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A CASE REPORT ON OPIOID INDUCED DELIRIUM

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ABSTRACT

Opioids have been associated with the development of delirium in the cancer patients. Demulcent of pain with Morphine in cancer patients can be complicated by adverse effects. Forbearance of these effects such as nausea and drowsiness occurs within a few days of morphine therapy. Still, some patients may develop intolerable adverse effects of morphine when the dose is increased. Strategies to diminish adverse effects of opioids includes dose reduction, symptomatic management, switching opioid and altering the route of administration. A case of opioid induced delirium in a cancer patient who was on a Morphine is discussed. A switch- over to Oxycodone resolved his delirium and gave him a new life. This case report is discussed with an evidence for opioid – switching and the intolerable effects of opioid.

KEYWORDS: Opioid; Palliative Care; Delirium.

INTRODUCTION

Opioid analgesic agents have been used for centuries for their analgesic effects and are considered to be the most commonly used pharmacological agents for the management and treatment of moderate to severe pain. Most opioid analgesics are well absorbed when administered through subcutanous, intramuscular and oral routes.

Opioid Induced Nephrotoxocity (OIN) can occur with all known opioid agonists that are used in cancer pain management, including morphine, Hydromorphone, Oxycodone, Fentanyl,

Methadone and Buprenorphrine.[1,2] Delirium occurring in advanced cancer is normally multifactorial in origin, with one frequent precipitating factor being the escalation of opioid dose in patients with uncontrollable pain.[3-5] Delirium is defined as a disturbance in attention (i.e reduced ability to direct, focus, sustain and shift attention), awareness and changes in cognition (i.e memory, deficit, disorientation, language disturbances, perpectual disturbances).

The disturbances develops over a short period (usually hours to days) and tends to fluctuate during the course of the day. This can be assessed by using two methods, Confusion Assessment Method (CAM) and Delirium Symptom Interview (DSM). It occurs in 10% of all hospitalized patients. However, the incidence increases to 26–44% in advanced cancer, and more than 80% become delirious.[6] Delirium also causes significant morbidity, increasing the length of hospital stay and also increasing the risk for falls and associated sustained injuries.[7,8]

Case Presentation

A 63 years old female patient who suffered from pancreatic cancer was admitted with a complaints of worsening nausea, vomiting, abdominal cramps and rigorous non – radiating back pain. Initially she tried a variety of analgesics from the family doctor including NSAIDS and oral morphine but adequate dosing was delayed by nausea and vomiting.

On evaluation she was found to have small bowel obstruction. Initially she was on fentanyl by transdermal patch with morphine for pain. Her initial management for nausea was treated with haloperidol, enemas for bowel obstruction and morphine for pain whereas transdermal fentanyl patch has been discontinued.

As her pain was difficult to control, a pain management team started a temporary intrathecal (IT) catheter for spinal. Opioids were removed later, then she was subsequently continued on intravenous morphine. Still she had a complaints of nausea, though she was on continous infusion of 10 mg of haloperidol over 24 hours, plus Octreotide. In order to treat the nausea, Haloperidol was switched to olanzepine by sublingual tablets of 5 mg twice daily or with 4 – 6 hours as needed.

Parentral morphine was increased from 1 mg / hour to 2mg / hour for 2 days because of rigorous pain. Two days after iniating Olanzepine and increasing the dose of morphine, she

was developed with the myoclonus, delirium and visual hallucinations. Her medications at the time of delirium onset includes Famotidine, Octreotide, Olanzepine, Morphine and Omeprazole. Morphine was switched to Oxycodone, then Famotidine and Mirtazepine were discontinued. Olanzepine was continued in order to control nausea.

The delirium and myoclonus resolved within two days after discontinuation of morphine. Her pain was managed with Oxycodone and nausea were treated with Olanzepine. She was stable and discharged.

DISCUSSION

This case demonstrates the potential for morphine to cause unbearable side-effects which can be resolved by a switch to an another opioid. Cherny et al reported on the guidance of the Expert Working Group of the European Association of Palliative Care on the management of the Adverse Effects of oral Morphine.[9] A single patient may have one or more comorbidities that impersonate opioid-induced adverse effects.

