Sodium Bicarbonate Lowers Intracranial Pressure After Traumatic Brain Injury

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Abstract

Background Hypertonic saline is routinely used to treat rises in intracranial pressure (ICP) post-traumatic head injury. Repeated doses often cause a hyperchloremic metabolic acidosis. We investigated the efficacy of 8.4% sodium bicarbonate as an alternative method of lowering ICP without generating a metabolic acidosis.

Methods We prospectively studied 10 episodes of unprovoked ICP rise in 7 patients treated with 85 ml of 8.4% sodium bicarbonate in place of our usual 100 ml 5% saline. We measured ICP and mean arterial pressure continuously for 6 h after infusion. Serum pH, pCO$_2$, [Na$^+$], and [Cl$^-$] were measured at baseline, 30 min, 60 min and then hourly for 6 h.

Results At the completion of the infusion ($t = 30$ min), the mean ICP fell from 28.5 mmHg ($±$2.62) to 10.33 mmHg ($±$1.89), $P < 0.01$. Mean ICP remained below 20 mmHg at all time points for 6 h. Mean arterial pressure was unchanged leading to an increased cerebral perfusion pressure at all time points for 6 h post-infusion. pH was elevated from 7.45 ± 0.05 at baseline to 7.50 ± 0.05, $P < 0.01$ at $t = 30$ min, and remained elevated. Serum [Na$^+$] increased from 145.4 ± 6.02 to 147.1 ± 6.3 mmol/l, $P < 0.01$ at $t = 30$ min. pCO$_2$ did not change.

Conclusions A single dose of 8.4% sodium bicarbonate is effective at treating rises in ICP for at least 6 h. Serum sodium was raised but without generation of a hyperchloremic metabolic acidosis.

Keywords Traumatic brain injury · Intracranial pressure · Osmotherapy · Sodium bicarbonate · Hypertonic solutions

Introduction

Protocols that target intracranial pressure (ICP) and cerebral perfusion pressure (CPP) for the management of traumatic brain injury (TBI) have been shown improved outcome over standard treatment [1, 2]. Hypertonic saline is well established in the treatment of intracranial hypertension following head injury [3] and this is reflected in the use of boluses of 100 ml 5% sodium chloride to treat sustained unprovoked rises in ICP at our institution. Unfortunately, there is a paucity of evidence showing an improved outcome with hypertonic saline use in TBI.

Saline solutions cause a metabolic acidosis derived from hyperchloremia [4, 5]. Several studies have demonstrated a fall in pH after administration of hypertonic saline solutions for raised ICP due to a hyperchloremic metabolic acidosis [6, 7]. It is not clear whether a metabolic acidosis associated with hypertonic saline use is harmful to patients but hyperchloremia may be implicated in the development of renal impairment [8, 9] and a coagulopathy [10–12].

We hypothesized that an equiosmolar infusion of 8.4% sodium bicarbonate would have a similar effect on ICP reduction as our standard therapy but with the potential advantage of avoiding a hyperchloremic metabolic acidosis. The aim of this study was to evaluate the effectiveness of 8.4% sodium bicarbonate for ICP reduction in humans after TBI.
Methods

This study was performed in the intensive care unit of a tertiary neurosurgical unit at Frenchay Hospital, Bristol. Ethical approval was obtained from the Guy’s and St Thomas’ Research Ethics Committee (08/H0802/28). The Medicines and Healthcare Products Regulatory Agency approved the use of 8.4% sodium bicarbonate solution in the study EudraCT (2008-000219-14).

Patients

Patients were recruited into the trial if they had suffered severe TBI (GCS < 8 requiring sedation, ventilation, and ICP monitoring). Patients were only recruited when the investigators were on duty (1 week in 6). They were excluded if they were expected to be woken and extubated within 24 h or were expected to require surgical intervention within 24 h. Personal legal representatives gave assent for entry into the study and all patients were aged >16 years.

Patients were treated in accordance with our institutional protocol for the management of raised ICP after TBI. Briefly this includes 4 sequential stages: Stage 1: use of osmotherapy (hypertonic saline, frusemide); Stage 2: hypothermia (down to 34°C as needed); Stage 3: hyperventilation (down to a pCO2 of 4 kPa as needed); Stage 4: either thiopentone infusion and/or decompressive craniectomy.

Intervention

An episode of raised ICP was defined as an increase in ICP > 20 mmHg for at least 5 min that was not related to an external noxious stimulus or correctable physiologic derangement. A bolus of 85 ml of 8.4% sodium bicarbonate was administered over 30 min via a syringe driver through a central venous catheter, in place of the 100 ml of 5% sodium chloride usually given in our institutional protocol.

