Original Article

Single-institutions experience with acute kidney injury in the brain injury population

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Background: Treatment of traumatic brain injury (TBI) in the hospital-setting focuses on prevention of the secondary insult sustained from elevated intracranial pressures. Hypertonic saline (HTS) as well as other agents are employed as part of the medical management armamentarium. A retrospective chart review was performed to analyze if more aggressive resuscitation with HTS can be tolerated by assessing the rate of acute kidney injury (AKI) using the Acute Kidney Injury Network (AKIN) criteria.

Methods: Retrospective review of prospectively collected data from January 2012 through December 2014 was performed on 157 patients. AKIN criteria were used to assess for AKI.

Results: In total, 93.6% of patients did not meet any AKIN criteria.

Conclusions: AKI is an uncommon adverse effect of HTS use. Aggressive resuscitation with HTS may be tolerated and shorten the time to treatment by reaching therapeutic sodium levels more expeditiously.

Keywords: Acute kidney injury (AKI); traumatic brain injury (TBI); trauma, kidney

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Introduction

Primary brain injury refers to the unavoidable cascade of events secondary to the trauma sustained to the brain at the moment of impact. Secondary brain injury is a direct result of the physiological processes that occur following the initial trauma. The resulting sequelae leads to the activation of different pathways involving inflammation, coagulation, oxidation, and apoptosis. During what is referred to as the "golden hours" following the primary insult the physician can intervene and interrupt the progression of the disease process. This can be accomplished through interventions targeted at decreasing intracranial pressure, proper tissue oxygenation, maintenance of blood pressure and cerebral perfusion pressure (1-4).

Elevated intracranial pressures can be managed through conservative medical measures *vs.* operative intervention. Hypertonic saline (HTS) is a crystalloid solution with higher than physiologic concentration of sodium chloride. Animal and human studies have demonstrated that HTS can affect cerebral blood flow, intracranial pressures, and inflammatory responses in neurotrauma. HTS increases oncotic pressure intravascularly, promoting fluid shifts that as a secondary effect lead to a decreased intracranial pressures and shrinkage of brain parenchyma. Its use has been employed for conservative management of elevated intracranial pressures in conjunction with mannitol (5,6).

Despite being an effective agent in the armamentarium toward managing elevated intracranial pressures, HTS does have possible side effects: rebound intracranial hypertension, central pontine myelinolysis, renal impairment, subarachnoid hemorrhage, natriuresis, high urinary water losses, hyperchloremic acidosis, masks the development of diabetes insidious (7). Hypernatremia secondary to the use of HTS is a well-known risk factor for developing acute kidney injury (AKI) (8-10). There

Table 1 Acute Kidney Injury Network (AKIN) classification and staging system of acute kidney injury (9)

Stage	Serum creatinine	Urine output
1	incr. SCr >0.3 mg/dL or 1.5–2× baseline	<0.5 mL/Kg/hours (>6 hours)
2	incr. SCr 2–3× baseline	<0.5 mL/kg/hours (>12 hours)
3	incr. SCr >3× baseline, or >4 mg/dL from baseline	<0.3 mL/kg/hours (24 hours or anuria >12 hours)

SCr, serum creatinine; incr., increase.

Table 2 Patient characteristics (N=169)

Epidemiology	Values
Male, N (%)	100 (59.2)
Female, N (%)	69 (40.8)
Age, mean ± SD, years	61.4±20.6
HTN, N (%)	103 (60.9)
DM, N (%)	40 (23.7)
CHF, N (%)	56 (33.1)
CAD/atrial fibrillation, N (%)	56 (33.1)
CKD/ESRD, N (%)	8 (4.7)
HLD, N (%)	46 (27.2)
Antiplatelet/anticoagulant, N (%)	62 (36.7)
Systolic <90 on admission, N (%)	6 (3.6)
Transfused blood products on admission, N (%)	15 (8.9)

HTN, hypertension; DM, diabetes mellitus; CHF, congestive heart failure; CAD, coronary artery disease; CKD, chronic kidney disease; ESRD, end-stage renal disease; HLD, hyperlipidemia.

have been reports of renal dysfunction in the pediatric patient population with prolonged elevations of serum osmolarity. The mechanism(s) responsible is thought to be a combination of intravascular volume depletion and effects of the renin-angiotensin-aldosterone system (10,11).

We decided to perform a retrospective analysis of all patients that sustained a traumatic brain injury (TBI) in order to assess the incidence of AKI using the Acute Kidney Injury Network (AKIN) criteria (12).

