TITLE: Tramadol Plus Acetaminophen for the Management of Pain in Adult Patients: Clinical Effectiveness

DATE: 03 November 2015

RESEARCH QUESTION

What is the clinical effectiveness of tramadol plus acetaminophen for the management of pain in adult patients?

KEY FINDINGS

Two randomized controlled trials and four non-randomized studies were identified regarding the clinical effectiveness of tramadol plus acetaminophen for the management of pain in adult patients.

METHODS

This report expands on a literature search conducted for a previous CADTH report. The original literature search was conducted on January 6, 2015 on key resources including PubMed, The Cochrane Library, University of York Centre for Reviews and Dissemination (CRD) databases, ECRI, Canadian and major international health technology agencies, as well as a focused Internet search. Methodological filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, and randomized controlled trials. Where possible, retrieval was limited to the human population. The initial search was also limited to English-language documents published between January 1, 2010 and January 6, 2015.

For the current report, database searches were rerun from January 1, 2014 to October 23, 2015, to capture any articles published since the initial search, but no filters were applied to limit retrieval by study type. To expand further to all study types from the initial search, the search was rerun for January 1, 2010 to December 31, 2013 with methodological filters applied to limit retrieval to all publication types except for health technology assessments, systematic reviews, meta-analyses, and randomized controlled trials. The search of major health technology agencies was also updated. Internet links were provided, where available.
The summary of findings was prepared from the abstracts of the relevant information. Please note that data contained in abstracts may not always be an accurate reflection of the data contained within the full article.

**SELECTION CRITERIA**

One reviewer screened citations and selected studies based on the inclusion criteria presented in Table 1.

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<th>Table 1: Selection Criteria</th>
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<td><strong>Population</strong></td>
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<td><strong>Comparator</strong></td>
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<td><strong>Outcomes</strong></td>
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<td><strong>Study Designs</strong></td>
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**RESULTS**

Rapid Response reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by randomized controlled trials and non-randomized studies.

Two randomized controlled trials and four non-randomized studies were identified regarding the clinical effectiveness of tramadol plus acetaminophen for the management of pain in adult patients. No health technology assessments, systematic reviews, or meta-analyses were identified.

Additional references of potential interest are provided in the appendix.

**OVERALL SUMMARY OF FINDINGS**

Two randomized controlled trials (RCTs)\(^1\)\(^-\)\(^2\) were identified regarding the clinical effectiveness of tramadol plus acetaminophen for the management of pain in adult patients. One RCT\(^1\) found tramadol plus acetaminophen to be equally effective as paracetamol and codeine plus meprobamate at relieving pain after third molar extraction. Both treatments were well tolerated by patients.\(^1\) The other RCT\(^2\) investigated the use of tramadol and acetaminophen compared to non-steroidal anti-inflammatory drugs in patients with low back pain and depression. This study found that patients in the tramadol-acetaminophen group reported statistically significant less depression and lower pain scores on the Numerical Rating Scale, but no statistically significantly different scores in the Oswestry Disability Index, Pain Disability Assessment Scale, or Pain Catastrophizing Scale when compared to the non-steroidal anti-inflammatory drug group.\(^2\) There was no significant difference in treatment related adverse events between the two patient groups.\(^2\)

Four non-randomized studies\(^3\)\(^-\)\(^6\) were identified regarding the clinical effectiveness of tramadol plus acetaminophen for the management of pain in adult patients. One study\(^3\) compared the use of tramadol plus acetaminophen to transdermal fentanyl for the control of postoperative pain following corrective eye surgery. Transdermal fentanyl was significantly better at controlling pain.
in these patients; however, patients in this group experienced significantly more adverse events.\(^3\) Tramadol was compared to tramadol plus acetaminophen following ambulatory surgery in another study.\(^4\) Both groups experienced a comparable proportion of patients with moderate to severe pain; however, patients in the tramadol plus acetaminophen group experienced more side effects and were less therapy compliant, but needed less escape medication than the tramadol group.\(^4\) One study\(^5\) examined the use of analgesics by patients seeking treatment for pain in general practice. This study found that tramadol plus acetaminophen and codeine plus acetaminophen had comparable reductions in pain and were well tolerated by patients.\(^5\) For the treatment of low back pain, the last identified study\(^6\) compared tramadol plus acetaminophen to tramadol plus acetaminophen and caffeine (novel combination group). Patients in the novel combination group had significantly better pain management with fewer side effects when compared to patients in the tramadol plus acetaminophen group.
REFERENCES SUMMARIZED

Health Technology Assessments
No literature identified.

Systematic Reviews and Meta-analyses
No literature identified.

Randomized Controlled Trials


Non-Randomized Studies


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APPENDIX – FURTHER INFORMATION:

Previous CADTH Reports


Randomized Controlled Trials

No Active Comparator Group, Placebo-Controlled


Non-Randomized Studies

Elderly Population, No Comparator Group


No Comparator Group


Review Articles


Elderly Population