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Spinal analgesia for advanced cancer patients: An update

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Abstract

In the nineties, spinal analgesia has been described as an useful means to control pain in advanced cancer patients. The aim of this review was to update this information with a systematic analysis of studies performed in the last 10 years. 27 papers pertinent with the topic selected for review were collected according to selection criteria. Few studies added further information on spinal analgesia in last decade. Despite a lack of a clinical evidence, spinal analgesia with a combination of opioids, principally morphine, and local anesthetics may allow to achieve analgesia in patients who had been intensively treated unsuccessfully with different trials of opioids. Some adjuvant drugs such as clonidine, ketamine, betamethasone, meperidine, and ziconotide may be promising agents, but several problems have to be solved before they can be used in the daily practice. In complex pain situations, spinal analgesia should not be negated to cancer patients, and oncologists should address this group of patients to other specialists.

Keywords: Cancer pain; Spinal analgesia; Intrathecal opioids; Local anesthetics

Most advanced cancer patients will experience painful symptoms that require opioid therapy. Even when the basic principles for the use of analgesic drugs are adhered to, some patients experience considerable side-effects from systemic opioids and/or poor pain relief. About 10–20% of patients may not respond well to standard analgesic measures, and

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thus, additional treatment options are necessary [1]. Aggressive opioid therapy using trials of different opioids in the same patient has been found to provide some benefit in pain relief [2]. However, opioid-induced hyperalgesia, particularly with increasing doses of opioids has been of concern in the last years. Moreover, some pain syndromes may strongly limit the quality of life of cancer patients. The proportion of cancer patients who may benefit from invasive therapies is small [3], but still extremely important, given the level of suffering of patients unresponsive to multiple trials of opioids, possibly receiving high doses of opioids unsuccessfully and having consistent adverse effects.

Spinal analgesia may provide an useful means to control pain in such difficult situations. The rationale behind spinal opioid therapy was that administration of small amounts of opioids in close proximity to their spinal receptors would achieve high concentrations at these sites, resulting in a superior analgesia and minimization of adverse effects. Moreover, other drugs with a different mechanism, for example local anesthetics, may provide additive or synergistic analgesia.

In 1999 a review on the use of spinal analgesia for the management of cancer pain provided information on status of art of this treatment, assessing the principal problems in long-term [4]. The aim of this review was to update this information with a systematic analysis of studies performed in the last 10 years.

1. Methods

A systematic literature search of literature on Pub-Med database was carried out from 2000 to 2010. The terms used were "spinal" OR "intrathecal" OR "peridural" OR "neuraxial analgesia" AND "cancer pain". Hand search of the references list of identified papers was also performed. Studies were included if performed in adult patients with chronic cancer pain. Because the expected paucity of studies available, no other limits regarding study design have been established. Case series with small number of patients were taken into consideration only when providing relevant information to be tested in larger studies. The goal was to find publications that meaningfully update the literature in the last decade as regards a previous review [4], also providing challenging new ideas to be explored in future studies.

2. Results

27 papers pertinent with the topic selected for review were collected according to selection criteria. Many papers included patients both cancer and non-malignant pain. Only one paper was a randomized-controlled trial of IT treatment with an implantable drug delivery system compared with comprehensive medical management, and two were follow-up analyses [5–7]. In a multicenter study, 119 cancer patients were treated with a patient-activated implanted delivery system [8].

Two retrospective studies of patients who received an implanted pump system were retrieved. A retrospective analysis was performed in 64 of 87 patients who received a trial of neuraxial analgesia, and then treated with long-term epidural and IT analgesia by an implanted pump [9]. Stability, compatibility, and safety of IT BU and opioids administered via an implantable delivery system was assessed in 56 patients with cancer pain [10].

Only three papers reported a series of cancer patients implanted with a subcutaneous port system. One reported prospective data of 55 advanced cancer patients who were unresponsive to multiple trials of systemic opioids [11], and another two were retrospective analyses of patients who were treated with IT opioids and BU [12,13] (Table 1). Fifty cancer patients who were implanted with a subcutaneous port system were assessed for risk of infection [14].

Small case reports provided interesting information about IT adjuvants. Six patients with cancer pain were included in a phase I/II study of IT clonidine [15] and a case report on the use of IT dexmedetomidine has been described [16]. Small case series dealt with the use of IT betamethasone [17,18], meperidine [19,20], and ketamine [21–23]. Controlled and double blind studies, open-label experiences as well an alarming report regarding serious toxicity have been reported on the use of IT ziconotide [24–27].

The use of cervical–thoracic catheter insertion was described in two small series [11,28]. Local anesthetics were described for breakthrough pain in patients receiving high doses of opioids intrathecally, unresponsive to systemic opioids given as breakthrough pain medication [13,29,30]. Papers were conveniently grouped for different clinical problems.

3. Discussion

3.1. Indications and frequency of use of spinal analgesia

In a previous review it was stressed as in pioneer studies of spinal analgesia in cancer pain no clear indications were provided to start this complex treatment [4]. It seems that patients should optimize their treatment by using multiple trials of opioids administered by different routes and administering other indicated non-opioid analgesics and symptomatic drugs, before being defined as refractory [8,11]. After an appropriate selection, neuraxial analgesia is used in a selected number of patients with cancer pain, accounting for approximately 2% of those seen for pain consultation [9].

3.2. IT morphine

The rate and extent of opioid distribution within cerebrospinal fluid, spinal cord, epidural space, and systemic circulation after intrathecal injection has been recently assessed. Integral exposure (area under the curve divided by dose) of the spinal cord (i.e., effect compartment) to the