Early Changes in Brain Oxygen Tension May Predict Outcome Following Severe Traumatic Brain Injury

J.K. Rhodes, S. Chandrasekaran, and P.J. Andrews

Abstract We report on the change in brain oxygen tension ($P_{bt}O_2$) over the first 24 h of monitoring in a series of 25 patients with severe traumatic brain injury (TBI) and relate this to outcome. The trend in $P_{bt}O_2$ for the whole group was to increase with time (mean $P_{bt}O_2$ 17.4 [1.75] vs 24.7 [1.60] mmHg, first- vs last-hour data, respectively; $p=0.002$). However, a significant increase in $P_{bt}O_2$ occurred in only 17 patients (68 %), all surviving to intensive care unit discharge ($p=0.006$). Similarly, a consistent increase in $P_{bt}O_2$ with time occurred in only 13 patients, the correlation coefficient for $P_{bt}O_2$ versus time being ≥0.5 for all survivors. There were eight survivors and four non-survivors, with low correlation coefficients (<0.5). Significantly more patients with a correlation coefficient ≥0.5 for $P_{bt}O_2$ versus time survived in intensive care ($p=0.039$). The cumulative length of time that $P_{bt}O_2$ was <20 mmHg was not significantly different among these three groups. In conclusion, although for the cohort as a whole $P_{bt}O_2$ increased over the first 24 h, the individual trends of $P_{bt}O_2$ were related to outcome. There was a significant association between improving $P_{bt}O_2$ and survival, despite these patients having cumulative durations of hypoxia similar to those of non-survivors.

Keywords Brain oxygen tension • Traumatic brain injury • Hypoxia • Outcome

Introduction

The measurement of intracranial pressure (ICP) is an established monitoring modality in many units managing patients with traumatic brain injury (TBI). However, despite control of ICP and maintenance of cerebral perfusion pressure (CPP) to guideline targets, significant cerebral hypoxia can still be measured [16]. In recent years, the direct measurement of brain tissue oxygen tension ($P_{bt}O_2$) is also possible with the use of commercially available parenchymal catheters.

Experience with $P_{bt}O_2$ monitoring has demonstrated that both episodic cerebral hypoxia and the cumulative hypoxic period are significantly associated with adverse outcome [15, 19]. Furthermore, manipulation of physiological variables such as CPP and the control of ICP, aiming to maintain cerebral blood flow, can improve $P_{bt}O_2$. Management based on such a $P_{bt}O_2$-guided approach is associated with improvement in outcome after TBI [1, 12, 14, 15], although this is not yet supported by high-quality, randomised, controlled trials. In this chapter we report our experience of introducing $P_{bt}O_2$ monitoring in a series of patients with severe TBI who were admitted to a tertiary neurosurgical referral centre and university teaching hospital.

Materials and Methods

The Western General Hospital is the tertiary referral centre for neurosurgical emergencies in South East Scotland. Since May 2010, patients with severe TBI admitted to intensive care and requiring intubation, sedation and ICP management have also received $P_{bt}O_2$ monitoring using the Integra Licox system (Integra, France). Patients were managed in accordance with Brain Trauma Foundation guidelines [17]. Patients were admitted either directly to the intensive care unit (ICU) or following surgical intervention for mass lesions. Patients were intubated and ventilated (to achieve a partial pressure of carbon dioxide [$PaCO_2$] of 4.5–5.0 kPa), sedated and nursed with 30° head elevation. CPP was controlled (≥60 mmHg) by the regulation of mean arterial pressure (MAP) with fluids and noradrenalin and the limitation of ICP (≤20 mmHg).

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B.-T. Ang (ed.), *Intracranial Pressure and Brain Monitoring XV*, Acta Neurochirurgica Supplement, Vol. 122,
DOI 10.1007/978-3-319-22533-3_2,

$P_{bt}O_2$, ICP and brain temperature were measured via oxygen electrode, fibre-optic pressure catheter and thermistor, respectively; these were inserted into brain parenchyma via a dedicated triple lumen bolt placed through a burr hole (Integra Neurosciences, Andover, UK). The bolt was placed so that the monitors were inserted into the frontal white matter. In the case of diffuse injuries this was into the non-dominant hemisphere. If the dominant injury was focal, the bolt was placed on the side of maximal injury, unless this would place the oxygen electrode in non-viable tissue.

