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Association of 6% hetastarch resuscitation with adverse outcomes in critically ill trauma patients

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Abstract

BACKGROUND: Six percent hetastarch is used as a volume expander but has been associated with poor outcomes. The aim of this study was to evaluate trauma patients resuscitated with hetastarch.

METHODS: A retrospective review was performed of adult trauma patients. Demographics, injury severity, laboratory values, outcomes, and hetastarch use were recorded.

RESULTS: A total of 2,225 patients were identified, of whom 497 (22%) received hetastarch. There were no differences in age, gender, injury mechanism, lactate, hematocrit, or creatinine. The mean injury severity score was different: 29.7 ± 12.6 with hetastarch versus 27.5 ± 12.6 without hetastarch. Acute kidney injury developed in 65 hetastarch patients (13%) and in 131 (8%) without hetastarch (relative risk, 1.73; 95% confidence interval [CI], 1.30–2.28). Hetastarch mortality was 21%, compared with 11% without hetastarch (relative risk, 1.84; 95% CI, 1.48–2.29). Multivariate logistic regression demonstrated hetastarch use (odds ratio, 1.96; 95% CI, 1.49–2.58) as independently significant for death. Hetastarch use was independently significant for renal dysfunction as well (odds ratio, 1.70; 95% CI, 1.22–2.36).

CONCLUSIONS: Because of the detrimental association with renal function and mortality, hetastarch should be avoided in the resuscitation of trauma patients.

The ideal fluid for the resuscitation of trauma patients has been the subject of much controversy. Crystalloid solutions were the first to be used and are still the recommended first-line treatment by the Advanced Traumatic Life Support course.[1] However, there is evidence that isotonic crystalloids may be proinflammatory.[2–4] Colloids have been proposed as an alternative because of their ability to remain in the intravascular space for a longer period. They also have been shown to reduce inflammation compared with crystalloids.[5,6] A recent study, however, suggested that there is no difference between the protein colloid albumin and crystalloid resuscitation in critically ill patients and that the subgroup of injured patients may have worse outcomes with albumin, particularly those with traumatic brain injuries.[7] Furthermore, synthetic starch-based colloids have been associated with worse outcomes in patients with sepsis characterized by a higher rate of renal dysfunction and a trend toward increased 90-day mortality.[8]

Because the ideal fluid for resuscitation of the trauma patient has not been established, we sought to evaluate if 6% hetastarch use within the first 24 hours of a traumatic injury was associated with adverse outcomes. Specifically, this study was designed to evaluate differences in rates of acute

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kidney injury and mortality between critically ill trauma patients who received 6% hetastarch compared with those who did not.

Methods

The University of Maryland Medical Center institutional review board approved the study. The trauma data registry of the R Adams Cowley Shock Trauma Center, an academic tertiary care regional referral trauma center, was queried for all patients between July 1, 2003, and June 30, 2008, aged >18 years. Patients who were admitted for a primary traumatic mechanism to an intensive care unit and had injury severity scores (ISS) $\geq$ 9 were identified. Patients who survived for <24 hours after admission were excluded because early deaths of unsalvageable patients dilute the impact of an intervention. Most of those deaths occurred within 1 hour of hospital admission and were likely unpreventable. Demographic variables, ISS, trauma and ISS probability of survival (TRISS), admission vital signs, and mechanism of injury were recorded. Total fluids received during the first 24 hours were recorded. Initial laboratory values, including lactate, creatinine, and hematocrit, were recorded as well. Outcome variables included death, diagnosis of acute kidney injury, and the combined outcome of death or acute kidney injury. Acute kidney injury was defined using the creatinine estimate of glomerular filtration on the basis of the RIFLE (risk for kidney dysfunction, injury to the kidney, failure of kidney function, loss of kidney function, and end-stage kidney disease) criteria. Patients were considered to have acute kidney injuries if they met injury criteria or greater: a rise in creatinine >2 times above the patient's baseline, corresponding to a 50% reduction in glomerular filtration.[9] End-stage kidney disease present on admission was excluded from consideration of acute kidney injury. A pharmacy billing database was queried to identify which patients were administered 6% hetastarch within 24 hours of arrival to the hospital.

