The medical treatment of cancer pain

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Summary

Pain is still one of the most feared symptoms in cancer patients and the vast majority of these patients require treatment with opioids for severe pain. Correct use of therapeutic approaches should lead to a satisfactory pain control in nearly 95% of patients with cancer. Unfortunately, about 50% of cancer patients still experience insufficient pain control. Moreover, cancer pain relief is particularly difficult to achieve in specific subgroups such as patients with breakthrough pain, neuropathic pain, impaired cognitive function or communication barriers. Despite the medical advances occurred in recent years, cancer pain still remains a relevant issue throughout the world. This review aims to discuss the current critical issues and future challenges in the medical treatment of cancer pain.

KEY WORDS: cancer pain, pharmacotherapy, opioids, nonopioids, adjuvant drugs.

Introduction

Despite the advances occurred in recent years in terms of knowledge of pathogenic mechanisms of pain and the development of new highly effective opioid drugs, cancer pain still represents a global hearth concern and the unsatisfactory pain management in oncology is a prevalent issue. As stated by International Association for the Study of Pain (IASP), pain is an unpleasant sensory and emotional experience associated with actual and potential tissue damage (1). The physical component is only a single aspect of a wider suffering: to better describe the global essence of pain Cicely Saunders coined the term of “total pain” that, beyond the physical aspect, incorporates psychological, social, emotional and spiritual components (2). Mainly in cancer patients, uncontrolled pain negatively affects activities, motivation, relationships with family and friends and, globally, quality of life.

Methods

A selective review of pertinent literature from October 1998 to October 2013 was performed using PubMed. The following key terms were searched by Medline: “Cancer Pain”, “Management”, “Pharmacotherapy”, “Opioids”. Most recently updated versions of World Health Organization (WHO), National Comprehensive Cancer Network (NCCN) and European Society of Medical Oncology (ESMO) guidelines have been also included.

Cancer pain: still a major issue

World Health Organization estimates that over 80% of the world’s population is undertreated for moderate to severe pain (3). Based on the results of one published systematic review, pain is a commonly reported cancer-related symptom: its prevalence varies from 25% in newly diagnosed patients to 64% in patients with ad-
advanced cancer (4). In several cases pain is related to the underlying disease and its prevalence seems to be higher in specific neoplasms as pancreatic (44%) and head and neck cancers (40%) (5).

In many other circumstances it is mainly iatrogenic and related to chemotherapy (e.g. neuropathy due to taxanes or platinum-compounds), radiotherapy (e.g. brachial plexopathy in patients treated with adjuvant radiotherapy for breast cancer) or surgery (e.g. postmastectomy pain) (6).

Cancer patients with pain are often undertreated. In 2008 Deandrea et al. published a complete and systematic review with negative results: undertreatment of cancer pain was reported in about 50% of cases (7). Moreover, Breivik et al. reported discouraging data: their survey screened more than 5000 cancer patients experiencing pain and a high proportion (56%) of these reported from moderate to severe pain during the last month of care (8).

Several barriers exist between pain and its satisfactory control: insufficient assessment, patient’s refusal to take opioids and patient’s difficulty in referring pain (9). The scarce attention that clinicians dedicate to pain management is a relevant factor: for example, in a national survey conducted in about 2000 oncologists, frequent referrals to pain or palliative care specialists were reported by only 14 and 16%, respectively (10).

The critical first step in the treatment of cancer pain is represented by the practice of comprehensive pain assessment. Visual analogue scale (VAS), verbal rating scale (VRS) and the numerical rating scale (NRS) are the most used tools for self-reporting assessment of pain intensity. Moreover, physicians must evaluate the quality of pain, onset, duration and they should understand how the pain is improved or exacerbated by specific actions (11).

Pharmacotherapy represents the cornerstone of cancer-related pain. Commonly used drugs are opioids, non-opioids and adjuvant analgesics. In 1986 WHO designed the 3-step analgesic ladder that still guides the treatment of cancer pain (12). Since then, several guidelines have been promulgated (APS, NCCN, ESMO) to support physicians in the treatment of cancer pain. In all these published guidelines opioids remain the mainstay of treatment of cancer pain and morphine still represents the reference drug for cancer patients with severe pain (13-15).

