Amantadine

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Summary: Amantadine (Symmetrel®) is a medication that may be helpful for helping people with challenging behaviours in neurobehavioral disorders (e.g. traumatic brain injury, autism spectrum disorder) with poor executive functioning.

What is Amantadine?

Amantadine (Symmetrel®) is a medication that may be helpful for helping people with challenging behaviours in neurobehavioral disorders (e.g. traumatic brain injury, autism spectrum disorder) with poor executive functioning. It has the following features:

- Glutamatergic antagonism, i.e. it inhibits the NMDA receptor by binding to it, thus preventing excessive NMDA excitation by the glutamate neurotransmitter. By preventing the toxic effects of excessive glutamatergic neurotransmission, it may thus be helpful with various brain conditions.
- Enhancing dopamine function by enhancing dopamine release indirectly via antagonism of the NMDA receptor.

Amantadine has been around a while, having been originally approved in 1976 by the US Food and Drug Administration (FDA) as an antiviral drug to treat Influenza A, however it is no longer used for this purpose.

What Might It Be Helpful For?

Evidence suggests it may be helpful for the following:

- Behaviours
    - Aggression, challenging behaviours
- Symptoms:
    - Fatigue, distractibility, rigidity, arousal level, initiation, purposeful movement, attention and concentration, sequencing skills and processing time (Green, Hornyak, & Hurvitz, 2004).
- Side effects
    - Counteracting excessive weight gain in children/youth on atypical antipsychotics
- Brain conditions such as
    - Attention deficit hyperactivity disorder (ADHD)

- Autism spectrum disorder (ASD)
- Depression: Amantadine has been used to augment treatment-resistant depression (Stryjer et al., 2003; Rogoz et al., 2007)
- Obsessive-compulsive disorder (OCD)
- Traumatic brain injury (TBI): Amantadine is felt to have neuroprotective properties.

What is the Dosage for Amantadine?

For adolescents and adults, typically, it is started at 25-50 mg daily and increased up to 200 mg daily.
For OCD

- A study of 100 adults (aged 18-60) looked at patients with OCD who were already on Fluvoxamine 100-200 mg/day, and where amantadine was added at a dosage of 100 mg daily added (Naderi, 2018).
  - Dosage: Amantadine 100 mg daily.

For ADHD

- A study of 40 children with ADHD looked at amantadine vs. methylphenidate (20-30 mg daily) (Mohammadi, 2010), and showed that amantadine was equivalent to methylphenidate.
  - Dosage of amantadine
    - 100 mg/day for <30 kg
    - 150 mg/day for >60 kg
- A study of 24 children/youth aged 5-13 with ADHD (Donfrancesco, 2007).
  - Dosage
    - Start 50 mg / daily, increase every 4-7 days, up to 150 mg daily total.

For autism spectrum disorder (ASD)

- A study of 39 children/youth aged 5-19 with ASD (King, 2001).
  - Dosage
    - Week 1: Amantadine 2.5 mg/kg/day (as a single dose)
    - Week 2: Amantadine 5 mg/kg/ day (divided in two doses)
    - Up to 200 mg/day.

For autism spectrum disorder (ASD), where amantadine being added to other medications

- A study of 40 patients aged 4-12 looked at amantadine added to Risperidone (Risperidone dose ranged from 1-2 mg daily), and found that amantadine the combination appeared helpful, more so than Risperidone alone.
  - Dosage was
    - For children < 30 kg : Up to 100 mg/day (Mohammadi, 2013)
    - For children > 30 mg : Up to 150 mg/da

Side Effects

Amantadine is well tolerated and most taking amantadine did not report more side effects than those on placebo (King, Wright, Handen, et al., 2001).
Side effects reported most frequently (5–10% incidence) include:

- Nausea
- Dizziness (lightheadedness)
- Insomnia.

Side effects / adverse reactions reported less frequently (1–5%) include:

- Confusion,
- Somnolence,

- Anorexia,
- Dry mouth, constipation, headache, orthostatic hypotension, agitation, irritability and hallucinations.

Rarer side effects (0.1–1%) include:

- Psychosis/ paranoia, delusions, abnormal thinking, slurred speech, hypertension, urinary retention, livedo reticularis (a skin reaction) and skin rash (Endo Pharmaceuticals Inc., 2007).

References

Donfrancesco R, Calderoni D, Vitiello B. Open-label amantadine in children with attention-deficit/hyperactivity disorder. J Child Adolesc Psychopharmacol. 2007 Oct;17(5):657-64. doi: 10.1089/cap.2006.0128. PMID: 17979585.
https://pubmed.ncbi.nlm.nih.go...

Green LB, Hornyak JE, Hurvitz EA. Amantadine in pediatric patients with traumatic brain injury: a retrospective, case-controlled study. Am J Phys Med Rehabil. 2004 Dec;83(12):893-7. doi: 10.1097/01.phm.0000143400.15346.c8. PMID: 15624567.
https://pubmed.ncbi.nlm.nih.gov/15624567/
Hosenbocus S, Chahal R. Amantadine: a review of use in child and adolescent psychiatry. J Can Acad Child Adolesc Psychiatry. 2013 Feb;22(1):55-60. PMID: 23390434; PMCID: PMC3565716.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3565716/
King BH, Wright DM, Handen BL, Sikich L, Zimmerman AW, McMahon W, Cantwell E, Davanzo PA, Dourish CT, Dykens EM, Hooper SR, Jaselskis CA, Leventhal BL, Levitt J, Lord C, Lubetsky MJ, Myers SM, Ozonoff S, Shah BG, Snape M, Shernoff EW, Williamson K, Cook EH Jr. Double-blind, placebo-controlled study of amantadine hydrochloride in the treatment of children with autistic disorder. J Am Acad Child Adolesc Psychiatry. 2001 Jun;40(6):658-65. doi: 10.1097/00004583-200106000-00010. PMID: 11392343.
https://pubmed.ncbi.nlm.nih.gov/11392343/
McGrane IR, Loveland JG, Zaluski HJ. Adjunctive Amantadine Treatment for Aggressive Behavior in Children: A Series of Eight Cases. J Child Adolesc Psychopharmacol. 2016 Dec;26(10):935-938. doi: 10.1089/cap.2016.0042. Epub 2016 Aug 2. PMID: 27483360.
https://pubmed.ncbi.nlm.nih.gov/27483360/
Mohammadi MR, Kazemi MR, Zia E, Rezazadeh SA, Tabrizi M, Akhondzadeh S. Amantadine versus methylphenidate in children and adolescents with attention deficit/hyperactivity disorder: a randomized, double-blind trial. Hum Psychopharmacol. 2010 Nov;25(7-8):560-5. doi: 10.1002/hup.1154. Epub 2010 Dec 8. PMID: 21312290.
https://pubmed.ncbi.nlm.nih.gov/21312290/
Naderi S, Faghih H, Aqamolaei A, Mortazavi SH, Mortezaei A, Sahebolzamani E, Rezaei F, Akhondzadeh S. Amantadine as adjuvant therapy in the treatment of moderate to severe obsessive-compulsive disorder: A double-blind randomized trial with placebo control. Psychiatry Clin Neurosci. 2019 Apr;73(4):169-174. doi: 10.1111/pcn.12803. Epub 2018 Dec 25. PMID: 30488617.
https://pubmed.ncbi.nlm.nih.gov/30488617/

About this Article

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