

Hydromorphone for Cancer Pain in HIV Patient: A Case Report

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Received date: December 13, 2016, Accepted date: December 28, 2016, Published date: December 31, 2016

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Abstract

Background: Antiretroviral therapy has been implicated in significant interactions with a variety of drug classes used to treat comorbid conditions in patients with HIV.

Case report: Male, under oral antiretroviral therapy (emtricitabine 200 mg+tenofovir diproxil fumarate 300 mg id, atazanavir 300 mg id, ritonavir 100 mg id) diagnosed with end-stage pancreatic cancer. Treated orally for pain with paracetamol 1 g 3id, metamizol 575 mg 2id and tramadol 100 mg 3id with poor analgesic control, a Numerical Pain Rating Scale=8. All the analgesic drugs prescribed were discontinued and started hydromorphone extended-release formulation 8 mg id per os with a reduction in the pain to Numerical Pain Rating Scale=0.

Discussion: There is a lack of precise scientific evidence to infer safety conclusions from the concomitant administration of hydromorphone and antiretroviral therapy. Limited existing studies suggest that there is no clinically significant interaction between either emtricitabine or tenofovir with hydromorphone. Regarding atazanavir and ritonavir, coadministration with hydromorphone has not been studied, they both induce glucuronidation and could decrease the opioid analgesic effect.

Conclusions: Since there is a lack of precise scientific evidence to infer safety conclusions from the concomitant administration of these drugs, more studies need to be performed.

Keywords: Hydromorphone; Analgesia; HIV; Cancer

Introduction

Hydromorphone, a semi-synthetic opioid used in the management of acute and chronic pain, is one of a family of closely related μ -agonist opioid drugs with dose-dependent analgesic properties. Hydromorphone has clinically been used to treat pain since the 1920s and it is routinely administered orally, rectal, intravenous, subcutaneous and spinal (epidural and intrathecal) routes [1-3].

Similar to other opioid agonists, hydromorphone does not have a ceiling effect for analgesia and doses can be increased as needed to relieve moderate to severe pain. Hydromorphone has its major effects on the central nervous system and on gastrointestinal. These include analgesia, drowsiness, mental clouding, changes in mood, euphoria or dysphoria, respiratory depression, cough suppression, decreased gastrointestinal motility, nausea, vomiting, increased cerebrospinal fluid pressure, increased biliary pressure and miosis [4].

Hydromorphone is extensively metabolized via glucuronidation in the liver mainly by uridine diphosphate-glucuronosyltransferase 2B7 pathway (UGT2B7) to hydromorphone-3-glucuronide, which has no analgesic effects but it has been found to have significant neuroexcitatory properties [5].

Antiretroviral therapy (ART) represented a huge breakthrough in the treatment of HIV. As a result, HIV is becoming manageable as a chronic disease in the setting of lifelong medication adherence [6].

The success of ART has allowed individuals infected with HIV to suppress viral replication, preserve immune function and reach similar life expectancies as non-infected individuals [7].

However, ART has been implicated in significant interactions with a variety of drug classes used to treat comorbid conditions in patients with HIV [8].

There will be much more to be learned about drug interactions between opioids used in the treatment of pain and ART. Most medications in combination with opioids have not been directly studied in humans. *In vitro* studies indicating the likelihood of drug interactions are not always predictive of what will occur in patients. The ongoing study of frequently prescribed medications with opioids will help to enhance clinical outcomes and to increase safety with medication treatments in this high risk and challenging population.

The author describes a case report of an HIV patient with cancer pain treated with hydromorphone.

Case Report

A 46-years-old Caucasian male, HIV positive since 2005, under oral ART (emtricitabine 200 mg+tenofovir diproxil fumarate 300 mg id, atazanavir 300 mg id, ritonavir 100 mg id) diagnosed with end-stage metastatic pancreatic cancer with hepatomegaly, jaundice, asthenia and intractable lumbar and abdominal pain.

The patient has a history of chronic alcohol abuse, averaging 1 bottle wine/day for the past few years. He also endorsed a 45-pack-year smoking history.

He has been treated for oncologic pain (lumbar and abdominal pain) for the previous week with paracetamol 1 g 3id per os (P.O.), metamizol 575 mg 2id P.O. and tramadol 100 mg 3id P.O.. Regarding this information the Chronic Pain Management Unit has evaluated the patient and applied the Numerical Pain Rating Scale (NPRS). The patient is asked to indicate the intensity of current, best, and worst pain levels over the past 24 hours on a scale of 0 (no pain) to 10 (worst pain imaginable) [9]. The average of the 3 pain ratings, current NPRS=8, best NPRS=6, worst NPRS=10, was used to represent the patient's level of pain over the previous 24 hours [9]. With this therapeutic regimen he presented a NPRS=8.

