Sufentanil: an overview of its use for acute pain management

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Authors' objectives
To evaluate peri-operative sufentanil with a view to designing the optimal peri-operative sufentanil regimen.

Searching
MEDLINE (from 1997 to June 2001), EMBASE (from 1998 to 1999), BIOSIS Previews (from 1998 to 1999) and SciSearch (from 1998 to 1999) were searched. In addition, the reference lists in relevant reviews (1988 to 1996) were handsearched. The keywords were not stated.

Study selection

Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion in the review.

Specific interventions included in the review
Studies that used sufentanil either alone or in combination with local anaesthetics, morphine, clonidine or ketamine in peri-operative analgesia (defined as intra- and post-operative) were eligible for inclusion. The routes of administration could be intravenous (i.v.), intrathecal, epidural, combinations of routes, patient-controlled analgesia (PCA) or epidural analgesia (PCEA), or fixed interval.

The included studies used various doses of sufentanil as peri-, intra- or post-operative analgesia. The treatments used in the studies were: epidural morphine with and without bupivacaine; epidural sufentanil with and without bupivacaine; intramuscular morphine at fixed intervals; epidural ropivacaine with and without sufentanil; i.v. plus epidural remifentanil or sufentanil; patient-controlled sufentanil (i.v. or via epidural); i.v. or epidural sufentanil or fentanyl; different doses of i.v. or epidural fentanyl; epidural sufentanil plus adrenaline; i.v. or epidural clonidine; various doses of i.v. or epidural ketamine used in conjunction with epidural bupivacaine, sufentanil and clonidine mixture; i.v. ketoprofen plus epidural sufentanil; intrathecal sufentanil; intrathecal morphine with and without sufentanil; i.v. propofol or midazolam; and i.v. midazolam plus sufentanil.

Participants included in the review
The inclusion criteria were not explicitly defined in terms of participants. The studies included in the review were of patients undergoing abdominal surgery (including gynaecological surgery and Caesarean section), paediatric surgery, and other types of surgery (including orthopaedic, maxillo-facial, thoracotomy and lithotripsy).

Outcomes assessed in the review
The inclusion criteria were not explicitly defined in terms of outcomes. The review assessed efficacy and adverse effects. The following outcomes were mentioned in the text of the review: post-operative analgesia, speed of onset of analgesia, pain relief, plasma concentration of analgesic agents, heart rate, mean arterial pressure, sleep quality, sufentanil consumption, haemodynamics, oxygen consumption, myocardial ischaemia, recovery time, hypercapnia, respiratory rate, time to extubation, and circulating catecholamines. Some studies used a visual analogue score to assess pain, but the review did not state the range of scores. It was not stated how the outcomes for other studies were measured.

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

Assessment of study quality
The authors did not state that they assessed validity.

**Data extraction**
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction. The tabulated information included sample size, details of the treatment regimen including route of administration, and whether the analgesia was intra- and/or post-operative.

**Methods of synthesis**
How were the studies combined?
The stated intent was to group the studies by the type of surgery (abdominal, paediatric or other) and the patients’ age (adult or child). The studies were tabulated in these groups, but this grouping was not adhered to in the 'Results' section of the review. The individual studies were described rather than synthesised in the text of the review.

How were differences between studies investigated?
Differences between the studies were not mentioned.

**Results of the review**
Twenty-four RCTs (n=1,205) were included.

The main results of review are summarised below.

PCA (i.v.) versus PCEA sufentanil (1 study, 27 patients): the study reported that there was no advantage of one technique over the other. Intravenous versus epidural sufentanil (2 studies): one study (45 patients) that compared i.v. sufentanil with epidural sufentanil reported similar efficacy between the two routes of administration. Another study (20 patients) reported that plasma concentrations between i.v. and epidural sufentanil were comparable.

Sufentanil alone or in combination with ropivacaine or bupivacaine (3 studies): one study that investigated sufentanil infusions with and without bupivacaine, in 171 patients undergoing upper and lower abdominal surgery, reported that sufentanil infusions without bupivacaine were less effective than combined analgesia. One study, in 120 patients undergoing major gastrointestinal surgery, evaluated different doses of combined ropivacaine and sufentanil. One study in 30 patients undergoing elective hip replacement, reported that treatment with a continuous epidural infusion of ropivacaine and sufentanil was more effective than ropivacaine alone.

