Guidelines for the Use of Vasopressin in the NICU

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Therapeutic Use: Vasopressin is indicated as a first line vasoconstrictor in the following patient populations:

1. ***First line*** - Term or preterm infants with *hypotension* [particularly low diastolic and/or mean arterial pressure] and known or suspected *concurrent pulmonary hypertension*
2. ***First line*** – hypotension in the presence of septal hypertrophy/*hypertrophic obstructive cardiomyopathy* [e.g. due to maternal diabetes]
3. First line or adjunctive therapy – hypotension due to vasodilator shock in the presence of sepsis/necrotizing enterocolitis or massive hemorrhage until intravascular volume status is restored using blood products, etc.

Contraindications: Vasopressin should be used cautiously and only with echo guidance in patients with primary *left ventricular* dysfunction [increases afterload without positive inotropy] or infants in whom systemic circulation is dependent on right-to-left ductal shunt [e.g. aortic obstruction, Vein of Galen malformation].

Pharmacology: Vasoconstriction is via V_1 receptors and predominantly affects splanchnic and skin circulation [coronary, CNS circulation are less potently vasoconstricted]. Pulmonary vasodilator effect is via pulmonary vascular endothelial V_1 receptor mediated nitric oxide release. Water reabsorption is via V_2 receptors which mediate aquaporin insertion in the renal collecting duct.

Dosing Range: The usual therapeutic dose is between 0.1 and 1.2mU/kg/min. Recommended starting dose is 0.3mU/kg/min with titration up every 15-60 minutes [depending on the magnitude of the illness severity] in intervals of 0.2-0.3mU/kg/min to achieve target arterial pressure.

Considerations:

1. Significant increase in arterial pressure may occur. Once stability is achieved, titrate down to the lowest tolerated dose to achieve arterial pressure > 3rd centile for gestational age AND adequate organ perfusion. Avoid maintaining supra-normal arterial pressure to minimize exposure to side effects and to prevent hypertension-related cerebral reperfusion injury.

2. Vasopressin is NOT an inotrope. For patients with mild to moderate right ventricular dysfunction, vasopressin may indirectly improve *right ventricular* performance via afterload reduction ['pulmonary vasodilator effect'], improved coronary perfusion pressure, or improved systemic (IVC/SVC) venous return [improved RV preload]. In patients with significant heart dysfunction, a second agent [e.g. dobutamine, milrinone, epinephrine (dose < 0.1mcg/kg/min)] which is a positive inotrope is often required.

3. Urinary output of both water and sodium may be impacted by vasopressin in several phases and which vary from patient to patient and by clinical situation:

    a. For patients with shock, restoration of normal renal perfusion pressure [by improving arterial pressure] should result in improved renal function and increased

urinary output. This may be followed by a phase of *polyuria due to acute tubular necrosis* which is unrelated to vasopressin.

b. Insertion of aquaporins results in increased absorption of free water and therefore oliguria. *Oliguric patients being treated with vasopressin may have a dilutional hyponatremia* if fluids are not appropriately adjusted.

c. In many babies, exposure to vasopressin results in adaptation of the more proximal nephron to mitigate V_2 effects in the collecting duct. This results in an increase in proximal sodium excretion and associated water excretion in the convoluted tubules. Thus, vasopressin is also a naturetic. *Patients on vasopressin who are making urine are at risk for hyponatremia due to urinary sodium losses*.

Monitoring: Follow serum sodium closely. Recommended every 2-4h if Na < 135 until both serum sodium and urinary output are stable. If patients are voiding > 0.5ml/kg/h while on vasopressin urinary sodium should be measured and urinary excretion of sodium calculated [using concentration and volume of urine produced] at least once per nursing shift.

Weaning/Discontinuation: Vasopressin weaning is recommended in increments of 0.1 to 0.2mU/kg/min. The half-life is 10-20 minutes and therefore dose changes every 30-90 minutes are reflected in a patients' condition. It is recommended to wean vasopressin dose every 2-3h until discontinued. Considerations:

1. Vasopressin is a hormone which is also endogenously secreted. Prolonged administration [e.g. > 48-72h] may result in suppression of endogenous production. If this is the case, vasopressin discontinuation may be associated with immediate polyuria and fluid dysregulation. Urine output should be calculated hourly x 4h after stopping vasopressin. If UO is > 4ml/kg in the first hour, vasopressin at a dose of 0.05mU/kg/min should be restarted x 12h and fluid/sodium status reassessed. Another trial of discontinuation after 12h is recommended.

2. Because of the local effect of vasopressin in the pulmonary vascular bed, both vasopressin and iNO should not be weaned simultaneously. It is recommended to wean vasopressin preferentially if the arterial pressure is adequate and the patient remains in FiO_2 > 50% and iNO preferentially if the arterial pressure is borderline and the FiO_2 is < 50%. Weaning should be at the discretion of the attending and is variable from patient to patient.

3. If prolonged use is expected and there are concerns either for hyponatremia or requirements for excessive sodium supplementation, norepinephrine is a reasonable alternative. Situations in which norepinephrine should be used cautiously include: patients with tachycardia [HR>170] and those with hypertrophic obstructive cardiomyopathy as the beta- 1 agonist properties of norepinephrine may produce undesirable side effects in those situations.

References:

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