



TITLE: Duration of Dosage Effect for Methylphenidate SR and Dextroamphetamine SR for Patients with Attention Deficit Hyperactivity Disorder

DATE: 01 September 2015

RESEARCH QUESTION

What is the clinical evidence for the duration of dosage effect for methylphenidate SR and dextroamphetamine SR for patients with attention deficit hyperactivity disorder?

KEY FINDINGS

One systematic review, two randomized controlled trials, and two non-randomized studies were identified regarding the duration of dosage effect for methylphenidate SR for patients with attention deficit hyperactivity disorder.

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 August 18, 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.

Disclaimer: The Rapid Response Service is an information service for those involved in planning and providing health care in Canada. Rapid responses are based on a limited literature search and are not comprehensive, systematic reviews. The intent is to provide a list of sources of the best evidence on the topic that CADTH could identify using all reasonable efforts within the time allowed. Rapid responses should be considered along with other types of information and health care considerations. The information included in this response is not intended to replace professional medical advice, nor should it be construed as a recommendation for or against the use of a particular health technology. Readers are also cautioned that a lack of good quality evidence does not necessarily mean a lack of effectiveness particularly in the case of new and emerging health technologies, for which little information can be found, but which may in future prove to be effective. While CADTH has taken care in the preparation of the report to ensure that its contents are accurate, complete and up to date, CADTH does not make any guarantee to that effect. CADTH is not liable for any loss or damages resulting from use of the information in the report.

Copyright: This report contains CADTH copyright material and may contain material in which a third party owns copyright. **This report may be used for the purposes of research or private study only.** It may not be copied, posted on a web site, redistributed by email or stored on an electronic system without the prior written permission of CADTH or applicable copyright owner.

Links: This report may contain links to other information available on the websites of third parties on the Internet. CADTH does not have control over the content of such sites. Use of third party sites is governed by the owners' own terms and conditions.

Table 1: Selection Criteria

Population	Patients of any age with attention deficit hyperactivity disorder (ADHD)
Intervention	Methylphenidate SR (e.g., Ritalin SR); and dextroamphetamine SR (e.g., Dexedrine Spansule)
Comparator	None
Outcomes	Perceived duration of dosage effect
Study Designs	Health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, non-randomized studies

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 (RCTs) and non-randomized studies.

One systematic review, two RCTs, and two non-randomized studies were identified regarding the duration of dosage effect for methylphenidate SR for patients with attention deficit hyperactivity disorder (ADHD). No relevant health technology assessments or meta-analyses were identified. Further, no relevant evidence regarding the duration of dosage effect for dextroamphetamine SR was identified.

Additional references of potential interest are provided in the appendix.

OVERALL SUMMARY OF FINDINGS

One systematic review,¹ two randomized controlled trials,^{2,3} and two non-randomized studies^{4,5} were identified regarding the duration of dosage effect, measured using Permanent Product Measure of Performance (PERMP) and Swanson, Kotkin, Agler, M-Flynn, and Pelham combined rating scale (SKAMP) scores, of methylphenidate SR products for patients with ADHD.

The systematic review¹ reported results from 15 RCTs in adults (n = 1) and children (n = 14). Based on PERMP mathematics scores, duration of efficacy ranged from eight hours with long-acting methylphenidates, to 14 hours with lisdexamfetamine dimesylate.¹ Most agents exhibited a 12 hour duration of efficacy.¹

One RCT² reported that NWP06, a novel extended-release formulation of methylphenidate, was effective from 45 minutes onward up to 12 hours post-dose, as measured by SKAMP scores and the PERMP mathematics test in children aged six to 12 years. Another RCT³ reported effects of osmotic-release oral system methylphenidate (Concerta) from one hour onward up to 12.5 hours post-dose as measured by SKAMP and PERMP scores in children aged nine to 12.

One prospective observational study⁴ reported that Ritalin LA resulted in significantly prolonged effect duration (outcome measure not specified) compared to pre-treatment in children (mean age 10.9 years) with an insufficient response to previous ADHD medication. Another retrospective observational study⁵ comparing the effects of novo-methylphenidate extended-release versus Concerta reported that 43% of pediatric patients who were switched to the bioequivalent product observed a shorter duration of effect (outcome measure not specified).

