Use of oxycodone in polytrauma patients: the “Gemelli” experience

F. FRANCESCHI1, M. MARINI3, S. URSELLA1, L. CARBONE1, M. CANDELLI1, G. PIGNATARO1, M. GABRIELLI1, L. SANTARELLI1, V. OJETTI1, B. GIUPPONI1, V. FIORE1, F. BARBARO1, G. DE MARCO1, F. BUCCELLETTI1, F. MANCINI1, D. ROCCARINA1, G. GIGANTE1, A. GASBARRINI2, G. GASBARRINI2, N. GENTILONI SILVERI1

1Emergency Department and 2Internal Medicine Institute, Catholic University of Rome (Italy)
3 Istituto di Anestesia e Rianimazione, Catholic University of Rome (Italy)

Abstract. – Introduction: This is the first study investigating the effect of oxycodone in polytrauma patients. The management of pain in polytrauma patients has become a very relevant issue. Nonsteroidal anti-inflammatory drugs (NSAIDs) represent the most used drugs in polytrauma patients, even though their use is associated with an increased hemorrhagic risk. Previous studies have demonstrated the efficacy of oxycodone for the treatment of acute pain. The aim of this study was to assess the efficacy of oxycodone administration in polytrauma patients, with minor injuries.

Patients and Methods: 15 polytrauma patients (10 males, mean age 40 ± 13 years; 5 females, mean age 49 ± 26 years) were admitted to the Emergency Department of the Catholic University, A. Gemelli Hospital in Rome, Italy. All patients underwent physical examination, FAST ultrasound, total body CT scanning and blood tests. Three patients had multiple costal fractures, three had pelvic fracture, two had tibial fracture, five had vertebral fractures, one patient had clavicle fracture and ulnar fracture, one patient a severe trauma of the left leg, which required amputation. Five patients also reported minor head trauma, with a Glasgow Coma Score (GCS) 15. All patients reported abdominal trauma, while none of them had severe thoracic or kidney damage. Patients with head trauma also underwent a second CT head scanning 12 hours after admission, which excluded the occurrence of cerebral damage. All patients were then treated with oral administration of oxycodone 10 mg two times per day (bid) for 3 days. Pain intensity, before and after the administration of oxycodone, was evaluated using a scale ranging from 0 to 10.

Results: The mean pain score at admission was 8 ± 0.7. All patients reported significant pain improvement after the administration of oxycodone (8 ± 0.7 vs 1.8 ± 0.9; p < 0.0001). A dosage increase of oxycodone from 20 to 40 mg bid was required in only one patient with a clavicle fracture. The main side effects were light-headedness (5 patients), constipation (4 patients) and nausea (3 patients).

Conclusions: These data indicate that oxycodone is a safe and effective drug for pain relief in polytrauma patients without severe thoracic, kidney or brain damage.

Key Words: Oxycodone, Polytrauma, Pain

Introduction

Polytrauma is a clinical condition defined by the presence of at least two long bone fractures, or one life-threatening injury and at least one additional injury, or severe head trauma and at least one additional injury1.

Polytrauma patients usually undergo complex medical management; in particular, treatment of these patients will generally require resuscitation, emergency surgery, intensive care and complex reconstructive surgery. Nevertheless, a satisfactory pain control is also required for those patients2.

Treatment of acute pain in polytrauma patients is always a great challenge. In fact, one of the most important characteristic for polytrauma is the high risk of internal bleeding. The use of nonsteroidal anti-inflammatory drugs (NSAIDs) is very common in the management of pain in polytrauma patients but it is associated with an increased hemorrhagic risk1.

Corresponding Author: Francesco Franceschi, MD; e-mail: castrv@terra.es
Oxycodone is a semisynthetic analgesic opioid derived from opium alkaloid thebaine. Despite it has been used for many years as hydrochloride salt in combination with acetaminophen in the management of chronic pain, new clinical trials proved its safety and more efficacy when used alone as controlled release or immediate release formulation. In fact, pharmacodynamic data pointed out that oxycodone does not require conversion to oxymorphone to be active, making this drug to have a higher oral bioavailability and to be about twice as potent as morphine. In addition, due to the lack of detectable clinically relevant active metabolites, which in turn may trigger toxic reactions, oxycodone could be also used in patients with renal failure. Although its precise mechanism of action is still unknown, some studies have shown that oxycodone is a mu-and kappa-opioid receptor agonist, which confers to this drug strong analgesic properties, as demonstrated by its efficacy in the treatment of different kind of pain, including postoperative, malignant and non-malignant diseases related pain. Finally, oxycodone has no effect on platelet aggregation differently from NSAIDs, thus not increasing the hemorrhagic risk. All those characteristics make this drug ideally suitable for pain management in polytrauma patients, more than NSAIDs. Based on these observations we designed a study aimed at evaluating the efficacy of oxycodone in the treatment of pain in polytrauma patients.

### Patients and Methods

We enrolled 15 polytrauma patients (10 males, mean age 40 ± 13 years; 5 females, mean age 49 ± 26 years; Table I), admitted to the Emergency Department of the Catholic University, in Rome, Italy. All patients underwent physical examination, focused assessment with sonography for trauma (FAST), total body CT scanning and blood tests. In all patients, the injury severity score (ISS), in which the degree of injury severity is determined on a scale of 1 to 6 for 6 physical regions, such as head or neck, face, chest, abdomen, extremities, and external was also calculated.

