Injury, Int. J. Care Injured 45 (2014) 2084–2088

Contents lists available at ScienceDirect

Injury

journal homepage: www.elsevier.com/locate/injury

Responsiveness to therapy for increased intracranial pressure in traumatic brain injury is associated with neurological outcome

K. Colton [a,b,*], S. Yang [a], P.F. Hu [a], H.H. Chen [a], L.G. Stansbury [a], T.M. Scalea [a], D.M. Stein [a]

[a] Shock Trauma Anesthesia Research Organized Research Center, University of Maryland School of Medicine and R Adams Cowley Shock Trauma Center, Baltimore, MD, USA
[b] Duke University School of Medicine, Durham, NC, USA

ARTICLE INFO

Article history:
Accepted 28 August 2014

Keywords:
Intracranial pressure
Traumatic brain injury
Hypertonic saline
Hyperosmolar therapy

ABSTRACT

In patients with severe traumatic brain injury, increased intracranial pressure (ICP) is associated with poor functional outcome or death. Hypertonic saline (HTS) is a hyperosmolar therapy commonly used to treat increased ICP; this study aimed to measure initial patient response to HTS and look for association with patient outcome.

Patients >17 years old, admitted and requiring ICP monitoring between 2008 and 2010 at a large urban tertiary care facility were retrospectively enrolled. The first dose of hypertonic saline administered after admission for ICP >19 mmHg was recorded and correlated with vital signs recorded at the bedside. The absolute and relative change in ICP at 1 and 2 h after HTS administration was calculated. Patients were stratified by mortality and long-term (≥6 months) functional neurological outcome.

We identified 46 patients who received at least 1 dose of HTS for ICP > 19, of whom 80% were male, mean age 34.4, with a median post-resuscitation GCS score of 6. All patients showed a significant decrease in ICP 1 h after HTS administration. Two hours post-administration, survivors showed a further decrease in ICP (43% reduction from baseline), while ICP began to rebound in non-survivors (17% reduction from baseline). When patients were stratified for long-term neurological outcome, results were similar, with a significant difference in groups by 2 h after HTS administration.

In patients treated with HTS for intracranial hypertension, those who survived or had good neurological outcome, when compared to those who died or had poor outcomes, showed a significantly larger sustained decrease in ICP 2 h after administration. This suggests that even early in a patient's treatment, treatment responsiveness is associated with mortality or poor functional outcome. While this work is preliminary, it suggests that early failure to obtain a sustainable response to hyperosmolar therapy may warrant greater treatment intensity or therapy escalation.

Introduction

Traumatic brain injury (TBI) is the leading cause of death after injury [1], with incidence peaks in children, adolescents, and adults over the age of 65 [2]. One study estimated the economic impact of TBI at $9.2 billion in lifetime medical costs and $51.2 billion in lost productivity [3].

Management of severe TBI focuses on preventing and treating secondary insults caused by hypoxia, hypotension, and intracranial hypertension (ICH). Treatment for severe TBI is algorithmic [4] and directed at maintenance of intracranial pressure (ICP) and cerebral perfusion pressure (CPP) within ranges that do not further exacerbate secondary injury such as oedema, inflammation, and ischaemia. Hyperosmolar therapy, traditionally with mannitol, has been commonly accepted as an acute treatment of cerebral oedema for decades. More recently, hypertonic saline (HTS) has become popular [5–7]. While there is as yet no definitive evidence to support one agent as clearly superior, one meta-analysis suggests that equi-osmolar HTS may be more effective than mannitol [8]. At our institution, HTS is regularly used as the first-line hyperosmolar therapy as part of a larger tiered protocol.

Accurate prediction of outcome after severe TBI has proved difficult. The large International Mission for Prognosis and Clinical Trial design in TBI (IMPACT) study found various admission characteristics such as patient demographics, Glasgow Coma Score

* Corresponding author at: R Adams Cowley Shock Trauma Center, 22 S. Greene Street, T1R52, Baltimore, MD 21201, USA. Tel.: +1 410 328 3495.
E-mail addresses: Katharine.colton@duke.edu, krcolton@gmail.com (K. Colton).

http://dx.doi.org/10.1016/j.injury.2014.08.041
0020–1383/

(GCS), presence of secondary insults or structural abnormalities on imaging, and laboratory abnormalities to be predictive of eventual outcome [9]. However, clinical course after TBI is often unpredictable, and most prognostic models are unable to incorporate information gleaned from the patients' treatment and recovery. In this study, we sought to evaluate the actual effect of early ICP-directed treatment on prognosis following severe TBI.

Materials and methods

Patients

Study subjects were admitted to the R Adams Cowley Shock Trauma Center, a level I tertiary medical center, between 2008 and 2010. With approval from the Institutional Review Board (IRB), data were collected retrospectively on patients older than 17 years of age admitted to the Neurotrauma Critical Care Unit (NTCCU) with severe TBI who required invasive ICP monitoring. Severe TBI was defined as post-resuscitation GCS < 9 and TBI confirmed by computed tomography (CT). Patients were then included if they received at least one dose of hypertonic saline for the reduction of intracranial pressure during the duration of ICP monitoring.

