



# Patient-controlled analgesia with hydromorphone treatment for advanced colon cancer with severe pain in an older adult patient: a case report and literature review

Mao-Dong Zheng<sup>1</sup>, Yan-Xia Li<sup>2</sup>, Ze-Yu Wang<sup>3</sup>, Huan Ma<sup>4</sup>, Yu Wang<sup>1</sup>, Ting-Ting Qiao<sup>1</sup>, Michael S. Krasovitsky<sup>5,6,7</sup>, Cihad Tatar<sup>8</sup>, Mohana Karlekar<sup>9</sup>, Juan Yan<sup>1</sup>

<sup>1</sup>Department of Pharmacy, The First Affiliated Hospital of Hebei North University, Zhangjiakou, China; <sup>2</sup>Department of Clinical Pharmacy, Lingcheng District's Traditional Chinese Medicine Hospital, Dezhou, China; <sup>3</sup>Department of Pharmacy, Hebei North University, Hebei Key Laboratory of Neuropharmacology, Zhangjiakou, China; <sup>4</sup>Department of Radiotherapy, The First Affiliated Hospital of Hebei North University, Zhangjiakou, China; <sup>5</sup>The Kinghorn Cancer Centre, St Vincent's Hospital, Darlinghurst, NSW, Australia; <sup>6</sup>St Vincent's Clinical School, University of New South Wales, NSW, Australia; <sup>7</sup>St Vincent's Clinical School, University of Notre Dame, NSW, Australia; <sup>8</sup>Department of Colorectal Surgery, Acibadem Taksim Hospital, Istanbul, Turkey; <sup>9</sup>Division of General Internal Medicine and Public Health, Department of Medicine, Vanderbilt University Medical Center, Nashville, TN, USA

**Contributions:** (I) Conception and design: MD Zheng, J Yan; (II) Administrative support: H Ma; (III) Provision of study materials or patients: YX Li, ZY Wang; (IV) Collection and assembly of data: Y Wang, TT Qiao; (V) Data analysis and interpretation: MD Zheng; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

**Correspondence to:** Juan Yan, PhD. Department of Pharmacy, The First Affiliated Hospital of Hebei North University, 14 Changqing Road, Zhangjiakou 075000, China. Email: yjazmd520@126.com.

**Background:** Unrelieved cancer pain can seriously reduce patients' quality of life. Hydromorphone based patient-controlled analgesia (PCA) is widely used in surgery. In recent years, it has also gained attention in the field of cancer pain. We report the case of an older patient with refractory pain secondary to colorectal cancer for whom PCA therapy led to improved symptomatic outcomes.

**Case Description:** We present the case of a 79-year-old male with severe pain from advanced colon cancer. After receiving anti-cancer therapy for 7 years, the patient developed pain in the right groin with a pain score of 7/10. The results of whole-body bone imaging suggested the underlying cause to be a pelvic osseous metastasis. Contemporaneous computed tomography (CT) scanning confirmed disease progression in previously noted non-osseous sites of disease. Systemic therapy with bevacizumab, oxaliplatin, and raltitrexed was commenced. For pain palliation, the patient was treated with morphine hydrochloride tablets, morphine hydrochloride injections, compound codeine phosphate and ibuprofen sustained release tablets, incadronate disodium for injection, and oxycodone hydrochloride sustained-release tablets; despite this, his pain remained poorly controlled. The patient was admitted to hospital with a pain score of 8/10. Other symptoms at presentation included fatigue, anorexia, distress and insomnia. A hydromorphone PCA was initiated, which led to a rapid improvement in the patient's pain. The patient died peacefully 17 days later; his family was highly satisfied.

**Conclusions:** Older patients with cancer experience pain in myriad ways. Patients with advanced cancer pain should receive safe, rapid, and effective pain relief. Hydromorphone-based PCA therapies may provide a valuable therapeutic option for individuals with malignant pain.

**Keywords:** Patient-controlled analgesia (PCA); hydromorphone; severe pain; colon cancer; case report

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## Introduction

Pain is one of the most common symptoms of advanced cancer, with an incidence of between 70% and 80%. One in three patients will experience self-assessed severe pain (1). Oral and injectable opioids are traditionally used to address mild-to-moderate malignant pain, but they may have limitations in treating acute, severe pain, where rapid analgesia may be required. In order to meet the psychological and physical needs of patients with advanced cancer in pain crisis, the integration of palliative care is increasingly recognized as a benefit (2). Patient-controlled analgesia (PCA) technology is a patient-controlled drug-delivery technology that can be personalized and controlled by the patient. PCA therapy is widely used in surgery (3,4). In recent years, it has also gained attention in the field of cancer pain (5).

