

# A comparative evaluation of fentanyl and hydromorphone efficacy profiles in palliative cancer pain management: a case report

## Abstract

Optimal pain management plays a pivotal role in enhancing the quality of life among cancer patients. Opioids, notably Fentanyl and Hydromorphone, are frequently employed for alleviating cancer-related pain. Cancer patients necessitate effective pain management to enhance their overall well-being. Opioids, such as Fentanyl and Hydromorphone, are prominently employed to address cancer-related pain. This case report delves into the comparative analysis of the efficacy profiles of Fentanyl and Hydromorphone in the context of a 65 years old female diagnosed with advanced metastatic rectosigmoid cancer. Inadequate pain relief from prior interventions necessitated a referral to Palliative Care services for optimized pain management. Despite previous utilization of non-opioid analgesics, weak opioids, and adjuvant therapies, the patient experienced persistently uncontrolled pain. Given the severity of the pain and the progressive nature of the disease, strong opioid therapy was introduced. The subsequent analysis of the outcomes showcases the individualized approach required for effective opioid therapy in cancer pain management, providing noteworthy implications for the optimization of treatment strategies.

**Keywords:** Fentanyl, Hydromorphone, cancer pain, efficacy, opioid metabolism

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## Introduction

Pain is a prevalent symptom in individuals with cancer. It is of utmost importance to accurately assess and effectively manage pain to enhance patients' well-being, quality of life, and overall health outcomes. Administration of opioids for long period may result in tolerance and hyperalgesia, and decreases the efficacy even with titrating or rotating the doses.<sup>1,2</sup> Hence, it is necessary to implement an efficient pain management strategy.<sup>3,4</sup>

The selection of opioid analgesics for managing cancer-related pain is often based on individual patient factors, response patterns, and medication profiles. Recently considerable attention towards the new approach of pharmacogenetics and genetic background, which affect pain perception, opioid prescription, response and sensitivity to ensure the most suitable painkiller for patient, to provide satisfactory pain control and to improve oncologic consequences.<sup>5</sup> As long as different genes adjust pain and painkillers, the above pharmacogenetics may be encouraging.<sup>6</sup> It may improve treatment outline and determine the safest and effective adjusted dose.

Fentanyl and Hydromorphone are potent opioids commonly utilized in patients with cancer pain with distinct pharmacokinetic and pharmacodynamic properties.<sup>7</sup> Hence, understanding their comparative efficacy, mechanism of action, and optimal dosing is essential. Fentanyl and Hydromorphone both act as agonists of the mu-opioid receptor, which helps to alleviate pain by modulating pain signals in the central nervous system. Fentanyl exhibits a stronger binding affinity to the mu-opioid receptor when compared to Hydromorphone.<sup>8</sup> The observed variations in pain relief and side effects between Fentanyl and Hydromorphone may be attributed to differences in their pharmacokinetics and individual responses of patients.<sup>7-9</sup> In regards to metabolism, Fentanyl undergoes hepatic metabolism primarily through the cytochrome P450 enzyme system, mainly CYP3A4, while Hydromorphone undergoes hepatic

metabolism primarily through glucuronidation via the UDP-glucuronosyltransferase (UGT) enzyme system.<sup>10</sup>

Individual variations in drug metabolism, such as genetic polymorphisms in drug-metabolizing enzymes, can influence the metabolism of opioids.<sup>11</sup> Additionally drug interactions involving enzyme induction or inhibition can impact the metabolism and clearance of these opioids.<sup>12,13</sup> Close monitoring of patients, especially those with hepatic or renal impairment, is essential to ensure appropriate dosing and minimize the risk of adverse effects.

## Case report

We report the case of a 61-year-old female with mid-lower locally advanced rectal cancer B-RAF mutant with invasion to anal canal and vaginal wall and metastasis to liver and lung. Firstly, she underwent neo-adjuvant concurrent chemoradiation therapy (CCRT) 50.4 gray with Capecitabine and had 28 fractions completed June 01, 2020, followed by posterior pelvic exenteration - low anterior resection, hysterectomy with bilateral salpingo-oophorectomy on August 25, 2020. Furthermore, she had extensive residual tumor directly invading adjacent structures (vagina) with no evident tumor regression. For which she was started on FOLFOX chemotherapy with dose adjustment due to low platelets and completed 8 cycles on February 22, 2021. Unfortunately, disease progression and recurrence with peritoneal disease developed. Then, she was started on FOLFIRI + Bevacizumab on November 01, 2021 and completed 8 cycles on April 10, 2022 followed by Cetuximab and Vemurafenib from April 2022 until December 2022. The patient went for second opinion at USA and she was started on Encorafenib + Cetuximab however she showed further disease progression. Then received 2 cycles of TAS102. During the course of her illness, she developed partial bowel obstruction due to extensive peritoneal disease, two times, and underwent palliative resection and ileostomy and conservative management, respectively. The patient presented to emergency

