Management of Acute Painful Crisis and Chronic Pain in Adults with Sickle Cell Disorder

North East & Yorkshire Haemoglobinopathy Coordinating Centre

This guideline has been developed by the NE&Y HCC and is intended for use by hospital trusts within the North East & Yorkshire region, as deemed appropriate by the local haematology team. If being adopted for use in a hospital trust, localisation information below must be completed and standard trust processes for approval of new or updated guidelines followed.

Trust localisation information

This guideline applies to

Setting: eg Trust Wide
Individuals: eg All clinical staff
Specialty: eg Haematology
This guideline does not apply to: eg N/A

Admission pathway

eg Direct admission to haematology, ambulance pathways, admission via Emergency Department

Local guidance where this differs from network guideline

eg relating to availability of particular opioids or other medication

Location of individualised care plans for sickle cell patients

Availability of PCA

Contact and referral pathway for acute pain specialist team

Contact and referral pathway for chronic pain specialist team

Other relevant localisation information including local support organisations for those with opioid dependence

Trust owner of guideline:

Trust approval date:

Trust approval body:

Trust review date:

Introduction

Sickle Cell Disorder (SCD) is an inherited disorder of haemoglobin with an autosomal recessive pattern of inheritance. The clinical phenotype of SCD results from homozygous inheritance of the sickle gene (HbSS); or compound heterozygosity with haemoglobin C (HbSC), β-thalassaemia (HbSβthal) or other haemoglobin variants.

SCD is a chronic illness punctuated by acute crises, the commonest of which is a vaso-occlusive painful crisis. Common triggers for vaso-occlusive crises include dehydration, stress, or infection, but can often occur without an obvious trigger. Pain can be excruciating and has been likened to the pain of a broken bone or a myocardial infarction.

Part A: Sickle Cell Painful Crisis

Assessment and Investigation of a Sickle Cell Crisis

Admission

See localisation information above of details of admission pathway. If patient presentation is not directly to haematology, the on-call haematology registrar or consultant should be contacted urgently on presentation for discussion and to arrange admission.

Assessment

Acute painful sickle cell crises should be treated as a medical emergency, requiring prompt assessment and treatment. Appropriate analgesia must be offered within 30 minutes of presentation.

Patients known to the haemoglobinopathy team should have an individualised Care Plan – please consult this where available.

Patients (and/or carers) are experts in their condition, listen to their views on:

- Planned treatment regimen for the episode
- Treatment received during previous episodes
- Any specific concerns they have about the current episode
- Any psychological and/or social support they may need

Establish what analgesia has been used prior to coming to hospital, and what analgesia has been required in previous admissions.

Ask the patient whether the pain is similar to the pain of a sickle cell crisis, or is it different in any way? Patients with SCD can usually differentiate pain due to a sickle cell crisis from other causes of pain. Atypical pain should prompt consideration of alternative diagnoses.

Document relevant medical history, including:

- Frequency of admissions
- Any known complications of sickle cell disorder (prior chest crises, exchange transfusions etc)
- Any chronic complications of sickle cell disorder or any other significant co-morbidities/medical history

Assess for any 'red flags' or complicating features such as:

- Acute chest syndrome: shortness of breath / cough / chest pain / hypoxia / chest signs on examination - *See separate guideline*
- Confusion: this can indicate hypoxia, worsening anaemia or other acute deterioration and must be treated as a medical emergency
- Stroke: headache/neurological symptoms: a full neurological examination and urgent CT scan are warranted if neurological features are evident - *See separate guideline*
- Abdominal pain
- Priapism - *See separate guideline*
- Features to indicate infection - *See separate guideline*

Observations

Observations (respiratory rate, oxygen saturations, pulse rate, blood pressure, temperature, and pain score) should be documented using the NEWS2 chart.

Observations should be repeated initially every 30 minutes, including a pain score, until pain is controlled. Observations should then continue hourly for at least 6 hours after initiation or increased opioid dosing. Observations can then be reduced to 4-hourly unless there are clinical concerns. Particular note should be made of oxygen saturations, respiratory rate, pain score and level of sedation.

