

# Wessex Paediatric Oncology Supportive Care Guidelines: Symptom Management & Palliative Care

## **Scope**

This guideline applies to all Paediatric Oncology patients in the region. It does not apply to neonates on neonatal units.

## **Purpose**

Children receiving treatment at the Southampton Paediatric Oncology Principal Treatment Centre (PTC) have open access to the designated Paediatric Oncology Ward at either the PTC or their Paediatric Oncology Shared Care Unit (POSCU). Their parents/carers will be in possession of contact details for these wards and have been instructed to contact them for any medical problems that arise while they are receiving treatment. These Guidelines are intended for the use of the medical teams at the PTC or POSCU. If one of the Paediatric Oncology patients presents to a medical service outside of the PTC or POSCU, please contact the medical teams at the PTC or POSCU for advice.

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Valid from 31/03/16

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**Do not hesitate to contact the Paediatric Oncology team, the Paediatric Palliative Care Consultant or the Paediatric Oncology Outreach Nurse Specialist (POONS) for advice. Refer to the BNFC and “Piam Brown Guidelines for Symptom Management in Paediatric Oncology and Haematology Palliative Care 2015” for more specific drug doses and information.**

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# Symptom Management

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## 1.1 Introduction to Symptom Management

Symptom management is important from presentation, throughout oncological treatment as well as the non-curative/palliative phase of care. For children and young people whose disease cannot be cured, palliative care, including rigorous attention to symptom management, will help to provide as good a quality of life as possible for the time that remains.

Each child/young person and their family respond to their symptom experience differently. The wide spectrum of cognitive ability and chronological age amongst this patient group necessitates an individualised approach to assessment and management. In addition, the patient and family's preferred place of care should be taken into consideration when planning management. The benefits and disadvantages of each intervention must be carefully considered.

It is helpful to approach the management of any symptom systematically:

1. History and assessment
2. Identify likely causes
3. Plan treatment
4. Regular review

When choosing pharmacological treatments in the management of symptoms for children and young people, it is important to remember that some drugs are used 'off license' or 'off-label' and there are often little data to support their use in the younger age groups.

A lack of clinical trial data within this population means that some drugs discussed within this document reflect the experiences of paediatric oncology centres rather than published evidence.

Close collaboration and communication amongst health and allied healthcare professionals is essential. Advice should be sought from the specialist palliative care team if needed. In addition standard references such as the BNFC and APM formulary should be used.

This chapter will discuss the pharmacological management of common symptoms the child/young person may experience. It is important to also consider non-pharmacological strategies for example: distraction therapy, hypnotherapy, physiotherapy and occupational therapy.

## 1.2 Nausea and Vomiting

In palliative care identifying the cause of nausea and vomiting, which may be multifactorial, can help in making the logical choice of antiemetics. For further advice regarding chemotherapy related nausea and vomiting please see the separate guideline (CINV).

### ***Causes of nausea and vomiting***

- **Cancer related causes**
  - Irritation of the upper GI tract
  - Gastric outflow obstruction
  - Blood in stomach
  - Constipation
  - Abdominal mass
  - Anxiety
  - Uraemia
  - Cough
  - Pain
  - Raised intracranial pressure
  
- **Treatment related causes**
  - Radiotherapy
  - Drug therapy e.g. opioids
  - Chemotherapy
  - Carbamazepine
  - NSAIDs
  - Monoclonal antibodies

### ***Antiemetics and sites of action***

- Vomiting centre
  - Cyclizine
  - Hyoscine
- Chemoreceptor trigger zone and Vomiting centre
  - Levomepromazine
- Chemoreceptor trigger zone
  - Haloperidol
- Chemoreceptor trigger zone and GI tract
  - Metoclopramide
  - Domperidone
  - 5 HT<sub>3</sub> antagonists e.g. Ondansetron, Granisetron

### ***Nausea and vomiting during therapy***

Managing nausea and vomiting aggressively from the start helps to gain the confidence of the child and parents, and reduces the difficult problem of anticipatory vomiting. All modalities of oncological therapy – chemotherapy, radiotherapy and surgery – have the potential to cause nausea and vomiting and as such should be assessed and treated appropriately. For further details see CINV guideline.