Sustained elevations of ICP (>20 mmHg for >5 min, not secondary to inadequate sedation, high intrathoracic pressures, poor positioning, cardiovascular instability, hypoxia or hypercapnia) led to an escalation of therapy that included the use of hypertonic fluids (5 % NaCl 125 ml or 20 % mannitol 200 ml boluses), paralysis and further computed tomography scanning. Lesions amenable to surgical intervention were resected. Cerebrospinal fluid was not drained. Barbiturate coma to burst suppression, mild hypothermia (32–35 °C) and decompressive craniotomy were all therapeutic options for refractory ICP elevation. Pyrexia >38 °C was managed with paracetamol and cooling blankets. All patients received loading with phenytoin (20 mg/kg) and maintenance treatment (4–5 mg/kg/day) for 7 days after injury.

Minute to minute physiological data, including $P_{bt}O_2$, brain temperature, heart rate, CPP, MAP and ICP, were recorded on a bedside computer. ICU Pilot software (CMA, Kista, Sweden) was used to integrate the data from different sources. Data were continuously collected, except for interruptions due to CT scanning or surgical intervention, until ICP monitoring was no longer required or the patient died. Data from the first 2 h of $P_{bt}O_2$ monitoring were excluded from the analysis to ensure that the results were not influenced by the time required for the oxygen electrode to stabilise. During the study a simple treatment algorithm was developed to guide the management of patients based on $P_{bt}O_2$, the target $P_{bt}O_2$ being ≥20 mmHg This included steps to optimise partial pressure of oxygen (PaO_2), $PaCO_2$, ICP, CPP, haemoglobin concentration and cardiac output (Fig. 1).

Non-parametric data are given as median with 25th and 75th percentiles and compared using the Mann–Whitney rank sum test for unpaired and the Wilcoxon signed rank test for paired data. Multiple groups were compared using the Kruskal–Wallis test. Parametric data are given as mean ± standard error of mean (SEM) and compared using either the *t* test or analysis of variance (ANOVA) with adjustment for multiple comparisons made using the Holm–Sidak method.

Results

Between May 2010 and May 2012, a total of 30 patients with TBI required ICP monitoring. Of these 1 patient did not have $P_{bt}O_2$ monitoring. So far, data from the first 24 h of admission have been analysed in detail. Three patients were excluded from the analysis because of damage to the brain oxygen electrode on insertion. These cases occurred early in the series. One further patient was excluded because they deteriorated and died of their injuries before the 2-h settling period for $P_{bt}O_2$ data had passed. There were no infections or haematomas complicating $P_{bt}O_2$ and ICP monitoring.

The mean age of the 25 patients with successful $P_{bt}O_2$ monitoring was 40.4 ± 3.4 years, 23 (92 %) being male. TBI was caused by a fall in 11 (44 %), assault in 4 (16 %) and road traffic accident in 7 (28 %). In 2 (12 %) the cause was uncertain, the patient having been found unconscious by a passerby. The median post resuscitation Glasgow coma score in the emergency room was available for 22 patients and was 7.5 (range 3–14). Further details of the patients are given in Table 1.

To look at the adequacy of resuscitation early in the ICU, mean CPP, ICP and $P_{bt}O_2$ values over the first 4 h of stable data collection were calculated. Nineteen patients (76.0 %) had mean CPP ≥70 and ICP ≥20 mmHg respectively. However, despite the achievement of adequate CPP and the limitation of ICP, 9 of these 19 (47.4 %) had a mean $P_{bt}O_2$ of <20 mmHg. During the same 4-h period 8 patients (32.0 %) had a mean CPP ≥80 and ICP ≥20 mmHg. Of these, 3 (37.5 %) had a $P_{bt}O_2 < 20$ mmHg.

Over the first 5 days of monitoring the median absolute total length of time when $P_{bt}O_2$ was <20 mmHg showed no significant differences between survivors and non-survivors, being 28.6 (6.2–59.6) vs 56.0 (43.0–79.4) h respectively. Similarly, the total length of time when $P_{bt}O_2$ was <20 mmHg expressed as the median percentage of monitored time that $P_{bt}O_2 < 20$ mmHg was 42.6 (11.0–61.6) vs 66.5 (58.3–76.1) % for survivors vs non-survivors respectively, which was not significant.

