Letter to Editor

Pegylated Naloxone in the Treatment of Persistent Opioid-Induced Constipation in Patients with Hematological Malignancies

Gregorio Antonio Brunetti¹, Giovanna Palumbo¹, Giorgia Annechini¹, Michelina Santopietro¹, Andrea Tendas²*, Pasquale Niscola²* and Claudio Cartoni¹

¹Department of Cellular Biotechnology and Hematology, University La Sapienza of Rome, Rome, Italy and ²Hematology Unit, S.Eugenio Hospital, Rome, Italy

To the Editor,

In the course of Hematological Malignancies (HM) several pain syndromes, often troublesome and difficult to treat, may be suffered from affected patients [1]. Therefore, for a significant proportion of HM patients, up to 50% in advanced phase of disease [2], opioids are a mainstay of pain management, offering an effective treatment for both acute and chronic pain conditions [1]. Likelihood pain patients with solid tumors, the use of opioids in the setting of HM may be complicated by several side effects, including Opioid-Induced Constipation (OIC), which may add their negative effects to other causes of bowel dysfunctions in HM, such as the use of some chemotherapeutic drugs, other supportive therapies as well as mechanical obstruction and/or intestinal neoplastic compression. OIC is the most common symptom of Opioid-Induced Bowel Dysfunction (OIBD), which comprises several other Gastrointestinal (GI) complaints (such as nausea, bloating, and incomplete evacuation with abdominal pains of a colic type [3]); OIC could be highly debilitating, thus significantly deteriorating patients' Quality of Life (QoL). OIC could induce secondary complications, such as haemorrhoidal bleeding and anal fissures (which may be more frequent among HM patients due to increased bleeding and infection risk). Finally, OIC could result in reduced compliance with opioid schedule and, consequently, undertreatment of pain. Therefore, HM patients on pain requiring opioids are at high risk of OIC which should be prevented by a correct evaluation of diet, age, intestinal habits, the history of prior bowel disorders as well as the constipating effects of other concomitant medications [3, 4]. However, the occurrence of OIC during treatment with opioids requires pharmacological interventions for which several agents, such as pegylated naloxone (naloxegol), methyl-naltrexone and lubiprostone, are now approved. These agents represent an emerging class of drugs which target the opioid receptors in the gastrointestinal tract neutralizing the constipating effects of opioid medications without any interference with their centrally mediated mechanism of action in ensuring a stable pain relief [3-5]. Given their unique and beneficial therapeutic mechanisms, these drugs represent a paradigm shift in the prevention and treatment of OIC [6]. Herein, we report our experience on the use of one of these medications, such as naloxone pegylated (naloxegol), [6, 7], in a small series of HM elderly patients who developed OIC once having achieved a stably maintained pain relief by long term opioid medications. There were 9 (5 female) patients with a median age of 78 years (range 69-87). All patients were in advanced phase of disease (mean Karnofsky Performance Status: 51) and were followed in a home palliative care program. Diagnosis was multiple myeloma in 6 patients; the remaining 3 patients suffered from Hodgkin disease, non Hodgkin lymphoma and myelodysplastic syndrome, respectively. Regarding the underlying mechanism, pain was diagnosed as nociceptive, neuropathic and mixed in 3, 5 and 1 patients, respectively. According to Numerical Rating Scale (NRS) [8], the mean basal pain was 7.3; Breakthrough cancer Pain (BtcP), requiring short acting opioids, were suffered by 7 out of 9 patients. Again, 6 patients presented a single source of pain whereas in the remaining 3 multiple painful sites were recorded. In our experience we evaluated the response and resolution times of OIC, which was resistant to standard laxa-
tives with osmotic action, following the administration of naloxegol (25 mg once a day by oral route) in our group of advanced oncohematological patients receiving opioids. In addition we observed the impact of this agent on pain control, OIC-associated symptoms and QoL through the longitudinal assessment (Table 1) performed by NRS [8], the constipation assessment scale [9] and M.D. Anderson Symptom Inventory Score [10] respectively at baseline [time (T) 0], at 3 days (T1) and at 7 days (T2). Table 1 shows the favorable treatment results in terms of reduction of symptoms burden and increased QoL achieved in treated patients over time. Indeed, naloxegol was effective to resolve OIC and associated symptoms as well as improving QoL without interfering with opioid-induced pain control. In addition, no side effects attributable to naloxegol were recorded. Therefore, once-daily oral antagonist naloxegol represented in our experience effective and well-tolerated agents in the treatment of OIC in HM patients receiving opioids resistant to oral laxatives. Our report dealing with a limited experience on a small series of patients demonstrated favorable results which should stimulate further larger studies in the setting of HM, in order to better identify patients at risk of OIC, the appropriate strategy of its prevention and optimal management of this disabling and troublesome iatrogenic complication of opioid treatment.

Table 1. Course of symptoms and quality of life of treated patients.

<table>
<thead>
<tr>
<th>Evaluation Time</th>
<th>CSA Score</th>
<th>Pain NRS</th>
<th>BTcP°</th>
<th>Rectal Pain*</th>
<th>Nausea*</th>
<th>Somnolence*</th>
<th>Dry Mouth*</th>
<th>MDASI Symptom Score</th>
<th>MDASI Interf. Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>T0</td>
<td>9</td>
<td>4.3</td>
<td>9</td>
<td>6</td>
<td>4</td>
<td>5</td>
<td>7</td>
<td>3.8</td>
<td>7.4</td>
</tr>
<tr>
<td>T1</td>
<td>3.3</td>
<td>2.8</td>
<td>5.6</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>3</td>
<td>3.4</td>
<td>6.1</td>
</tr>
<tr>
<td>T2</td>
<td>3.1</td>
<td>3.0</td>
<td>3.8</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>2</td>
<td>2.7</td>
<td>4.9</td>
</tr>
</tbody>
</table>

To: basal, T1: after three days, T2: after 7 days, CSA: Constipation Assessment

REFERENCES


Gregorio Brunetti
Department of Cellular Biotechnology and Hematology
University La Sapienza of Rome
Rome
Italy
Tel: +390685795740
Fax: +390644241984
E-mail: brunetti@bce.uniroma1.it