Recognizing and Managing Opioid Induced Neurotoxicity

Effective pain control can be achieved with the use of opioids and other medications. However, there may be some rare instances where metabolites from opioids, usually in conjunction with other factors, can accumulate in the body leading to opioid induced neurotoxicity (OIN).

Opioid induced neurotoxicity includes symptoms such as hyperalgesia (heightened sensitivity to the existing pain), allodynia (pain response from a non-painful stimuli), agitation, delirium with visual, tactile and auditory hallucinations, with or without myoclonus. Myoclonus appears as involuntary single or irregularly repetitive movement. It usually involves one part of the body associated with brief, shock-like muscle contractions or jerks. Myoclonus can be uncomfortable for the patient to experience and the family or caregivers to observe. It is a hallmark sign of OIN.

To understand how we treat opioid induced neurotoxicity, it helps to understand how opioids act. Opioids act in both the ascending pain transmission system and in the descending inhibitory system. Morphine acts by at least three different mechanisms in preventing nerve transmission of pain signals from the periphery to the brain (ascending pain transmission).

1) Reducing stimulation (transduction) at the pain nerve ending.
2) Reducing transmission from peripheral nerves into the spinal cord.
3) Reducing flow in the cord.

Morphine is an opioid agonist, which means it is a drug that binds to an opioid receptor in the body for which it has an affinity to stimulate physiological activity. It is also known that morphine activates pain control pathways that descend from the midbrain to the spinal cord dorsal horn and further reduces the ascending transmission of pain signals. There are also other direct cerebral effects, many still with unknown action, that alter the perception of pain.
Accumulation occurs with repeated administration of any drug before all the previous dose has been cleared. As the plasma concentration increases, the rate of elimination should increase. However, when nearing end of life, patients may naturally have decreased intake of food and fluids with dehydration resulting in electrolyte imbalances, and have a reduced urine output due to impaired renal function. OIN can sometimes be misinterpreted by well-meaning health professionals as worsening pain and therefore there is a decision to increase the opioid, which will only worsen the symptoms (Black & Downing, 2006).

How can we attempt to treat OIN? Depending on the goals of care, presenting associated symptoms, and the illness trajectory, treatments such as opioid dose reduction, hydration (oral or artificial), opioid rotation, non-pharmacological and pharmacological management should be considered.

Start a dose reduction of the opioid as much as 50%. If pain is not well controlled and/or neurotoxicity is severe, an opioid rotation (switch) may be required to allow another opioid to bind to different receptors. With a rotation the dose reduction could also be up to 50% to take into account the lack of cross tolerance. We would use the equianalgesic scale to help us convert from one opioid to another and we should critically think about how many extra doses have occurred related to hyperalgesia (BC Centre for Palliative Care, 2019). Opioid switching is successful in 75-85% of cases (Pallium Palliative Pocketbook 2nd Ed).

Hydration may improve renal function, in turn helping to clear toxic metabolites. If your patient is unable to swallow, consider providing artificial hydration via hypodermoclysis (a bolus of normal saline subcutaneously as a trial to see if symptoms are improved).

Parenteral naloxone should not be used to treat OIN unless signs of overdose are present. OIN does not seem to relate to opioid receptors alone. Giving naloxone does not seem to be effective, and could precipitate opioid withdrawal accompanied by worsening pain. Myoclonus management involves assessing if pain is well controlled and if neurotoxicity is not severe. If so, an opioid dose reduction and encouragement of oral hydration may be all that is required. Severe myoclonus that presents clinically similar to ongoing seizing, should be treated temporarily with a benzodiazepine.
pine such as lorazepam or midazolam (1-3 days) to control the myoclonus, with oral or artificial hydration, until another strategy has taken effect (Pallium Palliative Pocketbook 2018, 2nd Ed).

Screen for and treat delirium in relation to the severity of any agitation/ restlessness. Mild delirium does not need to be treated with medications. Use non-pharmacological measures such as reorientation, ensure the availability of eyeglasses or hearing aids and oral hydration. Promote one-to-one observation to maintain safety, reduce fear, and support re-orientation (BC- CPC, 2019).

Pharmacological management should be considered if delirium is moderate to severe as evidenced by hallucinations, agitation and/or restlessness that is difficult to manage. If there is concern of patient self harm or harm and distress to the patient, family, or caregivers, use haloperidol as a first line therapy, or methotrimeprazine which is more sedating (or midazolam). Other causes of delirium could be managed in alignment with the patient’s goals of care. Is there an infection present? Have you assessed their bowel and bladder needs? Are there other medications that we could initiate, increase or reduce the dose, or discontinue?

Recognizing and treating opioid induced neurotoxicity is key to providing the best possible care for your patient wherever they are in their illness trajectory. Consider the utilization of palliative consultation services for complex situations such as unrelieved pain, unmanageable adverse effects or toxicity, particularly involving patients with renal or liver impairment (BC-CPC, 2019). Your Northern Health Palliative Care Consultation Team is here to help.

**References**

BC Centre for Palliative Care (2019). B.C. Inter-professional Palliative Symptom Management Guidelines.


Introductions

Welcome Jessica Kovacevic

Jessica joined our team as a Palliative Care Nurse Consultant at the beginning of November. She comes to us from BC Cancer Centre for the North where she worked in chemotherapy and the Pain and Symptom Management clinic over the past 4 years. She has also worked on Pediatrics at UHNBC since graduating from the nursing program at UNBC in 2007 and has been teaching for UNBC as a clinical instructor on Pediatrics since 2009. Jessica is excited about starting in her new role with the Palliative Care Team and expanding her current knowledge and practice.

When she's not at work, Jessica keeps busy at home with her husband, 4 kids, and 3 dogs. She loves downhill biking, skiing, camping, and coffee!

Palliative Care Team Photo Corner

On the left, Suzy Stever, our Palliative Pharmacist Lead, is shown here with another attendee during the ECHO training session that happened in October in Vancouver. Our team lead, Stacey Joyce and Jennifer Ferguson, Palliative Care Nurse Consultant, also attended.

Palliative Care F2F Meeting 2019

Our team came together October 2 & 3 to discuss the work plan and participate in some team building exercises.

Back Row (left to right): Jenny Kenny, NW NC; Suzy Stever, Pharmacist Lead; Jennifer Ferguson, NI NC; Seth Gysbers, NI NC; Stacey Joyce, Team Lead

Front Row (left to right): Janet Grainger, Admin; Annie Leong, NE NC; Jenna Hemmerich, NI NC
Upcoming Palliative Education Opportunities

Pallium’s LEAP Core

Palliative Care Consultation will be providing LEAP Core education sessions in the spring. Please watch for further information on dates and locations.

Education Sessions by Skype

A team of experts in palliative care will be presenting a series of interdisciplinary webinars on palliative care. Health professionals from all care settings are invited to attend. A specific subject will be taught each month and repeated throughout the month to allow more people to participate. Webinars are recorded and provided on OurNH and the external website.

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If you are interested in having your name added to our distribution list, please contact Palliative.Care.Consult.Team@northernhealth.ca