TITLE: High Dose Stimulants for Attention Deficit Hyperactivity Disorder: Clinical Effectiveness, Safety, and Guidelines

DATE: 29 January 2015

RESEARCH QUESTIONS

1. What is the effectiveness and safety of high dose stimulants in children and adolescents (six to 18 years) with attention deficit hyperactivity disorder (ADHD)?

2. What is the comparative effectiveness and safety of high dose stimulants in adults (>18 years) with ADHD?

3. What are the evidence-based guidelines regarding the use of high dose stimulants in patients with ADHD?

KEY FINDINGS

One systematic review, three randomized-controlled trials, and four non-randomized studies were identified regarding high dose stimulants for attention deficit hyperactivity disorder.

METHODS

A limited literature search was conducted on key resources including PubMed, The Cochrane Library (2015, Issue 1), 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, 2010 and January 26, 2015. Internet links were provided, where available.

SELECTION CRITERIA

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

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Table 1: Selection Criteria

<table>
<thead>
<tr>
<th>Population</th>
<th>Children and adolescents (six to 18 years) and adults (&gt;18 years) with ADHD, with or without co-morbidities in out-patient and in-patient (e.g., mental health facilities) settings.</th>
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<tbody>
<tr>
<td>Intervention</td>
<td>High dose of stimulants i.e., above the recommended dose. Drugs of interest: All short, intermediate, and/or long acting stimulants (e.g., methylphenidate, amphetamine, dextro-amphetamine, lisdexamfetamine)</td>
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| Comparator          | Standard of practice – Stimulants prescribed  
• within the recommended maximum dose and/or  
• in combination with non-stimulants  
Placebo |
| Outcomes            | Efficacy outcomes, including but not limited to: changes in severity of ADHD symptoms, cognitive and adaptive skills, functional outcomes, quality of life and psychiatric morbidity, caregiver satisfaction, time to onset of effectiveness, duration of effectiveness.  
Safety outcomes, including but not limited to: overall adverse events, withdrawals due to adverse events, missed dose, non-compliance, abuse potential, development of substance abuse disorder, long-term safety (e.g., cardiac safety, hepatotoxicity, growth effects, psychiatric effects, etc.). |
| Study Designs        | Health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, non-randomized studies, evidence-based guidelines |

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.

One systematic review, three randomized-controlled trials, and four non-randomized studies were identified regarding high dose stimulants for attention deficit hyperactivity disorder.

Additional references of potential interest are provided in the appendix.

Health Technology Assessments
No literature identified.

Systematic Reviews and Meta-analyses

PubMed: PM25230710
Randomized Controlled Trials

Children and Adolescents


Adults


Non-Randomized Studies

Children and Adolescents


Adults


Guidelines and Recommendations
No literature identified.

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APPENDIX – FURTHER INFORMATION:

Non-Randomized Studies - Maximum Daily Dose Not Specified


Clinical Practice Guidelines – Uncertain Methodology

   See: Supporting Document 7A, pages 7.11 – 7.16
   Supporting Document 7B, pages 7.17 – 7.20