85 ml of 8.4% bicarbonate contains a similar solute load (170 mOsm) and sodium load (85 mmol) to our standard therapy of 100 ml 5% saline (171 mOsm and 85.5 mmol sodium). The study protocol allowed for a second dose of bicarbonate if the ICP rose above 20 mmHg within 6 h. Treatment failure was defined as failure to respond to two doses of sodium bicarbonate or requirement for additional therapy such as muscle relaxants, osmotherapy or Stages 2 to 4.

Patients could receive further doses on subsequent days and these were considered as separate treatment episodes.

Patients could be entered into the study at any time during stage 1. Prior episodes of intracranial hypertension treated with osmotherapy did not preclude study enrollment. Failure of stage 1 and requirement for stage 2 therapy would preclude enrollment. Sedation was given according to sedation score and not altered to treat raised ICP.

Data Collection

ICP, MAP, and CPP were monitored continuously and data examined at baseline (prior to infusion of 8.4% sodium bicarbonate) and at 5 min intervals for the first hour and then at hourly intervals for 6 h after the infusion was commenced. An arterial blood sample was taken at baseline, 30 min after the infusion commenced, and then at hourly intervals for 6 h. pH, Na+, Cl−, were measured on the arterial blood sample.

Statistical Analysis

Data were compared with baseline values at the time intervals described above. Differences from baseline values were examined with paired t tests for single comparisons and ANOVA for repeated measures. Data are quoted as mean and standard deviation.

Results

Data from 7 patients were studied over a 12-month period. All had an admission GCS < 8, 4/7 had sub-dural hematomas plus contusions and 3/7 contusions only. Four patients received a single treatment dose. In one patient the ICP reached threshold for a further treatment at one hour post-commencement of the infusion and he received a second treatment dose. Two other patients received a second dose on separate days. Data was analysed from all 10 treatment episodes.

Data was obtained for all patients for ICP, CPP, MAP, Na+, Cl−, pH, and pCO2. No patients were excluded from the study for treatment failure.

ICP Reduction

Mean ICP was reduced at all times after commencement of the infusion (P < 0.01). At the completion of the infusion (t = 30 min), the mean ICP decreased to 36.2% of baseline value, from 28.5 mmHg (±2.62) to 10.33 mmHg (±1.89, P < 0.01). Mean ICP was less than or equal to 20 mmHg in all treatment episodes after 15 min from the start of the infusion. The greatest reduction in mean ICP, 63.13%, occurred 5 h after the infusion was commenced, mean 9.8 mmHg (±1.44, P < 0.01) (see Fig. 1).
Effect on MAP

MAP did not significantly change after infusion of 8.4% bicarbonate at any time point (see Table 1).

Effect on CPP

CPP was increased after infusion of 8.4% sodium bicarbonate solely by its effect on ICP reduction. Mean CPP rose by 29% from 62 mmHg (±4.1) to 80 mmHg (±3.3) $P < 0.01$, on completion of the infusion ($t = 30$ min) and remained above 70 mmHg at all times during the study period (see Table 1).

Effect on pCO$_2$

pCO$_2$ was not significantly altered from baseline by the infusion of 8.4% sodium bicarbonate at any point in the study period (see Table 1). Minute ventilation was not altered.

Effect on Serum [Na$^+$]

Serum [Na$^+$] increased after the infusion was completed from 145.4 ± 6.02 to 147.1 ± 6.30 mmol/l, $P < 0.01$ (see Table 1).

Effect on Serum [Cl$^-$]

Serum [Cl$^-$] was reduced from 119.4 ± 6.67 to 117.8 ± 6.43 mmol/l, $P < 0.01$ on completion of the infusion (see Table 1).

Effect on Serum pH

Serum pH increased after the infusion of 8.4% bicarbonate with the greatest increase seen at 30 min after the infusion commenced, 7.45 ± 0.5 to 7.50 ± 0.05 ($P < 0.01$), however, over the 6 h period this difference was not significant.