There were no resuscitation protocols in place during the study period. Fluid choice was based on physician preference. The general resuscitation strategy used at the institution is to resuscitate to normovolemia and to reverse shock as determined by the end points of lactate and/or mixed or superior vena cava oxygen saturation, or appropriate hemodynamic parameters.

Patients were divided into 2 groups: those who received 6% hetastarch 450/0.7 within the first 24 hours after hospital arrival and those who did not receive hetastarch within the first 24 hours after hospital arrival. Univariate analysis was performed to determine differences between these 2 groups in terms of demographics, injury mechanism and severity, physiologic variables, laboratory values, amount of fluids and blood given in the first 24 hours, and the categorical outcomes of acute kidney injury and death. Need for operative intervention was compared between groups as well.

Fisher's exact tests were used for categorical variables, and Student's t tests were used for continuous variables. Multivariate regression models were then constructed to determine if 6% hetastarch remained an independent risk factor for death and/or acute kidney injury after controlling for the other variables associated with hetastarch use and significantly different between the groups with and without hetastarch. Specifically, the variables included in the multivariate analysis were hetastarch use, ISS, systolic blood pressure, number of packed red cells infused, and total fluids infused. Next, interaction terms were included in the regression models to discern any effect of 6% hetastarch on outcomes within specific subgroups. An operative and a nonoperative subgroup were analyzed. The operative subgroup was defined as patients requiring operative intervention within the first 24 hours of hospital arrival. Furthermore, because of concerns that patients with traumatic brain injuries may have disproportionately increased mortality with synthetic colloid administration, a moderate or severe brain injury subgroup and a subgroup with no or minor brain injuries were analyzed separately. Moderate or severe brain injury was defined as a patient having a brain abbreviated injury score $\geq$ 2. Dependent variables included the outcomes of death, renal failure, and the combined end point of death or renal failure.

Results

A total of 2,225 critically injured patients were included in the study. Overall, there were 1,719 male patients (77%) and 1,921 blunt injuries (86%). The average age was 44 $\pm$ 19 years. Two hundred ninety-five patients died, for a mortality rate of 13%. The overall mean ISS was 28.0 $\pm$ 12.6, and the mean TRISS was .80 $\pm$ .24. One hundred ninety-six (9%) patients developed acute kidney injuries.

Of the 2,225 patients, 497 (22%) received 6% hetastarch 450/0.7 within the first 24 hours of hospital arrival. With the exception of 6 patients who received 6% hetastarch in a balanced salt solution (ie, lactated Ringer's), most patients (99%) received starch in a normal saline solution. The mean dose of hetastarch in the first 24 hours was 725 $\pm$ 400 mL (median, 500 mL). The demographics for the groups with and without hetastarch are listed in Table 1. Initial physiologic and laboratory variables are listed in Table 2. ISS and systolic blood pressure were different between groups. Lactate trended toward significance, but of note, lactate values were available for only 575 patients. The mean TRISS was .76 $\pm$ .27 in the hetastarch group compared with .81 $\pm$ .23 in the group without hetastarch ($P < .01$).

Total fluids given in the first 24 hours were 10,510 $\pm$ 5,585 cm^3 in the hetastarch group versus 8,785 $\pm$ 5,404 cm^3 in the group without hetastarch ($P < .01$). The hetastarch group received more blood than the group without hetastarch (5.0 $\pm$ 8.4 vs 3.0 $\pm$ 7.0 U packed red blood cells, $P < .01$) and more fresh frozen plasma (3.4 $\pm$ 6.6 vs 2.2 $\pm$ 5.4 U, $P < .01$).