

Opioids in non-malignant pain: Are they equivalent in safety profile?

A network meta-analysis Siddiqui MK¹; Gupta J¹; Bhutani M¹; Sehgal M¹ ¹HERON Group, Chandigarh, India



Introduction

All opioid analgesics are considered to be associated with similar adverse event profile. However, we identified a need to generate relative safety and tolerability of opioids indicated for non-malignant pain as little evidence is available to substantiate comparative safety.

The evidence to assess relative safety and tolerability was generated following a systematic review methodology. Sufficient direct evidence on comparative safety of opioids was not available. Potential differences in safety were then assessed using mixed treatment comparison followed by generation of probability ranking in WinBUGS.

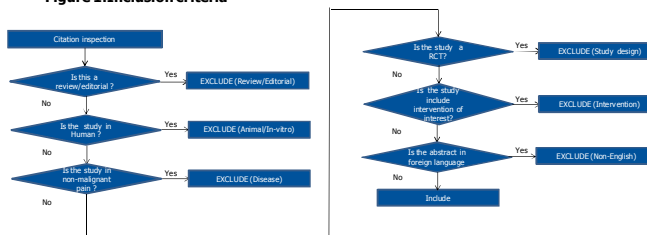
Objectives

The objective of this review was to compare the safety and tolerability of commonly used opioids (tramadol, oxycodone, hydrocodone, propoxyphene, and codeine) in non-malignant pain through network meta-analyses of randomized controlled trials (RCTs).

Methods

- Medline and Embase databases were searched from 2000 to 2011 for RCTs comparing commonly used opioids (tramadol, oxycodone, hydrocodone, propoxyphene, and codeine) in non-malignant pain.
- Studies were assessed for inclusion/exclusion by two independent reviewers based on a pre-specified protocol (Figure 1). Any disagreement was resolved by a third reviewer.
- A two-stage data extraction process was used to capture key outcomes including nausea, vomiting, somnolence, dizziness, headache, constipation, dry mouth, cardiovascular events, all cause mortality, gastrointestinal bleeding and fractures. Any disagreement in extracted data was resolved by a third reviewer.
- Based on the incidence of adverse events (AEs) associated with each intervention, a probability-based ranking (probability (P) of being worst) was generated using WinBUGS.

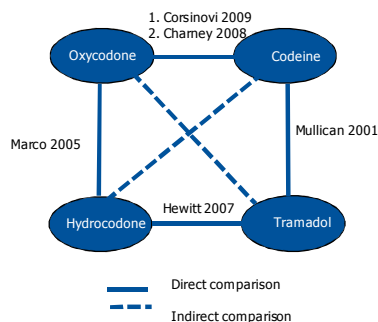
Figure 1: Inclusion criteria



Results

Of the 1156 studies screened, five RCTs enrolling 1399 patients were eligible for inclusion. Figure 2 shows network of evidences available in non-malignant pain. Of the five included studies, four studies (80%) were double blind, allocation was concealed in three studies (60%), and randomization was adequately generated in four studies (80%).

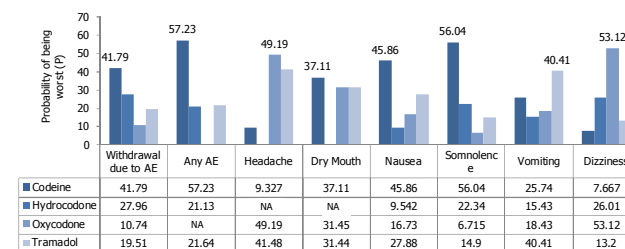
Figure 2: Trials network



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The most commonly reported AEs were nausea, vomiting, somnolence, dizziness, headache, constipation and dry mouth. The probability of an opioid being worst for each adverse event is shown in Figure 3. Withdrawals due to AEs were most commonly observed with codeine (P= 42%) followed by hydrocodone (P=28%), tramadol (P=19%), and oxycodone (P=10%). The probability of occurrence of nausea and somnolence was the highest with codeine. Dizziness was most frequently associated with oxycodone (P= 53%). However, the incidence of dizziness and headache was the lowest with codeine. Tramadol was observed to be associated with the highest (P=40%) incidence of vomiting, while hydrocodone had the lowest incidence (P=15%).

Figure 3: Probability of opioids being worst per each AE



Conclusions

Codeine was observed to have the highest incidence of withdrawals due to AEs. It was observed that the probability of occurrence of any particular AE varied across included opioid analgesics. Codeine was observed to have been more frequently associated with nausea/somnolence while tramadol and oxycodone had the highest incidence of vomiting and dizziness respectively.

References

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