Treating Autism Pharmacologically: Also Tacrine Might Improve Symptomatology in Some Cases

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Cholinergic drugs, mainly used for patients suffering from Alzheimer’s disease, are described to be effective in treating patients suffering from autism. In 2004, Chez et al published an open-label study demonstrating that rivastigmine leads to gains in overall autistic behavior and expressive speech. Hertzmann (2003) reported improvements in verbal fluency, caused by galantamine treatment, but also mentioned verbal and behavioral regression when the patient was on donepezil. Until yet we did not find any data with regard to tacrine’s efficacy for those patients.

For late stages of Alzheimer’s disease, also glutamate antagonists (memantine) have been recommended and proven to be effective.

For that reason, we checked this substance in an open trial for 3 patients (17.4 ± 33.2 years; IQ 68 ± 11 [Wechsler Intelligence Scale] without medical or neurological illnesses, suffering from autistic disorder, diagnosed by ICD-10 criteria, which had been medication-free for at least 2 weeks, completed an open trial of Tacrine [20 mg daily]). Written informed consent was obtained. Patients were included in the study if their irritability, motoric activity, eye contact, and expressive language were significantly impaired, according to the Aberrant Behavior Checklist (Aman et al., 1985). Combined both parent and teacher ratings of irritability (off 15.6 ± 5.3; on 11.7 ± 7.3, P = .0.038), hyperactivity (off 20.6 ± 14.9; on 17.5 ± 12.3, P = .0.034), inadequate eye contact (off 8.2 ± 5.6; on 7.4 ± 3.5; P = .0.047), and inappropriate speech (off 6.4 ± 2.5; on 4.2 ± 3.5; P = .0.047) showed an only very modest improvement. None of the patients appeared to have headaches or stomachaches, although report of such side effects was limited by the expressive language and social skills of these patients.

Tacrine was the first Acetylcholinesterase-inhibitor, developed for treating Alzheimer’s disease. It seems to be effective in treating Alzheimer’s disease and may also be modestly effective in the short-term treatment of irritability in children with autistic disorder. Because of its late proven hepatotoxicity its registration in many countries has been cancelled. In a short-term trial we did not see any sign for hepatotoxicity, which cannot be excluded in case of long-term treatment. Despite no excludable minimal benefits in some cases, Tacrine cannot be recommended as an helpful drug for patients suffering from autism, mainly because of its proven hepatotoxicity.

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References


Response to “Treating Autism Pharmacologically”

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I was interested in reading the correspondence from Dr Niederhofer regarding yet another clinical observation of improvement using drug therapy in autistic patients that modulates acetylcholinergic function. This use of tacrine is the only one I have read and shows similar promise to prior small reports with galantamine by Hertzmann and the small series by Harden and Handen using donepezil. This work is supported by basic anatomical studies reporting decreased a4b2 nicotinic receptors in basal forebrain and decreased parietal M1 muscarinic receptors in brain specimens from autistic individuals by Perry and colleagues. A published open-label and double-blinded experience was reported with donepezil by Chez et al and an open-label treatment with rivastigmine also exists that supports therapeutic benefit to autistic patients with these medications. Given the better safety profile of newer agents such as galantamine, donepezil, and rivastigmine over tacrine, it is probably advisable to use the newer cholinesterase inhibitors. The deficits in autism...
are cholinceptive from deficient receptor density, and this differs from Alzheimer dementia where acetylcholine-producing cells are reduced.

It is interesting that Dr Niederhofer mentions memantine as well in Alzheimer disease. In recent publications, Chez\(^7\) has shown that in 30 autistic spectrum disorder patients, clinical improvement in language and behavior using a clinical global impression rating was observed in clinical treatment with memantine. This drug, however, works in presumed excessive glutaminergic excitability also observed in autistic brain studies.

Most important, the scientific community is exploring therapeutic options that may impact improved quality of life in autistic patients based on clinical and basic scientific observations mentioned above. More work in this disease is warranted and should be encouraged in pediatric neurology.

Michael G. Chez, MD

References


**Long-Term Follow-Up of Hearing Loss in Biotinidase Deficiency**

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A young patient with biotinidase deficiency and high-frequency hearing loss was previously reported.\(^1\) Biotin supplementation therapy was initiated, and the patient experienced no further hearing loss. Long-term follow-up of the patient at 10 years of age has been obtained and shows that she continues to have high-frequency hearing loss (Figure 1A and 1B). Although her hearing has stabilized, it has not returned to the normal range as stated in the original case report. This case illustrates the importance of early recognition and treatment of biotinidase deficiency in preventing pediatric sensorineural hearing loss.

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**Reference**