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Pharmacotherapy for Impulsivity-hyperactivity Behaviors in Autism Spectrum Disorder

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Abstract

Hyperactivity is a shared behavior with ASD and Attention Deficit Hyperactivity Disorder (ADHD). Medications such as Methylphenidate (MPH) and α 2-a adrenergic receptor agonists are used to modify hyperactivity behavior in ADHD and thus have been used as management in ASD. A review of literature was done to evaluate the use of medications typically used for ADHD in the use of ASD. The databases searched included PubMED, PsycINFO, Cochrane, and Clinical Key. After reviewing the literature, it was found that both MPH and 2-a adrenergic receptor agonist have a potential role in pharmacotherapy for ASD. MPH may be slightly more effective at reducing hyperactivity-impulsivity behaviors than 2-a adrenergic receptor agonist, however the side effect profile in MPH has led to more discontinuations over 2-a adrenergic receptor agonist. More studies would need to be conducted to validate the findings of this review.

Keywords: *ASD, ADHD, PDD-NOS, Asperger syndrome, autistic disorder, Hyperactivity, Stimulants, MPH, Guanfacine, Clonidine*

Introduction

- Incidence of Autism Spectrum Disorder (ASD) in 8-year old children is 1 in 59.
- Autism includes deficits in social emotional reciprocity, non-verbal communication for social interactions, developing and maintaining relationships and in some cases, hyperactivity response to sensory input
- ASD often shares similar behavior profiles to ADHD. These behaviors include impulsiveness and hyperactivity.

Statement of the Problem

- ASD and ADHD behaviors interfere negatively with daily living for children, peers, teachers and parents/caregivers, which makes day to day life difficult for both the child and others involved.
- Pharmacotherapy is often used to help manage these behaviors and to make daily living more manageable for the child and those around them.
- The first line pharmacotherapy for children with ADHD is typically a stimulant. Due to similarities in behavior profiles, psychostimulants are used off-label for impulsivity-hyperactivity behaviors in children with ASD without a comorbid diagnosis of ADHD.
- Research needs to be done to investigate the effectiveness of these medications in children with ASD to help explore further management of these behaviors.

Research Questions

1. In children with ASD, are psychostimulants, such as MPH as effective at reducing impulsivity-hyperactivity behaviors as compared to children with ADHD according to teacher and parent reports?
2. In children with ASD, are α 2-a adrenergic receptor agonists, such as clonidine and guanfacine, more effective at reducing impulsivity-hyperactivity behaviors as compared to psychostimulants such as MPH, according to teacher and parent reports?
3. Are the rates of discontinuation of pharmacotherapy in children with ASD higher in treatment with MPH vs clonidine or guanfacine?

Literature Review

Methylphenidate as a treatment for impulsivity-hyperactivity in ASD

- 8 out of 13 children were deemed responders to MPH (Handen, Johnson & Lubetsky, 2000).
- According to research conducted by RUPP, “Our response rate of 49% is less than the previously described response rates of 70% to 80% seen in typically developing children with ADHD”
- MPH was found to be superior to placebo at reducing hyperactivity (Quintana et al., 1995).

Methylphenidate as a treatment for impulsivity-hyperactivity in ADHD

- 80% of the 314 subjects were deemed responders to MPH (Greenhill, Findling & Swanson, 2002).
- It was found that MPH was statistically significant over placebo. 52% of 177 subjects in the active medication group achieved some benefit from MPH (Wilens et al., 2006).

α 2-a receptor agonists as treatment for impulsivity-hyperactivity in ASD

- 19 of the 80 subjects (23.8%) were deemed as “responder” (Posey, Puntney, Sasher, Kem & Mcdougle, 2004).

FIG. 1. Global response to guanfacine in 80 subjects with pervasive developmental disorders based on the Clinical Global Impressions global improvement item.

- A study conducted by RUPP showed that 50% of participants were deemed responders to the active medication of guanfacine

Efficacy of α 2-a receptor agonists in ADHD

- Significant improvement was found in Clonidine over placebo (Jain et al., 2011).
- Guanfacine was found to be superior to placebo (Newcorn et al., 2013)
- All subjects receiving active guanfacine showed statistically significant improvement (Sallee et al., 2009).

Causes for discontinuation of pharmacotherapy with methylphenidate in the treatment of ASD

- There were no statistically significant side effects found when comparing MPH to placebo (Quintana, et al., 1995).
- Three of the thirteen children that participated in this study discontinued early due to adverse side effect (Handen, Johnson & Lubetsky, 2000).

Literature Review, cont.

Causes for discontinuation of pharmacotherapy with methylphenidate in ADHD

- Of the 314 children in the study, two discontinued the treatment due to adverse events (Greenhill, Findling & Swanson, 2002).
- Of the 220 subject, there was one serious adverse event requiring discontinuation in which a subject threatened suicide (Wilens, et al., 2016).

Causes for discontinuation of pharmacotherapy with α 2-a receptor agonists in ASD

- None of the subjects discontinued use of clonidine during the trial due to adverse side effects (Jaselskis, Cook, Fletcher & Leventhal, 1992).
- In no case did side effects lead to discontinuation of guanfacine in this study (Posey, Puntney, Sasher, Kem & Mcdougle, 2004).
- 16% of subjects withdrew due to adverse effects associated with guanfacine (Scahill et al., 2006).

Causes for discontinuation of pharmacotherapy with α 2-a receptor agonists in ADHD

- The total rate of discontinuation due to side effects in this trial were GXR of 7.4% and placebo at 7.6% (Sallee et al., 2009).
- There were nine participants that ultimately withdrew from the study due to adverse effects (Wilens et al., 2015).

Discussion

- The number of subjects in the ASD studies ranged from 9-13 compared to the ADHD studies which ranged from 220-314.
- The response rate to MPH in the ASD group ranged from 49-61%, whereas, responders in the ADHD population ranged from 52-81%.
- MPH and α 2-a adrenergic receptor agonists were both found to be statistically significant at modifying impulsivity-hyperactivity behavior in children with Autism.
- The most common reasons for discontinuation of MPH were irritability, crying, tantrums, skin picking and aggression
- The most common reasons for discontinuations of 2-a adrenergic receptor agonists were excessive fatigue, somnolence, irritability and emotional lability.
- Further research needs to be conducted with large scale studies to validate the data found.

Applicability to Clinical Practice

- Behaviors associated with Autism such as hyperactivity and impulsivity are often detrimental in various situations of life.
- The increasing incidence of autism is evidence that continued investigation and evaluation of the most efficacious medical management is needed to meet the needs of this increasing population.
- By identifying the most efficient pharmacological therapy for these behaviors, providers can help to prescribe an appropriate medication regimen to improve quality of life for both patients and caregivers.

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