Local infiltration with NSAIDs for postoperative analgesia: evidence for a peripheral analgesic action

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Authors' objectives
To investigate the evidence for a peripheral analgesic effect of local infiltration with non-steroidal anti-inflammatory drugs (NSAIDs) in post-operative pain.

Searching
MEDLINE was searched from 1966 to September 1999, EMBASE from 1989 to August 1999, and the Cochrane library in 1999, using the search terms 'NSAID', 'non-steroidal anti-inflammatory drug', individual drug names, 'postoperative pain', 'local infiltration', 'intra-articular', 'regional' and 'surgical site'. There were no restrictions on publication language. Additional studies were identified from the references lists of retrieved reports. Abstracts and unpublished studies were not considered.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) that were double-blind and had at least 10 patients per treatment group.

Specific interventions included in the review
Comparisons were made with NSAIDS administered intravenously or intramuscularly, or with placebo or no treatment. Comparisons had to be of a local NSAID with the same dose of systemic NSAID, of a local NSAID with placebo or no treatment, or of different doses of a local NSAID. The interventions included in the review were local infiltration with NSAIDs (30 or 60 mg ketorolac; 5, 7.5, 10 or 20 mg tenoxicam) administered either by intra-articular injection (i.a.), as intravenous regional anaesthesia (IVRA) or intra-wound (i.w.).

Participants included in the review
All patients with post-operative pain were eligible for inclusion in the review; of those studies included, participants were undergoing various surgical procedures such as arthroscopy, elective hand surgery, herniorrhaphy, mastectomy and tonsillectomy. There was a link between the mode of local application of NSAID and the type of surgery undergone by the participants. All studies of i.a. injection of NSAIDs involved patients undergoing arthroscopy. All studies of IVRA involved patients undergoing elective hand surgery. Studies of i.w. application were more varied, involving studies of patients undergoing herniorrhaphy, mastectomy and one each of elective hand surgery and tonsillectomy.

Outcomes assessed in the review
Difference between the treatments were assessed using pain scores, consumption of supplementary analgesics and/or time to first analgesic request. Weighted mean differences of visual analogue scale (VAS) scores were calculated.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the authors performed the selection.

Assessment of study quality
Studies were assessed for the adequacy of randomisation, blinding and description of withdrawals. Included studies (all double-blind RCTs) were scored between 2 and 5. All of the authors independently performed the quality assessment process.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the authors performed the data extraction. Information about drugs and doses, number of patients enrolled and analysed, types of surgery and anaesthesia (general or regional), study design, observation periods, outcome measures, and adverse effects was...
extracted from all reports.

**Methods of synthesis**

How were the studies combined?
A quantitative analysis was performed with calculation of Weighted Mean Differences (WMD) of VAS scores between treatment groups. Random-effects models were used to calculate WMDs. A narrative synthesis is also presented.

How were differences between studies investigated?
L’Abbe plots were constructed to analyse the degree of pain relief and homogeneity in studies comparing local NSAIDs with systemic administration, placebo or no treatment.

**Results of the review**

A total of 16 studies were included (n=844, of whom 660 received NSAIDs). These studies involved 28 comparisons.

All 4 studies comparing i.a. NSAIDs with systemic administration found a statistically-significant effect in favour of i.a. NSAID. Of the 3 studies that compared local i.a. NSAID with placebo or no treatment, only 2 showed clinically-improved pain relief with the i.a. injection. The results may have been confounded by the use of rescue analgesia.

The one study that compared IVRA NSAID with systemic administration showed a significant treatment effect in favour of IVRA administration, although the treatment effect was of limited clinical significance.

In the 5 studies comparing i.w. with systemic administration, 2 showed improved pain relief after i.w. administration, with no difference seen between treatments in the other 3 studies. Four of the 5 studies comparing local infiltration with placebo showed a significant effect in favour of local administration.

No adverse effects attributed to the local infiltration of NSAIDS were reported, although such information was only provided in 7 of the 16 studies.

**Authors’ conclusions**

There is evidence for a clinically relevant peripheral analgesic action of i.a. NSAIDs, while results for IVRA and i.w. are inconclusive. Trials without a systemic control group were not considered to provide evidence for a local effect.

**CRD commentary**

The review addressed a broad question. The question was in fact three separate questions about i.a., IVRA and i.w. administration of NSAIDs and the review did deal with them separately. The inclusion and exclusion criteria were clearly defined. The literature search was comprehensive and the quality assessment of the studies appears to have been rigorous. Sufficient details of the primary studies are included in the review. The statistical methods for the meta-analysis employed a random-effects model to take into account heterogeneity. This was not as appropriate as the narrative synthesis employed. It was appropriate that there was no attempt to pool the findings for the different modes of local administration.

The authors’ conclusions are supported by the findings of the review, although it should be noted that the positive treatment effect identified for i.a. NSAID may only be applicable to arthroscopy, as it has not been tested adequately in other surgical procedures.

The review included several trials which were subsequently retracted.

**Implications of the review for practice and research**

**Practice:** The authors did not state any implications for practice.

**Research:** The authors state that more large-scale placebo-controlled trials comparing local NSAIDs with systemic administration are needed before final recommendations can be made.

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