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Elevated cytokine levels in peritoneal fluid from burned patients with intra-abdominal hypertension and abdominal compartment syndrome☆

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Abstract

Background: Burn patients with intra-abdominal hypertension (IAH) and abdominal compartment syndrome (ACS) undergo vigorous resuscitation and accumulate peritoneal fluid (PF) that is a plasma ultra-filtrate. This study compared antithrombin (AT) and cytokine levels in burn patient plasma and peritoneal fluid (PF).
Methods: Twenty-nine patients were studied; 22 developed IAH and 9 progressed to ACS. Burn + inhalation injury was present in 22 patients; 5 had burn only and 2 had inhalation only. Sixteen patients died; of these, 9 survived less than 48 h due to the severity of their injuries. Flow cytometry utilized the Cytometric Bead Array kit for Human Th1/Th2 cytokines. AT levels were determined by the Accucolor method spectrophotometrically.
Results: All cytokine levels were significantly elevated in burn plasma and PF compared to normal plasma, $p < 0.001$. AT plasma levels were decreased compared to normal. AT and cytokines were present in peritoneal fluid of burn patients with IAH and ACS. Patients who died had decreased plasma levels of AT and increased IFN-γ, IL-10, IL-6, IL-4, IL-2 peritoneal fluid levels compared to survivors.
Conclusions: Peritoneal fluid may be a reservoir for cytokines during initial resuscitation and contributes to homeostatic perturbations in burn patients.

Keywords: Peritoneal fluid; Antithrombin; Cytokines; Thermal injury; Abdominal compartment syndrome; Intra-abdominal hypertension

1. Introduction

Burn patients are at risk for developing secondary abdominal compartment syndrome (ACS) due to massive fluid resuscitation requirements and accumulation of tissue edema [1–6]. Intra-abdominal hypertension (IAH) and ACS may also develop during septic episodes and inhalation injury [5]. Percutaneous decompression (PD) of ACS in burns has been reported as a useful alternative to damage control laparotomy not only in burn but also in trauma patients [4,5,7]. Antithrombin and cytokine levels have been studied in peritoneal fluid obtained during peritoneal dialysis, adhesiolysis, and ascitic fluid [8–11]. This study is the first characterization of the peritoneal fluid obtained from burn patients during PD and a comparison of antithrombin and cytokine levels in burn plasma and peritoneal fluid. Since peritoneal fluid is an ultrafiltrate of plasma, the hypothesis was that the AT and proinflammatory

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cytokine levels in plasma and peritoneal fluid would be equivalent in concentration.

2. Materials and methods

2.1. Sample population

In a 59-month period (April 1999–February 2004), there were 1520 admissions to the Sumner L. Koch Burn Center at John H. Stroger, Jr. Hospital of Cook County. Twenty-two (1.4%) of 1520 patients developed IAH and 9 (0.6%) progressed to ACS. There were 29 patients (22 = burn and inhalation injury; 5 = burn only; 2 = inhalation only). Peritoneal fluid without concurrent plasma samples were collected and studied in the beginning of the project; once IRB approval occurred for collecting blood samples, concurrent plasma and PF samples became available on seven patients. Blood samples on patients admitted during the same time period without IAH or ACS were collected for comparison. The study was approved by the John H. Stroger, Jr. Hospital of Cook County Institutional Review Board and informed consent was obtained from patients, parents or guardians. Patients were resuscitated as per the Practice Guidelines for burn care [12]. Escharotomies were performed as needed, either in the Burn Operating Room or the Burn Intensive Care Unit. Hemodynamically stable patients underwent burn wound excision and temporary wound coverage within the first 48 h. Those patients too unstable to be transported to the operating room underwent debridement and topical antimicrobial wound therapy in the Intensive Care Unit. No diuretics or dialysis were utilized in any of the patients during the first 3 days after admission.

2.2. Intra-abdominal pressure measurements

All burn patients at risk for IAH and ACS (circumferential chest and abdominal burns; patients with $\geq$40%TBSA) were closely monitored for increased IAP with urinary catheter transducers [13,14]. For the purpose of this study, IAP $\geq$25 mmHg was considered indicative of IAH. Once the IAP exceeded 30 mmHg with impaired pulmonary and renal function, the IAH had progressed to ACS [14,15].

2.3. Peritoneal decompression

A percutaneous peritoneal lavage catheter was placed when the IAP reached $\geq$25 mmHg, using the standard diagnostic peritoneal lavage catheter placement technique. The peritoneal lavage catheters in this kit were 9.25 in. (24 cm) (Arrow International, Inc., Reading, PA). Percutaneous drainage was a continual process with fluid draining for several days. Once the drainage stopped, the catheter was removed.

2.4. Peritoneal fluid

The peritoneal fluid was analyzed for chemical composition, cell count, and the presence of bacteria. Since there are no ''normal values'' established for peritoneal fluid in burn patients, for study purposes, the fluid contents were compared to patient serum content and ''normal'' serum levels. Chemical analyses were performed on Olympus AU640 analyzers (Olympus America, Inc., Lake Success, New York) using the manufacturer's reagents and procedures.

2.5. Antithrombin

AT was studied to determine the severity of the coagulation dysfunction in these patients. AT levels were determined by the Sigma Diagnostics (Dorset, UK) Accucolor method. The spectrophotometer was a Beckman Coulter Du 640 (Fullerton, CA). Four normal plasma samples were titrated individually; because of minimal variation, they were pooled and used as the normal plasma standard. The samples were then assayed according to the manufacturer's directions. Diluted samples or standards (200 μL) were warmed to 37 °C and a bovine thrombin and heparin mixture was added. Then substrate was added and allowed to react for 2 min with uninhibited thrombin. The reaction was stopped with citric acid and read at 405 nm.

2.6. Cytokines

Flow cytometry (BD Biosciences, San Diego, CA) utilized the Cytometric Bead Array kit for Human Th1/Th2 cytokines (BD Biosciences Pharmingen, San Diego, CA) to measure Interferon-γ (IFN-γ), tumor necrosis factor-α (TNF-α), Interleukin-10 (IL-10), Interleukin-6 (IL-6), Interleukin-4 (IL-4), and Interleukin-2 (IL-2) plasma levels, using manufacturer reagents and standards and according to manufacturer instructions. These particular cytokines were studied because they were selected by the manufacturer and could be assayed in one kit. Three ''normal'' plasma samples were run as controls.

2.7. Statistical analysis

Statistical analyses were performed utilizing Statistica® (STATSOFT, Tulsa, OK). Comparison groups consisted of blood plasma and peritoneal fluid levels by severity of injury, and mortality, and admission (days 1–2) or acute (days 3–7) sampling day. The figures show the separation of samples by time of retrieval. Because there was no significant difference between the time intervals, statistical analyses were performed combining the intervals for a higher sampling number. Summary descriptive statistics such as median, means, standard deviation and error, one-way ANOVA, chi-square 2 × 2 summary frequencies (Pearson and Maximum Likelihood), were performed. Nonparametric analyses