Should we add clonidine to local anesthetic for peripheral nerve blockade: a qualitative systematic review of the literature

McCartney C J, Duggan E, Apatu E

CRD summary
Clonidine improved the duration of analgesia and anaesthesia when used as an adjunct to intermediate-acting local anaesthetics for some peripheral nerve blocks. The authors' conclusions reflected the evidence presented, but in light of both a lack of reporting, and the presence of several methodological concerns with the review, the authors' conclusions may not be reliable.

Authors' objectives
To determine the effectiveness of adding clonidine to local anaesthetics for peripheral nerve block.

Searching
PubMed and EMBASE were searched from July 1991 to October 2006 for English language, published peer-reviewed articles. Search terms were reported. References of eligible articles were also screened.

Study selection
Double blind randomised controlled trials (RCTs) in adult patients (over 18 years of age) investigating the effect of clonidine as an adjunct to local anaesthesia in peripheral nerve blocks, were eligible for inclusion in the review. Trials investigating the addition of clonidine to intravenous regional anaesthetics were excluded from the review.

Doses of clonidine ranged from 30 micrograms (μg) to 300 μg. Local anaesthetic techniques included in the review were: axillary, interscalene, peribulbar, psoas compartment, mid-humeral, infraclavicular, ankle/metatarsal, femsciatic and ilioinguinal/iliohypogastric. Local anaesthetics included: bupivacaine, levobupivacaine, lidocaine, mepivacaine and ropivacaine.

Outcome measures of post-operative pain included: time to first analgesia, results of visual analogue scale (VAS), verbal rating score (VRS) and total analgesic consumption.

Two reviewers independently performed the study selection. The authors did not state how disagreements were resolved.

Assessment of study quality
Although only double blind RCTs were eligible for inclusion in the review, the authors did not state that they formally assessed validity.

Data extraction
For each trial, data were extracted on: the number patients, regional anaesthetic technique used, dose of clonidine, name and dose of local anaesthetic used, outcome measures of post-operative pain, adverse effects, and if appropriate, a description of the systemic control used.

The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction.

Methods of synthesis
The trials were combined in a narrative synthesis, supported by accompanying data tables and bar charts. The authors classified trials as 'supportive' if the use of clonidine demonstrated reduced pain and total analgesic consumption, or prolonged block duration; or 'negative' if no difference was found between clonidine and control.

Subgroup analyses were performed according to whether or not the trials had a systemic control and whether an
intermediate versus a long-acting local anaesthetic was used.

Results of the review
Twenty seven RCTs were included in the review (n=1,386 patients), five of which had a systemic control group (n=226 patients). Sample size ranged from 20 to 120.

In the five RCTs with a systemic control group, three studies were supportive of clonidine and two failed to demonstrate a benefit.

Of the 22 RCTs without a systemic control, 12 were supportive of clonidine and 10 were not. The RCTs without a systemic control group used four main types of anaesthetic technique: upper limbs (13 trials), lower limbs (four trials), peribulbar (three trials) and ilioinguinal/iliohypogastric (two trials). Of the upper limb studies, eight RCTs were supportive of using clonidine and five were not. Of the lower limb studies, two RCTs were supportive of using clonidine and two were not. Of the peribulbar studies, two RCTs were supportive of using clonidine and one was not. Of the ilioinguinal/iliohypogastric studies, both RCTs were negative (i.e. not supportive of the use of clonidine).

The analgesic effect of clonidine appeared to be dose dependent, with a greater number of supportive RCTs seen at a dose of 150μg.

Nine RCTs reported significant differences in the incidence of adverse effects in the clonidine group compared to the control group. In five RCTs greater sedation was seen in the clonidine group. Five RCTs reported prolonged motor block with clonidine. In seven RCTs, hypotension and bradycardia was reported in the clonidine group, which resulted in some patients (number unspecified) requiring drug treatment and two patients having a prolonged hospital stay.

Authors’ conclusions
Clonidine improved the duration of analgesia and anaesthesia when used as an adjunct to intermediate-acting local anaesthetics for some peripheral nerve blocks. Side-effects appeared to be limited at doses up to 150μg. Evidence was lacking for the use of clonidine as an adjunct to local anaesthetics for continuous catheter techniques.

CRD commentary
The review addressed a clear research question and was supported by adequate inclusion criteria. The search strategy was adequate, but it was limited to published studies in English. The review was therefore subject to the possibility of publication and language bias, which means that relevant studies may have been missed. Study selection was performed independently by two reviewers, which minimised the risk of reviewer error and bias, but details were not provided on methods used in the data extraction process. Although the authors stated that only double blind RCTs were eligible for inclusion in the review, there was no formal validity assessment, which means the reliability of the evidence presented was unclear. A narrative synthesis was appropriate given the diversity of the included trials. However, there was often a lack of information about the comparator treatments used, making it difficult to interpret results. Interpretation was further restricted by the authors only presenting very basic result details. The authors’ conclusions reflected the evidence presented, but in light of both a lack of reporting, and the presence of several methodological concerns with the review, the authors’ conclusions may not be reliable.

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

Research: The authors stated that further RCTs with systemic and control groups are required to determine if: clonidine is only effective when added to intermediate-acting local anaesthetics; the effect of clonidine is systemic or local; clonidine prolongs analgesia when added to intermediate-acting local anaesthetics for lower limb blocks; there is a role for clonidine in continuous catheter infusions.

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