department with severe abdominal pain and found to have recurrent partial small bowel obstruction. Fentanyl was initially administered at a dose of 12.5 mcg/hour via continuous intravenous infusion. Despite adequate conservative management of bowel obstruction, use of different adjuvant medications such as Dexamethasone and Hyoscine butyl bromide, and Fentanyl dose titration over the course of seven days, the patient reported persistent pain scores ranging from 6 to 8 on the Numeric Rating Scale (NRS) and consumed Fentanyl breakthrough doses ranging from 8 to 18 times daily. Furthermore, despite proper hydration, the patient started to experience adverse effects, namely increasing drowsiness and myoclonus, warranting a switch in opioid therapy. Considering the inadequate pain relief and adverse effects, Fentanyl was rotated to Hydromorphone at a starting dose of 1.5 mg intravenous every 4 hours and 1 mg intravenous every 1 hour for breakthrough cancer pain. Moreover, the Hydromorphone dose was reduced to 0.6 mg subcutaneous every 4 hours which continued to demonstrate further pain control. Subsequently, the patient experienced a significant reduction in pain scores, ranging from 1 to 3 on the NRS, and reported improved functionality, overall satisfaction with pain control, and reduction of the experienced adverse effects from Fentanyl.

## Discussion

Pain is a significant issue faced by individuals diagnosed with cancer, and it is one of the most prevalent symptoms reported by cancer patients. Inadequate management of cancer pain can profoundly affect the quality of life experienced by these patients.<sup>14,15</sup> although significant progress has been made in the field of anti-cancer treatment in recent years, the management of cancer-related pain has seen limited advancements wither pharmacological or non-pharmacological. A systematic review revealed that a substantial proportion, around 32%, of patients suffering from cancer-related pain were not adequately treated.<sup>16</sup> Fentanyl and Hydromorphone are both potent opioid analgesics considered as mainstays in pain management, with Fentanyl commonly used for acute and chronic pain, and Hydromorphone often utilized in various clinical settings, including postoperative pain control and palliative care. They act as mu-opioid receptor agonists, providing analgesia through modulation of pain transmission in the central nervous system. Fentanyl has a higher binding affinity for the mu-opioid receptor and is approximately 50 to 100 times more potent than morphine. Hydromorphone is also a potent opioid but has approximately 5 to 10 times the potency of morphine. The observed variations in pain relief and adverse effects between Fentanyl and Hydromorphone may be attributed to differences in their pharmacokinetics and individual patient response.<sup>7-9</sup> In this case, the goal of the Palliative Care Team was to control the patient's pain quickly and reduce the number of used medications for pain control and side effects to enhance her quality of life. Firstly, the patient experienced none to only mild pain relief with Fentanyl. The initial starting dose of Fentanyl was carefully titrated to achieve optimal analgesia without significant side effects. However, due to inadequate pain control and adverse effects, the patient was rotated to Hydromorphone, which required dose adjustments to achieve adequate pain relief. Hydromorphone was initiated at a lower dose compared to Fentanyl taking into consideration the calculation for incomplete cross-tolerance. The dose of Hydromorphone was titrated once in order to achieve better pain management while closely monitoring for any possible side effects. However, the patient reported a dramatic improvement in her pain for which we started tapering down the dose gradually over the course of nine days until we reached to a Hydromorphone dose of 0.6 mg subcutaneous every 4 hours. After switching to subcutaneous Hydromorphone, the patient

achieved sustained pain control with a reduction in pain intensity to less than 3/10 on the NRS. The sedative effects and myoclonus were also notably reduced, which allowed the patient to maintain better alertness and participate in social interactions.

## Conclusion

Optimizing personalized pain management in cancer patients requires a thorough understanding of the pharmacological profiles, varying potency of different opioids. Regular evaluation of pain intensity and careful adjustment of opioid dosages are essential for achieving adequate pain relief while minimizing adverse effects. This case report highlights the potential advantages of Hydromorphone compared to Fentanyl in managing cancer-related pain in this specific patient. Nevertheless, it is essential to consider individual patient characteristics and preferences, including opioid pharmacokinetics and metabolism, when selecting the most appropriate opioid.

Further research and larger-scale studies are necessary to validate these findings and establish more comprehensive guidelines for selecting opioids in cancer pain management. The main step to achieve an effective "personalized" therapy will be by detecting how a patient may react to a certain medication. Better biological activity of medication may affect direct costs, and the prevention of side effects (especially addiction in non-cancer patients) may decrease an indirect cost.<sup>17</sup>

Costs, patient selection, and ethical issues continue to be barriers to the widespread adoption of genetic testing in opioid prescription. Given the lack of data and the lack of information needed to determine whether pharmacogenetics information can vary based on racial or ethnic origin, it is probably too early to predict who will respond better and require lower doses. These restrictions might be overcome if our knowledge grows and new data continue to support the accuracy of genetic profiling.

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## Conflicts of interest

There are no conflicts of interest.

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