



Activated Protein C and Corticosteroids Decrease the Rate of Albumin Transudation in Septic Shock

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Introduction:

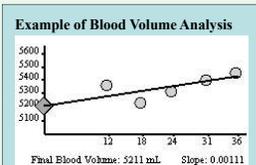
Monitoring rates of I-131 labeled albumin transudation from the intravascular compartment gives an estimate of capillary leak, a sign of inflammation. This information is available as part of blood volume measurement using Blood Volume Analyzer (BVA-100, Daxor, NY, NY).

Plasma volume is measured based on the dye dilution principle:

1. Known dose of a tracer in a known volume is injected into the patient
2. Complete mixing and equal distribution of the tracer occurs in the circulating blood volume
3. Blood samples are taken to measure the new tracer concentration in the patient and the unknown volume is then calculated

$$\text{Plasma volume} = \frac{\text{Total amount of I-131 albumin injected}}{\text{Measured amount of I-131 albumin in sample injected}} \times \text{volume}$$

After obtaining a baseline sample, albumin tagged with I-131 (in a known 1mL volume) was injected intravenously. After complete mixing, to correct for albumin transudation, serial measurements (5 samples every 6 minutes) were drawn and extrapolated to time zero to calculate plasma volume. The slope of albumin transudation is presented as a numeric value with 0.0025 (0.25 of 1% per minute exiting the circulation) as being normal. Estimation of capillary permeability may provide a tool to assess efficacy of certain treatments.

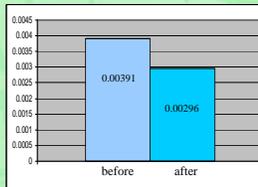


Hypothesis: Activated protein C (APC) and steroids may affect capillary permeability, as measured by the rate of albumin transudation, in patients with severe sepsis/septic shock.

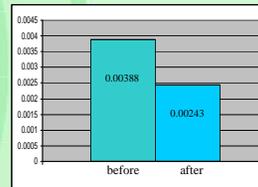
Methods: Blood volume analysis was performed in surgical patients with septic shock on days 1,2,3, and 5-7 after resuscitation. Patients were treated per protocol to early goal directed therapy. Those with evidence of adrenal failure (baseline cortisol <18µg/dL or post-cosyntropin stimulation change <9 µg/dL) were given 50mg hydrocortisone every six hours. Failure to meet endpoints of resuscitation, including transcutaneous pressure of O₂ (PtcO₂) goal via oxygen challenge test prompted initiation of APC in addition to steroids.¹ Sequential analysis of BVA allowed measurement of albumin transudation rate before and 24 hours after starting steroids and/or APC.

Results: Seventy five patients with severe sepsis or septic shock were included in the study. Of these, 50 patients contributed 116 instances of steroid therapy alone and 25 patients contributed 35 instances of concurrent treatment with steroids and APC. All patients had elevated pretreatment rate of albumin transudation (>.0025) and a follow-up analysis 24 hours after treatment initiation.

Albumin Transudation Rate with Steroids & APC



Albumin Transudation Rate with Steroids Alone



	Steroids (n=50)	Steroids & APC (n=25)
Age	58 15	67 18
M:F	35:15	15:10
Septic shock	21 (42%)	19 (76%)
Severe sepsis	29 (58%)	6 (24%)
APACHE II	27 3	28 4
Mortality	6/50 (12%)	7/25 (28%)
Pretreatment transudation rate	0.00388 0.00144	0.00391 0.00117
Posttreatment transudation rate	0.00243 0.00191	0.00294 0.0017
p-value	<0.0001	<0.004

Conclusions: Elevated rates of albumin transudation were significantly decreased with use of APC and steroids in severe sepsis and septic shock. While steroids have a debatable effect on mortality in severe sepsis and septic shock, patients given steroids experience earlier reversal of their shock states with a hastened wean off vasopressors.^{2,3} In our patients we observed that the elevated pretreatment rates of albumin transudation returned to normal within 24 hours of initiating steroid therapy alone. For patients who failed to meet PtcO₂ goals by the oxygen challenge test, APC was given in addition to steroids. APC has been shown to temper endothelial dysfunction by decreasing leukocyte adherence, leukocyte emigration, and venular permeability to protein in a hypoxic injury model.⁴ Patients receiving both APC and steroids also demonstrated a significant decrease in albumin transudation rates, though a normal level of 0.0025 was not observed within 24 hours of initiating therapy. This group had a higher proportion of patients with septic shock, higher mortality, and a greater degree of microcirculatory dysfunction would have been expected. It is difficult to separate out the effects of APC independent of steroids since patients who required APC required steroids as well. Measuring albumin transudation rates may provide an additional tool to assess microvascular integrity and an objective marker of response to treatment.

References

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