Investigations

Urgent investigations on admission:

- FBC & reticulocyte count
- Group and screen
- U+Es
- LFTs
- Urine dipstick
- Pregnancy test in women of childbearing age

Please note that CRP, white cell, and neutrophil counts are often raised in the context of sickle cell crisis, therefore a single value is often unhelpful in suggesting or excluding infection.

Additional investigations if indicated:

- Cultures from blood, urine and other sites if signs of infection
- CXR if patient has chest signs on examination or is hypoxic
- Patients on iron chelating drugs (e.g. desferrioxamine) admitted with abdominal pain/diarrhoea/fever should have blood and stool screened for *Yersinia* and the iron chelator suspended
- X-rays of painful areas are rarely useful and should **not** be done routinely

Management of a Sickle Cell Painful Crisis

Immediate control of acute pain

First dose of appropriate analgesia should be administered within 30 mins of arrival (see patient's care plan if available). Pain is often excruciating and delays in administering analgesia cause severe distress and risk of clinical deterioration. Do not wait until you have taken a full history or sent off baseline bloods, for example - the first dose of analgesia must be administered urgently, as soon as possible after arrival.

Prior to prescribing check for:

- **Pregnancy** (avoid NSAIDs after 20 weeks of pregnancy but a short course can be given before 20 weeks if required; avoid Pregabalin)
- **Renal impairment** (avoid NSAIDS, decrease / omit pregabalin)
- **Analgesia taken prior to presentation at hospital**
- **The patient's Individualised Care Plan, if available** – if so, please refer to dosing outlined in this over generic guidance below

Offer a bolus dose of strong opioid such as oxycodone 2.5 - 5mg SC or 5 – 10mg PO; or morphine 5-10mg SC or 10-20mg PO (avoid pethidine) to:

- All patients with severe pain
- All patients with moderate pain who have already had analgesia before presentation
- Subcutaneous (SC) delivery should be offered for severe pain on presentation, or if patient is vomiting / unable to take oral medication

Consider a weak opioid such as codeine 30mg PO instead for:

- Patients with milder pain who have not had any analgesia

In addition to an opioid, offer all patients (unless contraindicated):

- Regular pregabalin (usual starting dose 75mg bd PO)
- Regular paracetamol (PO or IV)
- Regular NSAID (e.g. ibuprofen) + PPI for gastric protection

Adjunctive treatment:

Prescribe the following for all patients prescribed opioid medication:

- Regular laxatives eg docusate, laxido
- Anti-emetics PRN eg metoclopramide, ondansetron (avoid IV cyclizine)
- Anti-pruritics PRN eg chlorphenamine
- Naloxone for emergency treatment of opioid overdose

Early control of pain is vital as it will reduce complications and lead to faster resolution of vaso-occlusive crisis. Early and adequate pain relief has been demonstrated to reduce length of admission, reduce the risk of acute chest syndrome, reduce the risk of developing chronic pain and longer-term opioid use.

Reassessment and On-going Management

Ongoing pain management in the first 24 hours:

1. Assess effectiveness of pain relief every 20 - 30 minutes and provide further doses of appropriate analgesia until satisfactory pain relief achieved. Assessment should include asking the patient what their pain score is, how well the last pain killer worked, and whether they feel they need further pain relief.
2. If the patient still has severe pain on re-assessment, offer a further bolus dose of SC strong opioid.
3. Patients with a level of opioid tolerance (frequent or long-term opioid exposure) may require increased doses of strong opioids to control pain.
4. If patients are not settling with standard treatment by 2 hours, reassess clinically considering the possibility of alternative diagnoses and consider starting a PCA (patient-controlled analgesia) pump if available.
5. Once initial pain relief is effective, PRN doses of ongoing opioid medication should be prescribed (unless PCA has been started). Prescribe opioid PRN doses to be given up to 2-hourly: if the patient requires repeat dosing more frequently than 2-hourly this should prompt clinical review.

After 24 hours:

Aim to convert any remaining SC PRN opioid dosing (including PCA) to oral by 24 – 48 hours following admission, unless patient is vomiting. Oral opioids are as effective as SC opioid doses; they just take a little longer to achieve peak efficacy. Therefore, patients can be reassured that oral dosing will be effective for them.