### ***Nausea and vomiting in palliative care***

Cyclizine and Levomepromazine are commonly used for nausea and vomiting associated with raised intracranial pressure.

Short pulses of Dexamethasone can also be of benefit in this situation and Haloperidol is a useful alternative if Cyclizine or Levomepromazine are ineffective.

Haloperidol or Levomepromazine (generally not used together) may also be effective for nausea/vomiting secondary to metabolic disturbance e.g. renal failure.

Nausea and vomiting due to bowel obstruction requires specialist advice, and treatment may include steroids or chemotherapy/ radiotherapy to reduce the obstruction, as well as anti-emetics, and potentially include Octreotide (to reduce secretions) for inoperable bowel obstruction (if needed discuss with PTC before starting).

(Cyclizine, Levomepromazine and Haloperidol are all compatible with Morphine for subcutaneous/intravenous infusions).

### **1.3 Constipation**

Constipation is defined as a decrease in frequency of the passage of stools. Constipation is most likely to occur as a side effect of drug treatment. Other factors such as intra-abdominal disease, poor fluid intake, inactivity, poor nutrition, cord compression, hypercalcaemia and hypokalaemia should also be considered. These underlying causes should be treated where appropriate/possible. Prophylaxis or treatment for constipation should start with Movicol (Lactulose is less effective). If Movicol as a single agent is insufficient, other oral stimulants and softeners will be required. Doses of laxatives should be titrated up before adding in a new laxative. Co-danthramer should only be used in children/young people with non-curative disease and should be used with caution in those who are incontinent, catheterised or in nappies as skin excoriation may occur. Occasionally, rectal preparations may be needed provided the patient is not neutropenic or thrombocytopenic and all oral measures have been tried.

### **1.4 Pain**

Pain is a complex symptom related to physical, social, psychological and cultural reasons, which need to be considered in the assessment of a child/young person's pain and to select the best choice of treatment. Pain can be a problem throughout the disease process.

- **Causes of pain related to the disease process**
  - Tumour
  - Infection
  - Procedures (e.g. needles, LP, bone marrows)
- **Pain whilst on treatment**
  - Side effects of treatment (e.g. mucositis)
  - Tumour
  - Progressive disease
  - Other (e.g. pressure areas, infection)

#### **1.4.1 Assessment of Pain**

Pain is a subjective experience and the child/young person's own opinion is the best guide as to what they are feeling, but their level of understanding and communication skills may limit their ability to report their pain. Signs such as irritability and restlessness, reluctance to be held or unnatural stillness may represent pain. Parents are usually able to interpret their child's pain cues.

Specific pain assessment tools are available; tools appropriate for the child's age and ability should be used. Body charts may be helpful in identifying sites of pain, whilst the Faces, numeric and visual analogue scales can be used to measure severity. When assessing pain

it is also important to consider psychological and cultural factors influencing the child and family and their coping skills.

#### **1.4.2 Pain Tools**

**For those aged under 4 years of age and non-verbal children: FLACC Chart**

**For 4 years of age and above: Baker-Wong Faces chart or Numerical pain scale**

##### **Definitions of pain**

##### **Procedure-related pain**

Some of the tests or procedures that children undergo during their treatment may be uncomfortable or painful. The need for appropriate analgesia should be anticipated. Some examples are central line insertions, bone marrow aspirations or lumbar punctures.

The duration of pain/discomfort experienced may be variable from a few hours to a few days and should be managed with a step-wise approach.

#### **1.4.3 Persisting Pain**

The WHO persisting pain guidance 2012, defines children with cancer related pain (either from treatment or tumour related causes) as having persisting pain.

Persisting pain is therefore considered to be any pain that is not related to a procedure or investigation.

The current WHO guidelines (2012) no longer recommend the use of Codeine as a weak opioid for the management of persisting pain. It advocates a two-step approach from simple analgesia e.g. Paracetamol, followed by the use of low doses of a strong opioid e.g. morphine.

