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Parenteral Ketoprofen in the Management of Painful Sickle Cell Crises

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Abstract

Sickle cell disease (SCD) is characterized by recurrent painful vaso-occlusive crises (VOCs) that commonly require hospital admissions and narcotic pain killers. In most cases of VOC, pain control is achieved by narcotic analgesics such as pethidine, pentazocine or codeine. Patients with VOC are commonly undertreated either because of inavailability of strong analgesic or physician's suspicion of drug addiction. In this prospective pilot study we evaluated the safety and efficacy of parenteral ketoprofen, a non-steroidal anti-inflammatory drug (NSAID), in controlling pain of VOC in 31 VOC episodes. Ketoprofen was given in doses of 100mg intravenously every 4-8 hours. The results of pain control during the first 48 hours were compared with conventional pain killers (pethidine, codeine and paracetamol) in 31 historical VOC episodes in the same patients. The results showed that intravenous ketoprofen produced profound analgesia and sedation that was superior to the conventional narcotic analgesic without any gastrointestinal, nervous and respiratory side effects. We conclude that intravenous ketoprofen is safe and effective in controlling pain in VOC. However, larger double-blind, controlling studies are needed to confirm our observation.

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Introduction

Painful VOC represent the most unpleasant complications of SCD (1) that require hospital admission and narcotic analgesics for pain control (1-4). Commonly, patients are undertreated because (a) inavailability of strong analgesic in outpatients in many small hospitals; (b) the physician may suspect that the patient is a drug addict and is exaggerating the pain in order to get the narcotic drug; (c) sub therapeutic doses of narcotic pain killers to patients who are used to these drugs and required higher doses. On the other hand, many patients are given narcotic analgesics freely to the extent that they develop drug habituation and addiction (2-5). Unfortunately, parental NSAIDs have not been evaluated in the management of VOC (6). Ketoprofen is a NSAID with profound analgesic and sedative effect and safety especially when given intravenously. It lacks the common adverse effects of pain killers on the gastrointestinal tract, kidney and nervous system.

In this communication, we present our experience with intravenous ketoprofen in controlling severe pain of VOC.

Patients and Methods

Fourteen patients (9 males and 5 females, aged 15-31 years, mean 20.3 ± 5.1) who were admitted to the hospital 31 times for the management of severe VOC agreed to participate in this study (Table 1). Pain evaluation was carried out by using a visual scale (Fig 1). The painkiller requirements were evaluated for the first 48 hours after admission. All patients were hydrated with normal or 1½ normal saline supplemented with potassium chloride 20 mEq/l by continuous intravenous (1 V) infusion at 75 cc/kg/day.

Acknowledgement

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Table 1
COMPARISON BETWEEN PARENTERAL KETOPROFEN AND
CONVENTIONAL PAIN KILLERS IN CONTROLLING PAIN OF 52 VOC'S

<table>
<thead>
<tr>
<th>Patients</th>
<th>Group A</th>
<th>Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>Sex/Age</td>
<td>No. of VOC</td>
</tr>
<tr>
<td>1</td>
<td>M 21</td>
<td>4</td>
</tr>
<tr>
<td>2</td>
<td>F 23</td>
<td>4</td>
</tr>
<tr>
<td>3</td>
<td>M 24</td>
<td>3</td>
</tr>
<tr>
<td>4</td>
<td>M 19</td>
<td>3</td>
</tr>
<tr>
<td>5</td>
<td>F 16</td>
<td>3</td>
</tr>
<tr>
<td>6</td>
<td>M 15</td>
<td>2</td>
</tr>
<tr>
<td>7</td>
<td>M 25</td>
<td>2</td>
</tr>
<tr>
<td>8</td>
<td>M 18</td>
<td>2</td>
</tr>
<tr>
<td>9</td>
<td>F 17</td>
<td>2</td>
</tr>
<tr>
<td>10</td>
<td>F 18</td>
<td>1</td>
</tr>
<tr>
<td>11</td>
<td>M 15</td>
<td>1</td>
</tr>
<tr>
<td>12</td>
<td>F 15</td>
<td>1</td>
</tr>
<tr>
<td>13</td>
<td>M 28</td>
<td>1</td>
</tr>
<tr>
<td>14</td>
<td>M 31</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>31</td>
</tr>
</tbody>
</table>

Mean: 803.4 ± 45.4
Mean: 10967.6 ± 768.0

± SD: 255 ± 46.4
± SD: 177.9 ± 1067.7

Group A: Patient received intravenous ketoprofen only.
Group B: Control group who received conventional analgesic (codeine, paracetamol and pethidine).
VOC: Vasculo-occlusive crisis
K: Ketoprofen (Intravenously)
P: Pethidine (intravenously / intramuscularly)
V/C: Paracetamol / Codeine (Tylenol No. 3 containing 500 mg paracetamol + 30 mg codeine sulphate/tablet).

Conventional pain killers:

(a) Pethidine 50-100 mg I.V. or I.M every 4-6 hours as needed.

(b) Codeine phosphate 60 mg with paracetamol 1gm (Tylenol # 3 Cilag AG International, Switzerland) orally every 4-6 hours.

Ketoprofen: (Profenid Rhone-Poulenc, Paris, France) was given as 100 mg in 25 cc normal saline intravenously over 5-10 minutes and repeated every 4-8 hours.