- *To convert SC to equivalent oral dose, double the dose given SC (SC dosing is approximately twice as strong as oral dose).*
- *To convert morphine to equivalent oxycodone dose, halve the dose (oxycodone is twice as strong as morphine).*
- *To convert oxycodone to morphine dose, double to dose (morphine is half as strong as oxycodone).*

Please note that modified release (MR) opioid preparations are no longer considered appropriate for the management of acute pain in most patients. There has been withdrawal of their MHRA license for post-operative pain, and the evidence is compelling that they cause harm and confer limited – if any – benefit in such situations. Therefore this guideline recommends avoiding their use for acute sickle cell crisis pain.

Indications for pain specialist team involvement

This is only required for a minority of complex patients

Consider referral to local pain specialist team for the following patients:

- Pain uncontrolled despite optimal dosing with strong opioid, pregabalin, paracetamol and NSAID medication (unless contraindicated).
- Patient should first have been discussed with registrar / consultant haematologist to optimise standard analgesia treatment.

Supportive care measures

Hydration

For patients who are nauseous or vomiting, or those with severe pain (who are unlikely to drink well), IV fluids should be started on admission. Fluid balance should be monitored in all patients, whether or not they are on IV fluids. Patients who can drink should be encouraged to take oral fluids (aim for approximately 3L in 24hrs for average sized adults).

Oxygen therapy

This should be administered if pulse oximetry shows oxygen saturation < 95%. Low oxygen saturations should prompt an urgent clinical review and consideration of complications including acute chest syndrome, lower respiratory tract infection or pulmonary embolism.

Thromboprophylaxis

Patients with sickle cell disorder are pro-thrombotic and have a higher risk of VTE during inpatient stays. Commence low molecular weight heparin prophylaxis (or continue DOAC if already taking this) in all patients unless contraindicated.

Antibiotics

Broad-spectrum antibiotics should be administered if the patient is febrile (≥38°C), has evidence of lower respiratory tract infection, or other clinical features of infection.

Local heat / cold packs

Some patients find warm or cool packs applied to the painful area are helpful. Discuss with patient whether they would like to trial this, and with ward staff regarding availability.

Alternative therapies

If alternative therapies such as acupuncture or massage are available, consider offering these to patients as an adjunct to medical management of pain.

Blood transfusion

Any decision to transfuse should be discussed with the Haematology Registrar or Consultant. HbS is a low affinity Hb, therefore patients usually have low baseline Hb level and tolerate this relatively well. Typically, transfusions are only required if the haemoglobin falls by at least > 20g/l or to a level of < 50g/l. Exchange transfusions are indicated for severe chest crises, suspected cerebrovascular events or multi-organ failure, but not for straightforward painful crises.

Mental health support and the importance of compassion

Crises can be frightening, exhausting, and emotionally draining. Make sure to check on patients' mood and coping, offer reassurance and compassion to everyone, and involve clinical psychology when distress is identified. Letting patients know that you believe their reported pain and you care about their experience is vital.

Remember that people show pain, distress and fear in different ways. These can include being very quiet and withdrawn, raising the voice and speaking loudly, or feeling a need to leave the situation – the 'flight, fight, freeze' responses to pain and fear. These are all natural responses when people feel their safety and wellbeing is under threat, and should be met with understanding and care.

Discharge

Principles
• To be ready for discharge, the patient must be pain controlled (i.e. pain score ≤ 4/10) with oral analgesia *and not required any SC injections* for at least 24 hours
• Discharging before a patient is ready could lead to early 'revolving-door' re-admission
Practice
TTO drugs to include – • Prescribe regular paracetamol for at least one week • Prescribe regular ibuprofen 3-5 days together with PPI • Prescribe laxatives for at least 3-5 days • Stop pregabalin on discharge
If the patient is still needing a strong opioid at time of discharge: • If not needing regular or frequent strong opioid at time of discharge, wean to a weaker opioid e.g. Tramadol 50-100mg 3-4 times daily PRN or Codeine phosphate 30-60mg 4 times daily PRN for not more than 5 days. • If strong opioid is still required, use the minimum dose possible and give a prescription for not more than 5 days, with a plan for weaning dose over this time • Document on the discharge paperwork that strong opioids should only be prescribed by the hospital team – NOT to be continued by GP • Include an instruction to pharmacy to dispense exact dosage in the prescription to avoid rounding of doses and over- or under-supply • *Exception: patients who are receiving chronic strong opioid treatment – discuss with haemoglobinopathy team to develop an individualised weaning plan*
Follow-up: Request a Haematology O/P Appointment within 2 weeks of discharge