The overall trend for $P_{bt}O_2$ with time for the whole group over the first 24 h of monitoring was to increase with time (mean $P_{bt}O_2$ 17.4 [1.75] vs 24.7 [1.60] mmHg, first-hour data vs last-hour data respectively, $p = 0.002$). However, closer inspection of the data revealed that this was an oversimplification. A significant increase in $P_{bt}O_2$ from the first hour of monitoring to the last hour of monitoring occurred in 17 patients (68 %), no change in 1 (4 %) and a significant fall in 7 (28 %). In the 7 patients in whom the $P_{bt}O_2$ fell it ended the 24-h period <20 mmHg in 3, of whom 2 died. All the patients in whom $P_{bt}O_2$ increased over the first 24 h survived to ICU discharge. The single patient with no change in $P_{bt}O_2$ ($P_{bt}O_2$ remained >20 mmHg), and 3 of the 7 in whom $P_{bt}O_2$ fell ($P_{bt}O_2 < 20$ mmHg in 2 and >20 mmHg in 1 at the end of the 24-h period), died whilst in the ICU. More patients with a significant increase in $P_{bt}O_2$ between the first and last hour of monitoring survived intensive care vs those with no increase or in whom $P_{bt}O_2$ fell ($p = 0.006$). Mean $P_{bt}O_2$ in the last hour of monitoring showed no significant differences in survivors and non-survivors (25.9 [1.7] vs 18.4 [2.8]) respectively.

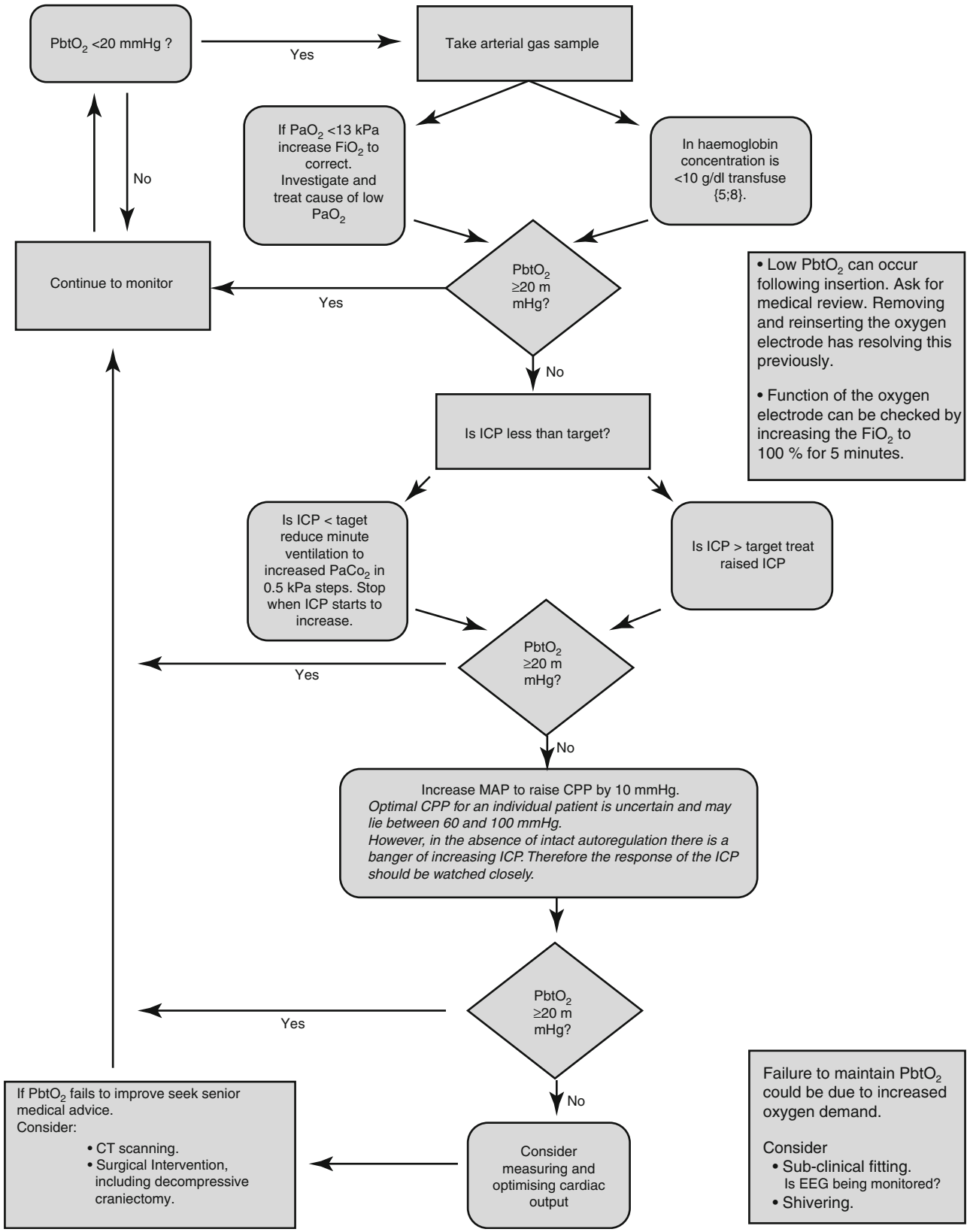

Fig. 1 The Edinburgh Treatment Algorithm for the management of brain oxygen tension ($P_{bt}O_2$). Flow diagram of suggested steps to correct a low $P_{bt}O_2$ by manipulation of physiological parameters including partial pressure of oxygen (PaO_2), partial pressure of carbon dioxide ($PaCO_2$), cranial perfusion pressure (CPP), intracranial pressure (ICP) and haemoglobin concentration in patients with severe traumatic brain injury (TBI)