### Pain management

#### Nonopioids analgesics

Nonopioids analgesics represent an important class of drugs in cancer pain treatment (Tab. 1). One of the most traditional drugs of this class is paracetamol. It is an analgesic and antipyretic without anti-inflammatory effects. Due to its relatively safe profile in terms of gastrointestinal toxicity, for many years it represented the preferred treatment in elderly patients with pain; recently, several studies have highlighted its moderate efficacy, interactions with some anticancer agents and potentially serious adverse effects in terms of renal and hepatic toxicity; such data should lead physicians to cautious prescriptions (16, 17).

Non-steroidal anti-inflammatory drugs (NSAIDs) relieve pain mainly blocking the biosynthesis of prostaglandins although they can act also influencing the peripheral or central nervous system. NSAIDs can be divided in two principal groups: unselective and COX-2 selective. Unselective NSAIDs can cause gastrointestinal ulceration, renal impairment and bleeding due to altered platelet aggregation (18). COX-2 selective drugs were introduced several years ago in order to reduce the risk of gastrointestinal bleeding but, unfortunately, this advantage diminishes after their prolonged use (19). Moreover, these drugs have been related with cardiovascular and cerebrovascular adverse events (20).

NSAIDs are active in cancer pain and they are mainly indicated for the treatment of mild pain although they can be useful in combination with opioids in order to reduce their dose and adverse events such as constipation, nausea and confusion. Also in cancer patients use of NSAIDs should be limited to few days and caution is mandatory in case of renal and/or hepatic dysfunctions or coagulative disorders (21).

#### Opioids

Opioids represent the cornerstone of treatment of cancer pain. Clinical response to a specific opioid can be dramatically different case by case and, to date, no opioid can be considered as superior to another. Opioids are traditionally divided in weak and strong opioids (Tab. 2).

<table>
<thead>
<tr>
<th>DRUG</th>
<th>MAXIMUM DAILY DOSE AND PRINCIPAL ROUTE OF ADMINISTRATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paracetamol</td>
<td>3000-4000 mg/day (oral)</td>
</tr>
<tr>
<td>Aspirin</td>
<td>2000-4000 mg/day (oral)</td>
</tr>
<tr>
<td>Naproxen</td>
<td>1000 mg/day (oral)</td>
</tr>
<tr>
<td>Ketorolol</td>
<td>15-30 mg every 6 hours (parenteral)</td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>400 mg four times a day (oral)</td>
</tr>
<tr>
<td>Celecoxib</td>
<td>100-200 mg twice daily (oral)</td>
</tr>
</tbody>
</table>
In several randomized clinical trials weak opioids demonstrated to be superior to placebo (22). Tramadol is a weak opioid receptor agonist and blocks the reuptake of serotonin and norepinephrine. Due to this modality of action tramadol should be avoided in patients receiving SSRIs or tricyclic antidepressants. Its metabolization is influenced by CYP2D6 with a consequent increased potential for interactions with several drugs. The ceiling dose of tramadol is 400 mg/day and its principal adverse events are nausea/vomiting, dizziness and weakness (23).

Codeine is a weak opioid generally administered in combination with paracetamol. It is a prodrug metabolized by glucuronidation mainly to codeine-6-glucuronide and this process largely depends on the action of CYP2D6. This cytochrome has showed polymorphism among various ethnic groups and among individuals. Poor metabolizers can experience reduced or no analgesic effects by the administration of codeine (24, 25). Propoxyphene is no longer recommended because of neurotoxicity related to the effect of norpropoxyphene, its main metabolite (26).

Despite the recent introduction in clinical practice of new strong opioids as fentanyl, methadone, hydromorphone and oxycodone, morphine is still the traditional reference drug: it is available in a wide range of formulations and routes; its main metabolite, morphine-6-glucuronide, is responsible for analgesia and may worsen the intensity of adverse events in case of patients with renal impairment (27).

