Acta Neurochir (2006) [Suppl] 96: 114–118

Printed in Austria

Monitoring and interpretation of intracranial pressure after head injury

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Summary

Objective. To investigate the relationships between long-term computer-assisted monitoring of intracranial pressure (ICP) and indices derived from its waveform versus outcome, age, and sex.

Materials and methods. From 1992 to 2002, 429 sedated and ventilated head-injured patients were continuously monitored. ICP and arterial blood pressure (ABP) were recorded directly and stored in bedside computers. Additional calculated variables included: 1) Cerebral perfusion pressure (CPP) = ABP − ICP; 2) a PRx calculated as a moving correlation coefficient between slow waves (of periods from 20 seconds to 3 minutes) of ICP and ABP.

Results. Fatal outcome was associated with higher ICP ($p < 0.000002$), worse PRx ($p < 0.0006$), and lower CPP ($p < 0.001$). None of these parameters differentiated severely disabled patients from patients with a favorable outcome. Higher average ICP, lower CPP, worse outcome, and worse pressure reactivity were observed in females than in males (age-matched). Worse outcome, lower mean ICP, worse PRx, and higher CPP were significantly associated with the older age of patients.

Conclusion. High ICP and low PRx are strongly associated with fatal outcome. There is a considerable heterogeneity amongst patients; optimization of care depends upon observing the time-trends for the individual patient.

Keywords: Head injury; intracranial pressure; pressure reactivity; outcome.

Introduction

Several novel methods of brain monitoring, including brain tissue oxygenation, cerebral microdialysis, and cerebral blood flow, have recently been studied and compared to more traditional techniques. However, intracranial pressure (ICP) and mean arterial blood pressure (ABP) are still gold standards in neurocritical care monitoring. Although there is no class-1 evidence that monitoring of ICP has the potential to improve outcome [7], there is consensus that without this modality the management of severely head injured patients is far from optimal. Cerebral perfusion pressure (CPP) and ICP have become therapeutic targets to prevent potentially life-threatening cerebral hypoperfusion. Therefore, several protocols for the management of acutely head-injured patients are based on a CPP-oriented therapy [9], an ICP-oriented management [6], or a mixture of both [8].

Beginning in September 1991, bedside computer-supported systems were used in our Neurosurgical Critical Care Annexe until 1993, and then in our Neurosciences Critical Care Unit (NCCU) from 1994 onward [3]. Its purpose has been to continuously monitor physiological parameters such as ICP, ABP, and CPP, and pressure-derived indices describing the state of brain homeostasis. The resultant large dataset has been used to examine our 10-year experience with head-injury monitoring. Some particular aspects are summarized, such as the relationship between Glasgow Coma Score (GCS) and outcome, influence of gender [1] and age [4] on outcome, and usefulness of ICP waveform analysis in order to predict complications associated with intracranial hypertension [2].

Patients and methods

This retrospective analysis is based on 492 head-injured patients admitted to the Annexe and NCCU between January 1992 and December 2001. Only patients with invasive monitoring of ICP and ABP over a period greater than 12 hours and connected to a bedside computerized system were included in the study. It is important to emphasize that the studied group is not representative of all admissions to the unit. Patients who were admitted and discharged promptly or died soon after admission are not included in the analysis.

Patients were sedated, mechanically ventilated, and paralyzed in order to maintain ICP below 25 mmHg. Systemic hypotension was treated with fluids and vasoactive drugs. CPP was kept above 60 to 70 mmHg to avoid secondary ischemic insults. Episodes of intracranial hypertension were treated with mild hyperventilation ($PaCO2 > 4.0$ kPa), moderate hypothermia, and boluses of mannitol and thiopentone. An external ventricular drain was inserted when

feasible, depending on the size of ventricles on computed tomography scan. In 1997, a standard ICP/CPP-oriented protocol for head injury was introduced, consisting of more aggressive management of intracranial hypertension and stricter control of ABP, aiming to minimizing the detrimental effects of hypoperfusion on brain tissue [8].

Data were analyzed retrospectively as part of the standard clinical audit and no additional intervention was associated with the bedside computer data capture of the monitored variables.

Monitoring and data analysis

ICP was monitored by an intraparenchymal probe (Camino ICP transducer in 12 patients [Integra Neurosciences, Plainsboro, NJ] or Codman ICP MicroSensors in 446 patients [Codman & Shurtleff Inc., Raynham, MA]) or through a ventricular drain and an external pressure transducer (34 cases; Baxter Healthcare Corp., Round Lake, IL) prior to 1994. ABP was monitored invasively. Signals were sampled from the analogue output of the monitors at 30 Hz, digitized (12 bits analogue-to-digital converter), analyzed as 6-second averages, and subsequently converted to 1-minute averages.