No relevant evidence regarding the duration of dosage effect for dextroamphetamine SR was identified; therefore no summary can be provided.

REFERENCES SUMMARIZED

Health Technology Assessments

No literature identified.

Systematic Reviews and Meta-analyses

1. Brams M, Moon E, Pucci M, Lopez FA. Duration of effect of oral long-acting stimulant medications for ADHD throughout the day. *Curr Med Res Opin.* 2010 Aug;26(8):1809-25.
[PubMed: PM20491612](#)

Randomized Controlled Trials

2. Wigal SB, Childress AC, Belden HW, Berry SA. NWP06, an extended-release oral suspension of methylphenidate, improved attention-deficit/hyperactivity disorder symptoms compared with placebo in a laboratory classroom study. *J Child Adolesc Psychopharmacol* [Internet]. 2013 Feb [cited 2015 Aug 27];23(1):3-10. Available from:
<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3696913>
[PubMed: PM23289899](#)
3. Armstrong RB, Damaraju CV, Ascher S, Schwarzman L, O'Neill J, Starr HL. Time course of treatment effect of OROS® methylphenidate in children with ADHD. *J Atten Disord.* 2012 Nov;16(8):697-705.
[PubMed: PM22084448](#)

Non-Randomized Studies

4. Haertling F, Mueller B, Bilke-Hentsch O. Effectiveness and safety of a long-acting, once-daily, two-phase release formulation of methylphenidate (Ritalin® LA) in school children under daily practice conditions. *Atten Defic Hyperact Disord* [Internet]. 2015 Jun [2015 Aug 27];7(2):157-64. Available from:
<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4449385>
[PubMed: PM25346231](#)
5. van Stralen JP. The clinical impact of switching attention deficit hyperactivity disorder patients from OROS(®)-MPH to Novo-MPH ER-C(®): A paediatric practice review. *Paediatr Child Health* [Internet]. 2013 Feb [cited 2015 Aug 27];18(2):70-3. Available from:
<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3567899>
[PubMed: PM24421659](#)

PREPARED BY:

Canadian Agency for Drugs and Technologies in Health

Tel: 1-866-898-8439

www.cadth.ca

APPENDIX – FURTHER INFORMATION:

Review Articles

6. Sugrue D, Bogner R, Ehret MJ. Methylphenidate and dexamethylphenidate formulations for children with attention-deficit/hyperactivity disorder. *Am J Health Syst Pharm.* 2014 Jul 15;71(14):1163-70.
[PubMed: PM24973373](#)
7. Childress A, Sallee FR. The use of methylphenidate hydrochloride extended-release oral suspension for the treatment of ADHD. *Expert Rev Neurother.* 2013 Sep;13(9):979-88.
[PubMed: PM24053342](#)
8. Maldonado R. Comparison of the pharmacokinetics and clinical efficacy of new extended-release formulations of methylphenidate. *Expert Opin Drug Metab Toxicol.* 2013 Aug;9(8):1001-14.
[PubMed: PM23611637](#)
9. McBurnett K, Starr HL. OROS methylphenidate hydrochloride for adult patients with attention deficit/hyperactivity disorder. *Expert Opin Pharmacother.* 2011 Feb;12(2):315-24.
[PubMed: PM21226641](#)
10. Weisler RH, Childress AC. Treating attention-deficit/hyperactivity disorder in adults: focus on once-daily medications. *Prim Care Companion CNS Disord* [Internet]. 2011 [cited 2015 Aug 27];13(6). Available from: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3304687>
[PubMed: PM22454805](#)

Additional References

11. Buck ML. Options for the management of attention deficit/hyperactivity (ADHD). *Pediatric Pharmacotherapy* [Internet]. 2011 Mar [cited 2015 Aug 27];17(3). Available from: <http://medicine.virginia.edu/clinical/departments/pediatrics/education/pharm-news/current/201103.pdf>