Fentanyl is a highly lipid soluble opioid that can be administered by all known routes of administration (parenteral, spinal, transdermal, transmucosal, intranasal, oral) (28). Although no substantial differences in serum levels were detected when fentanyl was intravenously administered in obese patients, concerns are emerged regarding the efficacy of this drug when transdermally delivered in cachectic cancer patients: in a comparative study conducted between normal-weight and low-weight cancer patients, fentanyl reached lower plasma levels in cachectic cancer patients (29, 30). Transdermal fentanyl is not indicated if a rapid opioid titration is necessary and should be administered only if pain is under control with other opioids. Transdermal formulation is recommended for patients with severe dysphagia, with unsatisfactory tolerance to morphine or poor compliance.

Oxycodone is a semi-synthetic thebaine derivative: this strong opioid displays a relevant affinity to κ-opioids receptors along with agonistic effects µ-opioid receptors-mediated (31). It is metabolized in the liver primarily to noroxycodone through CYP3A4 and, to a lesser extent, to oxymorphone through CYP2D6. In patients with liver cyrosis and hepatic diseases, the dose of oxycodone should be reduced of 50%. Oxycodone has renal excretion and patients with renal impairment should be treated with lower doses. CYP2D6 polymorphism probably does not alter the analgesic and adverse effects of oxycodone (32). Hydromorphone has properties similar to morphine and it is available in different formulations (immediate- and extended-release). Its main metabolite, hydromorphone-3-glucuronide, seems to be responsible for the neurotoxicity of the drug. Risk neurological effects seems to increase during treatment with high doses in presence of renal impairment (nevertheless, the metabolite is easily dialyzable) (33).

Methadone is available in oral tablet or oral solution: high inter-individual variability and long half-life in terms of pharmacokinetics make its administration particularly challenging in cancer patients. For these reasons methadone should be started at doses lower than calculated and slowly titrated providing adequate medications for breakthrough pain during the titration phase (34).

### Table 2 - Weak and strong opioids and their typical starting dose.

<table>
<thead>
<tr>
<th>DRUG</th>
<th>TYPICAL STARTING DOSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tramadol</td>
<td>25-50 mg every 4-6 hours (immediate release)</td>
</tr>
<tr>
<td></td>
<td>50-100 mg every 12 hours (controlled release)</td>
</tr>
<tr>
<td>Dihydrocodeine</td>
<td>30 mg every 4-6 hours (immediate release)</td>
</tr>
<tr>
<td></td>
<td>60 mg every 12 hours (controlled release)</td>
</tr>
<tr>
<td>Codeine</td>
<td>30 mg every 4-6 hours (immediate release)</td>
</tr>
<tr>
<td></td>
<td>60 mg every 12 hours (controlled release)</td>
</tr>
<tr>
<td>Morphine</td>
<td>5-10 mg every 4 hours (immediate release)</td>
</tr>
<tr>
<td></td>
<td>20-30 mg every 12 hours (controlled release)</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>One patch 25 mcg/hour every 72 hours</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>5 mg every 4-6 hours (immediate release)</td>
</tr>
<tr>
<td></td>
<td>10-20 mg every 12 hours (controlled release)</td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>One patch 35 mcg/hour every 84 hours</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>1-2 mg every 4 hours (immediate release)</td>
</tr>
<tr>
<td></td>
<td>2-4 mg every 12 hours (controlled release)</td>
</tr>
<tr>
<td>Methadone</td>
<td>3-5 mg every 8 hours</td>
</tr>
</tbody>
</table>

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- Opioid-related adverse events