Table 1 Patient demographics, surgeries and outcomes

Number	Age	Sex	GCS scene	GCS A&E	Injury mechanism	Principle CT findings	Surgery	ICU outcome
1	24	Male	5	4	Assault	DAI		Survivor
2	26	Male	14	7	Fall	[a]SDH, contusion/s	Evacuation of haematoma	Survivor
3	45	Male	4	3	RTA vehicle vs. pedestrian	SDH, contusion/s		Survivor
5	45	Male	15	8	Fall	[a]SDH, contusion/s	Evacuation of haematoma	Survivor
6	16	Male			Fall	Contusion/s		Survivor
8	53	Male		9	Fall	[a]SDH, SAH		Survivor
9	56	Male		14	Fall	[a]SAH, contusion/s		Survivor
11	56	Male		9	Uncertain	EDH, SDH	Evacuation of haematoma	Survivor
12	63	Male		14	Assault	SDH, contusions		Non-survivor
13	40	Male		6	Uncertain	[a]SDH, contusion/s	Evacuation of haematoma	Survivor
14	62	Female		4	Fall	SDH	Evacuation of haematoma	Survivor
15	61	Male	7	6	RTA motor cyclist	[a]SDH, contusion/s		Survivor
17	26	Male	8	7	RTA vehicle vs pedestrian	EDH, contusion/s	Evacuation of haematoma	Survivor
18	75	Male	12		Fall	[a]SAH, contusion/s		Non-survivor
19	29	Male	3	6	RTA vehicle driver	EDH, contusion/s	Evacuation of haematoma	Survivor
20	48	Male		11	Assault	[a]EDH	Evacuation of haematoma, contusionectomy and decompression	Survivor
21	17	Male	5		RTA vehicle vs livestock	[a]SDH, contusion/s	Contusionectomy	Survivor
22	33	Male	3	3	Uncertain	[a]SDH	Evacuation of haematoma and decompression	Non-survivor
23	22	Male		8	RTA cyclist	[a]SDH, contusion/s		Survivor
24	26	Male		6	Fall	EDH	Evacuation of haematoma	Survivor
25	25	Male	6	9	Fall	[a]SDH, contusion/s		Survivor
26	27	Male		3	Assault	SAH, DAI		Non-survivor
27	43	Male	3	12	Fall	[a]EDH, contusion/s	Evacuation of haematoma	Survivor
28	26	Male	14	14	RTA cyclist	[a]EDH, contusion/s	Evacuation of haematoma	Survivor
30	65	Female		12	Fall	[a]EDH, contusion/s	Evacuation of haematoma	Survivor

GCS Glasgow coma scale, *EDH* extradural haematoma, *SAH* subarachnoid haemorrhage, *SDH* subdural haematoma
[a]Fracture

Considerable variability in the change in mean $P_{bt}O_2$ over the first 24 h was seen both in patients in whom $P_{bt}O_2$ increased (range 0.7–25.2 mmHg) and in those in whom it decreased (range 0.7–10.1 mmHg). Therefore, to further describe the change in $P_{bt}O_2$ with time across the whole of the first day's monitoring the Spearman rank order correlation coefficient for $P_{bt}O_2$ vs time was calculated for each patient. Significant correlations were present in 22 of the 25 patients. In 13 patients the correlation coefficient for $P_{bt}O_2$ vs time was ≥0.5, all significant, $p<0.05$ (Fig. 2a). All of these patients survived to intensive care discharge. In 8 patients the correlation coefficients for $P_{bt}O_2$ vs time were lower, ranging from −0.564 to 0.459, $p<0.05$ in 7 of 8 (Fig. 2b). These patients also survived ICU. A final group of 4 patients with low correlation coefficients, 0.021 to 0.241, $p<0.05$ in 3 of 4, subsequently died of their injuries (Fig. 2c). Significantly more patients with a correlation coefficient ≥0.5 for $P_{bt}O_2$ vs time survived intensive care ($p=0.039$).