From each of the 40 samples of 6-second mean ICP and ABP, a moving correlation was calculated (pressure-reactivity index [PRx]). By averaging such a moving index over a minimum half an hour interval, pressure reactivity could be assessed. A positive correlation between ABP and ICP revealed a passive, non-reactive cerebrovascular bed. A negative correlation is specific for a reactive bed (Fig. 1A). A positive value of PRx has been previously demonstrated to be a strong predictor of fatal outcome following head injury [2, 10].

Apart from the calculation of global averaged values of ICP, ABP, CPP, and PRx, patients were classified as having gross intracranial hypertension if their mean ICP was above 35 mmHg for at least 4 hours continuously. Post-resuscitation GCS was used for analysis. The Glasgow Outcome Score (GOS) was determined at 6 months, either by follow-up clinic or by questionnaire.

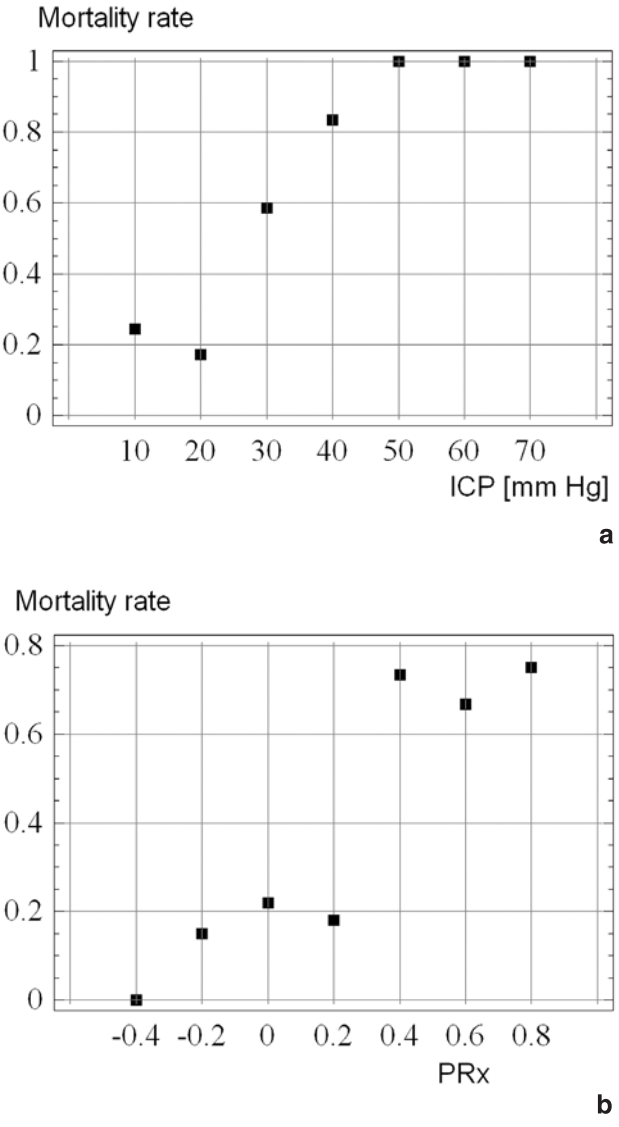

Fig. 1. (a) Mortality rate expressed as a function of intracranial pressure (*ICP*). (b) Mortality rate expressed as a function of pressure-reactivity (*PRx*)

Results

Of 492 patients included in the computer-supported monitoring, 429 were suitable for analysis, with adequate quality of the continuous recording of ICP and ABP and reliable outcome follow-up. Mean age was 34 ($\pm$16.7 years) and median admission GCS was 6 (range 3 to 15; 20% of patients had an initial GCS above 8); 21% of the patients were female. Overall, 28% of patients had a good outcome, 21% were moderately disabled, 22% severely disabled, 2% remained in a persistent vegetative state, and 27% died at 6 months.

Impact of ICP, CPP, and pressure reactivity on outcome

Outcome rates were distributed unevenly along the observed range of ICP. Mortality showed a clear breakpoint, increasing from 17% to 47% when averaged ICP increased above 20 mmHg ($p < 0.0001$; the exact threshold of ICP that minimized the p value of difference in mortality rate was 23 mmHg) (Fig. 1). This was mirrored by a decrease in good/moderate outcome rate. Severe disability rate did not show any remarkable changes dependent on ICP.

