TITLE: **Pentazocine versus Short-acting Opioids for Chronic or Acute Pain: A Review of the Clinical Effectiveness**

DATE: 29 May 2013

CONTEXT AND POLICY ISSUES

Pentazocine was introduced in the late 1960's and was the first agonist-antagonist analgesic to be marketed.[1,2] Pentazocine is available as oral and parental formulations marketed in Canada under the brand name Talwin.[3,4] It is chemically related to morphine however its mechanism of action differs by acting as a weak antagonist or partial agonist at the mu opioid receptor and partial agonist at the kappa receptor. Because of the weak antagonistic effects there is a maximal or "ceiling effect" seen with escalating doses as well as precipitation of withdrawal reactions in patients receiving opioids chronically or for a prolonged duration.[2,5]

This report will focus on the use of pentazocine in patients in the community setting experiencing, acute and chronic pain as well as pain control in palliative care and will not include the use of pentazocine post-operatively. Pentazocine will be compared to other opioids used in this setting such as codeine, morphine, oxycodone and hydromorphone. The aforementioned opioids differ from pentazocine in that they are agonists at the mu opioid receptor, therefore they do not precipitate withdrawal reactions.[2] Morphine is the prototypical opioid, alterations to its structure gave rise to the synthetic opioids oxycodone and hydromorphone.[1,2] Codeine is hepatically metabolized to morphine which is responsible for most of its analgesic effect.[5] It was thought that the development of agonist-antagonist combinations such as pentazocine would diminish some concerning side effects of opioid agonists such as central nervous system and respiratory depression.[1] However, a frequently stated consequence of pentazocine is psychomimetric effects, including visual and auditory hallucinations, dreams, delusions, euphoria, dysphoria, feelings of depersonalization, panic, and abnormal thoughts.[2,6-8]. These effects are thought to be mediated by receptors other than the usual opioid receptors because they are not reversed with naloxone.[2]

This review will examine the comparative clinical effectiveness and safety profile of pentazocine versus short-acting opioids for pain management.

RESEARCH QUESTIONS

1. What is the comparative clinical effectiveness of pentazocine versus short-acting opioids for the treatment of chronic pain?

2. What is the comparative clinical effectiveness of pentazocine versus short-acting opioids for the treatment of acute pain in the community setting?

3. What is the comparative clinical effectiveness of pentazocine versus short-acting opioids for palliative care?

KEY FINDINGS

No relevant literature was identified regarding the comparative clinical effectiveness of pentazocine versus short acting opioids for chronic pain, acute pain in the community setting or palliative care.

METHODS

Literature Search Strategy

A limited literature search was conducted on key resources including PubMed, The Cochrane Library (2013, Issue 4), University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. No filters were applied to limit the retrieval by study type. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 1992 and April 30, 2013 (with the exception of the Internet search which was restricted to 2003-2013).

Selection Criteria and Methods

One reviewer screened the titles and abstracts of publications, potentially relevant articles were retrieved and the full-text publications were evaluated for the final article selection. Full-text articles were considered for inclusion based on the selection criteria listed in Table 1.

Table 1: Selection Criteria

Population	Patients experiencing pain: -chronic pain -acute pain in the community setting (i.e. not post-operative) -pain in palliative care
Intervention	Pentazocine
Comparator	Short-acting opioid agonists: codeine, morphine, oxycodone, hydromorphone
Outcomes	Clinical effectiveness (pain control) Harms/adverse events - clinical events (e.g. hallucination, delusions)
Study Designs	HTA/ Systematic review/Meta-analysis Randomized controlled trials Non-randomized studies

Exclusion Criteria

Articles were excluded if they did not satisfy the selection criteria and if pentazocine was used for acute pain in the hospital setting. Additional exclusion criteria included articles using pentazocine for intrathecal administration, in bucoadhesive patches and formulated in combination with naloxone were excluded. Pentazocine used in the setting of anesthesia and procedural sedation, in women undergoing labor, in rodents and other animals, and for pretreatment of pain prior to extracorpeal shock wave lithotripsy was excluded. Lastly articles discussing the use of pentazocine in breastfeeding mothers were excluded.