Several side effects (constipation, nausea, vomiting, pruritus, delirium, sedation, respiratory depression and cognitive impairment) are related to administration of opioids. Each adverse effect needs a careful assessment and treatment: management of side effects from opioids should be consensual to their administration. Patients don’t develop tolerance to constipation: for this reason it should always be prevented and, when it occurs, aggressively treated. There is no consensus on medications to be administered in the prevention and treatment of opioid-related constipation. Apart from maintaining an adequate fiber intake, many physicians recommend a bowel regimen that includes a stool softener and a laxative (e.g. senna plus docusate), although a recent study has demonstrated the efficacy of senna alone (35). Once constipation occurs, stimulant or osmotic laxatives should be early administered: when response to common laxatives is unsatisfactory and constipation is clearly related to opioid treatment, methylaltrexone, an opioid antagonist that works on the receptors of the gastrointestinal tract, can be subcutaneously administered as a rescue therapy (36, 37). Although many drugs administered in cancer patients can be responsible of sedation, this symptom is generally attributed to opioid therapy. Tolerance to opioid-induced sedation generally develops within a few days but in rare circumstances it may persist: in these cases, opioid rotation or (with lesser evidence) administration of psychostimulants (e.g. methylphenidate 5-10 mg once or twice daily) can be considered (38). Nausea and vomiting are quite common in opioid-naive patients: tolerance generally shows a rapid onset. Despite the limited evidence, in presence of persisting and/or disturbing emetic events, metoclopramide and antidiopaminergic drugs are frequently administered (39). In patients with a prior history of opioid-related nausea, prophylactic antiemetic treatment can be recommended.

Pruritus is common and occurs in 10 to 50% of patients receiving opioids. After the exclusion of other possible causes of itching, a meticulous skin care should be advised and antihistamines may be useful. In case of refractory itching opioid antagonists have demonstrated some effectiveness (40). Other opioid-related adverse events, including respiratory depression, are really feared both by physicians and patients but their incidence is fortunately rare. These events must be taken into account but their overestimation can lead clinicians to underprescribe opioids: this attitude should be avoided.

- Breakthrough pain

Breakthrough pain (BTP) is defined as a transitory flare of pain that emerges in presence of well controlled baseline pain. BTP episodes are generally moderate/severe in terms of intensity, show rapid onset (frequency between 3-15 minutes) but their duration is generally short (15-30 minutes or even shorter). Their frequency varies and the number of daily events is also variable: more than 5-6 daily episodes are indicative of under-controlled baseline pain and, in these cases, physicians should revise their basal pharmacological approach. In literature, the prevalence of BTP ranges widely between 19 and 95% (41, 42). Several classifications of BTP exist. According to time pattern, BTP can be classified as either spontaneous or incidental. Incidental BTP can be divided in volitional (caused by a voluntary act), non-volitional (caused by an involuntary act) or procedural (related to therapeutic interventions) (43, 44). For BTP events “as-needed” medications should be prescribed. Several pharmacological therapeutic options are available and include oral immediate-release morphine sulfate (IRMS), opioids (subcutaneously or intravenously administered) and fentanyl (oral, buccal, transmucosal, or intranasal). Due to the few data emerged from randomized clinical trials, no definitive recommendations can be made about the best therapeutic option in this setting. According to the recommendations of the European Association for Palliative Care (EAPC) guidelines, BTP should be carefully assessed and should be treated with immediate-release oral opioids or with oral (or intranasal) fentanyl (45).

- Adjuvant analgesics

The term adjuvant refers to medications that are co-administered to counteract an adverse event of an opioid or to improve analgesia. Adjuvant drugs may be useful when pain is not completely responsive to opioids. Adjuvant analgesics include several drugs of different classes: anticonvulsants (e.g. gabapentin, pregabalin), corticosteroids, antidepressants (SSRIs, tricyclic antidepressants) and local anesthetics (Tab. 3) (46). Adjuvant analgesics demonstrated their role in management of bone pain, neuropathic pain and visceral pain. Moreover, they can be helpful in reducing opioids requirement. Adjuvant drugs have been extensively studied in neuropathic pain. Despite the lack of significant controlled studies in cancer pain, the tricyclic antidepressants are considered effective in relieving neuropathic pain (47). In 2007, an experts panel considered this class of drugs as one of several first-line therapies for neuropathic pain (48). Serotonin-norepinephrine reuptake inhibitor agents (e.g. venlafaxine, duloxetine) have demonstrated their effectiveness in relieving neuropathic pain (49, 50). The most prescribed antiepileptic drugs for the treatment of cancer pain are gabapentin and pregabalin. Acting at specific subunit of the voltage-gated calcium channel, both drugs were extensively tested and a recent review confirmed their significant clinical effect in neuropathic pain (51). These agents should be used in combination with opioids, especially when pain is moderate to severe. Recently, Bennett has published a review in which the addition of adjuvant analgesics to opioids provided significant pain relief and the strongest evidence emerged for gabapentin (52).
Corticosteroids are commonly administered to relieve neuropathic pain syndromes and, due to their anti-inflammatory effects, they demonstrated to improve cancer-related bone pain and symptoms related to malignant bowel obstruction. Despite this evidence, few data exist about their specific role in treating cancer pain (53). Local anesthetics are useful in preventing procedural pain and in improving neuropathic pain: they can be used topically, parenterally or spinally. Topical application of lidocaine is able to reduce both post-herpetic and cancer-related pain (54).