This article reports the case of an older patient with pre-treated advanced colorectal cancer who was managed with PCA technology. Despite traditional analgesic therapies, the patient experienced self-assessed severe pain. This occurred in the context of advanced disease with limited therapeutic options. The patient had an excellent response to PCA therapy, with a rapid reduction in pain severity. Hydromorphone PCA therapy has the potential to not only reduce pain and other symptoms associated with advanced cancer, but may have a significant quality of life benefit (6). We present this case in accordance with the CARE reporting checklist (available at <https://jgo.amegroups.com/article/view/10.21037/jgo-24-713/rc>).

### Highlight box

#### Key findings

- A 79-year-old male patient with advanced colon cancer developed severe pain following seven years of anti-cancer therapy

#### What is known and what is new?

- The patient's pain symptoms were controlled after treatment with hydromorphone patient-controlled analgesia.
- Management of cancer pain at the end of life is a critical component of optimising quality of life in older patients with cancer.

#### What is the implication, and what should change now?

- Hydromorphone PCA protocol is fast, convenient, safe, and effective in the management of advanced cancer pain among older adults.

## Case presentation

A 79-year-old, married male was admitted to the Department of Radiotherapy of The First Affiliated Hospital of Hebei North University on September 15, 2023, for systemic anti-cancer therapy and symptom management. He was undergoing radiotherapy for colon cancer at the time. Some 10 years earlier, the patient had undergone surgery for appendicitis. He had a 100-pack year history of tobacco, but had quit smoking 2 years prior. He did not drink alcohol. His father died of chronic obstructive lung disease at the age of 73 years, and his mother died of a myocardial infarction at the age of 63 years. He had no familial history of cancer, hypertension, or other genetic problems and no history of drug or food allergies.

In November 2016, the patient noted a change in his stool frequency. On January 26, 2017, the patient underwent abdominal and pelvic computed tomography (CT) examination that demonstrated a right colonic malignancy with locoregional lymphadenopathy. On January 28, 2017, the patient underwent laparoscopic right hemicolectomy and regional lymph node dissection for colon cancer. The pathological stage was T4N2M0. Between March 10, 2017, and August 08, 2017, the patient received eight cycles of adjuvant chemotherapy with oxaliplatin (200 mg, D1) plus capecitabine tablets (1,500 mg, bid, D1–14).

On October 25, 2021, a surveillance CT demonstrated recurrent colonic disease. On October 31, 2021, and November 17, 2021, the patient received two cycles of chemotherapy with bevacizumab (0.3 g, D1), oxaliplatin (130 mg, D1), leucovorin (600 mg, D1), fluorouracil (0.75 g as a bolus), and fluorouracil (4 g infused via CADD for 46 hours). Following induction chemotherapy, the patient underwent a left hemicolectomy; this confirmed metastatic colonic adenocarcinoma.

Between February 2022 and September 16, 2022, the patient received 12 cycles of chemotherapy combined with targeted therapy. The first to eighth cycle of treatment regimen was cetuximab (800 mg, D1), combined with a folinic acid, fluorouracil, and irinotecan (FOLFIRI) (irinotecan, 280 mg, D1; levoleucovorin, 300 mg, D1; fluorouracil, 0.7 g, D1; fluorouracil, 4.0 g, continuous infusion from D2 to D3). Cycles 9 to 12 consisted of cetuximab (0.8 g, D1) and irinotecan (280 mg, D1). A staging CT on September 22, 2022 suggested progressive nodal disease; a subsequent (18)F-fluorodeoxyglucose

positron emission tomography (FDG-PET) scan revealed thoracic and supraclavicular lymphadenopathy, hepatic metastases, and pericardial compression from subdiaphragmatic metastases. On October 15, 2022, the patient underwent radiofrequency ablation for a right-sided phrenic horn mass. Between December 04, 2022, and February 16, 2023, the patient received four cycles of anti-cancer therapy with bevacizumab (0.4 g, D1), oxaliplatin (200 mg, D1), and raltitrexed (4 mg, D1).