Correct use of analgesic medicines will relieve pain in most children with persisting pain due to medical illness and relies on the following key concepts:

- Selecting the appropriate drugs in a step-wise approach
- Dosing at regular intervals
- Using the appropriate route of administration
- Adapting treatment to the individual child

#### **1.4.4 Neuropathic pain**

Neuropathic pain is caused by structural damage and nerve cell dysfunction in the peripheral or central nervous system (CNS). Any process that causes damage to the nerves, such as metabolic effect, trauma, infection, ischaemia, toxin or immune-mediated pathology, can result in neuropathic pain. In addition, nerve compression or the abnormal processing of pain signals by the brain and spinal cord can cause neuropathic pain.

Nerve pain is characteristically associated with an area of altered sensation, and can be burning, stinging or shooting in nature. The patient may complain the area is hot or cold and may be relieved by rubbing or squeezing the site of pain. This pain is only partially relieved by opioids, although opioids should still be given as first line. Neuropathic agents such as Amitriptyline and Gabapentin may be helpful in this situation. However, these do not provide instant relief and each drug needs to be titrated to maximum benefit. In addition, a course of steroids may also be helpful if the pain is due to nerve compression. Severe neuropathic pain may require specialist palliative care advice on the use of NMDA receptor antagonists such as Ketamine and Methadone, and also the consideration of local or regional nerve blocks.

### 1.4.5 Management of Pain

In pain management, it can be helpful to combine a variety of approaches. Advice should be sought from the specialist team when pain is complex and unresponsive to treatment.

#### **Approaches to Pain Management Treatment of underlying disease**

Radiotherapy  
Chemotherapy  
Surgery

#### **Pharmacological management of pain**

Analgesic agents  
Non opioid analgesiacs  
NSAIDs  
Opioids  
Neuropathic agents e.g. antidepressants, anticonvulsants, NMDA antagonists  
Local agents e.g. EMLA, Ametop  
Sedating agents  
Inhaled anaesthesia e.g. nitrous oxide  
Regional blocks  
Epidural

#### **Non-pharmacological management of pain**

Education and explanation  
Psychological  
Distraction  
Relaxation  
Hypnosis  
Warmth e.g. hot water bottle  
Cold e.g. ice pack  
Massage  
Physiotherapy  
TENS  
Acupuncture

### 1.4.6 Analgesics

Although a variety of approaches to pain management are used, analgesics are still the backbone of any strategy. The principles of analgesic use are outlined below. Please refer to the BNFC for doses.

In most situations, analgesics of gradually increasing strength are used, according to the WHO analgesic ladder. However, the recent MHRA recommendation suggests that codeine should not be prescribed in children less than 12 years of age, and should only be prescribed in 12-18 year olds for up to three days for acute pain if Paracetamol and/or Ibuprofen cannot relieve pain.

It is essential that analgesics are given regularly, and that compliance is checked before moving on to the next step of the ladder.

Paracetamol is helpful in mild to moderate pain and has few side effects. The use of Paracetamol may mask infection and extra care should be taken if the patient is at risk of neutropenic sepsis.

The prescriber should be cautious in the use of NSAIDs due to their anti-platelet effect. When regular Paracetamol no longer relieves pain, an opioid at a low or standard starting dose is recommended. Anticipated side effects are constipation (laxatives should be prescribed routinely) and an antiemetic should also be prescribed for the first 3 days, due to the risk of nausea and vomiting. In a situation where pain is improving because of other interventions e.g. adjuvant radiotherapy or chemotherapy, analgesics should be reviewed regularly and reduced as the pain improves.

#### **WHO Guide to the Management of Persisting Pain in Children, 2012**

*Mild pain*

**Step 1: Paracetamol +/- co-analgesic**

*Moderate–severe or persisting or increasing pain*

**Step 2: Opioid at appropriate dose +/- non opioid +/- co analgesic**

### **1.4.7 Opioids**

Morphine is the first line opioid for moderate to severe pain. Adjuvants or alternatives may need to be considered, particularly, in neuropathic, bone and abdominal (especially liver) pain. Morphine Sulphate should be initiated on an 'as required', four-hourly basis using an immediate release preparation. Once the patient's opioid requirement is established, a regular twelve-hourly dose can be prescribed using a slow release preparation for background pain. Breakthrough, 'as required' 4 hourly doses of immediate release morphine should also be prescribed alongside the regular doses.

