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Bicarbonate and mannitol treatment for traumatic rhabdomyolysis revisited

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Abstract

BACKGROUND: A rhabdomyolysis protocol (RP) with mannitol and bicarbonate to prevent acute renal dysfunction (ARD, creatinine >2.0 mg/dL) remains controversial.

METHODS: Patients with creatine kinase (CK) greater than 2,000 U/L over a 10-year period were identified. Shock, Injury Severity Score, massive transfusion, intravenous contrast exposure, and RP use were evaluated. RP was initiated for a CK greater than 10,000 U/L (first half of the study) or greater than 20,000 U/L (second half). Multivariable analyses were used to identify predictors of ARD and the independent effect of the RP.

RESULTS: Seventy-seven patients were identified, 24 (31%) developed ARD, and 4 (5%) required hemodialysis. After controlling for other risk factors, peak CK greater than 10,000 U/L (odds ratio 8.6, $P = .016$) and failure to implement RP (odds ratio 5.7, $P = .030$) were independent predictors of ARD. Among patients with CK greater than 10,000, ARD developed in 26% of patients with the RP versus 70% without it ($P = .008$).

CONCLUSION: Reduced ARD was noted with RP. A prospective controlled study is still warranted. Published by Elsevier Inc.

Controversy remains regarding the use of a forced alkaline diuresis with mannitol and bicarbonate for the treatment of trauma-induced rhabdomyolysis.[1–3] Recent reviews and international consensus statements have not advocated for such a protocol.[3,4] While the results of numerous preclinical studies led to a widespread practice of inducing a forced alkaline diuresis to prevent myoglobinuric renal failure, clinical observational studies fail to consistently demonstrate a protective effect. The objective of this study is to examine the impact of using a mannitol

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and bicarbonate protocol to deter the development of acute renal dysfunction (ARD) after traumatic rhabdomyolysis. The hypothesis in this study was that the use of mannitol and bicarbonate is associated with preserved renal function.

Methods

Treatment protocol

The trauma service at Oregon Health & Science University developed and implemented a practice guideline for the identification and treatment of trauma patients with severe rhabdomyolysis in 1992. Based on a review of the literature, a serum creatine kinase (CK) level of 10,000 U/L was initially chosen as the indicator of severe rhabdomyolysis and the threshold for initiating a forced alkaline diuresis via the rhabdomyolysis protocol (RP; Fig. 1). Serum CK was chosen as the marker of rhabdomyolysis degree due to its speed of measurement, relatively low cost compared with other biochemical markers, and frequent use in previous studies.[2,5–9] The RP goals were to induce a brisk flow of urine within 1 hour and to raise the urine pH to greater than 6.0. The objective of choosing a specific treatment threshold was to include all patients at significant risk of developing ARD (defined as a serum creatinine [Cr] $>$ 2.0 mg/dL), while excluding patients at such low risk that use of an extensive protocol was unnecessary. Among patients who did not meet the threshold CK level for institution of the RP standard, nonprotocolized fluid management was provided, typically a urine output goal of .5 mL/kg/hour.

An interim analysis in 1997 revealed that no patients with a peak CK level less than 20,000 U/L required dialysis and only 13% of patients with a peak CK between 10,000 and 20,000 U/L developed ARD. This led to an increase in the CK threshold for initiating the protocol from 10,000 to 20,000 U/L. Consequently, there were patients with similar CK levels who did and did not receive RP to include in our analysis.

Data collection

The Oregon Health & Science University trauma registry was queried to identify patients with rhabdomyolysis treated at our Level 1 trauma center over a 10-year period (1993 to 2002). This time span included the 5 years before and after the increase in the CK treatment threshold from 10,000 to 20,000 U/L. Patients were selected for detailed chart review if they had an International Classification for Disease-9th Revision code for acute renal failure (584.9, 985.5), crush injury (925 to 929), rhabdomyolysis (728.88), myoglobinuria (791.3), or a procedure code for fasciotomy. Patient medical records were reviewed and individuals with a CK greater than 2,000 U/L (approximately 5 times the upper limit of normal, 4 to 397 U/L) were included in the study. Patients were excluded from the data analysis if they had pre-existing chronic renal insufficiency or a clearly established cause for developing renal failure other than rhabdomyolysis.

Data retrieved from the trauma registry for this analysis include age, gender, mechanism of injury, Injury Severity Score (ISS), shock on admission (systolic blood pressure $<$ 90 mm Hg), massive transfusion ($>$10 units of blood during the first 24 hours), interhospital transfer status, time of injury, time of arrival at a medical facility, time to treatment (time from injury to admission), and mortality. Information recovered from the medical record included exposure to intravenous contrast during the first 48 hours of admission, laboratory values, the use of dialysis, and whether the RP was employed.

Data analysis

The primary outcome measure was ARD, defined as having a serum Cr greater than 2.0 mg/dL. The secondary outcome measure was receiving renal replacement therapy. Univariate analyses were used to identify variables associated with ARD. Data with normal distributions were analyzed with the Pearson chi-square, Fisher's exact, and independent-samples t test, when appropriate. The Mann–Whitney U test was utilized for nonparametric data. Variables with a P value less than .2 on univariate analysis were included in a multivariable analysis using binary logistic regression to determine independent predictors of ARD with a P value less than .05. Variables that were inherently related were analyzed using separate models. Statistical analysis was performed using SPSS 22.0 software (SPSS, Inc., Chicago, IL) and STATA 13.1 software (StataCorp, College Station, TX). Our Institutional Review Board approved this project and a waiver of consent was granted.

Results

Using the inclusion criteria described, the records of 77 patients were analyzed. A peak CK less than 10,000 U/L was noted in 21 of these patients, 22 had a peak CK between 10,000 to 20,000 U/L, and 34 had a peak CK greater than 20,000 U/L. Most patients were seriously injured (mean ISS = 23 $\pm$ 14), including 35% who presented in shock, 29% who required a massive transfusion, and 27% who received a fasciotomy for extremity compartment syndrome (Table 1). Two thirds (66.3%) of patients had exposure to radiographic contrast agents (computed tomography scans and/or angiography). The mean time from admission to peak CK level was 21.7 $\pm$ 20.7 hours. Overall, 24 patients (31%) developed ARD, 4 (5%) received dialysis, and 9 (12%) died.

Fig. 2 illustrates the distribution of patients based on peak CK levels, use of RP, and renal function. Of the 21 patients with a CK less than or equal to 10,000 U/L, none were treated with the protocol. Forty-six of 56 patients