The mortality rate indicated a threshold rise from 20% to 70% when pressure reactivity deteriorated (averaged PRx increased above 0.3; $p < 0.01$) (Fig. 1). The relationship between CPP and the mortality rate revealed 2 areas where mortality rate increased. For CPP below 55 mmHg mortality was 81%, while above 55 mmHg it was only 23% ($p < 0.0001$). For

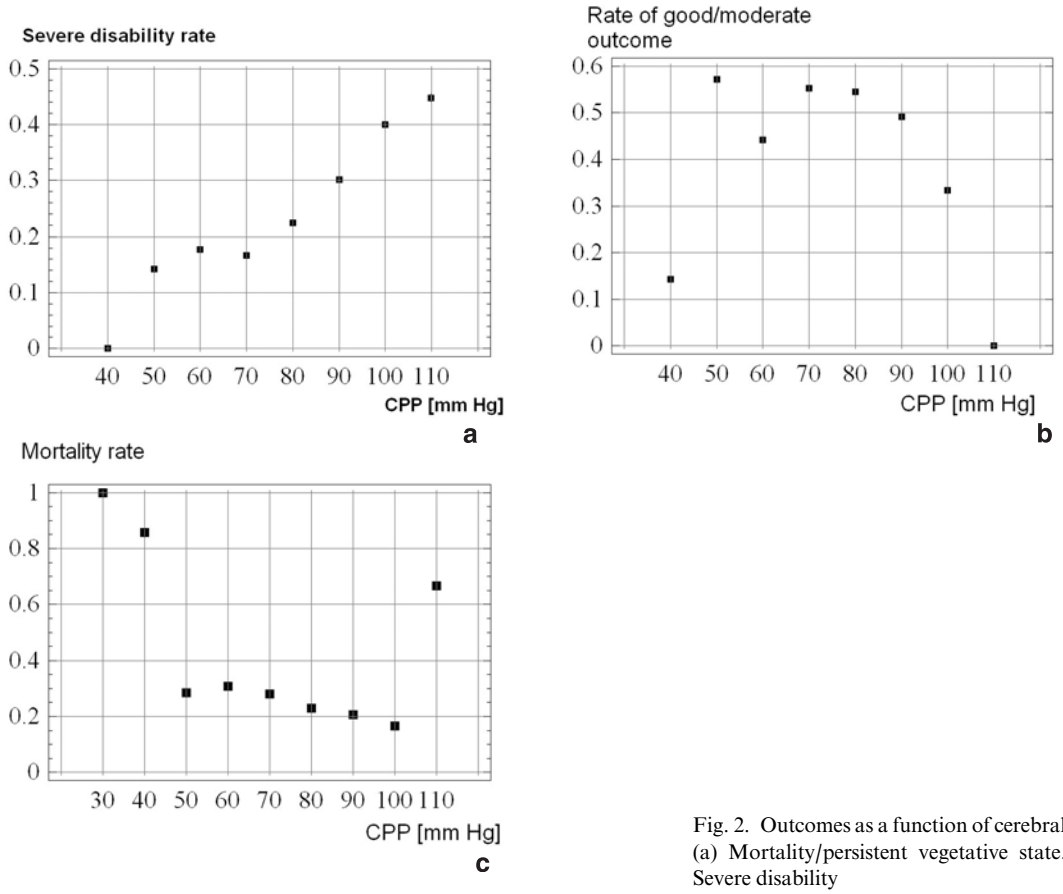

Fig. 2. Outcomes as a function of cerebral perfusion pressure (*CPP*). (a) Mortality/persistent vegetative state. (b) Good/moderate. (c) Severe disability

CPP above 95 mmHg mortality was 50%, while below was 20%, although this difference was not significant.

However, a CPP greater than 95 mmHg had a detrimental effect on good and moderate outcome. For CPP above 95 mmHg the rate of good and moderate outcome was 28%, while below it was 50% ($p < 0.033$).

The severe disability rate showed a tendency to steadily increase with CPP ($r = 0.87$; $p = 0.02$), suggesting either that a greater CPP does not help achieve a favorable outcome, or that these patients had more severe injury requiring greater intensity of treatment (Fig. 2).

Gender-related differences

ICP was significantly greater (median 15.9 mmHg, range 3.6 mmHg to 79 mmHg in males versus median 17.5 mmHg, range 5.7 mmHg to 106 mmHg in females, $p = 0.036$) and CPP significantly lower in females (males median: 76.7 mmHg vs. females 73.6 mmHg; $p = 0.007$). PRx was worse in females than males (females: 0.1 vs. males 0.04; $p = 0.022$). ABP was not different between the 2 groups. The mortality rate in females was significantly higher (females 35%, males 24%; $p = 0.029$) and rate of favorable outcome was lower (females 40%, males 25%; $p = 0.047$). The median GOS was worse in females (severe disability) than in males (moderate disability).

The rate of gross intracranial hypertension (averaged ICP above 35 mmHg) was greater in females (11%) than males (4.1%; $p = 0.012$). Averaged ICP was compared between both sexes in different outcome groups. Significant differences were only found in patients who died or persisted in a vegetative state: in females, mean ICP was 21.5 (range 9.4 to 106) mmHg in females versus 19.3 (range 3.6 to 75) mmHg in males; $p = 0.036$ (Mann-Whitney). In other outcome groups, ICP was distributed uniformly and reached a median of 16.2 mmHg both in females and males.

