

## Use of Intravenous Acetaminophen (Paracetamol) in a Pediatric Patient at the End of Life: Case Report

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### Abstract

**Background:** For the better part of 100 years, acetaminophen (or paracetamol as it is known outside of the United States) has been a common first-line analgesic in pediatrics and is typically well tolerated with minimal side effects. Its use as an anti-pyretic is also well-documented and thus it is used broadly for symptom control in the general pediatric population.

**Discussion:** In pediatric palliative care, acetaminophen is also used as an adjuvant to opioid therapy for pain as well as an anti-pyretic. For many pediatric patients near end-of-life, however, the ability to tolerate oral intake is diminished and rectal suppository administration can be distressing or contraindicated as in the setting of neutropenia, thus limiting use of acetaminophen by its usual routes. In Europe and Australia, an intravenous formulation of acetaminophen has been used for many years and has only recently become available in the United States.

**Conclusion:** Here, we describe a case using intravenous acetaminophen in a pediatric patient at the end of life.

### Introduction

FOR THE BETTER PART of 100 years, acetaminophen (or paracetamol as it is known outside of the United States) has been a common first-line analgesic in pediatrics and is typically well tolerated with minimal side effects. Its use as an antipyretic is also well documented and thus it is used broadly in the general pediatric population. In pediatric palliative care, acetaminophen is also used as an adjuvant to opioid therapy for pain as well as an antipyretic. For many pediatric patients near end-of-life, however, the ability to tolerate oral intake is diminished. Likewise, rectal suppository administration can be distressing or contraindicated as in the setting of neutropenia, thus limiting use of acetaminophen by its usual routes. In Europe and Australia, an intravenous formulation of acetaminophen has been used for many years and has only recently become available in the United States. Here, we describe a case using intravenous acetaminophen in a pediatric patient at the end of life.

### Case Description

M.A. is an 8-year-old girl with a history of metastatic Sertoli-Leydig cell tumor of the right ovary. She was first diagnosed at age 6 and underwent surgical resection of the mass. Despite no evidence of metastatic disease at the time of

diagnosis, the aggressive pathologic nature of the tumor led M.A. to undergo systemic chemotherapy, which she completed without significant toxicity. A little over a year later, M.A. presented with abdominal pain and was found to have a large abdominal mass that upon surgical resection was diagnosed as recurrent disease. At this time, she was noted to have metastatic lesions in multiple abdominal structures including the omentum, cecum, uterus, and mesentery. She again underwent systemic chemotherapy, which she tolerated well, but several months later developed an intermittent malignant small bowel obstruction with episodic nausea, vomiting, anorexia, and weight loss. M.A. underwent palliative radiation therapy in hopes of shrinking the mass and relieving her obstructive symptoms. Because of her inability to tolerate oral intake, MA was started on total parenteral nutrition (TPN) to maintain nutrition. She required frequent hospitalization for management of pain and other symptoms, including recurrent fevers. Eventually, M.A. was started on patient-controlled analgesia (PCA) for pain control, and her parents opted to enroll M.A. in hospice.

For her fevers, M.A. underwent evaluation with blood and urine cultures as well as abdominal imaging for possible abscess. When these studies were negative and her fever curve failed to respond to antibiotics, it was felt that they were most likely related to her metastatic disease. The fevers themselves

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caused M.A. significant discomfort manifested by increased irritability, diaphoresis, and tachycardia. Initially, M.A. was put on as-needed rectal acetaminophen, which she did not tolerate due to the discomfort and distress associated with the mode of delivery. After much discussion with her parents, a trial of intravenous acetaminophen at 15 mg/kg per dose scheduled every 6 hours was initiated. Twenty-four hours after initiation of intravenous acetaminophen therapy, M.A. experienced an improvement in her fever curve and subjective improvement in her fever-related symptoms. A few days later, she developed increasing bilirubin and imaging revealed the interval development of biliary obstruction from the tumor mass. Due to the risk of liver toxicity, scheduled intravenous acetaminophen was discontinued and M.A. was started on intravenous dexamethasone prior to receiving additional palliative chemotherapy. Eventually, M.A. was discharged home with hospice services. On follow-up with oncology, M.A. was fever-free on daily dexamethasone. She died a little less than 1 month later.

## Discussion

Fevers related to malignancy are common in patients with metastatic disease and can be a cause of discomfort for patients and distress for parents. Acetaminophen remains the mainstay of antipyretic therapy, although the lack of an intravenous formulation has limited its use in end-of-life care. Propacetamol, an intravenous water soluble pro-drug of acetaminophen, has been widely used in Europe for over 20 years but is not available in the United States.<sup>1</sup> Although well tolerated with a low side effect profile, the use of propacetamol has been associated with rare cases of contact dermatitis and pain at the site of injection.<sup>2,3</sup> Developing alternatives has been challenging due to acetaminophen's poor solubility in water. Recently, however, the development of an intravenous formulation of acetaminophen has been approved by the FDA in children older than 2 years of age and is associated with a decreased risk of local reaction compared to propacetamol.<sup>3</sup>

The majority of data on the use of intravenous acetaminophen involve postoperative analgesia,<sup>4-6</sup> although in the past several years increasing evidence has accumulated regarding the safety and efficacy of intravenous acetaminophen in pediatric populations, including neonates.<sup>7-9</sup>

The standard dosing of intravenous acetaminophen in pediatric patients is the same as for oral acetaminophen (15 mg/kg every 4–6 hours with a maximum of 60 mg/kg per day or 4 g/d) with each dose being run over 15 minutes. Noninferiority trials in pediatric patients have shown that in terms of analgesic and antipyretic effects, intravenous acetaminophen is no less effective than a comparable dose of intravenous propacetamol.<sup>10</sup> In a number of countries including Australia and most of Europe, intravenous acetaminophen has been available for more than 5 years, and has recently been approved for use in the United States. The side effects and toxicity of intravenous acetaminophen compared to oral acetaminophen appear to be similar, despite higher plasma levels seen with intravenous acetaminophen.<sup>10</sup> In our case, the patient developed worsening liver function after initiation of intravenous acetaminophen, though this was likely related to her metastatic disease. Caution should be used in patients with liver disease, chronic malnutrition, or severe renal impairment.<sup>11</sup> In addition, careful attention should be paid in

dosing intravenous acetaminophen as several cases of iatrogenic dosing errors have been reported related to calculating the dose based on milliliters rather than milligrams; given that the solution comes in 10 mg/mL preparations, this results in a tenfold overdose.<sup>12</sup>

In general, the oral route is the preferred method for medication delivery in pediatric palliative care patients given the relative discomfort associated with other preparations. In this case, our patient had a preexisting central line for TPN, and her parents, both medical professionals, had a great deal of comfort with delivering intravenous medications. In other situations, the difficulty of establishing and maintaining an intravenous access and parental anxiety or uneasiness may limit the utility of intravenous acetaminophen for pediatric patients at the end of life. Furthermore, the cost of intravenous acetaminophen (typically \$5–\$10 per 1000 mg) may limit widespread use by hospice agencies.<sup>7</sup>

To the best of our knowledge, this is the first reported use of intravenous acetaminophen in a pediatric patient at the end of life. Our patient's fever curve responded well to intravenous acetaminophen and administration improved overall comfort. This suggests a future role in select pediatric patients at the end of life who cannot tolerate other forms of acetaminophen.

## Author Disclosure Statement

No competing financial interests exist.

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