Liver Failure- prescribing at the end of life

Background information

Chronic liver disease is more predictably associated with impaired metabolism of drugs than acute liver dysfunction. The greater the liver dysfunction, the greater the impairment of drug metabolism.

This guideline applies to patients with synthetic liver dysfunction i.e. Low albumin/raised INR (above1) /low platelet count /raised bilirubin level.

In moderate to severe liver dysfunction rates of drug metabolism could be reduced by 50% but will vary according to severity and aetiology of disease and additional co-morbidities.

There are no endogenous markers for hepatic clearance that can be used as a guide for drug dosing.

Child-Pugh score can be calculated to assess severity of liver disease, but lacks sensitivity to estimate the liver's ability to metabolise individual drugs. Patients with Child-Pugh B or C liver disease will likely require dose reduction and an increase in intervals between doses.

Altered drug metabolism can precipitate symptoms of decompensated liver disease e.g. hepatic encephalopathy.

Cirrhotic patients will often have impaired renal function despite a normal creatinine level due to reduced muscle mass and poor nutrition.

There is a lack of good quality data examining the pharmacological and adverse effect profile of analgesia in end stage liver disease.

This guideline is based on the limited evidence available and on expert opinion.

Liver Failure- prescribing at the end of life

For patients with synthetic liver dysfunction e.g. Low albumin/raised INR/low platelet count /raised bilirubin.

This document is intended to highlight special considerations when prescribing for this group of patients. For further guidance on symptom management please refer to LCH Symptom Management in the Last Days of Life Guidance or Y&H Symptom Management Guidance

Assess the patient

- Assess for liver failure: albumin, clotting, evidence of decompensation (ascites, hepatic encephalopathy, variceal bleed).
- Further indication of severity of liver failure can be given by Child-Pugh score - usually recorded in the notes.
- Consider nutritional status. If low muscle mass /low BMI, may require lower doses and increased dosing intervals.
- Monitor closely for constipation to avoid precipitation of hepatic encephalopathy. However in the last days of life it is more appropriate to treat the patient's symptoms than to be overly concerned about the development of hepatic encephalopathy.

Pain management

Special considerations:

- If already on regular opioids seek specialist palliative care advice.
- Caution with NSAIDs; increased bleeding tendency and risk of renal function deterioration. This is less relevant in the last days of life-please seek specialist advice
- Paracetamol is safe to use: max oral dose 3g daily. For patients less than 50kg, IV dose to 15 mg/kg.
- Dihydrocodeine is preferable to codeine as it relies less on hepatic metabolism.
- First line opioid is morphine-starting at a low dose
    - Morphine Sulfate solution 2.5 mg PO orally p.r.n (minimum frequency 2 hours, up to 4 doses in 24 hours before medical review)
    - In the last days of life Morphine Sulfate 1.25 to 2.5 mg SC p.r.n. (minimum frequency 1 hour, up to 4 doses in 24 hours before medical review)
- If morphine is contraindicated or GFR <20 mL/min prescribe oxycodone. (i.e. below a GFR of 20 mL/min prioritizing renal dysfunction is felt to be safer). Start at a low dose. In the last days of life oxycodone 1 to 2 mg SC. minimum frequency 2 hours, up to 4 doses in 24 hours before medical review
    - Estimate of GFR (eGFR) reported by pathology labs can be used for most patients However, consider calculating creatinine clearance(ml/min) using the Cockroft - Gault formula in the following circumstances:
        - At extremes of muscle mass (BMI <18 kg/m2 or > 30 kg/m2)
        - Elderly patients (aged 75 years or older)
        - Patients taking nephrotoxic drugs / drugs with narrow therapeutic index
        - Other comorbidities or clinical concern

Cockcroft-Gault formula:

- $$\text{CrCL (mls/minute)} = \frac{n \times (140 - \text{age}) \times \text{weight (Kg)}}{\text{Serum creatinine (micromoles/L)}}$$

where n = 1.04 (females) n= 1.23 (males) or online calculator at www.mdcalc.com

Agitation - Consider reversible causes. **If not in the last days of life local delirium guidance**

Special considerations:

- May have hepatic encephalopathy.
- Beware of increased sensitivity to sedatives and so may need to consider increasing dosing intervals
- If medication is needed in the last days of life start with a low doses:
    - midazolam 1.25 mg SC p.r.n (minimum frequency of 30 minutes).Dose may need increasing if not effective. It is suggested that a p.r.n dose range is prescribed (1.25 to 5 mg)
    - haloperidol 0.5 mg SC p.r.n. (minimum frequency of 1 hour) Dose may need increasing if not effective. It is suggested that a p.r.n dose range is prescribed (0.5 to 3 mg)
    - Medical review is needed if doses are ineffective or after 3 doses in 24 hours.

Nausea and vomiting

Special considerations:

- If using haloperidol start with a low dose e.g. 0.5mg SC p.r.n. A dose can be repeated after one hour. Maximum 3 doses in 24 hours then medical review required.
- If using levomepromazine start with a low dose, e.g. 2.5 mg SC p.r.n. A dose can be repeated after one hour. Maximum 12.5mg in 24 hours then medical review required.
- Metoclopramide should only be used under specialist advice- it can accumulate and is centrally acting so can worsen encephalopathy.

Retained respiratory secretions in the last days of life

- Non-pharmacological management is the most important component of treatment.
- Hyoscine butylbromide is the favoured drug treatment as it is non-sedating, 20mg SC 1 hourly p.r.n. It is short-acting therefore if effective consider a continuous subcutaneous infusion (typical starting dose 60mg SC over 24 hours)
- Avoid hyoscine hydrobromide because of its central effects.

Breathlessness

- Trial non-pharmacological measures first line when possible
- Opioids can be used for breathlessness. See prescribing advice under pain.

Pruritus

- Aqueous cream and menthol.
- Antihistamine - e.g. chlorphenamine.
- Seek specialist advice if symptoms are persisting.

For further advice or information please contact your local Specialist Palliative Care Team:
Wheatfields Hospice: 0113 2787249 St Gemma's Hospice 0113 2185500

Leeds Palliative Care Network

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