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TITLE: CONSUMPTIVE COAGULOPATHY AS PREDICTOR OF OUTCOME IN PURPURA FULMINANS

AUTHORS: M.L. McManus and K.B. Churchwell
AFFILIATION: Dept. of Anesthesia, Children's Hospital, Harvard Medical School, Boston, MA 02115

Purpura fulminans, most commonly associated with meningococcemia, has been the subject of clinical study for decades. Many studies have focused upon the search for accurate predictors of mortality, yet have neglected significant morbidity. Common to most scoring systems is the identification of both a consumptive coagulopathy and an overwhelmed immune system. Recently it has been suggested that risk factors and prognostic scoring systems deemed valid in the 1960's and 70's are no longer relevant- perhaps due to improvements in medical care (1). Additionally, some authors have attempted to identify single tests, rather than multiple factors, as predictive of mortality (2). Rapid identification of patients at high risk for mortality or serious morbidity is helpful for triage, family counseling, and early direction of the medical team toward aggressive or even experimental interventions.

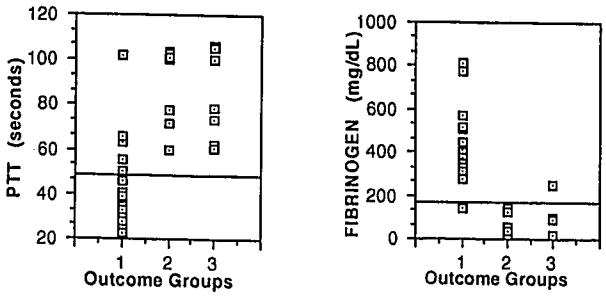
In order to determine current and accurate predictors of morbidity and mortality in patients presenting to our intensive care unit, we reviewed the records of 44 children aged 18d-17y (mean= 3.73yr) admitted with infectious purpura since 1982. Blood or CSF cultures in thirty-five of these was positive for N. Meningitidis. For all patients, mean PRISM score was 7.9 with a range of 1-34. Significant morbidity was defined as serious debilitating or disfiguring injury including CNS damage, limb amputation, and skin loss with the requirement for grafting.

In this population, there were 7 deaths (15.9%) and 7 patients with significant morbidity (15.9%). Mean PRISM score for these patients was 15.7. Regarding mortality, application of the criteria of Niklasson, et. al. (3) gave a sensitivity of 71.4% and specificity of 91.1%. Sensitivity/ specificity analysis of the criteria of Stelm and Damosh (4) gave values of 71.4% and 91.4% respectively.

Detailed record review and multivariate analysis identified consumptive coagulopathy on admission (ie. fibrinogen< 150 mg/dl or PTT> 2 x control) as most informative. Of 10 patients presenting with low fibrinogen, 4 died and 5 experienced significant morbidity (90%). Of 19 patients presenting with PTT>2x control, 14 experienced death or significant morbidity (73.7%). Sensitivities and specificities for fbgn< 150 were 90% and 95% respectively, while those for PTT> 2x control were 100% and 82.7%. The Positive Predictive Value of low fibrinogen in predicting mortality or serious morbidity was 90% and of elevated PTT was 73.7%. Accuracy was not improved by addition of other classical risk factors such as low white blood cell count.

We conclude that, in our practice, the most accurate predictor of death or serious morbidity in patients presenting with purpura fulminans is the presence of significant consumptive coagulopathy (particularly low fibrinogen) at the time of admission. Accuracy is sufficient to render elaborate, expensive or invasive assays for this purpose unnecessary.

Outcome and Coagulation Parameters at Time of Admission:
Group 1- intact survival
Group 2- survival with significant morbidity
Group 3- expired



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2. Crit Care Med 19(3):430, 1991
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4. Scan J Infect Dis 3:17, 1971

A287

Title: **PHARMACOKINETICS AND COMPARATIVE EFFICACY OF EPINEPHRINE DURING OUT-OF-HOSPITAL CPR**

Authors:J. Schüttler, M.D., U. Hörnchen, M.D., and F.Bremer, M.D.

Affiliation:Institut für Anästhesiologie der Universität,Bonn, Germany

Introduction: Although epinephrine is currently the vasopressor of choice in CPR there is great concern about its optimal dose and route of administration (1,2). We studied the clinical efficacy and pharmacokinetics of epinephrine (E) after IV and endobronchial (EB) administration in out-of-hospital CPR.

Methods: One hundred patients with witnessed cardiac arrest undergoing out-of-hospital CPR were included into this study which was approved by the local ethical committee. BCLS and ACLS were performed by a mobile emergency care service following a regional protocol with AHA algorithms including early ecg-diagnosis, immediate defibrillation in case of ventricular fibrillation (VF), and rapid endotracheal intubation. Pharmacological support was provided by E with IV administration (1 mg) or deep EB instillation (2.5 mg) with a 45cm catheter in cases were IV access was delayed for more than 1 min. Repetitive IV doses of E (1 mg) were given thereafter as necessary. A detailed documentation was performed and up to 4 blood samples were taken for E measurement by HPLC. Pharmacokinetic analysis was performed by multiple nonlinear regression of population data (NONMEM). Statistical significance ($p<0.05$) was assessed by U-test and chi-square-test.

Results: 43 patients demonstrated VF the other were asystolic. 11 patients (9 VF) were successfully resuscitated without requiring therapeutic E. Their initial E plasma concentrations were extremely elevated (113.7 ± 90.2 pmol/ml) (Fig.1). In 13 patients IV E was the initial treatment during ACLS while the EB route of administration was preferred in 76 patients in order to minimize time delays of drug therapy. There were no significant differences in the primary success rate (53.8% IV vs. 57.9% EB) and discharged survivors (23.1% IV vs. 21.1% EB) within the two groups. Peak plasma concentration of E (1928 ± 1313 pmol/ml) following IV injection (Fig.2) was observed after 2 min which was significantly faster when compared to EB administration (Fig.3) with 4 min (295.8 ± 228.8 pmol/ml). There was no linear relationship between the initial E peak plasma level and success rate of CPR. However, there was a threshold concentration of 50 pmol/ml E which was exceeded in most patients with successful CPR. Total doses of 4 to 10 mg of E were necessary for the primarily restoration of spontaneous circulation in 27 patients.

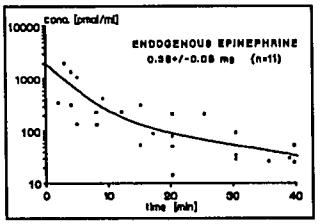

Fig.1

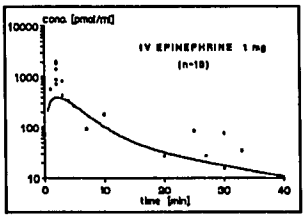

Fig.2

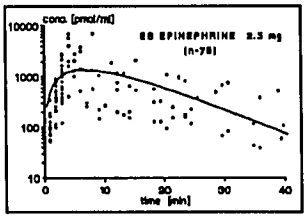

Fig.3

Conclusions: While the EB administration of 2.5 mg of E is equally effective as 1 mg of IV E, and an endotracheal tube can often be placed more rapidly than an IV line this route of drug administration should be the preferred one in CPR. Higher total doses of E than currently recommended with total doses of up to 10 mg may be necessary to guaranty initial CPR success. Survival rates become extremely low (<2%), however, when more than 3 mg of E have been exceeded.

References: 1. Crit.Care Med.17:437 (1989) 2. Lancet I:828 (1987)