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Altered thyroid function in severely injured patients

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ABSTRACT

Background: Hemorrhagic shock profoundly affects the neuroendocrine profile of trauma patients, and we hypothesized that massive resuscitation would negatively impact thyroid function.

Methods: A prospective, observational study investigating thyroid function in hypotensive trauma patients (systolic blood pressure <90 mm Hg × 2) who survived >48 h was conducted at a Level I center over a 6-mo period. Blood samples for thyroid function were collected at time of presentation to the trauma bay and serially for 48 h. Collected data included demographics, injury data, vital signs, transfusion needs, crystalloid use, and vasopressor requirements. Patients receiving >5 units packed red blood cells (PRBC) within 12 h were compared with those receiving ≤5 units.

Results: Patients who required >5 units of PRBC/12 h had significantly lower total and free T4 levels on initial presentation, and levels remained significantly depressed over the next 48 h when compared with patients who required a less aggressive resuscitative effort. T3 values were markedly suppressed during the initial 48 h post trauma in all patients, but were significantly lower in patients requiring >5 units PRBC. TSH levels remained within the normal range for all time points. Lower trauma admission T4 levels were associated with the need for greater crystalloid resuscitation within the first 24 h.

Conclusion: Measurements of thyroid function are significantly altered in severely injured patients on initial presentation, and low T4 levels predict the need for large resuscitation. Further research investigating the profile and impact of thyroid function in trauma patients during resuscitation and recovery is warranted.

1. Background

Although not typically considered a "stress hormone," thyroxine may play a critical role in maintaining vasomotor tone during times of physiologic stress. Abnormalities in thyroid function are known to influence cardiovascular stability and diminished levels of circulating thyroxine are associated with reduced myocardial energy, hemodynamic

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instability, and increased need for inotropic support [1–4]. Thyroid hormone replacement may reverse these metabolic derangements and dramatically improve myocardial dysfunction [1,5–7]. Intravenous thyroxine has recently been shown to improve the hemodynamic stability in severely brain-injured patients awaiting organ procurement and may be a useful cardiovascular adjunct following cardiac surgery [2,8].

Relative hypothyroidism has been observed following hemorrhagic shock and may contribute to decreased hemodynamic reserve and poor survival. Experimental models of hemorrhagic shock have demonstrated a strong association between degree of blood loss and the development of thyroid dysfunction. Specifically, T3 and T4 plasma concentrations fall drastically within minutes of experimental hemorrhagic shock [9,10]. These levels further decline during resuscitation and remain depressed for several days post hemorrhage. Animal studies also suggest that the magnitude of the T3 and T4 reduction may serve as a useful predictor of survival, with a higher mortality noted when thyroid indices failed to improve following hemorrhage [10]. Supplemental intravenous T3 following experimental hemorrhagic shock, however, appears to improve both cardiac function and survival [6,7,11].

Depressed thyroid function appears to be a harbinger of poor clinical outcome and increased mortality in critically ill patients [12]. To date, however, limited clinical data exist characterizing thyroid function in trauma patients [9,13,14]. Moreover, we hypothesize that alterations in thyroid function may be particularly pronounced in severely injured trauma patients who require massive resuscitation. In order to address this question, we investigated the profile of circulating thyroid hormone levels in severely injured trauma patients during their initial hospitalization and evaluated the potential impact of resuscitation.

2. Methods

A prospective observational study of trauma patients admitted to the Hospital of the University of Pennsylvania was conducted from March 2008 through September 2008. The Institutional Review Board of the University of Pennsylvania approved the study protocol. Initial blood samples were collected under waiver of informed consent and stored until consent and Health Insurance Portability and Accountability Act authorization were obtained from the patient or next of kin. If informed consent or Health Insurance Portability and Accountability Act authorization were not granted, samples were discarded without analysis.

2.1. Patients

All consecutive trauma patients (≥18 y old) assessed during the study period were evaluated prospectively. Patients who were hypotensive (systolic blood pressure <90 mm Hg × 2) and/or those who received packed red blood cells (PRBC) during their initial trauma resuscitation were considered for enrollment. The decision to initiate transfusion was made by the attending trauma surgeon. Exclusion criteria were pregnancy, significant intracranial injury requiring neurosurgical intervention, significant neck trauma, dialysis dependence, and thyroid supplementation or corticosteroid use within the prior 3 mo. Because of difficulty in obtaining consent, patients who died within 48 h of admission also were excluded.

2.2. Data collection

Demographic information, past medical history, mechanism of injury, Glasgow coma score, and injury severity score were documented for all patients. Serial blood samples were drawn at the following time points: on presentation to the trauma bay, on admission to the intensive care unit (ICU), and 24 and 48 h post admission. The total amount of PRBC and total crystalloid volume infused were also recorded. A PRBC requirement of >5 units within 12 h was deemed a large-volume resuscitation *a priori*. Vital signs and the use of vasopressors also were documented. The use of medications known to depress hormonal secretion (dopamine, haloperidol, and corticosteroids) was noted.

2.3. Blood sample analysis

Blood samples were collected in the trauma bay prior to the administration of intravenous fluids or blood products. Samples were processed but were discarded if patients did not meet inclusion criteria. Blood samples were collected in serum vacutainers (BD, Franklin Lakes, NJ) and were processed immediately upon collection. Serum samples were stored at −80°C until *post hoc* analysis. Thyroid hormone levels were quantified by the Diabetes and Endocrinology Research Center at the University of Pennsylvania using commercially available radioimmunoassay kits (MP Biomedicals, Solon, OH) to determine free thyroxine (unbound T4), total thyroxine (both bound and unbound T4), total triiodothryonine (total T3), free triiodothryonine (free T3), and thyroid stimulating hormone (TSH).

2.4. Statistical analysis

Mann-Whitney tests allowed comparison of T4, T3, free T3, and TSH in patients receiving >5 units of PRBC and patients receiving ≤5 units within 12 h of admission. P values of <0.05 were considered statistically significant.

3. Results

During the 6-mo study period, the trauma service evaluated 936 injured patients, of whom 96 met inclusion criteria of hypotension and/or blood transfusion for presumed hemorrhagic shock. Seventy-five of these patients were excluded due to survival <48 h, family declining consent, age <18 y, recent history of thyroid supplementation or steroid use, or chronic renal failure requiring dialysis. Eighteen patients met the inclusion criteria and all were transported directly from the scene. Patients were predominantly male (89%), between the ages of 18 and 75 y (mean age 31 ± 15 y), with injury severity scores ranging from 10-50 (mean 27 ± 14). Over 70% of these patients had sustained penetrating injuries ($n = 13$). Twelve patients received >5 units of PRBC and six patients