SUMMARY OF EVIDENCE

Quantity of Research Available

The literature search yielded 324 citations. Upon screening titles and abstracts, 321 citations were excluded and 3 potentially relevant articles were retrieved for full-text review. Of the potentially relevant reports none met the inclusion criteria and all were excluded. The process of study selection is outlined in the PRISMA flowchart (Appendix 1). Additional references of potential interest are provided in Appendix 2.

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING

No relevant literature was identified; therefore, no conclusions can be presented regarding the comparative clinical effectiveness of pentazocine versus short acting opioids for chronic pain, acute pain in the community setting, or palliative care.

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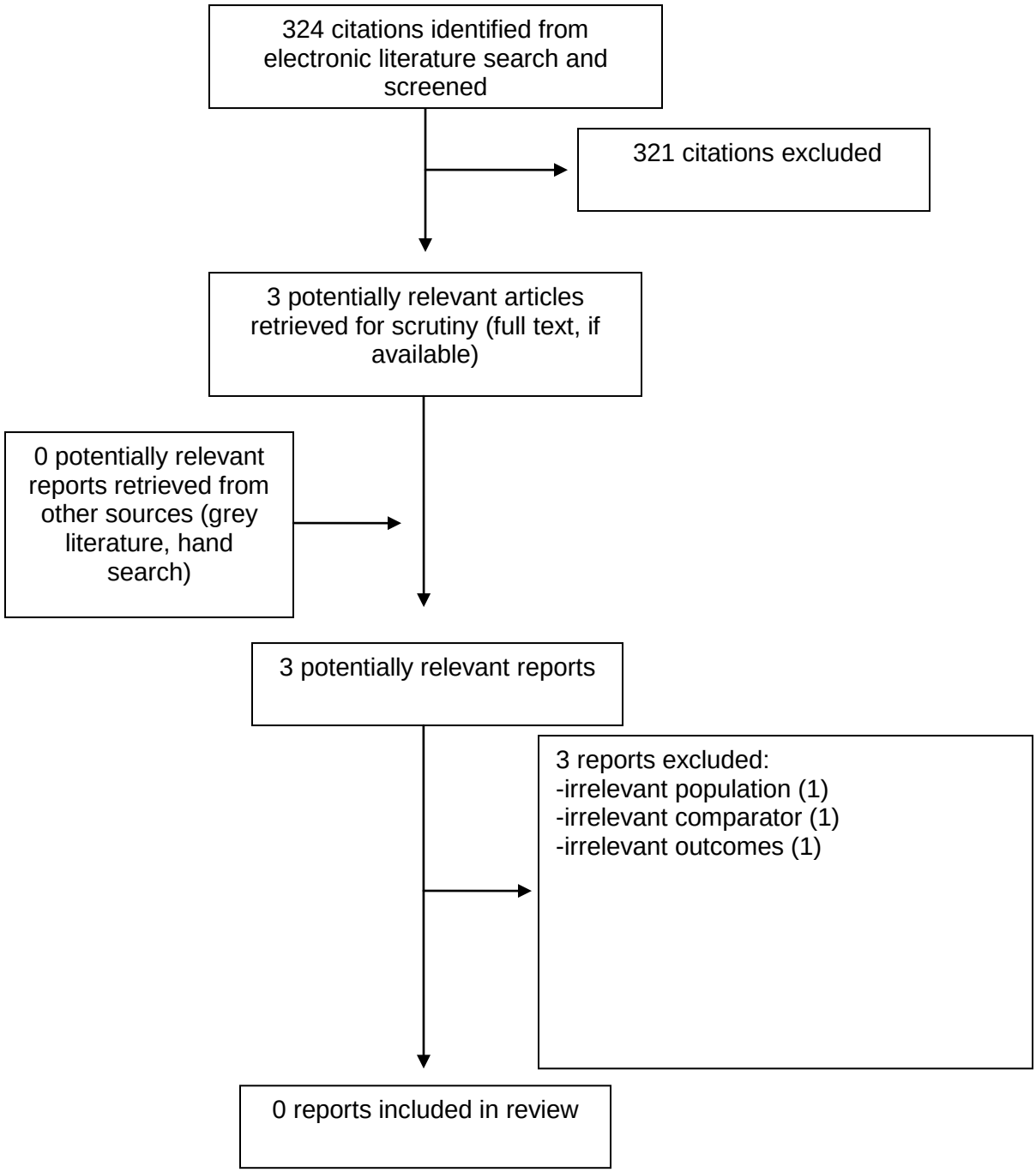
APPENDIX 1: Selection of Included Studies