Data collection

Patient demographics, mechanism of injury, routine vital signs, method of ICP monitoring, and need for surgical intervention with cranial decompression were recorded. Admission head CT was assigned a Marshall Classification score [10] according the presence of basal cistern compression, midline shift >5 mm, and lesions $>25\ cm^3$. Outcomes measured included in-hospital mortality (on discharge from the Shock Trauma Center) and long-term functional outcome as measured by the extended Glasgow Outcome Scale (GOSE) [11], evaluated at least 6 months after discharge. Neurological outcomes were divided into 'poor neurological outcome' (GOSE 1–4 at least 6 months after discharge or in-hospital mortality) or 'good neurological outcome' (GOSE 5–8).

Routine vital signs including ICP, cerebral perfusion pressure (CPP), and mean arterial pressure (MAP) were recorded from manually documented bedside records. When ICP > 19, values were recorded every 15 min; otherwise, hourly measurements are used. The timing of the first dose of HTS administration was correlated with recorded vital signs data and only included for analysis if ICP in the hour of administration was >19 to exclude instances of HTS administration for purposes other than amelioration of ICH.

Management protocol

Patients with severe TBI admitted to the R Adams Cowley Shock Trauma Center are admitted to a dedicated NTCCU and managed according to a standardized tiered protocol in accordance with the Brain Trauma Foundation Guidelines [Brain Trauma Foundation 2007]. Treatment targets the maintenance of ICP < 20 mmHg and CPP > 60 mmHg, as previously described elsewhere [12]. All patients included in the study had placement of a clinically indicated intraparenchymal monitor (Camino®; Integra NeuroSciences) or intraventricular catheter (Codman; Raynham, MA).

Only the first administration of a bolus dose of HTS was included for each patient to avoid confounding effect of multiple treatments. Patients received a bolus dose of 3% NaCl solution with a volume of either 250 ml or 500 ml, at the clinician's discretion.

Statistical analysis

Statistical analyses were performed in Excel (Microsoft; Redmond, WA), SAS (Cary, NC) and Matlab Student v7.10 (Natick, MA). Demographic data were summarized as percentages or means with standard deviation or error and medians with interquartile range. Ninety-five percent confidence intervals are reported. The Student's *t*-test was used to compare means and non-parametric tests were used to compare medians. Probability values for results being due to chance (p) of 0.05 or less were considered statistically significant. p-Values of more than one decimal place below 0.01 are shown as <0.001.

Results

Inclusion criteria were met by 46 subjects. Subjects were primarily male (80%), mean age 34.4 ± 4.0 with a median post-resuscitation GCS score of 6, IQR 6–7 and a median Marshall CT score of 2.5, IQR 2–3 (Table 1). Median Injury Severity Score was 29, IQR 25–37.5. 95.7% of patients suffered blunt injury; 45.7% had multiple severe injuries. In-hospital mortality was 19.6%. The median length of stay (LOS) was 15.3 days (IQR 11.9–21.8), with a median Intensive Care Unit (ICU) stay of 13.2 days (IQR 10.8–18.6). Craniectomy or craniotomy for ICP control was required by 45.6% of patients. Patients received either 250 ml or 500 ml 3% NaCl solution. 500 ml was administered to 5/9 patients who went on to die in-hospital, 18/37 patients who survived, 9/17 patients who had poor long-term outcome, and 11/26 with good long-term outcome.

In all patients, after the first dose of HTS for ICH, ICP was 7.1 ± 7.4 mmHg lower after 1 h and 8.7 ± 7.3 mmHg lower after 2 h ($p < 0.05$), a relative decrease of 30% and 38%, respectively (Table 2).

Table 1
Patient and injury characteristics.

	All ($n=46$)	Alive at discharge ($n=37$)	In-hospital death ($n=9$)	p	Good outcome* ($n=26$)	Poor outcome** ($n=17$)	p
Age (y), mean ± SD	34.4 ± 13.8	33.4 ± 13.0	38.4 ± 16.9	ns	30.3	37.2	ns
Males, *n* (%)	37 (80.4)	31 (83.8)	6 (66.7)	ns	84.6	70.6	ns
GCS, post-resuscitation, median (IQR)	6 (6–7)	6 (6–7)	6 (3–6)	<0.05	6 (4–6)	6 (6–7)	ns
Marshall CT score, median (IQR)	2.5 (2–3)	2 (2–3)	3 (2–3)	ns	2.5	2.7	ns
Blunt injury, *n* (%)	44 (95.7)	35 (94.6)	9 (100)	ns	26 (100)	15 (88.2)	ns
ISS, median (IQR)	29 (25–37.5)	26 (21–36)	34 (29–43)	ns	26 (21–37.5)	29 (26–43)	ns
Polytrauma, *n* (%)***	21 (45.7)	15 (40.1)	6 (66.7)	ns	11 (42.3)	9 (52.9)	ns
LOS (days), median (IQR)	15.3 (11.9–21.8)	17.6 (13.1–22.9)	6.5 (5.1–7.2)	<0.001	16.6 (12.9–22.0)	11.8 (6.5–17.4)	ns
ICULOS (days), median (IQR)	13.2 (10.8–18.6)	14.6 (11.6–19.3)	6.2 (4.6–6.8)	<0.01	13.9 (11.7–18.7)	10.6 (6.4–15.2)	ns
Craniotomy/craniectomy, *n* (%)	21 (45.6)	19 (51.4)	2 (22.2)	ns	26 (46.2)	8 (47.1)	ns

GCS, Glasgow Coma Scale; CT, computed tomography; ISS, Injury Severity Score; LOS, Length of stay; ICU, intensive care unit; ns, not statistically significant.
* 6-month GOSE 5–8.
** 6-month GOSE 1–4 or in-hospital death.
*** Defined as non-head ISS > 15.