Pain was evaluated by a visual scale between zero (no pain) and 10 (intolerable pain). Efficacy and side effects were evaluated according to the form shown in Fig.1.
Controls: The same number of previous admissions of the same patients were taken as a control group.

Results

All patients responded to intravenous ketoprofen within 5-10 minutes with complete disappearance of pain. The duration of response varied between 1-12 hours. (Table 2).

<table>
<thead>
<tr>
<th>Duration of response (Hours)</th>
<th>Ketoprofen Group n = 31</th>
<th>Pethidine Group n = 31</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7 (22.5)</td>
<td>5 (16.1)</td>
</tr>
<tr>
<td>4</td>
<td>9 (29.0)</td>
<td>20 (64.5)</td>
</tr>
<tr>
<td>6</td>
<td>7 (22.5)</td>
<td>6 (19.3)</td>
</tr>
<tr>
<td>8</td>
<td>5 (16.1)</td>
<td>-</td>
</tr>
<tr>
<td>12</td>
<td>3 (9.6)</td>
<td>-</td>
</tr>
<tr>
<td>Total</td>
<td>31 (100%)</td>
<td>31 (100%)</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>5.19 ± 3.26</td>
<td>3.90 ± 1.15</td>
</tr>
</tbody>
</table>

Side effects of ketoprofen were limited to transient local pain at the site of administration but only when the drug was pushed rapidly. More than two thirds of the patients slept after the injection and in 12 out of 31 episodes, patients experience euphoria. There was no nausea, vomiting, diarrhea or abdominal pain. No other side effects were noticed (Table 3).

<table>
<thead>
<tr>
<th>Side effects</th>
<th>Ketoprofen (intravenously)</th>
<th>Pethidine</th>
<th>Codeine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local pain</td>
<td>(+)</td>
<td>-</td>
<td>(NA)</td>
</tr>
<tr>
<td>Sedation</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Nausea / Vomiting / epigastric pain</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Euphoria</td>
<td>± (12/31)</td>
<td>± (14/31)</td>
<td>± (9/31)</td>
</tr>
<tr>
<td>Constipation</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

+ = Present, ± = Present in some cases (No. of cases), - = Absent, NA = Not applicable, (+) 8 = Present only when ketoprofen administered rapidly intravenously.

Discussion

This study indicated that parental ketoprofen was equal or superior to narcotic analgesics, i.e., pethidine and codeine. This confirms several international reports of excellent pain control with parental ketoprofen comparable to morphine, pentaazocine in post-operative conditions, severe renal colic and severe arthritis (6-10).

In addition to its efficacy, parental ketoprofen has a wide margin of safety without any recordable side effects on the gastrointestinal tract, nervous system or kidneys (9-16). Doses up to 1000 mg/day could be given intravenously in divided doses or by continuous infusion (in normal saline) (9).

References

Symposium
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College of Medicine - King Saud University - Riyadh
Parenteral Ketoprofen in the Management of Painful Sickle Cell Crises


College of Medicine and King Khalid University Hospital, King Saud University, Riyadh, Saudi Arabia

Frequent painful vaso-occlusive crises (VOC) are the most unpleasant complications of severe sickle cell disease. In most cases, VOC requires hospital admission and administration of narcotic pain killers such as pethedine, pentazocine, morphine and codeine. Ketoprofen is a non-steroidal anti-inflammatory drug with a powerful pain killing effect when used parenterally. The analgesic effect of the parenteral form of ketoprofen is comparable to pethedine, pentazocine and morphine. To ameliorate pain of VOC without using narcotic analgesics, we started a pilot study on adult patients with severe sickle cell disease who presented to King Khalid University Hospital with VOC. Each patient received 200 mg ketoprofen in 10 ml normal saline (NS) intravenously slowly to be followed by 100 mg in 5 ml NS every 6-12 hours thereafter until the end of the VOC. Evaluation includes site, severity and duration of pain, degree and duration of response as well as any side effects. Our preliminary results on the first 11 patients indicated that parenteral ketoprofen is effective in ameliorating the pain of VOC.

The full results of this study will be presented and discussed.

REFERENCES


Sickle cell disease (SCD) is characterized by recurrent painful vaso-occlusive crises (VOC) that commonly require hospital admissions and narcotic pain killers. In most cases of VOC, pain control is achieved by narcotic analgesics such as pethidine, pentazocine and codeine. Patients with VOC are commonly undertreated either because of unavailability of strong analgesics for outpatients or physicians suspicion of drug addiction. In this prospective pilot study we evaluated the safety and efficacy of parenteral ketoprofen (Profenid, Rhone-Poulenc, Paris, France), a non-steroidal anti-inflammatory drug (NSAID), in controlling pain of VOC in 31 VOC episodes. Ketoprofen was given in doses of 100 mg intravenously every 4-8 hours. The results of pain control during the first 48 hours were compared with conventional pain killers (pethidine, codeine and paracetamol) in 31 historical VOC episodes in the same patients. The results showed that intravenous ketoprofen produced profound analgesia and sedation that was superior to the conventional narcotic analgesics without any gastrointestinal, nervous or respiratory side effect. We conclude that intravenous ketoprofen is safe and effective in controlling pain of VOC. However, larger, double-blind, controlled studies are needed to confirm our observation.