

# Symptom management during chemotherapy

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## Abstract

Improvements in survival for children and young people with cancer have drawn increasing attention to the impact of symptoms on their experience of the disease and treatment. The symptom burden associated with chemotherapy treatment regimens continues throughout the illness trajectory, includes anticipatory symptoms, extends to prolonged treatment for refractory disease and beyond treatment completion in some circumstances. This review explores assessment and management of common symptoms, in particular those identified as sources of distress by children, parents and professionals. Included are pain, mucositis, nausea and vomiting, weight changes and poor nutrition, fatigue, sleep and mood disturbances. Attention is drawn to developing a holistic approach which considers relevant biological, psychological and sociocultural factors in assessment and management and the interrelationship of multiple symptoms.

**Keywords** chemotherapy; fatigue; mood disturbance; mucositis; nausea and vomiting; nutrition; pain; sleep disturbance; symptom assessment; symptom management; weight change

## Introduction

Globally there are an estimated 263 000 new cases of cancer affecting people younger than 20 years each year. Two-thirds of these cases will occur in children under the age of 15 years. In high income countries 80% of these children will survive joining the cohort of one in 1000 adult survivors of childhood or adolescent cancer in these countries. Multimodal chemotherapy has become the treatment that the majority of children and young people diagnosed with childhood cancer will receive. This approach to childhood cancer treatment and supportive care are credited with the significant improvements in survival over the last 40 years. Moreover improvements in supportive care have reduced the mortality and morbidity associated with intensive chemotherapeutic regimes.

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Chemotherapeutic regimes result in significant symptom burden for children and young people (CYP) in addition to those symptoms that arise as an indirect or direct result of the disease itself. Current trials in cancer therapies alongside a primary goal of increased survival are also directed towards the reduction of acute and long term side effects and the symptoms CYP experience during chemotherapy.

This review will discuss the most common symptoms experienced by CYP as a result of chemotherapy for childhood cancer, how these can be recognised, effectively assessed and managed as part of the child's holistic care. We include as symptoms, both measurable and observable phenomena (sometimes described as signs) such as mucositis and vomiting alongside events and experiences only discernible to the child and family and potentially less amenable to measurement, such as fatigue and mood. We recognise that although it may be possible to predict symptoms associated with specific chemotherapeutic agents and regimes, the experience of symptoms is unique to the child and variable over the illness requiring on-going assessment on an individual basis. In addition symptoms are not experienced in isolation, therefore we advocate a holistic approach to management that addresses the relevant biological, psychological and sociocultural factors which should be considered by healthcare professionals.

## Assessment of symptoms

Symptoms during treatment for childhood cancer have been reconceptualised as 'feeling' states rather than side effects. This perspective is validated in the accounts of children and young people (CYP) who speak of 'days when I wake up and feel like I have been hit by a truck' and 'Gastric Armageddon'. CYP accounts also draw attention to the limitations of assessment tools that consider symptoms as single entities that can be evaluated and compared through assigned numeric values. Research on symptom clusters, where two or more symptoms occur together such as pain and fatigue, show that co-occurrence of symptoms increases symptom severity affecting functioning and quality of life.

Recognition of symptoms as a complex biopsychosocial process requires clinicians to synthesise these elements, collected through physical observation and examination, clinical investigation, self-reporting by the CYP and proxy reporting by parents to achieve a comprehensive, meaningful and timely assessment. A number of assessment tools have been developed to determine the incidence, severity and impact on the child of single and multiple symptoms. These tools have been primarily utilised to research symptoms in children with cancer and therefore their utility for clinical practice has yet to be fully tested. Never the less they bear consideration as part of an initial, objective and on-going assessment process to determine the occurrence, cause and effectiveness of symptom management interventions.

Assessment must recognise that the occurrence and severity of symptoms can change over the course of chemotherapy. For example a recent longitudinal study of 236 children during Leukaemia treatment, showed that in addition to participants experiencing a range of symptom intensities mild, moderate and severe. Some symptoms decreased in occurrence over time whilst others changed little. The authors of this report demonstrated that despite a reduction in disease burden, symptoms

related to treatment continued. This is important for effective symptom management as increasingly short periods of hospitalisation become the norm for many chemotherapeutic regimes. In addition to the provision of clear information about potential symptoms and early specific intervention to manage them, paediatric oncology services should be organised to facilitate timely reassessment outside the hospital setting, utilising local health services (such as community nurses) and/or symptom review that can be initiated by the treatment centre, parents and CYP. Several centres have reported the benefits of web and phone based technology to support symptom assessment. On-going dialogue between healthcare professionals, parents and CYP is essential as under reporting of symptoms can relate to assessment tools that lack sensitivity and specificity and do not account for the developmental diversity in the paediatric oncology population. Furthermore both CYP and parents are reluctant to report symptoms which they anticipate cannot be alleviated and are seen as an inevitable part of the cancer experience.