Methods

A retrospective analysis was performed examining all patients that received HTS, 2% or 3%, from January 2012 through December 2014. IRB board approval was obtained for a retrospective chart review. A total of 169 patients were identified who sustained an injury that resulted in elevation of intracranial pressures. After excluding all deaths within 48 hours, and patients with baseline renal insufficiency 157 patients remained. Patients were admitted under a medical or surgical service pending their etiology. Use of 2% or 3% saline was under the discretion of the neurosurgeon and neurologist in coordination with the medical/surgical intensivist. All patients were managed per the recommended guidelines for patients with TBI. Intensive care unit admission with continuous hemodynamic monitoring, hourly neuro-checks, ventilatory support when indicated, and management of medical conditions or trauma burden was performed. Neurosurgery were consulted in all cases of intracranial hemorrhage regardless of etiology. A serum sodium between 150–159 meq was defined as therapeutic, and administration of HTS was held when sodium was greater than 160 meq or serum osmolality was greater than 320. AKIN classification was used as it relies solely on serum creatinine (Scr) levels and not glomerular filtration rate (GFR) changes. SCr levels at baseline, defined to be admission SCr, and at 48-hour interval were recorded. AKIN staging 1 through 3 was defined as per *Table 1*.

Results

A total of 157 patients were assessed. Patient population and demographics are illustrated in *Tables 2,3*; majority of the mechanism for TBI were non-traumatic including 32.0% hemorrhagic stroke and 20.1% ischemic stroke. As illustrated in *Table 4*, 93.6% of patients did not sustain any form of AKI, 5 patients (3.2%) sustained stage 1 injury, 2 patients (1.3%) sustained stage 2 injury and 3 patients (1.9%) sustained stage 3 injury.

Out of 157 patients that were treated with either 2% or 3% HTS, 65 people (41.4%) were at one point super-therapeutic with serum sodium measuring greater than 160 meq or serum osmolarity >320.

Table 3 Patient demographics (N=169)

Mechanism	N	Percent
MVA	8	4.7
Assault	10	5.9
Hemorrhagic stroke	54	32.0
Fall	25	14.8
Coiling	4	2.4
Ischemic stroke	34	20.1
Metabolic	7	4.1
Pedestrian struck	12	7.1
Ischemic stroke converted to hemorrhagic	10	5.9
Other	5	3.0

MVA, motor vehicle accident.

Table 4 Results (N=157)

Stage AKIN criteria	N (%)
1	5 (3.2)
2	2 (1.3)
3	3 (1.9)

147 patients (93.6%) did not sustain acute kidney injury that met AKIN criteria. AKIN, Acute Kidney Injury Network.

Discussion

Management of TBI focuses on the prevention of the secondary insult caused by increased intracranial pressure. This can be accomplished using hypertonic fluids, diuretics and surgical intervention. In a previous study, conducted by the authors in our institution, it was noted that continuous infusion of 3% HTS reached therapeutic levels, defined as serum sodium >150 meq, in 1.6 days from initiation of treatment. Our hypothesis is that more aggressive resuscitation with HTS could be tolerated without increasing the incidence of renal failure. Treatment of elevated intracranial pressure in the setting of TBI is a time sensitive issue; early aggressive treatment with HTS would be more efficacious and expeditious in reaching therapeutic serum sodium levels. However, possible side effects of HTS include: rebound in intracranial pressure, central pontine myelinolysis, renal impairment, subarachnoid hemorrhage, natriuresis, high urinary water losses, hyperchloremic acidosis, and masking of the development of diabetes insidious (7).

AKI has traditionally been classified by two major classifications, the AKIN classification and the RIFLE classification. For our study, the AKIN classification was used, as it offered several advantages. RIFLE classification is based on SCr and urine output, one major limitation of this classification is that it requires the baseline SCr, which, often in the trauma setting is not available. AKIN classification, developed in 2005, allows you to classify the stage of AKI based on two creatinine lab values obtained during a 48-hour time period. The diagnosis of AKI is only considered after achieving an adequate status of hydration and after excluding urinary obstruction; the AKIN classification only relies on SCr and not on GFR changes; baseline SCr is not necessary in the AKIN classification, and it requires at least two values of SCr obtained within a period of 48 hours (13).

In our study, 147 patients, 93.6% did not demonstrate any degree of AKI as classified by the AKIN criteria. Based on our observations the incidence of acute renal failure in the setting of HTS use is low. Thus, more aggressive use of HTS may be tolerated. Our study does carry limitations that are inherent to a retrospective review of prospectively collected data. Additionally, patients who met AKIN stage 2 or 3 criteria may have sustained AKI secondary to other physiologic insults associated with shock and trauma. However, the results are strongly favoring a low incidence rate. Further studies to develop a protocol that takes into account concentrate of HTS and route of bolus *vs.* continuous infusion are needed to shorten the time to treatment in the TBI patient population with HTS.

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Footnote

Conflicts of Interest: The authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/amj.2018.04.02). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki

(as revised in 2013). This study was approved by Lutheran Medical Center Health System Institutional Review Board (Protocol 652). Informed consent was waived due to the retrospective nature of the study.

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