INFUSION OF ARGININE-VASOPRESSIN (AVP) ENHANCES BLOOD PRESSURE AND RENAL FUNCTION WHILE PRESERVING CEREBRAL AND SPLANCHNIC PERFUSION IN PATIENTS IN SEPTIC SHOCK

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Introduction: Septic shock is characterized by profound peripheral vasodilation and hypotension refractory to norepinephrine (NE). Septic patients are exquisitely sensitive to the vasopressor effects of exogenous arginine-vasopressin (AVP) at the V1-receptor. We designed a prospective, randomized, double-blind study to test the hypothesis that in patients with septic shock supported by norepinephrine, addition of AVP infusion provides superior blood pressure (BP) support and improves renal function without worsening splanchnic or cerebral perfusion.

Methods: After IRB approval and informed consent from patients or their proxies, patients who met criteria for septic shock and who required an infusion of NE for BP support were randomized to the AVP (n = 12) or placebo (n = 11) group. Baseline measurements were made after a 30 min stabilization period (T0), followed by a blinded 4 hr infusion of either AVP (1-6 u/hr) or saline placebo during which a second set of measurements were made (T1). Fluid was administered to keep pulmonary artery occlusion pressure (PAOP) = 12 mmHg and NE was adjusted to keep mean arterial pressure (MAP) > 65 mmHg. Data collected included hemodynamics, intramucosal gastric pH (pHi) by gastric tonometry, Doppler cerebral artery flow velocity and 30 min creatinine clearance (CCr). During the study the dosage of all other vasoactive drugs was kept constant. Statistical analysis was performed by ANOVA.

Results: Data are expressed as mean ±SD % change from baseline (T1 vs. T0). There was no significant difference in hemodynamic profile between the two groups at either T0 or T1. However, in the AVP group the dose requirement for NE was decreased by 65 ±34 % ($p < 0.0003$ compared to placebo). CCr (125% vs 49%, $p < 0.05$) and urinary flow (78% vs 65%, $p < 0.04$) increased significantly with AVP compared to placebo. There were no significant changes in pHi, cerebral artery flow velocity, or arterial lactate acid levels between the two groups. Plasma AVP was decreased in both groups at T0 (1.5 ±0.5 vs 1.72 ±0.72 pg/mL, NS) but increased significantly in the AVP group at T1 (32.3 ±7.69 vs 1.84 ±0.59 pg/mL, $P < 0.05$).

Conclusions: This study was not powered to detect a difference in outcome between the two groups. Nonetheless, it provides compelling evidence that in patients in septic shock, the enhancement in BP induced by low dose AVP infusion (1-6 u/hr) is associated with improved renal function and does not have adverse effects on gastric or cerebral perfusion. The addition of AVP infusion should be considered for the management of septic shock whenever response to NE alone is inadequate.