On March 09, 2023, the patient complained of pain in the right groin, which he rated as 7 out of 10. Restaging investigations at this time confirmed a left clavicle bone metastasis. Contemporaneous CT examination demonstrated progressive disease within the lung and lymph nodes. Oxycodone hydrochloride sustained-release tablets 10 mg twice daily was initiated. Over the following 4 months, the dose of oxycodone was increased according to analgesic response to a maximal dose of 320 mg twice daily on August 30, 2023. Morphine hydrochloride tablets (128 mg) and morphine hydrochloride injection (5 mg) were used to treat breakthrough pain. Concurrently, compound codeine phosphate (30 mg, three times a day), ibuprofen sustained release (0.6 g, twice daily), and incadronate disodium for injection (300 mg, once a day, D1–5) were used. The patient received seven cycles of bevacizumab (0.4 g, D1) and trifluridine and tipiracil hydrochloride tablets (60 mg, D1–5 and D8–12).

Due to worsening pain, the patient was admitted to hospital on September 15, 2023. He rated his pain an 8 out of 10 at presentation, complaining of pain in the right groin and right leg. Additionally, he complained of fatigue, anxiety, anorexia, constipation, distress and insomnia. Pain worsened with position changes, with intermittent paroxysms of severe pain occurring approximately six times a day. Screening biochemical investigations did not demonstrate a clear metabolic or haematological cause of the patient's worsening pain, though it was noted that he had a mild hyponatraemia (126 mmol/L), a raised bilirubin (11.58  $\mu\text{mol/L}$ ) and a raised CRP without infective symptoms (151 mg/L). Thrombocytopenia was also noted. Despite an increase in oral analgesia, the patient's pain worsened. A hydromorphone PCA was initiated to treat refractory, severe pain on September 16, 2023. The patient's psychosocial distress was treated conservatively.

The patient's hydromorphone dose was calculated based on the total daily dose of opioid used in the previous 24 hours which totaled 640 mg of oxycodone hydrochloride sustained-release tablets, and 120 mg

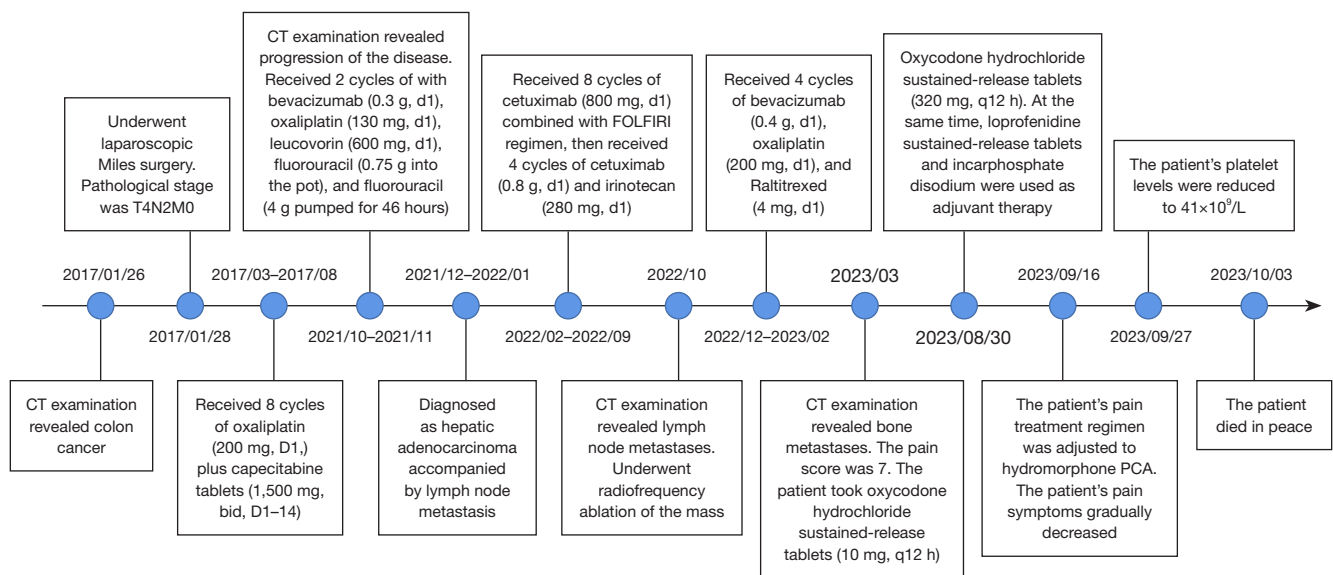
of subcutaneous morphine hydrochloride. In the context of thrombocytopenia, hepatic dysfunction and hyperbilirubinemia, a 25% dose reduction in the total hydromorphone dose was calculated. The patient was initiated on a PCA with a total dose of 66 mg of intravenous hydromorphone combined with 54 mL of 0.9% sodium chloride. The concentration of hydromorphone was 0.55 mg/mL, and the parameters of PCA were set as follows: the maintenance dose was 2.7 mL/h, the bolus dose was 5 mL (2.75 mg) and the lockout time was 10 minutes. Before the hydromorphone PCA was used, the patient's pain score was 8 out of 10. After 30 min, the patient's pain symptoms had decreased to 5/10, with improved ability to converse with family and an improved ability to move in bed. Over the following 72 hours, the patient's pain remained controlled; he was also more physically active, with improved insomnia control and a reduction in nausea; there was, similarly, and improvement in constipation and self-rated anxiety. No direct toxicities from the PCA were observed.

