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Association of high volumes of hydroxyethyl starch with acute kidney injury in elderly trauma patients

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ABSTRACT

Introduction: Initial fluid resuscitation in trauma is still controversial. Hydroxyethyl starch (HES), a commonly used fluid for resuscitation in trauma patients, has potential nephrotoxic effects. Advancing age is a known risk factor for acute kidney injury (AKI) in trauma patients. Therefore, the objective of this study was to evaluate the impact of large volumes of HES 130/0.4 on renal function in trauma patients, with a particular focus on the significance of age.

Methods: A retrospective review of all patients admitted to the Trauma Centre of the University Hospital Regensburg from September 1, 2007 to December 31, 2012 was performed. This investigation used data from the TraumaRegister of the German Trauma Society (DGU®), including preclinical data from the prehospital emergency physician's protocol, the patient data management system of the intensive care units and the anaesthesia protocols of the emergency room and the operating room. AKI was evaluated according to the risk, injury, failure, loss, or end-stage kidney disease (RIFLE) criteria. The rate of AKI and the rate of renal replacement therapy (RRT) were compared between patients who received $<$ 2000 ml HES 130/0.4 during the first 24 h (L-HES) after trauma and patients who received $\geq$ 2000 ml HES 130/0.4 during the first 24 h (H-HES) after trauma. An additional sub analysis of patients older than 59 years of age was performed.

Results: A total of 260 patients were included. Although patients in the H-HES group showed a higher injury severity score, the incidence of AKI and RRT were comparable. Furthermore, the sub analysis of patients older than 59 years of age also demonstrated similar results regarding incidence of AKI and the rate of RRT.

Conclusions: Fluid resuscitation with more than 2000 ml HES (130 kD/0.4) during the first twenty four hours after trauma was not associated with an increased incidence of AKI or need for RRT in trauma patients compared to patients who were administered $<$ 2000 ml HES (130 kD/0.4). The analysis of patients older than 59 years of age did not demonstrate any difference in the incidence of AKI or the need for RRT.

Introduction

Due to the fact that haemorrhagic shock is one of the most common causes of death in trauma, fluid administration is an essential part of trauma resuscitation. Although crystalloids are recommended as the first line treatment for trauma patients [1], there is evidence that large volumes of isovolemic solutions are associated with possible complications [2]. Conversely, colloid solutions may sustain intravascular volume for a longer duration and likely minimize resuscitation volume [3,4]. Furthermore, initial resuscitation with HES, a synthetic colloid, seems to have beneficial effects in trauma patients [5–8].

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Recent investigations of volume resuscitation in septic patients have demonstrated a detrimental effect of HES on renal function and mortality [9,10]. These detrimental effects of HES seem to increase with accumulating doses [11]. Because of these recent findings, the European Medicines Agency (EMA) has restricted the use of HES in patients with acute hypovolemia caused by sudden blood loss. However, the expected benefit should be considered. Because of the lack of safety data regarding the use of HES in trauma patients, the EMA recommends additional studies in these patients [12].

AKI is a frequent complication in trauma patients with a profound impact on survival. The incidence of AKI in trauma patients ranges between 15% and 36% [13,14]. Advancing age and blunt trauma are known risk factors for AKI in trauma occurrence [14,15]. It is essential to evaluate the data regarding safety of HES 130/0.4 because of the known risk factors of AKI in trauma and the possible detrimental effects of HES.

Consequently, the aim of this study was to compare the rate of AKI and the rate RRT in patients treated with low doses of HES or high doses of HES during the first 24 h after trauma, with particular focus on the significance of age on AKI in trauma. Thus, we conducted a retrospective observational survey that included all trauma patients during a five-year period at a level one trauma centre.

Methods

Design

A retrospective review of all patients admitted to the Trauma Centre of the University Hospital Regensburg from September 1, 2007 to December 31, 2012 was performed. This investigation used data from three databanks and included the preclinical data from the prehospital emergency physician's protocol. The database includes the TraumaRegister of the German Trauma Society (DGU®) (TR) (with its own variables), the patient data management system (PDMS) of the intensive care units (MetaVision®) and the anaesthesia protocols of the emergency room and the operating room (MedLink®). The study was approved by the Ethics Board of the University Hospital of Regensburg (approval number: 14-101-0004).

