Effects of Patient Controlled Analgesia Hydromorphone during Acute Painful Episodes in Adolescents with Sickle Cell Disease: A Pilot Study

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Abstract

The use of hydromorphone is increasing but little is known about its effects during painful episodes in adolescents with sickle cell disease. This pilot study examined the intensity, location, and quality of pain and evaluated the amount of relief and side effects from PCA hydromorphone during acute painful episodes in five adolescents with sickle cell disease. Data suggest that hydromorphone may provide a better alternative than morphine, the most commonly prescribed opioid in patients with sickle cell disease. Hydromorphone may provide improved pain control and recovery from acute painful episodes in patients with sickle cell disease.

Keywords

Hydromorphone (Dilaudid); sickle cell disease; patient controlled analgesia; acute painful episodes

Introduction

The acute painful episode is the hallmark of sickle cell disease and accounts for the most frequent reason for emergency department visits and hospitalization in these patients (1,2). The mainstay of pain therapy is treatment of the underlying cause, rest, hydration and opioids, predominantly morphine (3). The use of hydromorphone is increasing (4), particularly for...
patients who are experiencing intolerable itching, increased sedation, or unresponsive to and requiring high doses of morphine (clinical experience). However, data on the effects of hydromorphone on pain intensity ratings, pain location, and pain quality are lacking in children and adolescents with sickle cell disease.

Hydromorphone may be more preferable over morphine because of its solubility and speed of onset (5,6). Patients also report few troublesome side effects. Furthermore, hydromorphone has lower dependence liability as compared to morphine. As part of a larger study that examined analgesic response to morphine in patients with sickle cell disease, we examined the intensity, location, and quality of pain in patients receiving hydromorphone. The specific aims of this report are: 1) to examine the intensity, location, and quality of pain and 2) to evaluate the amount of relief and side effects from PCA hydromorphone during acute painful episodes in adolescents with sickle cell disease.

**Methods**

The data presented here were part of a study that examined the effects of different PCA regimens in children and adolescents with sickle cell disease during hospitalization for acute painful episodes. Patients with sickle cell disease were recruited from the hematology unit of a large children's hospital in the central southern United States. The Sickle Cell Program in this facility follows about 900 patients per year and provides comprehensive services for patients with sickle cell disease.

All hospitalized patients with sickle cell disease, eight years and older, were eligible. The age of eight years was chosen as the cut-off point because the outcome measures for pain were validated for patients eight years and older. In addition, patients younger than eight years old were less likely prescribed patient controlled analgesia for pain management during acute painful episodes. Patients were included in the study if: 1) they were English-speaking (data collection instruments available only in English); 2) the primary reason for admission was for management of acute pain as documented by the attending physician in the admission records, and 3) the pain was severe enough to require the administration of intravenous PCA opioids. Patients with sickle cell disease were excluded if pain was not related to an acute painful episode (infection, surgery, burns, trauma). Patients were also excluded if they had cognitive and neurological impairments that precluded them from completing the pain tool. The study was approved by the Institutional Review Board of the medical center.

**Procedures**

Children were asked to rate pain using 0 to 10 numerical rating scales (NRS; 0=no pain to 10=a lot of pain) for 1) worst pain, 2) least pain, and 3) amount of pain relief during treatment (0=no relief to 10=complete relief). The 0 to 10 numeric rating scale is a well-established valid and reliable tool (14), and was previously used by children with sickle cell disease (7-8). A checklist that consisted of common side effects of morphine (hypotension, bradycardia, respiratory depression, drowsiness, dizziness, tremors, sedation, pruritus, nausea, vomiting, constipation, urinary retention) was used to record side effects.

The patient was also asked to complete the Adolescent Pediatric Pain Tool (APPT) to measure the intensity, location, and quality of pain. Reliability and validity of the APPT is well established (9-13). Previous APPT data from children with sickle cell disease showed that pain location and spatial distribution of pain changed during acute painful episodes even when pain intensity remained the same (14).

The patient’s Medication Administration Record was reviewed for the dose, route, and time of all medications that were administered for pain (e.g. nonsteroidal anti-inflammatory drugs...
[NSAIDs] such as ibuprofen and ketorolac) and for side effects (e.g., diphenhydramine for itching, hydroxyzine and ondansetron for emesis). In addition, the following information were also collected from the medical records: 1) demographic information such as age, gender, weight, height, hemoglobin genotype; and 2) health related information such as CBC, pain ratings in the ED, presence of fever, oxygen saturation, other signs and symptoms at time of admission, history of past complications and sickle cell related treatments.

Data Analyses

Scatter plots were used to describe worst and least pain patterns across the five days: Descriptive statistics (frequencies, means, standard deviations) were used to describe worst and least pain, location of pain, and quality of pain, type and amount of medications, and amount of relief.