On September 27, 2023, the patient's platelet level reduced to  $41 \times 10^9/\text{L}$ , the creatinine level was 20.6  $\mu\text{mol/L}$ , and the direct bilirubin level was 102.15  $\mu\text{mol/L}$ . Despite daily transfusions of platelets, by October 02, 2023, the platelet count continued to drop to  $18 \times 10^9/\text{L}$ . Worsening renal function and obstructive jaundice were noted at this point. Following numerous discussions with the patient and his family, the decision was made to transition to best supportive care. The patient died comfortably on October 03, 2023, 17 days after the initiation of the hydromorphone PCA (Figure 1).

All procedures in this study were performed in accordance with the Institutional Ethics Committee of The First Affiliated Hospital of Hebei North University and with the Declaration of Helsinki (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report. A copy of the written consent is available for review by the editorial office of this journal.

## Review of the literature

This case report has suggested that hydromorphone PCA therapy may improve pain control in individuals with cancer. Lin *et al.* (7) evaluated the efficacy of intravenous PCA versus non-PCA hydromorphone titration for severe cancer pain; this study demonstrated that the median time to successful analgesia for PCA and non-PCA hydromorphone



**Figure 1** The timeline of diagnosis, treatment, and follow-up. CT, computed tomography.

were 0.50 and 0.79 hours, respectively. The successful titration time of opioid tolerant patients in the PCA and non-PCA groups was 0.50 and 1.00 hours, respectively. In opioid-naïve patients, there was no significant difference in the time to successful titration between the PCA and non-PCA groups. Compared with the non-PCA group, the 24-hour pain score in the PCA group was significantly lower than that in the non-PCA group, and the satisfaction with pain control in the PCA group was significantly higher.

Zeng *et al.* (8) found that PCA with hydromorphone and morphine can effectively and safely relieve short-term moderate-to-severe cancer pain. Sixty patients were randomly divided into hydromorphone and morphine groups, and the study found that postoperative pain scores decreased significantly in both groups compared to baseline. After 30 minutes of administration, patients in the hydromorphone group had significantly lower pain scores than those in the morphine group. Compared to baseline, the incidence of daily, severe pain decreased significantly at 48 and 72 hours in both groups. There was no statistically significant difference in the doses of additional opioids taken daily between the two groups. There was no significant difference in the incidence of nausea, vomiting, dizziness and constipation between the two groups.

Xiao *et al.* (9) studied the efficacy and safety of hydromorphone PCA and oral oxycodone hydrochloride sustained-release tablets in the titration of opioids for cancer pain. This study showed that, compared with

oral oxycodone hydrochloride sustained-release tablets, hydromorphone PCA therapy in the treatment of cancer pain had a shorter titration duration ( $P < 0.001$ ) and did not significantly increase the incidence of adverse events ( $P = 0.32$ ).

### International multidisciplinary team (iMDT) discussion

Pain is a highly prevalent symptom among individuals with advanced cancer. This pain may present in multiple ways, and cause numerous different pain syndromes, including nociceptive pain, neuropathic pain, inflammatory pain and a combination of these. Treating pain in advanced cancer requires a balance between efficacy and the management of toxicities. In the case presented here, PCA administration of hydromorphone was performed according to the principle of individual patient care, and the dose was adjusted according to the patient's tolerance. In this case, the PCA effectively treated the patient's background pain, as well as incident and breakthrough pain. In so doing, the patient was able to communicate with more ease with his family.