Three patients had multiple costal fractures, three had pelvic fracture, two had tibial fracture, five patients had vertebral fractures, one patient had clavicle fracture and ulnar fracture and one patient a severe trauma of the left leg, which required amputation. Five of those patients also reported minor head trauma, with a Glasgow Coma Score (GCS) 15 in the absence of any relevant neurological symptom. All patients also reported abdominal trauma. None of the patients had severe thoracic or kidney damage. Patients with head trauma also underwent a second CT head scanning 12 hours after admission, which excluded the occurrence of cerebral damage. All patients were then treated with oral administration of oxycodone 10 mg two times per day (bid) for 3 days. Pain intensity, before and after the administration of oxycodone, was evaluated using a scale ranging from 0 to 10, where 0 was the equivalent of no pain and

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex</th>
<th>Age</th>
<th>Main pain site</th>
<th>NSAIDs pre-treatment</th>
<th>ISS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>32</td>
<td>Chest</td>
<td>Yes</td>
<td>17</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>45</td>
<td>Chest</td>
<td>Yes</td>
<td>24</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>39</td>
<td>Chest</td>
<td>Yes</td>
<td>17</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>47</td>
<td>Pelvis</td>
<td>Yes</td>
<td>24</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>42</td>
<td>Pelvis</td>
<td>Yes</td>
<td>17</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>48</td>
<td>Heel</td>
<td>Yes</td>
<td>17</td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>28</td>
<td>Tibial</td>
<td>Yes</td>
<td>17</td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>54</td>
<td>Tibial</td>
<td>Yes</td>
<td>17</td>
</tr>
<tr>
<td>9</td>
<td>F</td>
<td>92</td>
<td>Lumbo-sacral</td>
<td>Yes</td>
<td>14</td>
</tr>
<tr>
<td>10</td>
<td>M</td>
<td>19</td>
<td>Lumbo-sacral</td>
<td>Yes</td>
<td>29</td>
</tr>
<tr>
<td>11</td>
<td>F</td>
<td>23</td>
<td>Lumbo-sacral</td>
<td>Yes</td>
<td>17</td>
</tr>
<tr>
<td>12</td>
<td>M</td>
<td>44</td>
<td>Neck</td>
<td>No</td>
<td>17</td>
</tr>
<tr>
<td>13</td>
<td>M</td>
<td>30</td>
<td>Ulna-clavicle</td>
<td>Yes</td>
<td>22</td>
</tr>
<tr>
<td>14</td>
<td>M</td>
<td>39</td>
<td>Leg</td>
<td>Yes</td>
<td>33</td>
</tr>
<tr>
<td>15</td>
<td>M</td>
<td>61</td>
<td>Leg</td>
<td>Yes</td>
<td>22</td>
</tr>
</tbody>
</table>
10 was given for severe pain. Statistical analysis was performed using the Student’s t test.

The general characteristics of the patients are summarized in the Table I.

**Results**

The administration of 10 mg bid of oxycodone was significantly effective for the reduction of pain in all patients. In particular, we observed that the mean value in the pain scale was 8 ± 0.7 at the admission into the Emergency Department, 2.3 ± 0.8 the day after and 1.8 ± 0.9 at the end of treatment ($p < 0.0001$) (Figure 1). In our series, the dosage of 20 mg bid was sufficient for a drastic sedation of the acute pain. Increasing dosage of oxycodone from 20 to 40 mg bid was only required in a patient with a clavicle fracture. No differences have been observed between males and females concerning the response to the treatment as well as among different ISS score values. The administration of oxycodone in our study caused only mild side effects to some of the patients such as light-headache (5 patients), constipation (4 patients) and nausea (3 patients), which did not required the suspension of the treatment as shown in Figure 2.

**Discussions**

In this pilot study, the administration of oxycodone 20 mg per day resulted to be very effective in the management of pain in polytrauma patients. Neither the site of pain nor the sex of the patient affects the efficacy of the treatment. Thus, according with previous studies oxycodone is able to control acute pain in a very reliable way.

Either pharmacodynamic or pharmacokinetic characteristics possessed by oxycodone may explain why it would be a good choice for the treatment of acute pain in polytrauma patients. First of all, oxycodone has been proved to show a rapid efficacy in pain control, comparable to morphine$^{6-11}$. The duration of activity of a single administration of controlled-release formulation of oxycodone is up to 12 hours$^{12}$, which may allow to reduce the frequency of analgesic administration to polytrauma patients. Finally, oxycodone does not exert any activity on platelet aggregation, differently from NSAIDs, thus not affecting the hemorrhagic risk, which in turn is typically increased in polytrauma patients$^{13}$.

In our knowledge this is the first study investigating the effect of oxycodone for pain management in polytrauma patients in an Emergency Department. There is only one study, in the general literature, investigating on the effect of oxycodone or hydrocodone in combination with acetaminophen in the treatment of acute pain associated with bone fractures, showing that both those drugs possess a good analgesic effect$^{14}$. Nevertheless, the characteristics of the subjects enrolled in that study differ from those shown by our patients; in particular we have enrolled patients with multiple sites of trauma and associated fractures, in which the pain was localized, at the same time, in different areas of the body. In-

![Figure 1](image-url). Global main pain score at admission and 1 and 2 days after the beginning of the treatment with Oxycodone. A drastic decreasing in the pain score was observed at either day 1 or day 2.
Interestingly, in our series, the administration of oxycodone determined a pain relief in all painful areas. Only few patients reported mild side effects, mainly represented by light-headache, constipation, and nausea, which did not require the suspension of the treatment. Finally, none of our patients required further administration of any other kind of analgesic during the clinical observation.

In conclusion, these data indicate that oxycodone is a safe and effective drug for pain relief in the emergency setting, in polytrauma patients without severe thoracic, kidney or brain damage. Further studies, enrolling a larger number of patients, are now needed in order to confirm our findings.

References