Over the first 24 h of monitoring the hypoxic time was not significantly different between patients in whom mean $P_{bt}O_2$ increased between the first and last hour and those in whom it did not change or fall (9.1 ± 1.8 vs 6.5 ± 2.2 h respectively). Similarly, the median cumulative hypoxic time did not show any significant differences among the three groups identified

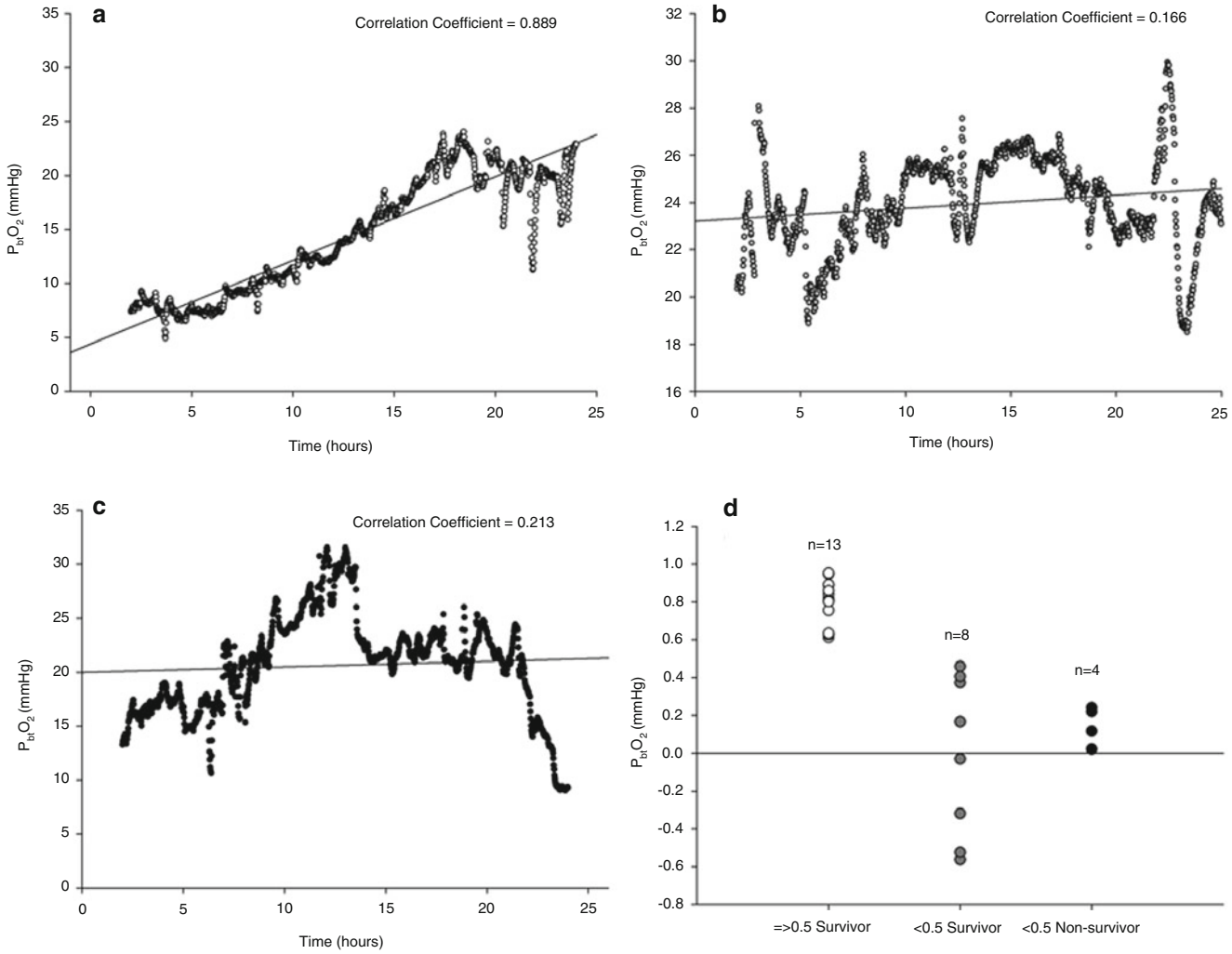

Fig. 2 Behaviour of $P_{bt}O_2$ with time during the first 24 h of monitoring. Example plots of minute to minute $P_{bt}O_2$ vs time for 3 patients with severe TBI. (**a**) Highly positive correlation of $P_{bt}O_2$ with time in a survivor. (**b**) Low correlation of $P_{bt}O_2$ with time in a survivor. (**c**) Low correlation of $P_{bt}O_2$ with time in a non-survivor. (**d**) Individual patient correlation coefficients for $P_{bt}O_2$ vs time grouped by high (≥0.5) survivors, low (<0.5) survivors and low (<0.5) correlation non-survivors

