Serum Testosterone Level in Pediatric Patients with Attention Deficit Hyperactivity Disorder

Thesis

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List of Abbreviations

Abbrev.	Full-term
ACTH	**:** Adrenocorticotrophic Hormone
ADHD	**:** Attention Deficit Hyperactivity Disorder
ADHD-C	**:** Attention Deficit Hyperactivity Disorder Combined
ADHD-PH	**:** Attention Deficit Hyperactivity Disorder Predominantly Hyperactive
ADHD-PI	**:** Attention Deficit Hyperactivity Disorder Predominantly Inattentive
ATX	**:** Atomoxetine
AUC	**:** Area Under the Curve
BMI	**:** Body Mass Index
CBT	**:** Combined Behavioral Therapy
CC	**:** Corpus Callosum
CEBM	**:** Center for Evidence-Based Medicine
CGI	**:** Conner's Global Index
CPRS	**:** Conner’s Parent Rating Scale
CPRS-L	**:** Conner’s Parent Rating Scale-revised; Long version
DA	**:** Dopamine
DAT	**:** Dopamine Active Transporters
DAT-1	**:** Dopamine Transporter 1
DBD	**:** Disruptive Behavior Disorders
DEX	**:** Dextroamphetamine
DHA	**:** Docosahexaenoic Acid
DHEA	**:** Dehydroepiandrosterone
DHT	**:** Dihydrotestosterone
DSM-V	**:** Diagnostic and Statistical Manual fifth edition

DTI : Diffusion Tensor Imaging
ECLIA : Electrochemiluminescence Immunoassay
EPA : Eicosapentaenoic Acid
FDA : Food and Drug Administration
FN : False Negative
FP : False Positive
FSH : Follicle Stimulating Hormone
GBG : Gonadal steroid Binding Globulin
G : Ginko
GnRH : Gonadotropin Releasing Hormone
GxE : Gene-Environment interactions
HPA : Hypothalamic–Pituitary–Adrenal axis
HREs : Hormone Response Elements
HS : Highly Significant
ICD-10 : International Classification of Diseases, tenth edition
LH : Luteinizing Hormone
MPH : Methylphenidate Hydrochloride
MRI : Magnetic Resonance Imaging
NE : Norepinephrine
NICE : National Institute for Clinical Excellence
ng/dl : Nanogram/desilitre
NS : Non-significant.
PUFAs : Polyunsaturated Fatty Acids
PET : Positron Emission Tomography
REM : Rapid Eye Movement
S : Significant
SDS : Standard Deviation Score
SHBG : Sex Hormone-Binding Globulin
sig. : Significant
T : Testosterone

TN **:** True Negative
TP **:** True Positive
TRT **:** Testosterone Replacement Therapy
WM **:** White Matter

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ABSTRACT

BACKGROUND: Attention deficit hyperactivity disorder (ADHD) is considered one of the most common neurobehavioral disorders of childhood. In recent years, the impacts of various hormones on ADHD have been studied. However, testosterone has received much less attention. The aim of this study was therefore to investigate serum total testosterone level in children with ADHD.

METHODS: This is a case control study of 70 ADHD patients were recruited from Child and adolescent psychiatry clinic in the children hospital, Ain shams university and 30 healthy controls were included in the study. The mean age of both groups was 7.82 $\pm$ 1.4 and 7.52 $\pm$ 1.4 years old respectively. Serum total testosterone was measured by Electrochemiluminescence immunoassay.

RESULTS: Serum total testosterone was found to be significantly higher in children with ADHD compared to healthy controls ($P < 0.01$).

CONCLUSION: This study has evidenced a significant high level of serum total testosterone in children with ADHD. There is an association between higher serum total testosterone concentration and ADHD in childhood. Therefore there is a need for regular monitoring of serum total testosterone levels and treatment of patients with high testosterone level.

KEYWORDS: attention-deficit-hyperactivity disorder; children; total testosterone

Introduction

Attention deficit hyperactivity disorder (ADHD) is a debilitating mental health disorder, which is marked by symptoms of inattention, overactivity and impulsiveness that have an early onset, and are age inappropriate, persistent and pervasive. It affects children over their school years and into adulthood and is associated with a number of impairments that impinge on a range of social and health care systems (education, criminal justice, mental health, social services and so on). Those with ADHD are at increased risk of delinquency, criminality, educational failure and mental illness ***(McCann et al., 2014).***

ADHD is considered to develop from an interaction between genetic and environmental factors, with numerous developmental neurotoxicants significantly increasing the risk for a diagnosis of ADHD ***(Malin and Till, 2015).***

Sex hormones play many roles in the development and function of the human body and brain. Organizational effects of hormones are believed to play an important role in the structural organization of the brain and body with subsequent effects on sex typed behavior ***(Roberts and Martel, 2013).***

Testosterone affects the behavior of adults, but little is known about how it might affect the behavior of children. The few available studies of children have focused on aggression, hyperactivity and other behavior disorders ***(Mehta et al., 2008).***

Aim of the Work

This study aims at:

- Evaluation of testosterone level in a group of pediatric patient with ADHD and comparison of these levels with a control children.
- Correlation of levels to disease severity.

Attention Deficit Hyperactivity Disorder (ADHD)

Attention Deficit Hyperactivity Disorder (ADHD) is considered one of the most common neurobehavioral disorders of childhood ***(Wolraich et al., 2011).*** ADHD is characterized by the early onset of age-inappropriate persistent and pervasive symptoms of inattention, hyperactivity and impulsivity ***(Banaschewski et al., 2010).***

Clinical presentation is heterogeneous with three subtypes identified according to the most prevalent symptoms (primarily inattentive, primarily hyperactive/ impulsive, and combined) and with a relative context dependence of symptom expression although the condition has a chronic course ***(Fair et al., 2012).***

ADHD is associated with cognitive impairments in inhibitory control and executive functions (Fair et al., 2012) but neuropsychological profiles of subjects with ADHD, despite significantly differing from controls in group comparisons, also show considerable inter and intra individual variability. This clinical heterogenecity is likely to reflect the multiplicity of causal pathways leading to the development of the disorder and of a series of moderating and mediating factors involved in symptom expression ***(Lahey et al., 2005).***

Diagnosis of ADHD:

There are two sets of diagnostic criteria used to define ADHD: the Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSMV) ***(American Psychiatric Association et al., 2013)*** (Previously the DSM-IV-TR which was used before May 2013) and the International Classification of Diseases, tenth edition (ICD-10) ***(World Health Organization et al., 1992).***

DSM-V-Diagnostic Criteria for Attention Deficit Hyperactivity Disorder *(American Psychiatric Association, 2013)* must meet criteria for inattention, hyperactivity/ impulsivity, or both.

1. Inattention

17 and younger: Six or more of these symptoms must be present for at least 6 months, be inconsistent with the child's developmental level, and have a negative effect on their social and academic activities. To be endorsed, the following must occur "often":

- Often fails to play close attention to details
- Often has trouble sustaining attention
- Often doesn't seem to listen when spoken to directly
- Often fails to follow through on instructions and fails to finish schoolwork or chores
- Often has trouble getting organized