Hydromorphone is a semi-synthetic opioid receptor agonist. Its analgesic effect is 5–10 times that of morphine and it has greater penetrance across the blood-brain barrier than other opioids. In addition to its rapid effect, PCA therapy allows patients to titrate opioids to their individual needs, bypassing traditional barriers of pharmacogenomic

and pharmacokinetic variability.

PCA devices are storage pump connected to the patient through a traditional intravenous line. This allows for both background and bolus delivery of analgesia. The self-control button on the PCA, which the patient can press to increase the dosage when in pain, allows for patient-directed bolus therapy at times of acute pain. In this way, patients can regulate the rate of analgesic administration according to their own needs, avoiding under-medication or overdose caused by individual differences. The patient presented in this report received a hydromorphone PCA late in his hospital course and suffered potentially avoidable pain.

Care services for patients with terminal cancer and their families have not been widely promoted and applied in various regions of China. Therefore, providing targeted professional services for patients with terminal cancer can make patient's feel cared for, engender meaning and understanding at the end of life, reduce the pain and fear of death, and afford these patients a dignified death.

*Discussion among physicians from the First Affiliated Hospital of Hebei North University, Lingcheng District's Traditional Chinese Medicine Hospital*

**Department of Radiotherapy**

A 79-year-old male patient with advanced colon cancer developed severe pain following seven years of anti-cancer therapy. The pain treatment of the patient was not significant, and the adverse reactions such as constipation were severe after long-term use of oxycodone sustained-release tablets, which the patient could not tolerate, and the pain broke out frequently, which was a refractory cancer pain. The doctor suggested that the patient should use PCA, replace the oral drug with hydromorphone injection with stronger analgesic effect and less adverse reaction, and relieve the pain quickly through intravenous analgesia. The adverse reactions were alleviated and the patients got satisfactory curative effect. The treatment of this case once again confirmed the analgesic effect of hydromorphone with good efficacy and light adverse reactions, and also showed that PCA technology is an important treatment method in cancer pain, fully proving its feasibility in clinical application in pain treatment.

**Department of Pharmacy**

This case is an advanced tumor patient with poor general condition and frequent outbreaks of pain. The use of

PCA treatment not only significantly reduces the patient's pain, but also can control the outbreak of pain in time and significantly improve the patient's quality of life.

*Several issues on PCA were further discussed as follows*

**Question 1: what is the role of PCA in the treatment of severe pain in cancer?**

*Expert opinion 1: Michael S. Krasovitsky*

PCA therapy is becoming important in the advanced management of malignant pain. Though still used significantly less frequently than subcutaneous therapy, PCA therapy offers the advantage of allowing patients to feel "in control" of their analgesia, and can facilitate both background and bolus therapy. In individuals with cancer pain, I feel that PCAs offer an excellent alternative to standard subcutaneous therapy.

*Expert opinion 2: Cibad Tatar*

In individuals diagnosed with terminal cancer, the implementation of PCA contributes significantly to the amelioration of their quality of life. This approach ensures the administration of a consistent basal level of analgesia, while also allowing for patient-managed dosing, which serves to mitigate the adverse effects commonly associated with the overuse of opioids. Empowering patients with the autonomy to manage their pain not only has physiological benefits but also fosters an improvement in psychological health. Conversely, it is imperative to ascertain the preservation of cognitive function in these patients. It must be recognized that cognitive capabilities may decline in the terminal phase of illness, potentially compromising the effective utilization of PCA.

*Expert opinion 3: Mobana Karlekar*

PCA was developed to allow patients to achieve rapid pain relief through self-administration of intravenous opioids (10). Cancer patients suffering from pain crises often require higher doses of opioids with rapid opioid dose titration to achieve effective pain relief (11). Although oral opioids can be effective, the longer time of onset limits their efficacy when used to treat advanced cancer pain (12). Additionally, oral opioids may be inappropriate in patients with dysphagia and or those experiencing nausea or vomiting.

PCA allows the patient to deliver a bolus dose in real time when their pain level spikes (10). The benefits of using PCA include improved efficacy without significant adverse effects and improved patient satisfaction as a result of having more autonomy in their pain management (7). PCA



is safe as the PCA pump can be programmed with a “lock out” to limit how often and how much opioid a patient may receive (10).