Biphosphonates act inhibiting osteoclast-mediated bone resorption and improve pain control in metastatic bone disease and multiple myeloma. Several biphosphonates are available in clinical practice: when compared with pamidronate, zoledronic acid demonstrated its superiority in relieving pain due to metastatic bone disease (55, 56).

### Treatment of cancer pain: few but important rules to follow

In 1986, WHO suggested a strategy for cancer pain treatment based on a sequential three-step analgesic ladder from non opioids to weak opioids to strong opioids according to pain intensity (3). Two decades after the publication of the first edition, this ladder still represents the reference strategy for pain management. According to WHO guidelines, opioids are the mainstay of analgesic therapy and are classified according to their ability to control pain from mild to mild–moderate to moderate–severe intensity. Opioid analogues may be combined with NSAIDs or paracetamol and with adjuvant drugs (57).

Opioid doses should be titrated to take effect as rapidly as possible. Titration is a process in which the dose of the opioid is modified to achieve the dose which provides satisfactory relief of pain with an acceptable profile of tolerability. Normal-release morphine has a short half-life and it should administered during the titration phase, in case of BTP episodes and for treating predictable episodes of acute pain in patients on regular analgesics (administration should take place 20-30 minutes before the predictable episode of acute pain). In patients with severe pain intravenous titration is recommended (58). All patients should be treated with “round-the-clock” analgesics’ administration with provision of a ‘rescue dose’ to treat exacerbations of pain. The ‘breakthrough dose’ is generally equivalent to 10-15% of the total daily opioid amount. If more than four ‘rescue doses’ per day are required, the baseline opioid treatment with a controlled-release formulation must be adjusted. Opioids with a rapid onset and short duration are preferred as rescue medications. Following the titration period, slow-release opioids are indicated. However, immediate release opioids must be always prescribed as a rescue medication.

Cancer patients should be informed about pain and its management: they should play an active role in their pain treatment (59). Onset of pain must be prevented by prescribing analgesics with “round the clock” administration. As-needed schedule of drugs administration should be avoided. It is important prescribing drugs that can be easily administered and managed by the patients and their relatives. Physicians should choose the less invasive and the easiest and safest route of administration. For chronic opioid treatment, oral route must be preferred. It should represent the first choice in patients able to take oral medicines. If oral administration is not feasible, several alternative routes exist. When patients are unable to swallow or adsorb opioids enterally, continuous parenteral infusion or transdermal formulations should be considered (60, 61). Traditionally, patients with mild-moderate pain have been treated with a combination of acetaminophen or NSAIDs plus a weak opioid such as codeine, dihydrocodeine or tramadol. The use of drugs of the second step of WHO ladder has some debated aspects.

