The Newcastle upon Tyne Hospitals NHS Foundation Trust

Guidelines for the use of vasopressin analogues in critically ill patients

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1 Introduction

Vasopressin analogues are frequently administered to the critically ill in the following situations:

- Vasodilatory shock refractory to noradrenaline
- Optimisation of the brain dead donor with diabetes insipidus
- Treatment of a patient with bleeding oesophageal varices from portal hypertension
- Hepatorenal syndrome

This guideline aims to give provide information on which to use, how to prescribe and the evidence supporting their use.

2 Guideline Scope

This document provides guidance for healthcare professionals working within an adult critical care unit in Newcastle Hospitals.

3 Main Body of Guideline

3.1 Rationale for Use

There are two available vasopressin analogues:

- Argipressin (pitressin®)
- Terlipressin (glypressin®)

Pitressin® (sometimes referred to as simply ‘vasopressin’) is usually used on ICU for patients with vasodilatory shock who remain hypotensive despite fluid resuscitation and increasing doses of first line vasopressors/inotropes. For consideration of vasopressin use, the patient should have good cardiac function but marked vasodilation (persistently low SVR) despite noradrenaline therapy.

Vasopressin is a constrictor of the systemic vasculature. Levels of vasopressin fall inappropriately as the shocked state becomes established (the patient develops a relative vasopressin deficiency). Vasopressin may enhance the sensitivity of the circulation to catecholamines and can reduce requirements.

There is no evidence to demonstrate clear benefit or adverse effects between noradrenaline and noradrenaline plus vasopressin as a second agent. Vasopressin is not recommended as a first line agent in sepsis and does not reduce the incidence of acute kidney injury when compared with noradrenaline alone in the setting of septic shock.

Vasopressin may be used earlier in the optimisation of a brain dead donor for organ donation due to it's effects on treating diabetes insipidus.
Terlipressin is a weaker agent than argipressin with a longer duration of action and milder side effects. It is usually given up to four times per day rather than as an infusion. It's main indications are for hepatorenal syndrome (where it reduces plasma renin activity, providing reduced RAAS activity and increased natriuresis) and to reduce bleeding in oesophageal varices (by reducing portal venous pressure). Treatment should usually be stopped after definitive haemostasis or after 5 days unless there is a continuing indication.

3.2 Adverse effects

Vasopressin use can cause myocardial ischaemia, mesenteric and digital ischaemia and should be used with caution in high risk patients.

3.3 Administration

Argipressin (pitressin ®)

- Add 20 units pitressin to 50mls 5% dextrose (the resulting solution is 0.4 units/ml)
- The infusion can be titrated up to 6mls/hour (0.04 units/min). Dose is not body weight dependant in adults.
- Infusion should be via a central venous line
- Reduce noradrenaline infusion prior to weaning off pitressin. Do not abruptly stop pitressin or rebound hypotension may occur. Aim to reduce the rate of pitressin by 50% hourly depending on the patient's response. Vasopressin is normally weaned before stopping other vaso-active drugs.

Terlipressin (glypressin®)

- 0.25mg – 2mg subcutaneously or intravenously up to 4 times in 24 hours
    - Increases in MAP are seen within 20 minutes and last at least 5 hours

4 Training, Implementation, Resource Implications

Education in this area will predominantly be delivered by consultants working on critical care. It should be noted that vasopressin is more expensive than noradrenaline.

5 Monitoring Section

Pharmacy staff will monitor prescribing habits of vasopressin analogues and the resultant cost implications. This will be published on a quarterly basis for all staff on critical care to review.

6 Evidence Review and Evaluation

Evidence for this guideline was taken from studies listed within the references and reviewed by the critical care guidelines committee.

7 References

1. Dellinger RP et al. Surviving Sepsis Guidelines. 2008: Critical Care Med; 36:296 –327.
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3. O'Brien A, Clapp L et al. Terlipressin for norephinephrine resistant shock. Lancet. 2002; 359: 1209-10
4. Russell JA, Walley KR et al. Vasopressin versus norepinephrine infusion in patients with septic shock (VAAST). N Engl J Med. 2008; 358: 877-887
5. Gordon A et al. Effect of early vasopressin vs norepinephrine on kidney failure in patients with septic shock. The VANISH Randomized Clinical Trial. JAMA. 2016; 316(5):509-518.
6. Rajekar H et al. Terlipressin in hepatorenal syndrome: Evidence for present indications. J Gastroenterol Hepatol 2011; 26: 109-14.