**Question 2: what are the advantages of hydromorphone for pain treatment compared to other opioids?**

**Expert opinion 1: Michael S. Krasovitsky**

There are numerous advantages here. PCA therapy is inherently empowering, as it allows patients to titrate their analgesia according to their needs. Furthermore, one of the advantages of PCA therapy is the rapidity of breakthrough options—currently, there can be a delay in receiving breakthrough analgesia due to nursing work load; PCA offers a practical option to address this. PCA therapy also has the advantage of decreasing opioid toxicity. Furthermore, for patients experiencing end of life care, PCA reduction (intermittent) can allow for periods of less analgesia, which may facilitate interaction with loved ones.

**Expert opinion 2: Cibad Tatar**

Hydromorphone, while possessing effects akin to those of other morphine derivatives, boasts a higher potency, a reduced half-life, and superior analgesic efficacy relative to its impact on respiratory depression.

**Expert opinion 3: Mobana Karlekar**

Cancer patients with advanced, refractory pain often require higher doses of opioids, as noted in our case study. Hydromorphone, a potent, predictable opioid with a favorable safety profile, has many advantages over other widely available opioids. Hydromorphone is more potent than morphine, codeine, and oxycodone (12). Unlike methadone, one of the most potent oral opioids available, hydromorphone has a more predictable pharmacological response (13,14). Hydromorphone has been proven to be an effective opioid analgesic including in patients with renal failure (15). Finally, hydromorphone PCA has been noted to be more effective in reducing pain in cancer patients as compared to those patients’ receiving hydromorphone without PCA (7).

**Question 3: how can we manage patients with advanced cancer pain and improve their quality of life?**

**Expert opinion 1: Michael S. Krasovitsky**

This is a very complex question, and really represents one of the cornerstone questions in palliative care. Pain management in palliative truly relies on the multidisciplinary team, with significant improvements possible with psychology, physiotherapy and occupational therapy, along with other fields such as diversional therapy.

Clearly, multimodal analgesia with therapies from numerous classes required; this may include paracetamol, non-steroidal anti-inflammatory drugs, opioids, neuropathic therapies, anxiolytics and possibly even dissociative therapies. Quality of life is optimised by comprehensive, holistic care, which pays attention to the physical, emotional, spiritual and practical needs of patients with cancer.

**Expert opinion 2: Cibad Tatar**

Managing advanced cancer pain involves a holistic and multidisciplinary approach, beginning with a detailed assessment of pain and regular reassessment as the patient’s condition evolves. Treatment includes pharmacological methods like the stepwise analgesic ladder, adjuvant medications, and specific drugs for breakthrough pain, as well as non-pharmacological interventions such as physical therapies, psychological support, acupuncture, and TENS. Additionally, interventional procedures, palliative care consultation, and hospice care play vital roles, alongside education, communication, and management of related symptoms. Regular review and adjustment of the pain management plan, creating a supportive environment, and ensuring effective communication among all parties are crucial for individualized care and maintaining the patient’s quality of life.

**Expert opinion 3: Mobana Karlekar**

Maximizing quality of life for patients with advanced cancer requires not just ensuring optimal pain control but also addressing the multiple issues that create distress including declining functional status, anxiety, depression, coping with illness and grief (16,17). Palliative care as a specialty aims to maximize quality of life for all patients facing serious illness and has been effective in improving quality of life (18). There is a growing consensus now recommending routine integration of palliative care for most all patients with advanced cancer to “foster coping strategies”, support the needs of patients and families with cancer and maximize symptom control and quality of life (19).

**Conclusions**

The hydromorphone PCA protocol was fast, convenient, safe, and effective in the management of advanced cancer pain in this older patient. PCA technology has the potential to improve quality of life and allow for rapid, effective palliation during the terminal phase of patients’ lives. Older patients with advanced cancer pain may be at risk of opioid toxicity due to age-related physiological changes; in this population, patient controlled analgesia may limit toxicity

while also providing efficacy. Hydromorphone-based PCA therapies may provide a valuable therapeutic option for individuals with malignant pain.

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### Footnote

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*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures in this study were performed in accordance with the Institutional Ethics Committee of The First Affiliated Hospital of Hebei North University and with the Declaration of Helsinki (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report. A copy of the written consent is available for review by the editorial office of this journal.

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