on the basis of correlation coefficient for $P_{bt}O_2$ vs time, 6.7 (3.7–15.4) vs 0.6 (0.1–17.4) vs 8.0 (6.8–9.1) h, $P_{bt}O_2 < 20$ mmHg for a correlation coefficient of $P_{bt}O_2$ vs time ≥0.5 survivors, <0.5 survivors and <0.5 non-survivors respectively (Fig. 3). However, examination of the group with a correlation coefficient <0.5, but who all survived to discharge suggested that this could be divided into two separate subgroups with significantly different cumulative hypoxic times (median cumulative hypoxic period 0.3 (0–0.5, $n=5$) vs 18.6 (16.8–19.2, $n=3$) h, $p<0.05$, Fig. 3). Thus, a total of 18 patients who survived either had a correlation of $P_{bt}O_2$ vs time ≥0.5 ($n=13$) or a low total hypoxic time ($n=5$) in the first 24 h of monitoring. There were no non-survivors who fulfilled these criteria. This distribution was also significant ($p<0.003$). In the group of patients with a correlation of $P_{bt}O_2$ vs time <0.5 in the first 24 h of monitoring, 3 patients with high hypoxic time survived and 4 died. Interestingly, the cumulative hypoxic time of the survivors with a low correlation coefficient but a large hypoxic time was significantly greater than that of non-survivors with a low correlation coefficient for $P_{bt}O_2$ vs time (median cumulative hypoxic time 18.6 [16.8–19.2, $n=3$] vs 8.0 [7.0–9.1, $n=4$] h, $p<0.001$, Fig. 3).

In the course of the data collection a treatment algorithm was introduced to direct the correction of low $P_{bt}O_2$ by manipulation of physiological parameters including CPP, $PaCO_2$, haemoglobin concentration and PaO_2 (Fig. 1). Mean CPP, averaged over the first and last 3 h of the 24-h monitoring period, increased significantly from 73.3±2.6 to 79.1±2.6 mmHg in survivors with a high correlation between $P_{bt}O_2$ and time ($p<0.05$). The change in CPP in the low-correlation groups was not significant (78.1±0.8 vs

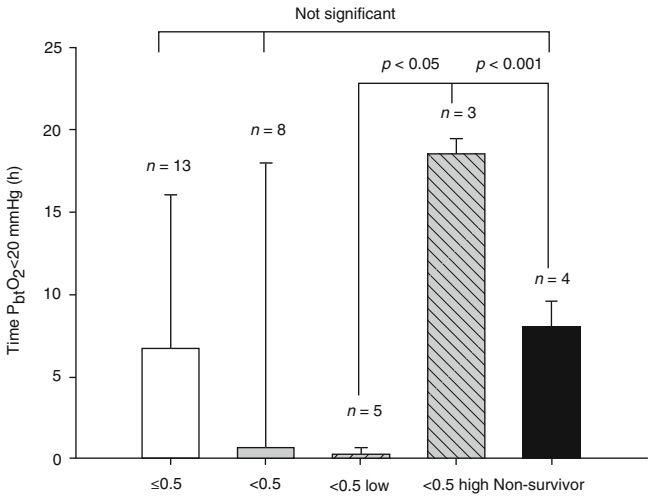

Fig. 3 Cumulative hypoxic times for each correlation coefficient outcome group. Median (25th and 75th percentiles) hypoxic time over the first 24-h monitoring period that was $P_{bt}O_2 < 20$ mmHg was 6.7 (3.7–15.4) vs 0.6 (0.1–17.4) vs 8.0 (6.8–9.1) hours for a correlation ≥0.5 in survivors (*white bar*) vs a correlation <0.5 in survivors (*grey bar*) vs a correlation <0.5 in non-survivors (*black bar*) respectively (not significant). Inspection of the correlation <0.5 survivor group suggested that it might be split into two subgroups with median hypoxic times of 0.3 (0–0.5) vs 18.6 (16.8–19.2) h, a correlation <0.5 in survivors with low hypoxic times vs a correlation <0.5 in survivors with high hypoxic times respectively, ($p < 0.05$)

