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Diabetes Insipidus After Discontinuation of Vasopressin Infusion for Treatment of Shock

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To the Editor,

Ferenchick and colleagues' report a series of 29 adult patients who developed diabetes insipidus after discontinuation of vasopressin infusion (DIDVI) for treatment of shock.[1] This intriguing observation was very uncommon with a single center occurrence rate of 1.53% (29 of 1,896 patients) but has been observed in patients who have been treated with both an adrenergic vasoconstrictor and vasopressin and in whom vasopressin is discontinued first. [2–5] The suggested mechanism of hypothalamic suppression associated with very high dose vasopressin infusion in cardiac surgery patients is unlikely to fully explain the phenomenon. Thus the report provides little insight regarding a potential mechanism or risk factor profile that could potentially identify patients at higher risk for DIDVI.

The authors acknowledge vasopressin receptor tachyphylaxis with prolonged agonist exposure. However alternative explanations include variations in vasopressinase (leucyl/cystinyl aminopeptidase [LNPEP]) activity coded by LNPEP rs4869317. In a post-hoc analysis of the Vasopressin in Septic Shock Treatment (VASST) trial, Nakada and colleagues reported that the rs4869317 TT genotype of LPENP was associated with increased 28-day mortality (51.0% [TT] vs 34.5% [AA/AT]; adjusted hazard ratio [HR], 1.58; 95% CI, 1.21–2.06; P = .00073) and confirmed this finding in a second independent replication cohort (38.6% vs 29.6%; HR, 1.36; 95% CI, 1.03–1.80; P = .030).[6] The TT genotype was associated with significantly increased plasma vasopressin clearance (P = .028) and the presence of the gene polymorphism accounted for 80% of serum sodium concentration variance in cardiac surgical patients.

Additionally, the numerous pharmacological agents and preparations have been associated with posterior pituitary suppression and would increase the risk for DI in the face of septic shock. However the authors do not provide a listing of concomitantly or historically administered medications and pharmacological preparations amongst the 29 patients and additional information about medication history could provide greater insight. While Lithium chloride is a prototypical etiology of nephrogenic DI similar adverse effects have been reported in patients treated with amphotericin B, cidofovir and foscarnet demeclocycline, ifosfamide, ofloxacin, orlistat, didanosine and vasopressin receptor antagonists.[7, 8] However in septic shock patients who develop DIDVI, central DI is likely

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to be more common. Idiopathic DI from infiltrative (e.g. sarcoidosis, Langerhans cell reticulocytosis) or autoimmune pituitary disorders (e.g. IgG4 syndrome) as well as anorexia nervosa have all been associated with subclinical or mild DI that could readily become clinically important in the context of complete pituitary vasopressin depletion in septic shock.[7]

Efforts to statistically control for these and other potential confounding and interacting factors (e.g. propensity matching) could be helpful in teasing out which characteristics might be predictive of a high risk subgroup at risk for DIDVI.

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