The starting dose should be calculated according to the child's weight (see BNFC for reference). Choosing a dose lower than the standard starting dose of morphine for the opiate-naïve patient either as a step up from Paracetamol or to relieve moderate pain, may be considered appropriate. Low dose Morphine is usually considered as 50% of the standard Morphine BNFC dose. For pain relief there is no ceiling Morphine dose.

#### **Side effects of opioids**

Opioids have many side effects. The side effect most likely to cause clinical problems is constipation, and laxatives should always be prescribed concomitantly. Nausea and vomiting are less frequent side effects (but can occur in up to 50% of cases) and antiemetics should be prescribed for the first three days. If the nausea and vomiting dissipate, the antiemetic can be stopped. Drowsiness is also common when initiating opioids or when escalating doses but almost always wears off within two or three days. It is useful to warn child/young person and their parents about this or they may worry that the disease has suddenly progressed or be concerned about the continued use of Morphine. Some patients experience itching; this may also wear off but if not, antihistamines or 5HT<sub>3</sub> antagonists (Ondansetron) are helpful. If itching persists, an opioid switch should be considered.

Respiratory depression does not cause problems in children being treated with opioid drugs for pain where it has been appropriately initiated and titrated. Children on opioids should be regularly assessed and reviewed to ensure they are on the correct dose for their degree of pain.

Once established, opioids should not be stopped abruptly as this may cause withdrawal symptoms. The dose should be reduced gradually (whilst monitoring for withdrawal) and then stopped.

#### **Parental concerns about opioids**

Sometimes parents are reluctant to consider the use of Morphine for their child's pain. The reasons for their concern need to be explored. It may not be the use of Morphine itself that concerns them, but that it represents an acknowledgement their child is seriously ill or dying. Parents may also be concerned about the risk of addiction and may need reassurance that psychological addiction does not occur in children requiring opioids for pain. It may be helpful to point out that Morphine can be reduced and stopped should the pain be relieved by other measures such as radiotherapy.

A patient can become physiologically tolerant to an opioid dose so they require a higher dose to achieve the same pain reduction. Physiological tolerance is not the same as psychological addiction.

#### **Alternative Opioids**

If you consider the patient has significant side effects to morphine, the use of alternative oral opioids may be considered. Please contact the Paediatric Treatment Centre (PTC).



## **Alternative routes of administration**

If the oral route is not possible, for example because of nausea and vomiting, difficulty swallowing, or gradual loss of consciousness, other routes should be considered:

### **- *Transdermal***

Transdermal Fentanyl is suitable for children who are on a stable dose of opioid, and who dislike or cannot tolerate oral medication. It is not suitable for children whose pain is changing and whose analgesic needs are therefore altering on a day-to-day basis. For very high doses of opioids, bear in mind that reliable dose conversion may become difficult.

### **- *Rectal***

During the palliative care phase some children tolerate rectal medication, and may prefer it to routes involving needles. When a child is no longer conscious (or during the last few hours) Morphine suppositories can be used (these are not routinely available so would have to be ordered via your pharmacy). The rectal route is not suitable for children having chemotherapy who may be neutropenic or thrombocytopenic.

### **- *Parenteral***

Analgesics can easily be given parenterally by continuous infusion. If a central intravenous catheter is in situ, this can be used, otherwise a needle can be placed subcutaneously. The site of a subcutaneous needle should be changed according to clinical need to avoid inflammation, and topical anaesthetic such as EMLA/Ametop can be used when the needle is re-sited if required. For the older child/young person a Patient Controlled Analgesia (PCA) infusion pump may be used and for younger children Nurse Controlled Analgesia (NCA) may be considered. Community PCA and PPCA (patient proxy controlled analgesia) are now available from some specialist services.

### **- *Epidural or spinal***

Epidural or spinal analgesia/anaesthesia can give very effective pain relief but is reserved for pain resistant to other measures and needs specialist management and care.

## **1.4.8 Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)**

For patients with bone tumours, NSAIDs can be used as second line analgesia instead of low dose oral morphine. Discuss with this with the oncology team if considered.