Influence of age

Elderly people had a worse outcome after brain trauma; the relationship between GOS and age was significant and positive ($R = 0.301$; $p < 0.0001$). The

initial GCS assessment correlated with age ($R = 0.14$; $p < 0.01$), indicating that there was a tendency to score better in elderly patients.

Monitored variables appeared to be associated with age: mean ICP had a weak tendency to decrease with age ($R = -0.14$; $p < 0.01$), ABP tended to increase with age although insignificantly ($p = 0.18$), and CPP increased with age ($R = 0.19$; $p = 0.0004$). Pressure reactivity indicated worsening of cerebrovascular control with age (PRx: $R = 0.24$; $p = 0.003$).

Discussion

Raised ICP determines outcome in terms of life and death. Above 20 to 25 mmHg, the mortality rate increases dramatically. An even more spectacular threshold can be demonstrated when PRx is considered. There is a sudden increase in mortality rate from 20% to 70% when averaged PRx increases above 0.3. Low CPP with aggressive CPP-oriented therapy is seldom an issue. The lower values of CPP observed in patients who died were mainly related to the higher values of ICP, as no significant difference was found between mean values of ABP in the different outcome groups.

The finding that a high CPP (above 95 mmHg) may reduce the rate of favorable outcome was surprising. This may suggest that an excessive increase in ABP to improve brain perfusion may be detrimental. Low ICP and CPP within the range of 50 to 90 mmHg are clinical findings that seem to justify a lower CPP target [6]. Our study is based on material gathered over a long time interval and has not been influenced by one consistent protocol. Our policy has changed a few times over the period, finishing with a mixed CPP- and ICP-oriented protocol [8].

In this group of traumatic brain injury (TBI) patients, females had a significantly greater rate of fatal outcome than males [1]. This was associated with a higher incidence of gross intracranial hypertension in females compared to males. One practical implication may be that aggressive treatment of intracranial hypertension should be administered more readily in young females than in males, as refractory intracranial hypertension is more likely to develop and lead to fatal outcome in females. Indeed, in patients with only moderately elevated global ICP (<25 mmHg), the gender-related difference in the mortality rate becomes non-significant and decreases further when this critical threshold is lowered. If ICP remains normal in TBI patients, the likelihood of a good outcome is comparable for females and males. However, if ICP rises, it appears to be more difficult to control in young females than males. In spite of the postulated neuroprotective role of estrogen in experimental studies, the susceptibility to brain swelling reported in the recently published clinical audit [5] is very likely to be an important factor.

The initial GCS in elderly patients admitted to Addenbrooke's NCCU indicates that the primary injury is usually slightly less severe. Also the post-injury course seems to be more favorable in the elderly from the point of view of brain protection against secondary insults: ICP seems to be lower and CPP higher in elderly patients. What, then, makes outcome worse if these traditionally outcome-linked factors are more favorable? It may be that critical thresholds may become less favorable in elderly patients. However, such an analysis would be impossible using our material. The only variables which deteriorated with age in our data were vascular pressure reactivity and autoregulation [4]. This association may suggest that worsening of the indices of blood-flow regulation with age is responsible for the worse outcomes. Indeed, in all our previous studies, when these indices were considered they were strong and independent predictors of outcome after TBI.

Conclusion

In addition to low CPP and high ICP, cerebral PRx should become a target in post-injury intensive care. Vasopressors should be used with moderation. Young women should be treated more aggressively when they develop intracranial hypertension (possibly including surgical decompression), as their mortality rate associated with raised ICP is greater than in males.

Acknowledgments

The authors are in debt to all team members participating in data collection: Dr. M. Hiler, Mrs. Pippa Al-Rawi, Mrs. Helen Seeley, Mrs. Carole Turner, Mrs. Colette O'Kane, Mrs. Shirley Love, Mrs. Diana Simpson, Dr. Eric Schmidt, Dr. Stefan Piechnik, Dr. P. Smielewski, Dr. Andreas Raabe, Mr. Eric Guazzo, Dr. David Menon, Dr. Arun Gupta, Mr. Peter Kirkpatrick, Mr. Rupert Kett-White, Mr. Pwawanjit Minhas, Mr. Rodney Laing, and all the nursing and research staff of NCCU.

P.J.H. is supported by an Academy of Medical Sciences Health Foundation Senior Surgical Scientifist Fellowship.

M. Czosnyka is on unpaid leave from Warsaw University of Technology, Poland.

This project was supported by the U.K. Government Technology Foresight Initiative, and the Medical Research Council (Grant No G9439390 ID 65883).

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