In concern to the patient's severe pain, Chronic Pain Management Unit discontinued all the analgesic drugs prescribed and started hydromorphone extended-release formulation (once daily) 8 mg id P.O. and morphine 5 mg P.O. 4id SOS. The patient was evaluated 24 h, 48 h and 72 h after beginning of new analgesic regimen, with a consequent reduction in the pain to average NPRS=0; pain evaluation in day 1, day 2 and day 3 with current NPRS=0, best NPRS=0, worst NPRS=1. There was no need of morphine SOS to control the pain. No adverse effects were identified with the introduction of hydromorphone in the treatment of pain.

Discussion

Because of the negative consequences on both patients and their families and wide variety of pain management techniques available nowadays, patients with cancer should be comforted with maximally achievable pain control and not live in fear of inadequately treated pain. As the survival of patients with cancer becomes longer, reliable pain relief is now a high-priority issue that warrants both scientific research and industrial development of new devices and pharmaceutical agents that would make this pain relief complete, safe, and lasting [2].

Clinicians should take caution when starting new medications in patients taking ART. A healthy respect for the influence of enzymatic modulation is necessary, as misadministration or inappropriate prescription of medications may have a devastating effect on the patient's viral control and/or may induce drug toxicity. HIV-infected individuals, and their providers alike, must be particularly mindful of the potential complications of new drug use and the susceptibility of this population for unique drug-drug interactions.

Some of the most important drug-drug interactions for ART medications involve opioids because of the significant risks of either supratherapeutic or subtherapeutic concentrations. Drug accumulation may cause oversedation, respiratory depression, hypoxia, and hypercapnia. Alternatively, decreased concentrations, as might be caused by enhanced enzymatic metabolism, could result in withdrawal symptoms or decreased analgesic effect.

When the Chronic Pain Management Unit first evaluated the patient, he presented poor analgesic control with severe pain (NPRS=8). Optimization of pain medication was made, stopping paracetamol, metamizol and tramadol, and starting hydromorphone. With the new opioid analgesic regimen, the author did not observe a supratherapeutic nor subtherapeutic pain control, in fact, by the evaluation from the NPRS=0 measured in day 1, day 2 and day 3, an

adequate and proper pain control was obtained with hydromorphone extended-release formulation 8 mg id P.O. with no need of morphine 5 mg P.O. 4id SOS. Periodical re-evaluation of patient's medication regimen is essential to finely tune their analgesia and to minimize the exposure to potentially dangerous adverse effects [2].

In fact, there is anecdotal evidence that HIV patients may respond to lower doses of opioids and starting doses may need to be reduced, being the recommended starting dose 4-8 mg once daily [10].

When adding a new medication to an ART regimen, if the clinician is unsure about the possible interaction, consultation with a drug-drug interaction database and/or consultation with a clinical pharmacist/pharmacologist or HIV specialist are recommended [6].

Regarding the patient ART regimen, limited existing studies in the literature suggest that there is no clinically significant interaction between either emtricitabine or tenofovir with hydromorphone, being secure the concomitant administration [11]. Regarding atazanavir and ritonavir, coadministration with hydromorphone has not been studied [11-12].

They induce glucuronidation and coadministration with hydromorphone could potentially decrease the opioid analgesic effect [11]. Careful initial opiate dose adjustment should be made in the setting of these interactions, patients monitored closely, and doses titrated accordingly.

Conclusions

The therapeutic management of a patient with HIV and comorbidities can be a challenge. It is imperative that clinicians should be taught about the consequences of drug metabolism and interactions and how it can affect therapeutic outcomes. Understanding the pharmacokinetics of opioids can help guide-prescribing decisions and optimize pain management, while minimizing the risk for pain resistance due to drug interactions associated with ART.

Hydromorphone and ART interactions are not well known; there is a lack of precise scientific evidence to infer safety conclusions from the concomitant administration of these drugs.

Since an adequate pain control should be a major concern in medical practice, more studies need to be performed to infer the safety of new opioids in HIV patients under ART.

Acknowledgments

The author reports no conflict of interests regarding this case.

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