TITLE: Pharmacologic Pain Management Interventions for Patients with Bleeding Disorders: Clinical Effectiveness and Guidelines

DATE: 6 August 2015

RESEARCH QUESTIONS

1. What is the clinical effectiveness of pharmacologic interventions for pain management in patients with bleeding disorders?

2. What are the evidence-based guidelines regarding pharmacologic pain management in patients with bleeding disorders?

KEY FINDINGS

Two evidence-based guidelines were identified regarding pharmacologic interventions for pain management in patients with bleeding disorders.

METHODS

A limited literature search was conducted 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. 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, 2010 and July 22, 2015. 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.

Table 1: Selection Criteria

<table>
<thead>
<tr>
<th>Population</th>
<th>Patients of any age with bleeding disorders (e.g., hemophilia A and B; von Willebrand’s disease; factor II, V, VII, X, XII deficiency) who require acute or chronic pain management in any health care setting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention</td>
<td>Pharmacologic pain management interventions, for example, but not limited to: Acetaminophen, Non-steroidal anti-inflammatories, Steroid anti-inflammatories, Opioids, Cannabinoids, Anti-convulsants, Anti-depressants</td>
</tr>
<tr>
<td>Comparator</td>
<td>Other drugs; Placebo or no treatment; Non-pharmacologic pain management interventions; Usual care</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Q1: Clinical effectiveness, safety and harms (e.g., increased risk of bleeding) Q2: Guidelines</td>
</tr>
<tr>
<td>Study Designs</td>
<td>Health technology assessment reports, systematic reviews, meta-analyses, randomized controlled trials, non-randomized studies, evidence-based guidelines</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, non-randomized studies, and evidence-based guidelines.

Two evidence-based guidelines were identified regarding pharmacologic interventions for pain management in patients with bleeding disorders. No relevant health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, or non-randomized studies regarding the clinical effectiveness of pharmacologic interventions for pain management in patients with bleeding disorders were identified.

Additional references of potential interest are provided in the appendix.

OVERALL SUMMARY OF FINDINGS

Two evidence-based guidelines\(^1,2\) were identified regarding pharmacologic interventions for pain management in patients with Hemophilia.
The guideline by the World Federation of Hemophilia\(^1\) makes general recommendations that paracetamol/acetaminophen be used for analgesia and for the avoidance of drugs affecting platelet function; in particular, acetylsalicylic acid (ASA) and non-steroidal anti-inflammatory drugs (NSAIDs) with the exception of select COX-2 inhibitors. Recommendations regarding specific clinical scenarios are summarized in Table 2.\(^1\)

<table>
<thead>
<tr>
<th>Clinical reason for pain</th>
<th>Recommendation</th>
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<tbody>
<tr>
<td>Joint inflammation</td>
<td>COX-2 inhibitors can be used judiciously after an acute bleed and in chronic arthritis (page 12).</td>
</tr>
<tr>
<td>Venous access</td>
<td>No pain medication is given with the exception of local anesthetic for children (page 15).</td>
</tr>
</tbody>
</table>
| Joint or muscle bleeding | • Paracetamol/acetaminophen is the first line strategy.  
|                          | • This can be followed, if ineffective, by COX-2 inhibitors (e.g., celecoxib, meloxicam, nimesulide and others), or paracetamol/acetaminophen plus codeine or tramadol.  
|                          | • As a last step, morphine can be used.  
|                          | See page 15 for all |
| Post-operative pain      | • Intramuscular injection of analgesia should be avoided and pain should be managed in coordination with the anaesthesiologist.  
|                          | • Initially, intravenous morphine or other narcotic analgesics can be given, followed by oral opioids such as tramadol, codeine, hydrocodone and others.  
|                          | • As pain decreases paracetamol/acetaminophen may be used.  
|                          | See page 15 for all |
| Chronic hemophilic arthropathy | See ‘Joint or muscle bleeding’  
|                          | • In addition, select COX-2 inhibitors may have a greater role and other NSAIDs should be avoided (page 15). |

*Minimally paraphrased or verbatim recommendations are referred to by page number*

The guideline by the Australian and New Zealand College of Anaesthetists and Faculty of Pain Medicine\(^2\) states that COX-2 inhibitors may be of benefit in hemophiliacs due to their lack of platelet inhibitory affects, and that intramuscular analgesia should be avoided due to the risk of bleeding.
REFERENCES SUMMARIZED

Health Technology Assessments
No literature identified

Systematic Reviews and Meta-analyses
No literature identified

Randomized Controlled Trials
No literature identified

Non-Randomized Studies
No literature identified

Guidelines and Recommendations

   See: 1.2.18, page 9;
   1.5.5, page 12;
   1.9 Pain Management, page 15;
   12, page 57

   See: Haemophilia, pages 262 to 263

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APPENDIX – FURTHER INFORMATION:

Non-Randomized Studies - Descriptive Surveys


Clinical Practice Guidelines – Unclear Methodology

   See: Pain Management, page 63

   See: Pharmacologic Approach to Pain Management, pages 10 to 18


Review Articles


PubMed: PM22992238
See: Adjunctive Treatment – Pain control, page 462

PubMed: PM23207414

PubMed: PM21670647

PubMed: PM21645179

Additional References

PubMed: PM24602275