### Table 3 - Selected adjuvant drugs for cancer pain.

<table>
<thead>
<tr>
<th>DRUG CLASS</th>
<th>DAILY STARTING DOSE (ADULTS)</th>
<th>ROUTES OF ADMINISTRATION</th>
<th>INDICATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antidepressant</td>
<td>Nortriptyline, 10-25 mg/day</td>
<td>Oral, Oral, Oral</td>
<td>Neuropathic pain</td>
</tr>
<tr>
<td></td>
<td>Desipramine, 10-25 mg/day</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Venlafaxine, 50-75 mg/day</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Duloxetine, 30-60 mg/day</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antiepileptic Drugs</td>
<td>Gabapentin, 100 mg 3 times a day</td>
<td>Oral, Oral</td>
<td>Neuropathic pain</td>
</tr>
<tr>
<td></td>
<td>Pregabalin, 50 mg 3 times a day</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>Dexamethasone, 2-20 mg/day</td>
<td>Oral, parenteral</td>
<td>Neuropathic pain, spinal cord compression, bone and visceral pain, cerebral edema</td>
</tr>
<tr>
<td>Lidocaine</td>
<td>Lidocaine, patch 5% every day</td>
<td>Topical</td>
<td>Neuropathic pain</td>
</tr>
<tr>
<td>Biphosphonates</td>
<td>Pamidronate, 60-90 mg every 2-4 weeks</td>
<td>Intravenous</td>
<td>Bone pain</td>
</tr>
<tr>
<td></td>
<td>Zoledronate 4 mg every 3-4 weeks</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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The first critical area concerns the absence of a clear evidence of effectiveness of weak opioids: their use in clinical practice is not supported by significant data resulting from randomized clinical trials. In a meta-analysis on 13 RCTs which compared paracetamol or NSAIDs administered alone or in combination with weak opioids, no meaningful clinical advantage emerged in patients treated with combination regimen (62). In a recent systematic review, in 23 comparative studies between NSAIDs given alone or in combination with weak opioids only a weak and marginal benefit was observed in combination arm (63). In conclusion, data supporting the routine use of weak opioids in cancer patients with mild to moderate pain are controversial: a RCT should be warranted to address the relevant issue of the role of WHO second step.

Discussion

Under-treatment represents a relevant issue in treatment of cancer pain: as previously reported, in a comprehensive review were analyzed 26 significative studies: in 43% of cancer patients a negative Pain Management Index (PMI) was reported (7). Although useful in evaluating pain treatment, PMI does not take in account several components present in cancer pain treatment: patients’ compliance to the treatment, drug doses, routes of administration, interactions among different analgesics and effectiveness of adjuvant analgesics and other non-pharmacological treatments (64, 65). This review included published studies between 1997 and 2007: it is likely that this situation is evolving towards a positive progress due to a better medical education and attention.

Inadequate pain assessment is the leading barrier to adequate pain management (66). Identification of pain should take place early and its assessment should include a detailed medical history, psychosocial evaluation and physical examination. As previously reported, current guidelines recommend the use of one of 3 validated assessment tools: VAS, NRS and VRS. Moreover, several guidelines stated that baseline pain assessment, reassessment and analgesia efficacy must be documented within the patient’s record (67). In 2007, Sun et al. published an interesting paper: this article reported on pre-intervention findings related to barriers to pain management. Discouraging data emerged: only 7.8% of subjects were screened for pain at each clinic visit and in only 2.6% of subjects was clearly documented the quality of pain. In this study emerged a very limited (7.9%) documented pain screening without documentation of NRS values and evidence of reassessment (68).

In addition to inadequate assessment, physicians are still showing improper opinions that negatively influence their prescription of analgesics (mainly opioids). For example, lack of education has brought to misplaced beliefs over addiction and tolerance to analgesics as well as problems with critical concepts such as the management of adverse events and the utilisation of specific routes of administration or adjuvant drugs (69).

Patient’s reluctance to report his pain and hesitancy to comply with treatment are also a major drivers for inadequate pain management. Patients often consider pain as an inevitable part of having cancer and believe that admitting pain is a sign of weakness (70). Moreover, some patients are reluctant to report their pain because they don’t want to distract the doctor from treating their pain or may fear that pain is a sign of disease progression (71). The patient’s age and ethnicity can play a significant role in creating inadequate pain assessment: in elderly patients cognitive decline can represent a communication barrier and, moreover, it is well documented that ethnic minorities frequently experience under-treatment of their cancer pain (72).

According to the previously reported data, despite the pain management became an area of real interest and the significative improvement in our therapeutic armamentarium observed in the recent years, unsatisfactory pain management in cancer patients still represents a major issue.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

References

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47. Mc Nicol E, Strassels S, Goulds L, et al. NSAIDs or paracetamol, alone or combined with opioids, for cancer pain (Cochrane review). John Wiley & Sons, Ltd; In the Cochrane Library Issue 1 2009.