Suspected opioid toxicity

Excessive sedation is not usually a problem and immediate reduction of the opioid dose is usually all that is required. It is important to reduce the dose cautiously for over-sedation, e.g. by 30-50%. DO NOT GIVE NALOXONE FOR SEDATION ALONE.

If a patient on a syringe driver or PCA with opioid becomes over-sedated, stop the syringe driver / PCA and contact the specialist pain team to discuss further actions (e.g. reduction of dose).

RESPIRATORY DEPRESSION IS MORE SERIOUS AND MAY NEED SPECIFIC ACTION.

To diagnose respiratory depression -

- respiratory rate <8 breaths/min **AND** SaO_2 <90% on air on pulse oximeter

Discontinue opioid infusion / PCA. Treat with **naloxone** slowly to avoid precipitating rebound pain and withdrawal (unless in an emergency)

- Dilute Naloxone 0.4mg vial in 10mL saline for injection.
- Use an **IV** cannula or butterfly.
- Administer 0.5-1mL IV every 2 minutes until respiratory status satisfactory.
- Repeat further doses as needed (this is important if a sustained release opioid has been used, e.g. modified release tablet or patch)
- Be prepared for signs of acute opioid withdrawal and acute pain recurrence – treat once respiration is normal with 10-20% of the former opioid doses, given prn, and re-titrate up to adequate analgesia
- If patient has been on fentanyl or buprenorphine patch, naloxone will need to be given for longer period.

Patient Education and Self-Management

Discharge after an episode of crisis is a good opportunity to ensure your patient has information to optimise self-management and staying well at home. Provide, or revisit, information to help patients recognise the early signs of crisis, know how to manage pain safely at home and when they need to seek help. Consider providing written information such as the HCC patient information leaflet ‘Pain Management for Adults Living with Sickle Cell Disorder’ and recommend other trusted resources, such as the Sickle Cell Society.

Part B: Chronic Pain in Sickle Cell Disorder

Introduction

Some patients with sickle cell disorder develop chronic pain syndromes which are multifactorial and often highly complex to manage. Pain may be due to permanent bone or joint damage such as avascular necrosis, but for many there is no clear cause. Chronic pain leads to increased risk of fatigue, depression and anxiety, which in turn worsen the experience of long-term pain. Patients with high regular opioid consumption are at risk of central sensitisation and opioid induced hyperalgesia. These patients may describe atypical pain not in keeping with their usual sickle crises or allodynia/hyperalgesic symptoms.

Management of chronic pain

Medications

- Opioids are not very effective for chronic pain due to development of tolerance, dependence and side-effects with long-term use, therefore should be avoided for this indication
- Paracetamol can be used longer-term provided liver function is normal
- NSAID use may impact renal function where used long-term and this should be monitored closely, with NSAIDs withdrawn if eGFR falls. Ensure patient is given a PPI for gastric protection if of longer-term NSAIDs.
- Amitriptyline or duloxetine may be useful for pain with a possible neuropathic basis
- Magnesium (dose of approximately 375 mg daily) may be helpful for chronic pain - patients can be encouraged to purchase this over the counter or it can be prescribed (off-license)

Non-medical therapies

- Psychology involvement is important for all patients with chronic pain – refer for specialist health psychology input
- Maintaining good activity levels will help. Gentle strengthening exercises such as Yoga, Pilates or Tai Chi may be effective in reducing pain
- Physiotherapy input is often beneficial for patients with avascular necrosis, chronic back pain and may be helpful in other chronic pain conditions. Request outpatient physiotherapy referral via the primary care team for a graded exercise programme
- Where pain and other symptoms are limiting ability to work, or carry out activities of daily living, Benefits Advisor or Social Worker referral is recommended to explore financial and other support available
- Alternative therapies such as acupuncture, acupressure and massage may be beneficial
- Nerve block injections may have a role for some musculoskeletal pain conditions as determined by local or regional pain services.

