenon that systemic corticosteroid treatment can produce resolution of ODE [9]. Thus, the fact that our patients were routinely given dexamethasone can explain the lack of ODE in our series. Furthermore, since ODE first appears some days after ICP elevation [9, 16] and our severly head-injured patients died early, ODE had no chance to develop. Retinal hemorrhages, a funduscopic evidence of raised ICP, were found frequently in our study.

We conclude that the appearance of intraocular hypotony is a reliable sign for beginning brain death. Thus, early determination of hypotony allows adequate time to plan and carry out further diagnostic procedures to prove brain death.

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