Sufentanil alone or in combination with clonidine, adrenaline or ketamine (4 studies): one study (20 patients) reported that the addition of adrenaline to sufentanil significantly prolonged the duration of analgesia in comparison with epidural sufentanil alone. Patients who received adrenaline were also reported to have experienced less respiratory impairment. One study (40 patients) that compared sufentanil with and without clonidine reported that the duration of pain relief was 'significantly' longer in patients who received the combination therapy. One study (40 patients) reported that epidural clonidine provided a longer lasting residual analgesic effect than epidural sufentanil. One study (100 patients) investigated whether the addition of 'subanaesthetic doses' of ketamine to a combined infusion of bupivacaine, sufentanil and clonidine improved clinical outcome.

Sufentanil alone or in combination with morphine (2 studies): one study (90 patients) reported that post-operative analgesia with epidural sufentanil or morphine and bupivacaine after major abdominal surgery seemed to be better than the conventional method of intramuscular morphine. Efficacy and side-effects were similar between epidural sufentanil and morphine. A second trial (40 patients), which supported this finding, reported a more rapid onset of analgesia with epidural sufentanil in comparison with morphine.

Another study (49 patients) compared PCA with i.v. morphine to intrathecal morphine or combined sufentanil and morphine in patients undergoing thoracotomy. The study reported that superior post-operative pain relief was experienced in patients receiving intrathecal morphine or combined sufentanil and morphine. One study (96 patients) in patients undergoing major abdominal surgery compared PCA morphine and PCEA sufentanil and bupivacaine. Patients who received sufentanil and bupivacaine reported lower post-operative pain intensities on the visual analogue scale.
Other reported physiological outcomes were comparable between the two groups.

Paediatric surgery (3 studies): one study of 58 children undergoing major surgery evaluated the addition of ketoprofen bolus and continuous infusion to epidural sufentanil infusion. Children in the ketoprofen group reported a better analgesic effect, shown by a decrease in the need for sufentanil. The median pain scores at 24 and 72 hours were reported to be lower in children who received ketoprofen, and fewer children had inadequate pain relief during activity. Two other small studies (12 and 24 children) were reported: one compared combined epidural and general anaesthesia (including sufentanil) with deep opioid anaesthesia, while the other compared loading doses of either fentanyl or sufentanil.

Other studies evaluated the following: PCEA sufentanil compared with placebo infusion; the effects of adding small infusions of remifentanil or sufentanil to sevoflurane in combination with post-operative epidural analgesia; different doses of sufentanil in patients undergoing extra-corporeal shock wave lithotripsy; and infusions of propofol, sufentanil and bolus midazolam, and midazolam in patients undergoing aortic surgery.

Authors’ conclusions
Peri-operative epidural or i.v. sufentanil was as effective or better than other drugs. The addition of a local anaesthetic or adjuvant drugs increased the duration of its action and sometimes reduced adverse effects.

CRD commentary
This review was of a poor quality: the description of the methods used to conduct the review was lacking, the information on the included studies was incomplete, and the synthesis of the studies was inadequate. The review also suffered from its poor translation into the English language.

The review question was clear in terms of the study design and was broadly defined in terms of the intervention. The inclusion criteria were not defined in terms of the participants or outcomes. Several relevant sources were searched, but the search terms were not stated and it was unclear whether any language limitations had been applied. No attempt was made to locate unpublished studies, thus raising the possibility of publication bias. Validity was not assessed although only RCTs were included. The methods used to select the studies and extract the data were not described. Hence, the adequacy of the methods used cannot be judged. It was difficult to summarise the results adequately due to the lack of structure in the results section and the inconsistent reporting of the results and their statistical significance. The review included many different sufentanil regimes and many different comparators, which were generally tested in studies with a small number of patients in each treatment arm; this further limited the potential evidence. In addition, the quality of the evidence was not assessed. The evidence presented was insufficient to support the authors' conclusions.

Implications of the review for practice and research
The authors did not state any implications for further research and practice.

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Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.