APPENDIX 2: Additional Articles of Potential Interest

Studies that do not meet all the selection criteria but may be of interest are outlined below.

Guideline	Group	Recommendation
Pharmacologic Management. In: PDQ® Pain. 2013[8]	National Cancer Institute	*"Drugs to be avoided for Treatment of Cancer Pain: Pentazocine.* *- Risk of precipitating withdrawal in opioid-dependent patients.* *- Analgesic ceiling.* *-Possible production of unpleasant psychotomimetic effects (e.g., dysphoria, delusions, hallucinations)."* *Table 5*
Cancer-Related Pain Management. 2011 [9]	Program in Evidence-based Care, Cancer Care Ontario	*"Mixed agonist-antagonists (e.g., pentazocine) in clinical use have an analgesic ceiling (maximum daily dose). In contrast to full agonists, these drugs block opioid analgesia at one type of opioid receptor (μ) or are neutral at this receptor, while simultaneously activating a different opioid receptor (κ). Patients who receive a full opioid agonist should not be given a mixed agonist-antagonist, because it can precipitate a withdrawal syndrome and cause increased pain." p. 18*
Acute pain management: scientific evidence. 3rd ed. 2010[10]	Australian and New Zealand Colleage of Anaesthetists and Faculty of Pain Medicine.	*"…mixed agonist-antagonists (eg buprenorphine, pentazocine) should be also avoided as their use may precipitate acute withdrawal reactions" p. 430*
Cancer Care Ontario's Symptom Management Guides-to-Practice: Pain. 2010[11]	Cancer Care Ontario, the Ontario Cancer Symptom Management Collaborative (OCSMC) is a joint initiative of Palliative Care, Psychosocial Oncology and Nursing Oncology Programs	*"Meperidine and pentazocine should not be used in cancer patients with chronic pain." p. 19*
Guidelines on urolithiasis. 2008[12]	European Association of Urology	*"Pain relief for patients with acute stone colic: Pentazocine, preference 2 (second choice)."* *Level of evidence 4 ("Evidence obtained from expert committee reports or opinions or clinical experience of respected authorities")* *Grade C ("Made despite the absence of directly applicable clinical studies of*

Guideline	Group	Recommendation
		good quality")
Pain management guideline. 2006[13]	Health Care Association of New Jersey	*"Pharmacological Intervention: Considered but not recommended: Propoxyphene, Meperidine, Pentazocine, Butrophanol." p. 7*
Best Practice Guidelines for the Management of Cancer-Related Pain In Adults. 2005[7]	Cancer Care Nova Scotia	*"Mixed agonist-antagonist opioids should not be used for chronic treatment of cancer pain (e.g. pentazocine should not be used)" p. 24* *"Opioids which have an agonist action at the Kappa receptor (e.g. butorphanol, pentazocine) may cause psychotomimetic effects and chronic sedation not normally associated with other opioid agonists." p. 39* *"It is strongly recommended that Meperidine (Demerol), Pentazocine (Talwin) or Propoxyphene (Darvon) NOT be used for cancer pain management." p. 111*
Pain management in the long-term care setting. 2005[14]	American Medical Directors Association	*"Propoxyphene, meperidine, pentazocine, butorphanol, and other agonist-antagonist combinations are considered but not recommended."*