Follow up Study on Attention Deficit Hyperactivity Disorder Patients with and Without Comorbid Mood Disorders Receiving Non Stimulant Medication

Thesis

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List of Abbreviations

Abb.	Full term
AAP	*American Academy of Pediatrics.*
ADHD	*Attention deficit hyperactivity disorder.*
ADHD-C	*Attention deficit hyperactivity disorder - Combined type.*
ADHD-I	*Attention deficit hyperactivity disorder - Inattentive type.*
ADHD-RSIV	*Attention-Deficit Hyperactivity Disorder Rating Scale-IV.*
ASD	*Autistic spectrum disorder.*
ATX	*Atomoxetine.*
BD	*Bipolar disorder.*
BPD	*Bipolar disorder.*
CADDRA	*Canadian Attention Deficit Hyperactivity Disorder Resource Alliance.*
CBT	*Cognitive behavioral therapy.*
CC	*Corpus callosum.*
CD	*Conduct disorder.*
CDI	*Children Depression Inventory.*
CDRS-R	*Children's Depression Rating Scale-Revised.*
CNS	*Central nervous system.*
CPRS-R:L	*Conners' Parent Rating Scale-Revised: Long Version.*
CSF	*Cereprospinal fluid.*
DA	*Dopamine.*
DD	*Developmental disorder.*
DMDD	*Disruptive Mood Dysregulation Disorder.*
DSM-5	*Diagnostic and Statistical Manual of Mental Disorders, fifth edition.*
DTI	*Diffusion tensor imaging.*
EMs	*Extensive metabolizers.*
FDA	*United States Food and drug administration.*

List of Abbreviations cont...

Abb.	Full term
GIRK	*G-protein-coupled inwardly rectifying potassium channels.*
IQ	*Intelligence Quotient.*
K-SADS	*The Kiddie Schedule for Affective Disorder and Schizophrenia for School Age Children.*
MDD	*Major depressive disorder.*
MRI	*Magnetic resonance imaging.*
MTA	*Multimodal Treatment Study of Children with ADHD.*
NE	*Nor-epinephrine.*
NMDA	*N-Methyl-D-aspartic acid*
NNTH	*Number needed to harm*
NNTB	*Number needed to treat inorder to benifit*
ODD	*Oppositional Defiant Disorder.*
PBR	*Pediatric behavior rating scale.*
PFC	*Prefrontal cortex.*
QoL	*Quality of life.*
SD	*Standard deviation.*
SMs	*Slow metabolizers.*
SPSS	*Statistical Package for the Social Sciences.*
SSRI	*Selective serotonin reuptake inhibitors.*
TADS	*Treatment of Adolescent Depression Study.*
TMAP	*Texas Medication Algorithm Project.*
TMS	*Transcranial magnetic stimulation.*
WM	*White matter.*

INTRODUCTION

ADHD is a rather common condition that affects about 5 % of the children and adolescents and 2.5% of the adults ***(Polanczyk et al., 2014)***. ADHD frequently co-occurs with other psychiatric disorders ***(Skirbekk et al., 2011).*** It is characterized by cross-situational impairments in attention, activity and impulse control which in 60% of the childhood cases persists to adulthood ***(Sibley et al., 2017).***

Young people with ADHD and depression are more impaired than those with ADHD or depression alone. Therefore, identifying young people with ADHD who are at risk of depression and other comorbid mood symptoms or disorders is important, in terms of facilitating early intervention or prevention ***(Blackman et al., 2005).***

Mood symptoms such as irritability and its features are common in ADHD, even though it is not a defining diagnostic feature, it can be described as a propensity to react with anger, grouchiness, or tantrums disproportionate to the situation ***(Stringaris et al., 2010)*** and when included in the broader definition of emotional dysregulation, it is present in around 25-45% of children with ADHD ***(Shaw et al., 2013)***.

In recent years an "irritable" dimension of Oppositional Defiant Disorder (ODD) has been identified ***(Stringaris et al., 2010).*** This includes the items "often loses temper", "is often

angry and resentful", and "is often touchy or easily annoyed by others", all of which are common in ADHD and all of them are considered mood symptoms ***(Vidal-Ribas et al., 2016)***.

More recently, severely impairing childhood chronic irritability has been conceptualized as a new diagnostic category in the mood disorders section of the Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5) ***(American Psychiatric Association, 2013).*** This new diagnostic category, known as Disruptive Mood Dysregulation Disorder (DMDD), is characterized by severe temper outbursts that are grossly out of proportion in intensity or duration to the situation. Alongside these temper outbursts the child experiences a persistently irritable or angry mood most of the day, nearly every day ***(Copeland et al., 2013).***

Early research into DMDD in the general population, where existing data have been used to derive diagnoses retrospectively, suggests that the prevalence ranges from 0.8% to 3.3% ***(Copeland et al., 2013).*** Children with DMDD have been found to be very impaired, with high rates of comorbidity including depression ***(Dougherty et al., 2014).*** DMDD in the context of ADHD has not been studied widely. Results from community samples suggest that 4.3-23.5% of those with ADHD meet DMDD diagnostic criteria ***(Copeland et al., 2013; Mulraney et al., 2016).*** Therefore, the findings to date suggest that DMDD is more common in those with ADHD than in the general population ***(Mulraney et al., 2016).***

The comparative efficacy and safety of pharmacological and non-pharmacological treatments are largely unknown, mainly because of the paucity of head-to-head trials. A wide variety of interventions have been used for the treatment of ADHD, including pharmacological and psychological interventions, herbal and homeopathic remedies, and dietary management ***(CatalaÂ-LoÂpez et al., 2017)***.

Stimulant medications (e.g., amphetamine, and methylphenidate) and non-stimulant medications (e.g., atomoxetine, guanfacine and clonidine) are the two categories of medications approved for treating ADHD. Among these, long term treatment with atomoxetine and methylphenidate is not only proven to be clinically efficacious, but also improves a wide range of executive functions and focused attention among children with ADHD ***(Gau and Shang, 2010).***

Atomoxetine as a non-stimulant treatment, approved in the United States for the treatment of ADHD in November 2002, it is a non-stimulant that is thought to act presynaptically via the inhibition of norepinephrine reuptake. Atomoxetine has limited effect on the serotonin or dopamine transporters and has low affinity at dopaminergic, muscarinic-cholinergic, histaminic, serotonergic and a1- or a2-adrenergic receptors ***(Spencer et al., 2002).***

RATIONALE OF THE WORK

ADHD is a chronic disorder that may affect all aspects of a child's life including academic difficulties and social skills problems. It also causes a burden on families and society, which makes it a major public health problem. ADHD is very often associated with other comorbidities, particularly mood and anxiety disorders. Comorbid disorders, recognized or unrecognized, may also complicate the treatment process. However, there are a relatively few studies were conducted to assess the effect of ADHD associated comorbidities on the treatment process. In this study, Non-stimulant treatment (Atomoxetine) was chosen because of its availability and continuity at Ain Shams university child psychiatry clinics.

HYPOTHESIS

In this study it was expected that the presence of comorbid mood disorder with ADHD will affect or decrease the response of ADHD symptoms to non-stimulant treatment.