

## Letter to the editor

### First preliminary results of a single case report: Duloxetine might improve some symptoms of attention-deficit hyperactivity disorder

D-amphetamine, the mixed preparation of D, L-amphetamine [14], and methylphenidate [6] are first line agents for the treatment of attention deficit disorder (ADHD). Despite the impressive track record for the stimulants in the treatment of ADHD, they fail in 25% of patients due to lack of efficacy or the emergence of unwanted side effects [3]. Recently, the selective norepinephrine reuptake inhibitor Atomoxetine showed benefit in treating ADHD, having a lower abuse potential than psychostimulants [15]. With respect to nonstimulants in treatment of ADHD, the Alpha<sub>2</sub>-receptor agonist clonidine has been used for more than 20 years [2], also based on inconsistent results of controlled studies. Furthermore, the noradrenaline reuptake inhibitor Desipramine, also drugs, affecting the Serotonin system, and the novel antidepressant bupropion have also shown some benefit [13,9]. Duloxetine is a Serotonin and norepinephrine reuptake inhibitor. We found no study, investigating the efficacy of Duloxetine treating children suffering from ADHD. For that reason, this observation was conducted to examine the effects of Duloxetine on a variety of target behaviors in a patient with ADHD.

We gave Duloxetine (30 mg/d) for 4 weeks and than Placebo for 4 weeks to a 16-year-old female patient (WISC-R IQ = 102) who suffered from ADHD for at least 11 years and who did not suffer from tic symptoms (Yale Global Tic Severity Scale [7] total tic score < 22) or obsessive-compulsive symptoms (Children's Yale-Brown Obsessive Compulsive Scale [12] total score < 15), after having excluded combined disorders like hyperthyroidism, anxiety disorder, bipolar disorder, psychosis, EEG abnormalities and suicidality. She received prior to that medication Methylphenidate 20 mg daily for 6 years, which improved symptomatology, but led to insomnia and weight-loss. The patient was diagnosed with ADHD disattention type by clinical interview and Rating Scales [5]. The ADHD Rating Scale [4] is an 18-item measure of inattention and hyperactive/impulsive symptoms derived from DSM-IV. Each symptom was scored by the child, his/her parents and his/her teacher from 0 to 3 (0 = never [or rarely], 1 = sometimes, 2 = often and 3 = very often). The scale yields three scores: an inattention score and a hyperactive/impulsive score (range = 0–27 for each score) and a total score (range = 0–54). The screening included routine laboratory tests, ECG, measurement of pulse and blood pressure, height and weight measurement, medical history, and a physical

examination. The means of the three scores were compared. An improvement was observed for the inattention score (drop from 14 to 9), the hyperactive/impulsive score (drop from 13 to 7) and the total score (drop from 27 to 16). Placebo showed scores similar to those of the before-treatment period: inattention score: 12; hyperactive/impulsive score 13 and the total score 25. With respect to the Clinical Global Impression of improvement score (1 = very much improved, 4 = no change), there was an improvement in the verum period of 2 in ADHD symptoms rated by a clinician, who did not have any information about the Duloxetine medication.

With respect to Conners Continuous Performance Test [11], Duloxetine was not associated with an improvement (baseline six omission errors, 17 commission errors; at the end of the 4-week treatment period seven omission errors and 15 commission errors), although impressingly improvement has been reported e.g. for Methylphenidate. No serious side effects were observed in laboratory test results and using the Systematic Assessment for Treatment of Emergent Events (SAFTEE) [8].

To our knowledge, this is the first study of Duloxetine in children with ADHD. The observed improvement is lower than the 50%–60% improvement reported in stimulant trials, studied in a sample of 76 children [10], but is similar than the level of improvement observed in other nonstimulant studies such as that of Desipramine, studied in a group of 62 patients [1]. These finding also raises questions about the utility of combining Duloxetine with a stimulant. In patients with ADHD, this combination might permit lower doses of the stimulant. Furthermore, Duloxetine could provide protection against tics. Questions about these effects can be answered only with further placebo-controlled, randomized studies with larger samples that focus on safety and efficacy in monotherapy with Duloxetine in this population.