80.5 ± 4.6 mmHg for a correlation <0.5 in survivors with a low hypoxic time, 71.2 ± 4.3 vs 75.7 ± 5.0 mmHg for a correlation <0.5 in survivors with a high hypoxic time and 85.2 ± 6.6 vs 88.1 ± 6.3 mmHg for a correlation <0.5 in non-survivors. Mean $PaCO_2$ in the first and last hours of the 24-h monitoring period increased significantly from 4.1 ± 0.2 to 4.8 ± 0.2 kPa in survivors with a low correlation between $P_{bt}O_2$ and time and low hypoxic time ($p < 0.05$). The change in $PaCO_2$ in the other groups was not significant (4.5 ± 0.1 vs 4.7 ± 0.2 kPa for a correlation ≥ 0.5 in survivors, 4.6 ± 0.2 vs 4.7 ± 0.3 kPa for a correlation <0.5 in high hypoxic time survivors and 4.4 ± 0.2 vs 4.1 ± 0.3 kPa for a correlation <0.5 in non-survivors). Mean haemoglobin concentration in the first and last hours of the 24-h monitoring period did not change significantly with time (10.1 ± 0.6 vs 10.4 ± 0.4 g/dl for a correlation ≥ 0.5 between $P_{bt}O_2$ and time in survivors, 9.9 ± 0.6 vs 10.5 ± 0.5 g/dl for a correlation <0.5 in survivors with a low hypoxic time, 10.5 ± 0.6 vs 9.8 ± 0.9 g/dl for a correlation <0.5 in survivors with a high hypoxic time and 10.8 ± 0.6 vs 9.9 ± 0.6 g/dl for a correlation <0.5 in non-survivors). Mean PaO_2 in the first and last hours of the 24-h monitoring period decreased significantly from 19.8 ± 1.3 to 14.5 ± 0.7 kPa in survivors with a low correlation between $P_{bt}O_2$ and time and low hypoxic time ($p < 0.05$). The change in PaO_2 in the other groups was not significant (18.2 ± 1.5 vs 14.7 ± 0.9 kPa for a correlation ≥ 0.5 in survivors, 21.7 ± 5.5 vs 15.0 ± 1.7 kPa for a correlation <0.5 in survivors with a high hypoxic time and 24.0 ± 5.2 vs 12.5 ± 0.6 kPa for a correlation <0.5 in non-survivors.

Discussion

This paper reports the results of a retrospective analysis of prospectively collected data in the first 25 patients in whom $P_{bt}O_2$ monitoring was used as part of standard care in TBI patients requiring ICU support. It has been suggested that $P_{bt}O_2$ is a more reliable and sensitive monitoring system for the detection of cerebral hypoxia than jugular bulb saturation monitoring [9, 20] which can be influenced by the heterogeneity of regional cerebral blood flow following TBI [3]. So far, the first 24 h of admission have been analysed in detail. Three patients in whom $P_{bt}O_2$ electrodes were placed were excluded because of damage to the electrodes on insertion. These cases occurred in the first half of the series and were most likely due to the inexperience of the operators. To date, our total series of patients has grown to more than 60. There have not been any further failures of $P_{bt}O_2$ monitoring.

The prevention of secondary hypoxic insults, with their association with death and poor outcome [5, 8], remain the cornerstone of contemporary critical care management for traumatic brain injuries. Extensive guidelines have been developed advocating the invasive monitoring of ICP, the maintenance of CPP and the control of ventilation in an attempt to ensure that oxygenated blood continues to be delivered to the brain [2, 10]. The aim of our treatment algorithm was to maintain a $P_{bt}O_2 \geq 20$ mmHg, which is consistent with the contemporary literature [1, 14]. Despite the achievement of an adequate CPP and control of ICP, low $P_{bt}O_2$ was common early in the first 24 h of monitoring. This observation is consistent with previously reported data [6, 16].

Episodes of low $P_{bt}O_2$ and the cumulative duration of hypoxia have been associated with an adverse outcome following TBI [11, 12, 15, 19, 20]. However, in our series, over the first 5 days of monitoring neither the total time nor the percentage of monitored time that $P_{bt}O_2$ was <20 mmHg was significantly different in survivors and non-survivors. There was a strong trend towards less hypoxia in the survivors and this result may reflect the relatively small numbers. After 5 days, the total cohort size fell to <10 patients. The mean $P_{bt}O_2$ in the last hour of monitoring was not significantly lower in non-survivors than in survivors, although again this may reflect a lack of statistical power due to the small number of non-survivors. This finding contrasts with a recently published series in which $P_{bt}O_2$ was significantly different in survivors and non-survivors from 8 h onwards [4].

The overall trend in $P_{bt}O_2$ with time for the whole group over the first 24 h of monitoring was to increase with time.