Specialist referral

- Referral to a chronic pain specialist is advised for patients with intractable chronic pain and/or atypical manifestations of chronic pain syndrome.

Opioid Dependence and Weaning

Most patients only access opioid treatments for acute and severe pain, and it is important to avoid making an assumption of opioid dependence or addiction without good evidence. A small minority of patients with sickle cell disorder develop longer-term opioid dependence. This must be approached as an iatrogenic complication of their sickle cell disorder, in a supportive and understanding manner. Patients in whom opioid dependence is a concern should be discussed with the haemoglobinopathy team – if not previously identified, the assumption must remain against opioid seeking behaviour when patients present and report pain.

For those who have been exposed to long-term, high dose opioids, they are likely to have developed both physical and psychological dependence, and will need enhanced support to be able to successfully taper and stop opioid treatment. It is important to understand the distinction between dependence and addiction – the latter is less common and involves development of compulsive behaviours despite the negative consequences of opioid exposure.

Management of opioid dependence:

- Discuss with the patient the rationale for proposed tapering and stopping of opioids, including the benefits which primarily are to ensure opioids continue to work for when needed the most eg sickle crises; and the harms of opioid use. These include: constipation; hormonal effects including infertility and reduced sexual function; increased risk of falls and fractures; impact on mental health and cognitive function; immunosuppression; and increased mortality.
- Written information may be helpful for the patient, the following leaflet from the Faculty of Pain Medicine may be useful:

  FPM-OA-taking-opioids.pdf
- Consider optimising non-opioid management of chronic pain, if this is a factor (see above).
- Establish an accurate baseline of opioid use with the patient, including opioid doses accessed from primary care, any other secondary care providers or other sources.
- Agree the weaning plan with the patient – their agreement and engagement are key to success. They may feel very anxious and will probably need a lot of encouragement and reassurance that stopping the opioid is unlikely to worsen their pain and may actually help them feel better.
- Discuss symptoms of withdrawal. The aim of slow tapering is to avoid withdrawal symptoms, but encourage the patient to contact the haematology team if these occur for further review.

- Discuss the risk of potentially fatal overdose if previously high opioid doses are taken after long-term use is reduced.
- Involve psychology to support with anticipated anxieties around tapering and stopping long-term opioid use, and to manage the psychological aspects of opioid dependence.
- Enhanced support from the haemoglobinopathy MDT will often be required.
- Weaning plan should be based on regular (rather than PRN) dosing and should usually involve the opioid medication that is currently being taken (no need to switch to a different opioid preparation). Switching to modified release from immediate release preparation is usually recommended to reduce the risk of withdrawal symptoms.
- Rate of taper: 10% of original dose every 1-2 weeks. Slower taper (eg dose reduction every 4 weeks) may be required if opioid exposure is very long (eg >1 year) or high level of anxiety / psychological dependence.
- When prescribing tapering opioid doses, include an instruction to pharmacy to dispense exact dosage in the prescription to avoid rounding of doses and over- or under-supply.
- If there is evidence of drug-seeking behaviour or misuse discuss with patient a referral to local substance misuse services – this is only likely to be beneficial if the patient actively wants to engage with these services.

Referral to the Haemoglobinopathy Coordinating Centre (HCC) MDT:

Consider referring the patient for discussion in the HCC MDT, which includes a consultant pain specialist, if any of the following criteria are met:

1. Complex chronic pain unresponsive to standard treatment and unable to access specialist local pain services
2. Frequent presentations with pain, especially if considering escalating disease-modifying therapy, but challenges in clinically differentiating acute painful crisis from chronic or other pain as cause
3. Patient is dissatisfied with their individualised care plan, or with long-term pain management plan including any restrictions or weaning of opioids, and it has not been possible to find a suitable course of action to which patient is in agreement

References

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HCC Network Document Control

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