**Review: NSAIDs and adjuvant treatments such as hypnosis can help to reduce cancer related pain**


**QUESTION:** What is the effectiveness of drug and non-drug interventions for cancer related pain?

**Data sources**
Studies published from 1966 to December 1998 were identified by searching Medline, CancerLit, and the Cochrane Controlled Trials Registry databases. Bibliographies of relevant articles were reviewed, and experts were contacted.

**Study selection**
English language studies were included if they were randomised controlled trials (RCTs), cohort studies, or case series that assessed the effectiveness of analgesics (opioids, non-steroidal anti-inflammatory drugs [NSAIDs], and adjuvant analgesics) or different formulations and routes of administration; current adjuvant (non-pharmacological/ non-invasive) or psychological treatments, such as relaxation, massage, heat and cold, and music; and if outcomes included pain attributed to the cancer itself, cancer treatment, or the side effects of pain treatment.

**Data extraction**
Data were extracted on study design, sample size, patient characteristics, key components of the interventions, study quality, and outcomes. Main outcomes were pain intensity and pain relief.

**Main results**
Only the results of RCTs assessing the relative effectiveness of analgesics, various formulations and administration routes, and adjuvant physical and psychological interventions are reported here. **Relative effectiveness of analgesics:** 17 RCTs (n=1164) compared different types of NSAIDs with each other or with placebo. The NSAIDs evaluated included aspirin, diclofenac, diltiazem, dipyrrone, ibuprofen, indomethacin, indoprofen, ketorolac, ketoprofen, naproxen, nimuezide, paracetamol (acetaminophen), pirprofen, sulindac, and suprofen. NSAIDs were more effective than placebo for reducing pain intensity in each of 6 RCTs. Individual comparisons among different NSAIDs did not show any differences in effectiveness with one exception: dipyrrone was more effective than diltiazem. Meta-analysis of 3 RCTs (n=325) showed that NSAIDs did not differ from NSAIDs plus weak opioids or strong opioids alone for pain intensity (mean difference in visual analogue scale [VAS] 3.8 mm, CI –4.7 mm to 12.4 mm). In 3 RCTs, amantadine, amitriptyline, and capsaicin each were found to be more effective than placebo for surgical or postmastectomy neuropathic pain relief. Different formulations and administration routes: Meta-analysis of 8 RCTs (n=317) comparing controlled release tablets with aqueous solution of orally administered morphine showed no differences for average pain intensity at 4–14 days (mean difference in VAS scale 1.2 mm, 95% CI –1.6 mm to 4.0 mm), side effects, or other outcomes. Meta-analysis of 2 RCTs (n=58) comparing orally with rectally administered morphine showed no differences for changes in pain intensity (mean difference in VAS scale 2.3 mm, CI –4.3 to 8.0). One RCT comparing subcutaneous with rectal administration, and 1 RCT comparing subcutaneous with epidural administration of morphine, found no differences in pain relief or side effects.

**Adjuvant physical or psychological interventions:** 2 of 4 RCTs found that pain education for patients, medical staff, and the community at large decreased pain intensity and improved 1 measure of pain compared with the control. 4 of 5 RCTs found that hypnosis plus cognitive behavioural techniques reduced pain intensity and severity compared with the control in patients with acute procedure related pain and oral mucositis pain related to bone marrow transplant.

**Conclusions**
Different types of non-steroidal anti-inflammatory drugs are equally effective for mild to moderate cancer related pain, and as effective as weak opioids; different morphine formulations and administration routes have similar effectiveness. Adjuvant treatment such as hypnosis or cognitive behavioural treatment may help to reduce pain.

**COMMENTARY**
In this review of the efficacy of pharmacological and non-pharmacological treatments for cancer pain, Goudas et al used a broad definition of cancer related pain that included pain caused by the disease or its treatment and side effects; studies of acute postoperative pain and those using analgesics to control symptoms other than pain were excluded. Involving pain experts from diverse professional organisations in the development of the specific questions to be addressed enhanced the relevance, importance, and comprehensiveness of the review. Furthermore, a robust approach to the search strategy was used to minimise the number of studies that would be missed.

As the authors point out, this evidence report provides background information and synopses of evidence for use by health professionals and policy makers in developing clinical practice guidelines. Because the literature review only extends to the end of 1998, there is a time lag of almost 3 years between the end of the literature review and publication of the report. This lag does not necessarily mean that the review is outdated; however, the literature searches and summary updates required to ensure that the findings and interpretation of the evidence report are up to date are clearly beyond the scope of most clinicians and policy makers. Therefore, these stakeholder groups must formulate clinical practice guidelines and policies without the benefit of the most recent evidence.

There are no substitutes for the clinical judgments gleaned from comprehensive pain assessments, particularly patient reports of pain intensity. Accordingly, some important clinical caveats accompany the findings reported here. Although NSAIDs are effective for mild to moderate cancer pain, NSAIDs alone are inappropriate for pain of moderate to severe intensity. Furthermore, although the comparison of different routes of morphine administration did not show any differences in pain relief or side effects, these studies did not account for the rate of action. Again, pain severity is an important consideration in managing cancer pain effectively. The findings of this evidence report are applicable to nurses working with cancer patients and their families in any setting.

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Evid Based Nurs 2002 5: 115
doi: 10.1136/ebn.5.4.115

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