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Is guanfacine useful in the treatment of attention deficit hyperactivity disorder?

Guanfacine, an α_2-adrenergic agonist with more affinity for the α_{2A} receptor than clonidine, has been available for well over 2 decades. Recently, there has been a resurgence of interest in this centrally acting antihypertensive medication, including its possible use in the treatment of attention deficit hyperactivity disorder (ADHD). The α_2 receptors of the prefrontal cortex appear to be important in cognitive processes such as memory, learning and selective attention, particularly in preventing distractions of irrelevant stimuli. Specific syndromes of inattentiveness or age-related degeneration of the locus ceruleus with catecholamine depletion of the prefrontal cortex may account for significant functional impairment in many patients, and this has stimulated interest in the possible therapeutic utility of α_2 receptor agonists.

Guanfacine's potential benefit in ADHD, post-traumatic stress disorder, nightmares, Tourette's syndrome, age-associated memory impairment, substance abuse and cognitive impairment in schizophrenia has been studied. Compromised attention is a feature of many, if not most, psychiatric illnesses. In addition, ADHD is often comorbid with other disorders, including oppositional defiant disorder, learning disability, depression and anxiety.

In an open-label study of patients with comorbid ADHD and Tourette's disorder, Chappell and colleagues (Chappell et al, *J Am Acad Child Adolesc Psychiatry* 1995;34: 1140-6) found that guanfacine improved commission and omission errors on continuous performance tests. There was also a significant decrease in motor and phonic tics. A recent placebo-controlled study of guanfacine in the treatment of tic disorders and ADHD in children demonstrated similar results (Scahill et al, *Am J Psychiatry* 2001; 158:1067-74). After 8 weeks, there was a mean improvement of 37% in the total score on the teacher-rated ADHD Rating Scale. In the guanfacine group, continuous performance test measures declined by 17%–22% (in contrast with the increase in errors in the placebo group) and tic severity decreased by 31%. In a double-blind placebo-controlled crossover study comparing the efficacy of guanfacine with dextroamphetamine for the treatment of adult ADHD, both drugs significantly reduced attention deficit hyperactivity symptoms on behaviour checklists and cognitive measures of attention (Taylor et al, *J Clin Psychopharmacol* 2001;21:223-8).

Studies have demonstrated that regional blood flow in the frontal lobe increases after treatment with guanfacine, especially in the dorsolateral prefrontal cortex, without significant effect in the superior temporal cortex or auditory association area unrelated to task performance (Avery et al, *Neuropsychopharmacology* 2000;23:240-9). The hypothesis that the α_2-adrenergic receptor preferentially enhances functioning of the prefrontal cortex and thus working memory is supported by these data.

Most of the evidence to date suggests that guanfacine is well tolerated with few side effects; those commonly reported include fatigue and headache. Problems with hypotension are rarely reported, and manic symptoms are infrequent.

Although the role of guanfacine in ADHD is unclear, there is increasing evidence to support the view that guanfacine should be considered in patients with ADHD who have been nonresponsive to other medications. Some argue that guanfacine's favourable side-effect profile should move it higher in the treatment paradigm, and it has also been suggested that its properties in reducing tic severity should raise its profile in treating comorbid ADHD in Tourette's syndrome.

In summary, evidence to date suggests that guanfacine may have a role to play in the treatment of ADHD and other conditions, but further controlled studies are required.

Gary Hnatko, BMSc, MD, FRCPC
Department of Psychiatry
University of Alberta
Edmonton, Alberta, Canada

The information in this column is not intended as a definitive treatment strategy but as a suggested approach for clinicians treating patients with similar histories. Individual cases may vary and should be evaluated carefully before treatment is provided.