## Pain

Pain is common in children with cancer. It is one of the most prevalent, and also the most feared symptoms. Pain is an integral element of the cancer experience; often present at diagnosis, as a consequence of treatment therapies; as a feature in survivors; common in progressive disease and towards the end of life. Professionals working in the field need to be competent in the management of multiple pain states: acute pain, chronic pain, recurring pain, procedure related pain and pain at the end of life.

Pain is typically under-reported and under-treated in children with cancer. Patterns of opioid consumption in cancer patients show that children begin opioid treatment significantly later than comparable adult groups. Reasons for this are complex and include lack of acknowledgement, poor identification of pain, deficient assessment and management of pain. Concordance between nurse assessment/documentation and child reporting of pain is limited.

Agreement between child and parent pain assessment is also unclear. Parent–child agreement for nausea, pain and lethargy was only moderate in a review of symptoms aged 7–12 years. A recent study has found that many parents of children being treated for cancer reported concerns regarding analgesics used to treat their children's pain and misconceptions about how children express pain. It is essential that professionals provide adequate education and support to CYP and families to address these misconceptions to prevent under treatment of pain, particularly when care is home based.

## Pain management approaches

Pain specialists advocate a mechanism based, multimodal approach to the management of cancer pain. As pain is multi-dimensional, involving the emotional and sensory experience of the child within their developmental level and social and cultural framework, optimal pain relief can only be achieved through holistic assessment. Without attention to the psychological and existential wellbeing of the child, pharmacological management in isolation will not achieve desired effect.

Understanding the science of pain in relation to the pathophysiology of the disease and the clinical setting enables an

integration of psychological, physical, interventional and complementary therapies to optimize pain relief. For example, non-pharmacological and integrative therapies can stimulate efferent inhibiting pathways descending from the periaqueductal grey, thereby decreasing nociception, and providing effective self-coping skills for the child. The use of non-pharmacological therapies such as massage, acupuncture, hypnosis and guided imagery are recognised as essential elements to children's cancer pain management.

There are many causes of pain in this cohort. Chemotherapeutic agents, particularly the vinca-alkaloids, can cause persisting neuropathic pain; solid tumor infiltration into the somatosensory system or direct tissue invasion, and phantom limb pain can also be responsible. Bone pain is also common and is typically a focal, deep seated and intense pain that a child may describe as 'boring' or 'like a drill' and indicates to by pointing to a specific spot. Skills specific to the management of these unique pain syndromes are essential to support a child through cancer treatment. Failure to identify specific pain mechanism and use of targeted analgesia may be one reason for the considerable prevalence of pain in children with cancer.

Pain in cancer is often a combination of nociceptive (visceral and/or somatic), inflammatory and neuropathic pain. The choice of analgesic drug is made on the basis of assessment of pain and its severity and pain characteristics. Opioids are the cornerstone of pain management in cancer treatment and can be used alone or in combination with many other medications. Non-opioids (acetaminophen and non-steroidal anti-inflammatory drugs) and adjuvant medication such as anticonvulsant and tricyclic antidepressant drugs can work synergistically with opioids to improve analgesia.

Opioids are introduced once simple analgesia (paracetamol and ibuprofen) is no longer effective or if assessment indicates more than mild pain. Some analgesics do offer a genuine advantage over morphine, either because of the drugs pharmacokinetic profile such as other receptor activity or because of the formulations available. Examples include the use of methadone for complex cancer pain which is likely to involve several aetiologies (bone, nerve and visceral pain). Methadone has both  $\mu$ -opioid receptor activity and N-methyl-D-aspartate activity which target different pain pathways. Additionally, transdermal fentanyl may be advantageous in a child unable or refusing to take enteral medications.

Patient or nurse controlled analgesia (PCA/NCA) permits even very young children to self-administer small doses of parenteral opioid at frequent intervals and has the versatility to provide a continuous or background infusion at the same time. As children with malignancy have been found to have a high frequency of episodes of breakthrough pain (characterized by 'sharp' or 'shooting pain' lasting seconds to minutes) during treatment, a patient-controlled analgesia opioid bolus dose can be an extremely effective treatment.

Standard dosing of medication adequately treats most treatment related cancer pain in children; however, a significant group requires more extensive management. These challenging pain states are less well defined but occur more commonly among patients with solid tumors involving bone and organ (visceral) with additional neuropathic pain elements including the spine and major nerves. . These mixed pain states require

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