Other than patients with bone tumours, NSAIDs are generally avoided in haematology/oncology patients. This is because the increased risk of bleeding due to the antiplatelet activity of NSAIDs and thrombocytopenia. Once an NSAID has been given, and even after discontinuation of NSAID, the antiplatelet activity may be ongoing for weeks. Therefore, NSAIDs are generally avoided if a patient likely to be thrombocytopenic in the near future (eg if a patient with normal blood counts is due to start a block of chemotherapy). In this situation, NSAIDs are only used at PTC consultant's discretion or if there is a local policy stating otherwise.

### 1.4.9 Management of neuropathic pain

Mild pain (pain scale: 1- 4)	Consider simple analgesia first
Moderate pain (pain scale: 5-7) or Severe pain (pain scale: 8-10)	Consider a first line neuropathic agent - Gabapentin (gradual introduction, see BNFc) - Amitriptyline (2nd line agent) Both these drugs may take 1-2 weeks to be effective. Consider introducing Morphine during neuropathic pain titration. Opioids should be continued until pain score is <4

### 1.4.10 Bone pain

Non-steroidal anti-inflammatory (NSAID) drugs are particularly helpful for bone pain but use with caution when the patient is likely to be thrombocytopenic. (Refer to previous NSAIDs section). Steroids may also be helpful in bone pain and can be administered as a pulse over 3-5 days. Gastric irritation should be anticipated with NSAIDs and/or steroids and a H2 receptor or a proton pump inhibitor prescribed. Pain from discrete bony metastases may be relieved by a short course of palliative radiotherapy.

### 1.4.11 Headaches

A headache may have a simple underlying cause. Headache from central nervous system leukaemia is most effectively relieved by intrathecal chemotherapy. Headaches associated with raised ICP from brain tumours or cerebral metastases may be relieved with steroids. Steroids are often useful as a short-term measure but the disadvantages of long-term steroids, such as mood swings and changes in appearance, usually outweigh the advantages, and treatment with standard analgesics is preferable. Special consideration should be given if the patient has a shunt in situ as the raised ICP could be due to blockage or infection – seek advice from the PTC or paediatric neurosurgical team.

### 1.5 Dyspnoea

Dyspnoea is not just a symptom of disordered breathing. There is often the combination of physical, psychological, emotional and functional factors.

It can impact on a patient's day-to-day activities and if severe, can be a very frightening symptom for both the patient and the carers. Dyspnoea is common in patients who have pulmonary disease but may be caused by many factors, such as anxiety, anaemia, effusions, infection, SVC obstruction, pulmonary embolus, cardiac failure, central nervous system tumours and liver enlargement. Treatment of potentially reversible causes where possible, will help alleviate this symptom.

Radiotherapy or chemotherapy may be indicated.

If anaemia is a significant factor, the benefit of blood transfusion should be considered.

If bronchospasm is thought to be contributory, a trial of bronchodilators may be helpful. Furosemide may be of benefit in patients with cardiac failure.

Low dose Morphine (30-50% of the analgesic dose for the patient) can be very effective in reducing the sensation of dyspnoea.

A short course of steroids may be useful for dyspnoea secondary to obstructive mass.

In the palliative care setting, Midazolam given buccally may be useful for reducing the anxiety, which may be contributing and also be caused by the patient's breathlessness.

### **1.6 Seizures**

Seizures may occur in patients with brain tumours or those with metastatic central nervous system disease. Chemotherapy or radiotherapy may trigger a predisposition to seizures. Reversible causes such as electrolyte imbalances should be sought and treated appropriately. Occasional, short seizures may not require medication, although buccal Midazolam (and/or rectal Diazepam) should be available. Regular oral anticonvulsants may be appropriate for children with brain tumours or cerebral/CNS metastases having frequent convulsions.

Seizures can become difficult to control in the terminal phase and in these circumstances, a continuous subcutaneous or intravenous infusion of midazolam may be helpful.