Again this pattern is consistent with previously published reports [12, 18, 20, 21]. This suggests that $P_{bt}O_2$ should be commenced as soon as possible after injury if hypoxia is to be detected and corrected. However, inspection of the individual patient data revealed that whilst this was true for more than half of the cases, in the remaining 32 %, $P_{bt}O_2$ either fell or there was no change between the first and last hour of the first 24 h of monitoring. There was a significant association with survival in the 17 patients in whom $P_{bt}O_2$ increased significantly during the first day. Similarly, there was a strong correlation of $P_{bt}O_2$ with time during the first day in 13 survivors. Overall, there was no significant difference in cumulative hypoxic time between patients grouped according to the strength of the correlation of $P_{bt}O_2$ with time and survival. However, among the low-correlation survivors there were 5 patients with very low hypoxic times (< 1 h). These patients represent a group in which $P_{bt}O_2$ was maintained ≥20 mmHg throughout most of the first day. $P_{bt}O_2$ fell in 3 and increased in 2. When combined with the 13 survivors with a strong correlation of $P_{bt}O_2$ with time, the distribution with outcome is also significant. Interestingly, the other low correlation survivor subgroup had a much greater total hypoxia time than the non-survivors. In these 3 patients $P_{bt}O_2$ was <20 mmHg in both the first and last hours of monitoring, although it increased in 2 and fell in 1. With the small numbers in these subgroups it is difficult to explain this finding, but inspection of the trends in $P_{bt}O_2$ with time after the first 24 h suggests that this relationship might reverse with time, $P_{bt}O_2$ eventually improving in survivors. Taking the data together it might be suggested that although total hypoxic time during the entire patient stay may be related to outcome, this is less important within the first 24 h as there was no difference in hypoxic time between survivors and non-survivors in this period. However, a tendency for $P_{bt}O_2$ to increase with time is significantly associated with survival. Furthermore, patients in whom $P_{bt}O_2$ increases slowly (low positive correlation of $P_{bt}O_2$ with time) can still survive, even with times of high hypoxia in the first 24 h.

$P_{bt}O_2$ can be improved be manipulating CPP, ICP, $PaCO_2$, blood haemoglobin concentration [13] and inspired oxygen concentration. Although no large randomised controlled trials have been completed, small studies support the hypothesis that targeting and improving $P_{bt}O_2$ reduces the incidence of cerebral hypoxia and improves outcome after severe TBI, particularly when the threshold definition of hypoxia is high [12, 14, 15]. In our series a significant change in CPP between the beginning and the end of the first 24 h of monitoring was only seen in the group of patients with a strong correlation of $P_{bt}O_2$ with time. Conversely, significant increases in $PaCO_2$ or haemoglobin concentration were not seen in this group. The change in PaO_2 was either a significant fall or a strong trend towards a fall. Spontaneous variations in CPP have been used to define an optimal level of CPP based on pressure reactivity. Below this optimal CPP, $P_{bt}O_2$ has been shown to fall, with a decrease in CPP. Above the optimal CPP, $P_{bt}O_2$ reaches a plateau [7]. In our algorithm, increasing CPP is integral to the management of a low $P_{bt}O_2$. Therefore, our data support the hypothesis that increasing CPP might effectively improve $P_{bt}O_2$ and also suggests that $P_{bt}O_2$ might be an effective means of setting an ideal CPP for an individual patient.

In conclusion, $P_{bt}O_2$ and continuous multimodality monitoring has been successfully introduced in Edinburgh. Our initial results are consistent with those of the published literature. In particular, we have also demonstrated that despite adequate control of CPP and ICP, cerebral hypoxia is common. Whilst a general improvement in $P_{bt}O_2$ with time was also seen, this is an oversimplification. Although the total hypoxic burden for a complete patient stay may be related to outcome in some studies, within the first 24 h of data collection we did not observe this. However, the pattern of $P_{bt}O_2$ change in the first 24 h was related to outcome. There was a significant association between improving $P_{bt}O_2$ and survival, despite these patients having cumulative durations of cerebral hypoxia in the first 24 h similar to those of non-survivors. Analysis of the change in CPP from the first to the last hour of the 24 h period suggests that optimising this parameter might be responsible for the increase in $P_{bt}O_2$ seen in this group. Validation and further analysis of $P_{bt}O_2$ data over a longer period are required.

Acknowledgements We would like to acknowledge the support and enthusiasm of the doctors, nurses and management of the ICU, together with those of the neurosurgical trainees. Dr Rhodes would like to acknowledge the support of NHS Research Scotland.

Conflict of Interest Statement The authors declare that they have no conflict of interest.

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