Results

The patients who were prescribed PCA hydromorphone had a mean age of 16.2 ± 2.5 years, mostly female (4F; 1M), and had predominantly HgBSS genotype. In the ED, they received a morphine equivalent (0.07 mg/kg/dose) of hydromorphone (0.01 mg/kg/dose). The least pain was 2.7 ± 1.1 and the worst pain was 8.5 ± 1.3. The onset of pain was 2 ± 1.2 days prior to admission. The mean length of stay was 6.4 ± 4.4 days.

The recommended hydromorphone PCA dosing schedule as recommended by the American Pain Society (15) is presented in table 1. Patients self-administered 15 to 20 mg of hydromorphone (morphine equivalent to 0.3 mg/kg/day). See example of patient daily consumption of hydromorphone, table 1). The trends in worst (range 5.7 to 9.0 on 0 to 10 NRS) and least (range 2.5 to 5.5 on 0 to 10 NRS) pain intensity ratings during the course of hospitalization are illustrated in figure 1. The number of body areas marked with pain ranged from 5.8 to 9 areas (figure 2A). The number of quality word descriptors selected ranged from 5.3 to 17 words (figure 2B). The most frequent words were sensory quality (2.0 to 6.4), and fewer affective (0.5 to 2.8), evaluative (1.5 to 5.8), and temporal words (1.0 to 4.0). The perceived amount of pain relief (4.2 to 5.5 on 0 to 10 NRS) during the course of hospitalization is illustrated in figure 3.

Itching was the most common side effect, reported by 4 of the 5 patients in the PCA hydromorphone regimen. Nausea and vomiting were reported by one patient. No one had low blood pressure, heart rate, or respiratory rate. One patient had difficulty stooling, which was reported prior to enrollment.

Conclusion

While previous reports have examined the effects of morphine on the intensity, location, and quality of pain in children with sickle cell disease (7,8,14), very little if any reports were available that examined the effects of hydromorphone during acute painful episodes.

We found that pain intensity ratings decreased over time with PCA hydromorphone in this small sample of adolescents. We observed that with PCA hydromorphone, worst pain decreased by at least 20% (figure 1). Furthermore, our data showed that least pain intensity ratings were lower during the course of hospitalization than were reported in previous studies (7,8,14). Jacob and colleagues reported that patients with sickle cell disease showed that morphine decreased pain intensity ratings by 5% (14) which was not clinically significant. However, because our sample size was small for both the hydromorphone and morphine, we were not able to make any statistical analyses to tests for significance.
The number of body areas marked with pain was not affected by the use of hydromorphone. However, the number of word descriptors to describe the quality of pain showed a decreasing trend. The amount of pain relief from hydromorphone remained moderate throughout hospitalization. Very few patients reported side effects (itching, nausea, vomiting).

Although this study represented a small number of patients with sickle cell disease and would not be representative of the experience of all patients with acute painful episodes, our data suggest that hydromorphone may provide a better alternative than morphine, which is the most commonly prescribed opioid in patients with sickle cell disease (7,8). Therefore, we recommend future studies to examine whether hydromorphone is more effective in improving pain and recovery from acute painful episodes in children with sickle cell disease.

A report by Perlman and colleagues (4) showed that hydromorphone improved pain control and decreased admissions for acute painful episodes in adult patients with sickle cell disease.

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References

5. Taketomo, CK.; Hodding, JH.; Kraus, DM. Pediatric dosage handbook.

Example of Daily Hydromorphone Consumption for 60 kg Patient
Figure 1.
Worst and Least Pain Intensity Ratings on 0 to 10 NRS.
Figure 2.
Number of Body Areas Marked on the Body Outline Diagram (A) and Number of Quality Descriptors (B) Selected to Describe Pain in Adolescents with Sickle Cell Disease.
Figure 3.
Amount of Relief on 0 to 10 NRS.
**Table 1**

Hydromorphone Patient Controlled Analgesia Regimen

<table>
<thead>
<tr>
<th><strong>Recommendation for Patient Controlled Analgesia Settings (PCA) Hydromorphone</strong></th>
<th>Example PCA Settings for 60 kg Patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loading Dose</td>
<td>20 microgram/kg (max 1.5 mg)</td>
</tr>
<tr>
<td>Intermittent Push</td>
<td>5 microgram/kg/dose</td>
</tr>
<tr>
<td>Background Rate</td>
<td>1.5 microgram/kg/hour</td>
</tr>
<tr>
<td>Lock-out Interval</td>
<td>6 to 8 minutes</td>
</tr>
<tr>
<td>4 hour Maximum</td>
<td>20 microgram/kg/hour</td>
</tr>
</tbody>
</table>

meg: micrograms; mg: milligrams.