1. INTRODUCTION

Terlipressin is a vasopressin analogue, which acts as a vasoconstrictor predominantly in the splanchnic circulation. It is licensed to treat variceal bleeding\(^1\), but is also used to treat hepato-renal syndrome although it is unlicensed for this indication\(^2\).

Terlipressin should only be used with caution and under strict monitoring of the patients in the following cases\(^1\):

- Septic shock
- Bronchial asthma, respiratory deficiencies
- Uncontrolled hypertension
- Electrolyte derangements or if the patient is taking other medicines with a risk of hypokalaemia or hyponatraemia
- Cerebral or peripheral vascular diseases
- Cardiac arrhythmias, including QT prolongation or if patients are on other medicines that could prolong the QT interval
- Chronic renal insufficiency
- Acute coronary syndrome, coronary deficiencies or previous myocardial infarction
- Elderly patients >70 years as experience is limited in these groups
- Pregnancy or breastfeeding – seek specialist advice

Adverse effects and monitoring requirements

- Monitor daily U and E as terlipressin can cause hyponatraemia via weak anti-diuretic hormone effect
- An ECG must be checked before starting treatment
- As terlipressin can cause hyper and hypotension, peripheral vasoconstriction, bronchospasm and cardiac ischaemia, patients must be closely monitored and an ECG repeated if any adverse effects arise.
- GI adverse effects, including abdominal cramps and diarrhoea can occur but these are usually transient\(^1\)
2. **VARICEAL HAEMORRHAGE**

Variceal haemorrhage is caused by rupture of variceal wall due to excessive wall tension, and is one of the most immediate life threatening complications in patients with cirrhosis. 70% of GI bleeding events in patients with portal hypertension are due to variceal bleeds. Terlipressin has been shown to improve mortality in variceal bleeding compared to placebo and is as effective as endoscopic therapy at reducing mortality, haemostasis and preventing re-bleeding.

**Presentation of acute upper gastrointestinal bleeding**

Immediate action is required

- **Acute GI bleeding and portal hypertension**
- **Initial assessment (History, physical and blood examination, blood cultures) and resuscitation**
- **Immediate start of terlipressin 2mg QDS**
- **Hold beta-blockers while on terlipressin**
- **Confirmed variceal bleeding**
- **Maintain use of terlipressin at 2mg QDS for 48 hours then reduce to 1mg QDS for a further 3 days.**
- **Continue antibiotics for 5 days**

**Endoscopy <12 hours**

- **Band ligation**
- **Further bleeding**
- **Bleeding controlled**
- **Rescue with TIPS**
- **Check daily U&E to monitor for hyponatraemia**
- **Repeat ECG if any cardiac concerns**

**Rescue with TIPS**

- **Only consider early TIPS if high risk**

**Airway**

- **Breathing**
- **Circulation**
  - **Volume replacement**
  - **Restrictive transfusion**

**Antibiotic prophylaxis**

See [local guideline](#)
3. HEPATO-RENAL SYNDROME

Hepato-renal syndrome (HRS) is defined as renal failure in people with cirrhosis in the absence of ⁵⁻⁶:

- Pre-renal causes
- History of nephrotoxic drugs
- History of shock (acute tubular necrosis)
- Proteinurea +/- haematuria (parenchymal renal disease)

The classifications of HRS were changed in 2018 ³, ⁶

<table>
<thead>
<tr>
<th>Old classification</th>
<th>New classification</th>
<th>Diagnostic criteria</th>
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| HRS-1               | HRS-AKI (acute kidney injury) | a) Absolute increase in serum Cr ≥0.3mg/dL (27micromol/L within 48 hours)  
And/or  
b) Urinary output ≤0.5ml/kg ≥6 hours  
Or  
c) Percent increase in serum Cr ≥50% using the lowest available value of outpatient serum Cr within 3 months as the baseline value |
| HRS-2               | HRS-NAKI (no acute kidney injury) |  |
| HRS-2               | HRS-AKD (acute kidney disease) | a) eGFR <60ml/min for <3 months in the absence of other (structural) causes  
b) Percent increase in serum Cr <50% using the last available value of outpatient serum Cr within 3 months as the baseline value |
| HRS-2               | HRS-CKD (chronic kidney disease) | a) eGFR <60ml/min for ≥3 months in the absence of other (structural) causes |
Terlipressin dosing in hepato-renal syndrome

**Confirmed HRS-AKI**

(Do not use in HRS-2/NAKI due to high risk of recurrence)

**Concern over possible adverse effects?**

- Hyponatraemia
- Diarrhoea
- Abdominal pain
- Circulatory overload
- Cardiovascular ischaemic complications

**NO ↓**

Terlipressin IV 1mg QDS + Albumin 100ml OD – BD

**YES ↓**

Terlipressin IV 0.5mg QDS + Albumin 100ml OD-BD

**Decrease in serum Cr >25% from peak value**

**NO ↓**

Increase terlipressin in a stepwise manner up to a maximum of 2mg every 4 hours

**YES ↓**

STOP when AKI resolved to within 27 micromol/L of baseline

Or until maximum treatment course of 14 days is completed
References


4. Nevens F, Bittencourt P et al (2018); Recommendations on the Diagnosis and Initial Management of Acute Variceal Bleeding and Hepatorenal Syndrome in Patients with Cirrhosis; Digestive Diseases and Sciences; 64; p1419-1431