The TR is a study registry with multicenter, standardized and anonymous documentation of multiple injured trauma patients [16]. The data collection for this study included four consecutive post-trauma phases from the injury to hospital discharge: (I) prehospital phase; (II) emergency room/department and initial surgery; (III) ICU and (IV) outcome status at discharge. Additionally, 300 more preclinical and trauma room management variables were collected in our hospital.

All three databases were matched, and the following data points were abstracted: the patient's demographics (age, sex and weight), systolic blood pressure at presentation, pH, pO_2 and SpO_2 at admission, amount of catecholamines during the first 24 h, fluid resuscitation during the first 24 h (colloid and crystalloids [balanced electrolyte solutions or NaCl]) and blood products administered during the first 24 h. Furthermore, the following measurements were recorded: the injury severity score (ISS) [2,17,18], new injury severity score (NISS) [19], a scoring system for an anatomic classification of injuries, revised injury severity classification (RISC) [18,20], a scoring system for mortality, standardized mortality ratio (SMR), a ratio of recorded to expected mortality and Simplified Acute Physiology Score (SAPS) [21]. Moreover, the number of operations, number of emergency operations, length of hospital stay, mortality rate during the first 7 days and total mortality were recorded. Acute traumatic coagulopathy (ATC) was defined as a partial thromboplastin time > 60 s and/or an International Normalized Ratio ≥ 1.5 at presentation. Emergency operations included all operative procedures performed during the initial assessment.

AKI was determined by the risk, injury, failure, loss, or end-stage kidney disease (RIFLE) criteria [22] and was evaluated by comparing the daily urine output and creatinine measurements with baseline values during the first 7 days. The indications for RRT were at the discretion of the ICU clinicians and data were collected during the hospital stay.

Patients

This study includes all trauma patients within the mentioned period with ISS > 16 and age older than 16 years of age. Patients who were transferred from another facility, received colloids other than HES with a molecular weight of 130 kDa and a molar substitution rate of 0.4 (6% HES 130/0.4) or patients with missing data were excluded from further analysis. Furthermore, patients who died within 24 h were excluded from analysis (Fig. 1). Patients may have been excluded using multiple exclusion criteria.

Patients who were administered high volumes of HES were identified as having a total amount of HES during the first 24 h of ≥ 2000 ml (H-HES), whereas patients with a low volume of HES received < 2000 ml during the first 24 h (L-HES). The indications for the application of HES and the volume of HES were at the discretion of the clinicians. All patients received a crystalloid solution.

Statistics

Continuous variables were reported as the means (standard deviations) or medians (quartiles), and categorical variables were reported as the frequencies (percentages). While continuous variables were compared using Student's *t*-test or the Mann–Whitney *U*-test, the chi-squared *or Fisher's exact test* was

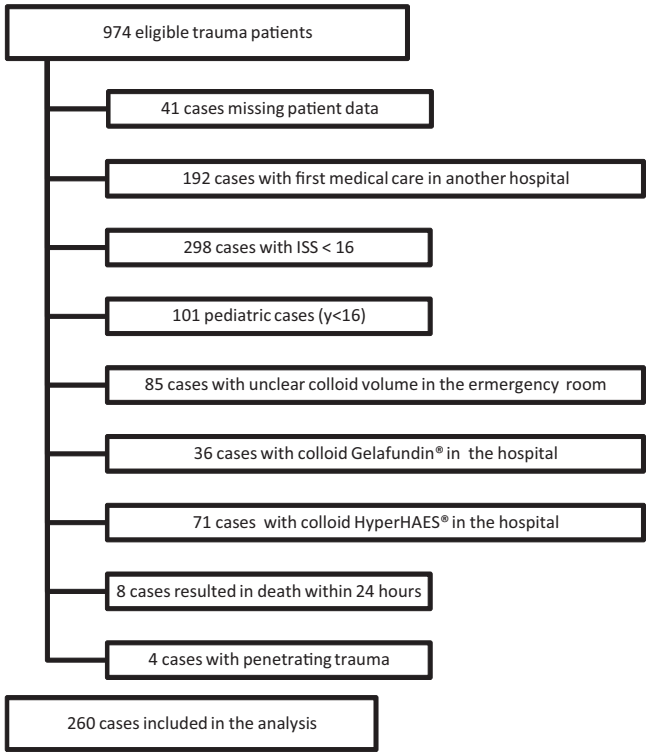

Fig. 1. Flow diagram of determination of our study population. ISS = injury severity score.