**Injected morphine in postoperative pain: a quantitative systematic review**

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**Authors’ objectives**
To compare the efficacy of single-dose subcutaneous, intramuscular or intravenous morphine with placebo in the control of post operative pain.

**Searching**
A number of different search strategies were conducted of MEDLINE (1966 to 1997), EMBASE (1980 to 1997), the Cochrane Library (1997 issue 2) and the Oxford Pain Relief Database (1950 to 1994). The last electronic search was conducted in March 1997. No language restrictions were applied. Reference lists of retrieved reports, review articles and specialist textbooks were examined. Review articles, letters and abstracts were excluded.

**Study selection**
Study designs of evaluations included in the review
Randomised placebo controlled trials of blinded design were included if they were full journal publications and reported data from which TOTPAR, SPID, VASTOTPAR OR VASSPID could be calculated.

Specific interventions included in the review
Single doses of placebo were compared with single doses of morphine given intramuscularly or intravenously in doses of 5 mg, 8 mg, 10 mg, 12.5 mg and 20 mg.

Participants included in the review
Adult patients experiencing non-surgical pain (due to acute trauma) or undergoing the following types of surgery with baseline pain of moderate to severe intensity were included: general; gynaecological; orthopaedic surgery including hip and knee replacements; third molar extraction; and day surgery.

Outcomes assessed in the review
Pain intensity or pain relief over 4 to 6 hours post operatively and adverse reactions were assessed. Outcome measures included total pain relief (TOTPAR), summed pain intensity difference (SPID) and visual analogue equivalents (VASTOTPAR, VASSPID).

How were decisions on the relevance of primary studies made?
Each report that could possibly be described as a randomised controlled trial was read independently by the three authors and consensus was achieved.

**Assessment of study quality**
Validity was assessed using the Jadad score (see Other Publications of Related Interest). Studies were scored independently by the three authors on validity criteria and consensus was achieved. Potential scores ranged from a minimum of 1 to a maximum of 5.

**Data extraction**
The number of patients in each treatment group who achieved at least 50% max TOTPAR was calculated from the data reported. Detail of analysis were presented elsewhere (see Other Publications of Related Interest). The following data were extracted: pain setting; study treatment groups; number of patients treated; study duration; route and dose of morphine; outcome measures; pain outcomes; withdrawals and exclusions; and adverse events as defined by authors of the primary studies.
**Methods of synthesis**

How were the studies combined?

The relative risk (RR) and 95% confidence intervals (CIs) and number-needed-to-treat (NNT) and 95% CIs were calculated by pooling data when available from at least three studies including both morphine and placebo groups with the same dose and route of administration. A random-effects model was used for data that were not homogeneous (P < 0.1) and a fixed-effect model used for adverse effects.

How were differences between studies investigated?

Homogeneity was assessed graphically and statistically. Sensitivity analysis was conducted by excluding a trial with non-surgical pain from the meta-analysis and by examining NNT according to study size.

**Results of the review**

Eighteen reports of 20 trials (1259 patients) were included.

Fifteen comparisons were used to compare 10 mg morphine with placebo in a meta-analysis (946 patients).

Quality scores were 2 for 2 reports, 3 for 6, 4 for 9 and 5 for 1. A funnel plot was reported to show no evidence of publication bias.

Meta-analysis comparing 10 mg intramuscular morphine with placebo: all but two of the reports had quality scores of 3 or more. The proportion of patients obtaining at least 50% pain relief ranged from 0% to 47% (mean 15%) in the placebo group and from 7% to 93% (mean 46%) in the morphine group. 8 of the 15 comparisons reported that morphine was statistically superior to placebo. Relative benefit of morphine = 2.8 (95% CI: 2.0, 3.8). NNT = 2.9 (95% CI: 2.6, 3.6). Omitting the trial that included nonsurgical pain did not affect the result. Trials with fewer than the median number of patients given morphine (32 patients) gave NNT similar to larger trials. NNT = 2.9 (95% CI: 2.3, 4.1) for smaller trials compared to NNT = 3.0 (95% CI: 2.5, 3.8) in larger trials.

Minor adverse effects occurred in 34% of patient given intramuscular morphine compared with 23% given placebo. RR = 1.49 (95% CI: 1.09, 2.04). Major side effects were rare (overall 1.2%) with no difference between morphine and placebo. No heterogeneity was detected in studies reporting adverse reactions (P > 0.01).

**Authors’ conclusions**

One in every three patients with moderate or severe postoperative pain treated with 10 mg intramuscular morphine had at least 50% pain relief and would not have achieved this had they been given placebo. Minor adverse effects were more common with morphine but drug related withdrawal was rare with no difference between morphine and placebo.

**CRD commentary**

The aims and inclusion criteria were stated. No language restrictions were applied to included studies. Details were given of methods used to select primary studies and assess validity. Heterogeneity was assessed though methods used were not stated in the review and may be included in another publication. Meta-analysis was limited to trials reporting on similar interventions. Trials included in the meta-analysis were all judged to be of high quality. Adverse events were considered. Publication bias was assessed and some sensitivity analysis was conducted.

The authors conclusions were supported by the evidence.

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

The authors did not state any implications for practice or further research.

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