### Table 1 Changes in pH, pCO$_2$, [Na$^+$], [Cl$^-$], MAP and CPP with time

<table>
<thead>
<tr>
<th>Time (minutes from start of infusion)</th>
<th>pH</th>
<th>pCO$_2$ (kPa)</th>
<th>[Na$^+$] (mmol/l)</th>
<th>[Cl$^-$] (mmol/l)</th>
<th>MAP (mmHg)</th>
<th>CPP (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>7.45 (0.05)</td>
<td>4.2 (0.35)</td>
<td>145.4 (6.02)</td>
<td>119.4 (6.67)</td>
<td>90.0 (11.23)</td>
<td>62 (4.31)</td>
</tr>
<tr>
<td>30</td>
<td>7.50 (0.05)</td>
<td>4.2 (0.42)</td>
<td>147.1 (6.30)</td>
<td>117.8 (6.43)</td>
<td>90.6 (5.76)</td>
<td>80 (9.76)</td>
</tr>
<tr>
<td>60</td>
<td>7.49 (0.05)</td>
<td>4.3 (0.37)</td>
<td>146.5 (7.31)</td>
<td>118.1 (6.96)</td>
<td>93.7 (10.95)</td>
<td>81 (12.71)</td>
</tr>
<tr>
<td>120</td>
<td>7.49 (0.04)</td>
<td>4.2 (0.42)</td>
<td>146.1 (5.15)</td>
<td>117.6 (6.37)</td>
<td>94.9 (12.58)</td>
<td>83 (12.47)</td>
</tr>
<tr>
<td>180</td>
<td>7.50 (0.05)</td>
<td>4.1 (0.29)</td>
<td>147.5 (5.95)</td>
<td>119.0 (6.72)</td>
<td>93.9 (14.5)</td>
<td>83 (15.28)</td>
</tr>
<tr>
<td>240</td>
<td>7.48 (0.05)</td>
<td>4.0 (0.43)</td>
<td>148.7 (4.79)</td>
<td>120.1 (7.93)</td>
<td>90.3 (11.08)</td>
<td>78 (15.42)</td>
</tr>
<tr>
<td>300</td>
<td>7.48 (0.06)</td>
<td>4.0 (0.31)</td>
<td>145.6 (5.61)</td>
<td>117.7 (7.50)</td>
<td>93.3 (14.5)</td>
<td>84 (15.56)</td>
</tr>
<tr>
<td>360</td>
<td>7.48 (0.06)</td>
<td>4.1 (0.35)</td>
<td>147.0 (6.05)</td>
<td>117.5 (6.19)</td>
<td>91.0 (14.37)</td>
<td>80 (15.84)</td>
</tr>
</tbody>
</table>

Values expressed as mean (SD)
Discussion

This study demonstrates that an infusion of 85 ml of 8.4% sodium bicarbonate over 30 min is effective for the treatment of raised ICP after TBI. Only one treatment episode required a second dose of 8.4% sodium bicarbonate and no patients were excluded due to treatment failure.

MAP was unchanged leading to a sustained rise in CPP throughout the 6 h study period.

Changes in ICP and CPP in this study can be attributed to the infusion of 8.4% sodium bicarbonate. All patients received identical standard care and no additional interventions to reduce ICP were instituted during the study period (such as CSF drainage, cooling, paralysis, diuretic, barbiturates, or decompressive craniectomy).

Hypertonic saline is postulated to lower ICP by several mechanisms including, osmotic, vasoregulatory, haemodynamic, and immunomodulatory [13]. Sodium does not cross the blood–brain barrier and therefore exerts osmotic effects on brain parenchyma resulting in the dehydration of brain tissue. We hypothesized that an equal sodium dose in the form of sodium bicarbonate would have a similar effect on ICP as sodium chloride.

Animal experiments performed over 90 years ago demonstrated that infusions of hypertonic sodium bicarbonate reduce CSF pressure and also result in a reduction in brain bulk [14, 15]. A study on neonatal dogs found that infusion of hypertonic sodium bicarbonate caused a significant reduction in brain water content [16]. Several human studies have demonstrated an increase in cerebral blood flow after sodium bicarbonate infusion [17, 18].

Our study is the first to describe the effect of sodium bicarbonate infusion on raised ICP after TBI in humans. Serum sodium concentration and osmolality were elevated after infusion of 8.4% sodium bicarbonate and we assume that at least some of the effect on ICP reduction is mediated by an osmotic mechanism. Although we did not measure cerebral blood flow, we suspect that sodium bicarbonate infusion would increase cerebral blood flow largely due to a reduction in ICP.

The magnitude and duration of ICP reduction with 8.4% sodium bicarbonate is similar to that found in previous studies examining the effects of hypertonic saline solutions on reduction of ICP [3]. In the present study, serum [Cl⁻] was reduced after infusion of 8.4% sodium bicarbonate and pH was elevated. This may convey an advantage over therapy with hypertonic saline in situations where an established metabolic acidosis exists.

There are some obvious weaknesses in this study. Firstly, treatment was not randomised or blinded. Secondly, a small number of episodes were studied and patients were only recruited in a single centre. The investigation was designed to evaluate the efficacy of sodium bicarbonate for ICP reduction and this study demonstrates the need for a prospective randomised trial to compare 8.4% bicarbonate with hypertonic saline in this setting.

Conclusions

This study demonstrates that an infusion of 8.4% sodium bicarbonate is effective for the reduction of raised ICP in patients who are sedated and ventilated in intensive care with a severe TBI.

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References