CADTH RAPID RESPONSE REPORT: SUMMARY OF ABSTRACTS

Sodium Hyaluronic Acid for the Treatment of Interstitial Cystitis: Clinical Effectiveness, Cost-Effectiveness, and Guidelines

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About CADTH: CADTH is an independent, not-for-profit organization responsible for providing Canada’s health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs, medical devices, diagnostics, and procedures in our health care system.
Research Questions
1. What is the clinical effectiveness of sodium hyaluronic acid for the treatment of interstitial cystitis?
2. What is the cost-effectiveness of sodium hyaluronic acid for the treatment of interstitial cystitis?
3. What are the evidence-based guidelines regarding the treatment of interstitial cystitis?

Key Findings
Two systematic reviews, two systematic reviews with meta-analyses, one randomized control trial, four non-randomized studies, and one economic evaluation were identified regarding the clinical and cost effectiveness of sodium hyaluronic acid for the treatment of interstitial cystitis/painful bladder syndrome. Additionally, two evidence-based guidelines were identified regarding the use of sodium hyaluronic acid for the treatment of interstitial cystitis/painful bladder syndrome.

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, 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. The search was limited to English language documents published between Jan 1, 2012 and Mar 21, 2017. Internet links were provided, where available.

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>Adult patients with interstitial cystitis</th>
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<tbody>
<tr>
<td>Intervention</td>
<td>Sodium hyaluronic acid (Cystistat) [may also be referred to as intravesical hyaluronic acid]</td>
</tr>
<tr>
<td>Comparator</td>
<td>Standard of care (e.g., dimethyl sulfoxide [DMSO])</td>
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<td>Outcomes</td>
<td>Q1: Clinical effectiveness</td>
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<td></td>
<td>Q2: Cost-effectiveness</td>
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<td></td>
<td>Q3: Evidence-based guidelines</td>
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<tr>
<td>Study Designs</td>
<td>Health technology assessments, systematic reviews, meta-analyses, randomized control trials, non-randomized studies, economic evaluations, evidence-based guidelines</td>
</tr>
</tbody>
</table>
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, economic evaluations, and evidence-based guidelines.

Two systematic reviews, two systematic reviews with meta-analyses, one randomized control trial, four non-randomized studies, and one economic evaluation were identified regarding the clinical and cost effectiveness of sodium hyaluronic acid for the treatment of interstitial cystitis/painful bladder syndrome. Additionally, two evidence-based guidelines were found regarding the use of sodium hyaluronic acid for the treatment of interstitial cystitis/painful bladder syndrome. No relevant health technology assessments were identified.

Additional references of potential interest are provided in the appendix.

Overall Summary of Findings

Four systematic reviews\textsuperscript{1-4} were identified regarding the clinical effectiveness of sodium hyaluronic acid (HA) for the treatment of interstitial cystitis (IC), two of which contained meta-analyses.\textsuperscript{1,3} One systematic review\textsuperscript{1} also presented conclusions regarding the cost-efficacy of HA to other instillation treatments. Three systematic reviews\textsuperscript{1,3,4} specifically examined the effects of intravesical hyaluronic acid instilled in patients with IC and one systematic review\textsuperscript{2} examined instillation of HA; however, it did not specify whether the therapy was intravesical. In one systematic review with meta-analysis,\textsuperscript{1} high molecular weight HA was found to be advantageous in clinical effectiveness, cost-efficacy, and cost-effectiveness over other instillation regimes; however, direct comparisons between the regimes were not possible. The authors additionally concluded that the number needed to treat to achieve a response for intravesical HA was 1.31.\textsuperscript{1} The authors of the second systematic review with meta-analysis\textsuperscript{3} also concluded that HA is an effective treatment regime for patients with IC, reporting improvement in pain symptoms, quality of life and other measured outcomes. The authors of another systematic review\textsuperscript{2} could not report definitive conclusions regarding the use of HA for IC, while the authors of the final systematic review\textsuperscript{4} did not report their conclusions from the systematic review in the abstract, only reporting positive efficacy results from the included case series.

One randomized control trial (RCT)\textsuperscript{5} was identified. The authors of this RCT concluded that instillation of HA is effective as a glycosaminoglycan substitution therapy in the treatment of patients with IC.\textsuperscript{5}

Four non-randomized studies\textsuperscript{6-9} were identified regarding HA for IC or painful bladder syndrome. Two studies\textsuperscript{6,8} examined refractory IC specifically. All four studies\textsuperscript{6-9} concluded that HA is effective in treating IC, although this beneficial effect was limited in one study.\textsuperscript{7} Pain was reduced after treatment with HA in three studies\textsuperscript{6-8} and there were limited side effects or complications with the treatment in two studies.\textsuperscript{8,9} Compliance with HA treatment was deemed good in one study.\textsuperscript{9} Finally, HA treatment for IC additionally improved sexual functioning in conjunction with reduction of IC symptoms.\textsuperscript{6}

One economic evaluation was identified\textsuperscript{10} and the analysis was performed on mid- and long-term economic costs of therapies for IC in Austria. The authors concluded that, in Austria, HA is cost saving when compared to all alternatives, and had the lowest treatment
costs at all three studied time points (1 year, 5 years, and 10 years) despite high initial costs of HA therapy.10

Finally, two evidence-based guidelines11-12 were identified regarding the treatment of IC using HA. The first guideline recommends that if conservative treatments, as well as oral medications, are unsuccessful in treating IC then, with an individualized approach, other therapies (including intravesical HA) can be added or substituted.11 The second guideline recommends intravesical HA as an option as part of multimodal therapy for IC12 but cautions that intravesical HA has had mixed results in the literature.

References Summarized

Health Technology Assessments

No literature identified.

Systematic Reviews and Meta-analyses

PubMed: PM26590137

PubMed: PM26272202

PubMed: PM27627755

PubMed: PM26166334

Randomized Controlled Trials

PubMed: PM24868341
Non-Randomized Studies


Economic Evaluations


Guidelines and Recommendations


See: 7.3 Intravesical treatments


See: Guideline: Based on published Level 3 evidence, intravesical HA may be considered part of multimodal therapy for IC/BPS. However, it should be kept in mind that three negative trials have been completed without published results.
Appendix — Further Information

Randomized Control Trials – Alternate Comparator


Non-Randomized Studies – Alternate Comparator


Clinical Practice Guidelines – Uncertain Methodology


Review Articles