### **1.7 Anxiety and Agitation**

Anxiety may reflect the patient's need to talk about their fears and concerns and may improve following discussion and explanation. Pain, breathlessness or nausea as underlying causes should be considered. Non-pharmaceutical measures are often helpful such as psychological intervention by a qualified team member, play therapist or child psychologist/psychiatrist where available. Low dose oral diazepam or sublingual Lorazepam may be helpful, particularly for panic attacks, episodic anxiety or for procedures likely to cause anxiety.

### **1.8 Terminal Restlessness**

Restlessness and agitation, sometimes termed terminal restlessness, is common in the final stages of life. It can be treated with Midazolam, Haloperidol or Levomepromazine, and can be given as a continuous infusion. Levomepromazine lowers the seizure threshold so is not generally used as first line in children with CNS disease. Haloperidol should be considered if there is a significant hallucinogenic or psychosis component to the agitation. Either Haloperidol or Levomepromazine should be considered if escalating Midazolam doses are not effective.

### **1.9 Retained respiratory tract secretions at the end of life**

This is a common symptom in patients who lose the ability to swallow secretions, and in those with decreased levels of consciousness in the final stages of life. It can be distressing for parents/carers but not necessarily for the patient who may be unconscious at this stage. Early intervention with anti-secretory agents can be of benefit. A Hyoscine Hydrobromide (Scopoderm) patch provides a non-invasive method of treatment but may not be of benefit as the symptom worsens. Subcutaneous/intravenous Hyoscine Hydrobromide can be used, although as it crosses the blood-brain barrier it may cause neurological side effects and agitation. Glycopyrronium is a useful alternative and may be used whilst the patient is still conscious, as it does not cross the blood-brain barrier and can be given orally or via subcutaneous/intravenous infusion. Repositioning to avoid pooling of secretions and gentle suction can be helpful. Deep pharyngeal suction and excessive frequent suctioning should be discouraged as this may stimulate more secretions.

## **2.0 Bleeding**

Significant bleeding is uncommon in children/young people. Persistent oozing e.g. bleeding

gums can be managed with topical agents such as Tranexamic acid or Adrenaline 1:1000 applied directly to the bleeding point. If low platelets are a contributory factor, a platelet transfusion should be considered as appropriate.

In the palliative phase, if a significant bleed is possible, this should be explained to the parents. Medication for anxiety, agitation and breathlessness (Midazolam, Diamorphine, Morphine) should be made available.

## **2.1 Syringe Drivers**

A syringe driver is an infusion pump used to give continuous medication parenterally, usually over a 24 hr period. Syringe drivers can deliver medication intravenously (e.g. via central venous catheter) or subcutaneously. It is particularly suitable for children who are unable to tolerate oral medication or who require immediate control of difficult symptoms, unresponsive to other intervention. Although it is a common route to administer medication at the end of life, it can also be used for short periods to gain control of difficult symptoms or when the oral route is temporarily impractical (e.g. persistent vomiting).

As recommended by MHRA an anti-syphon extension should be used with any syringe driver.

### ***Indications for using a syringe driver***

- Inability to absorb, tolerate or take oral medication
- Difficulty in swallowing
- Persistent vomiting
- Bowel obstruction
- Severe weakness/semi-unconscious state
- Alternative routes not appropriate
- Unsatisfactory response to oral routes

### **Advantages of using this delivery system are**

- Delivers drugs at an even rate continuously, maintaining plasma concentration without peaks and troughs
- May minimise the number of injections required
- Mobility and independence is maintained
- The ability to deliver complex drug combinations safely

Certain drugs can be mixed together and given in the same syringe driver. Others will require the use of a separate syringe driver. The compatibility of drugs should always be checked. In some situations up to 5 drugs can be mixed in one driver. Advice regarding mixing of 3 or more drugs should be sought from the pharmacist or specialist palliative care service.

### **Notes on using syringe drivers**

- It is usual practice to change the syringe every 24 hours
- Discuss with the pharmacist or specialist palliative care team if the mixing of more than three drugs in one syringe is indicated.
- Check with the pharmacist or specialist palliative care service before using any unusual combinations
- Avoid high concentrations of drug combinations.

Never use Chlorpromazine, Prochlorperazine and Diazepam subcutaneously.