Guidance of European Association of Palliative Care were stated below:

• Careful evaluation to differentiate between morphine- induced adverse effects from co-morbidities that impersonate these effects.

• Consider fall in the dose of morphine adding in co-analgesics or treatments targeting the definite pain syndrome (such as radiotherapy).

• Symptoms of the adverse effect can be managed by using neuroleptics such as haloperidol or benzodiazepines such as midazolam.

• Altering the route of opioid administration - even if the authors point out there is no strong evidence for this.

• Opioids switch over from morphine to oxycodone, fentanyl or methadone, consequently reducing the risks of adverse effects.

As per the above strategy to this case, other etiology for delirium were primarily sought, and a dose reduction of morphine was done. while adverse effects recurred as the morphine dose was increased, symptomatic management of these effects with olanzepine and mirtazepine was attempted. After this strategy was unsuccessful, a switch in opioid to oxycodone produced dramatic progress.

Nevertheless, CNS-excitatory adverse effects such as delirium, hallucinations and myoclonus might have a dose-response association and a chronicity reply relationship to morphine. According to expert opinion, extended exposure to morphine decreases the tendency to develop sedation and respiratory depression but increases the tendency to delirium and myoclonus.

Delirium residue the most common and destructive neuropsychiatric complication in patients with cancer.[10,11] Delirium causes significant pain to patients and their families.[12,13] Delirium impairs patient communication, hence challenging the evaluation of pain and other symptoms.[10]

The evidence for opioid switching

A statement of five cases by Galer *et al*, established the inter-individual variability in response to different opioids.[14] In every five cases, a switch to an another opioid resulted in better pain control and reduction of unbearable side-effects.

1. Pain characteristics (e.g. neuropathic, bone)
2. Drug characteristics (e.g. pharmacokinetic and pharmacodynamic properties, interaction with other drugs)
3. Individual characteristics (e.g. age, genetic variation in receptor subtypes, co-morbidities)

Pain characteristics

It is commonly accepted that the analgesia needs to target the pain syndrome. For instance neuropathic pain is not always opioid-responsive and co-analgesics may prevent the need for escalation of opioid dose.

Drug characteristics

The metabolism of morphine is through the UGT (Uridinediphosphoglyceryl transferase) system in the liver where the active metabolites M6G (Morphine 6-Glucuronide) and M3G (Morphine 3-Glucuronide) are produced. M6G has been shown to accumulate in renal failure and has been concerned in toxicity.

Oxycodone similar to codeine, at the same time it is metabolized in the liver by the enzyme cytochrome P450 2D6 (CYP2D6) to oxymorphone and by N-demethylation to noroxycodone, even if it is oxycodone that is mostly accountable for side effects and analgesia. Different opioids binds in a different way to the opioid receptors. Morphine,

oxycodone, methadone and fentanyl, are all μ opioid receptor agonists, moreover oxycodone works on the K opioid receptor. These differences plays an pivotal role in response to opioids.

Individual characteristics

Riley *et al*., conducted a retrospective study which intended to recognize individual characteristics including haematological and biochemical parameters that could predict morphine intolerance and the necessitate for opioid switching.[15]

CONCLUSION

In view of an opioid switch prior in the patient management would have, in observation, been less traumatic for mutually the patient and his family. It may be a better strategy to perhaps switch opioids if adverse effects are not subsiding within 48 hours and are causing pain to the patient. Even though delirium in this population is often associated with a poor prognosis, 50% of patients can improve with appropriate management of contributing etiologies. This study put forward that the availability of oxycodone in a wider variety of formulations and administration routes would provide a major benefit for the great majority of patients requiring palliative care, particularly those who are unable to endure parentral morphine. In conclusion, oxycodone is effective in treating chronic pain, and to be a safe analgesic for the elderly. In sight of evidence for efficacy, safety, tolerability, and cost, physicians may consider oxycodone as the main concern choice of pain management in the elderly.

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