### Conflicts of interests

I disclose direct or indirect financial or personal relationships, interests, and affiliations relevant to the subject matter of the manuscript that have occurred over the last two years, or that are expected in the foreseeable future. This disclosure includes, but is not limited to, grants or funding, employment, affiliations, patents (in preparation, filed, or granted), inventions, honoraria, consultancies, royalties, stock options/ownership, or expert testimony. This policy of full disclosure is similar to the policies of the International Committee of

Medical Journal Editors, the Journal of the American Medical Association, and other such organizations.

There are no acknowledgements.

I am the only author of the MS.

## References

- [1] Biederman J, Baldessarini RJ, Wright V, Knee D, Hartz JS. A double-blind placebo controlled study of desipramine in the treatment of ADHD. I: efficacy. *J Am Acad Child Adolesc Psychiatry* 1989;28:777–84.
- [2] Cohen DJ, Young JG, Nathanson JA, Shaywitz BA. Clonidine in Tourette's syndrome. *Lancet* 1979;2:551–3.
- [3] Crenshaw TM, Kavale KA, Forness SR, Reeve RE. Attention deficit hyperactivity disorder and the efficacy of stimulant medication: a meta-analysis. In: Scruggs TE, Mastropieri MA, editors. *Advances in Learning and Behavioral Disabilities*, vol. 13. Greenwich, Conn: JAI Press; 1999 p. 135–65.
- [4] DuPaul GJ, Anastopoulos AD, MacGoey KE, Power TJ, Reid R, Ikeda MJ. Teacher ratings of attention-deficit/hyperactivity disorder symptoms: factor structure and normative data. *Psychol Assess* 1998;9:436–44.
- [5] DuPaul GJ, Anastopoulos AD, Power TJ, Reid R, Ikeda MJ, MacGoey KE. Parent ratings of attention-deficit/hyperactivity disorder symptoms: factor structure and normative data. *J Psychopathol Behav Assess* 1998;20:57–81.
- [6] Greenhill LL, Abikoff HB, Arnold LE, Cantwell DP, Conners CK, Elliott G, et al. Medication treatment strategies in the MTA study: relevance to clinicians and researchers. *J Am Acad Child Adolesc Psychiatry* 1996; 35:1304–13.
- [7] Leckman JF, Riddle MA, Hardin MT, Ort SI, Swartz KL, Stevenson J, et al. The Yale Global Tic Severity Scale: initial testing of a clinician-rated scale of tic severity. *J Am Acad Child Adolesc Psychiatry* 1989;28: 566–73.
- [8] Levine J, Schooler N. SAFTEE: a technique for the systematic assessment of side effects in clinical trials. *Psychopharmacol Bull* 1986;22:343–81.
- [9] Niederhofer H. Tianeptine as a slightly effective therapeutic option for attention-deficit hyperactivity disorder. *Neuropsychobiology* 2004;49(3): 130–3.
- [10] Rapport MD, Denney C, DuPaul GJ, Gardner MJ. Attention deficit disorder and methylphenidate: normalization rates, clinical effectiveness, and response prediction in 76 children. *J Am Acad Child Adolesc Psychiatry* 1994;33:882–93.
- [11] Rosvold HE, Mirsky AF, Sarason I, Bransome ED, Beck LH. A continuous performance test of brain damage. *J Consult Psychol* 1956;20:343–50.
- [12] Scahill L, Riddle MA, McSwiggin-Hardin M, Ort SI, King RA, Goodman WK, et al. Children's Yale-Brown Obsessive Compulsive Scale: reliability and validity. *J Am Acad Child Adolesc Psychiatry* 1997;36:844–52.
- [13] Singer HS, Brown J, Quaskey S, Rosenberg LA. The treatment of attention-deficit hyperactivity disorder in Tourette's syndrome: a double-blind placebo-controlled study with clonidine and desipramine. *Pediatrics* 1995;95:74–81.
- [14] Swanson JM, Wigal S, Greenhill LL, Browne R, Waslik B, Lerner M, et al. Analog classroom assessment of ADHD in children with ADHD. *J Am Acad Child Adolesc Psychiatry* 1998;37:519–26.
- [15] Wee S, Woolverton WL. Evaluation of the reinforcing effects of atomoxetine in monkeys: comparison to methylphenidate and desipramine. *Drug Alcohol Depend* 2004;75(3):271–6.

H. Niederhofer

*Child and Adolescent Psychiatry,*

*Regional Hospital Bozen, Bolzano, Italy*

*E-mail address: [helmutniederhofer@yahoo.de](mailto:helmutniederhofer@yahoo.de)*

7 November 2007

Available online 2 October 2009