Aripiprazole Added on for DMDD in Youths with ADHD (AAOFDIYWA)

This study has been completed.

**Sponsor:**
Tri-Service General Hospital

**ClinicalTrials.gov Identifier:**
NCT03358277

First Posted: November 30, 2017
Last Update Posted: November 30, 2017

The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. Read our disclaimer for details.

**Collaborator:**
Ministry of Science and Technology, Taiwan

**Information provided by (Responsible Party):**
Chin-Bin Yeh, MD, PhD, Tri-Service General Hospital

#### Purpose

**Objectives:**

1. To investigate the effectiveness of adjuvant with aripiprazole to methylphenidate for disruptive mood dysregulation disorder (DMDD) in youths with attention-deficit/hyperactivity disorder (ADHD)
2. To investigate the neural basis of chronic irritability in youths with functional magnetic resonance imaging (fMRI)
3. To compare the clinical characteristics of youths with comorbid ADHD and DMDD to youths with ADHD only

<table>
<thead>
<tr>
<th>Condition</th>
<th>Intervention</th>
</tr>
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<tbody>
<tr>
<td>Disruptive Mood Dysregulation Disorder</td>
<td>Drug: MPH + APZ</td>
</tr>
</tbody>
</table>

Study Type: Interventional

Study Design: Intervention Model: Single Group Assignment

Masking: None (Open Label)

Primary Purpose: Treatment

Official Title: Aripiprazole Added on Methylphenidate in the Treatment of Youths With Comorbid ADHD and DMDD

Resource links provided by NLM:

Drug Information available for: Methylphenidate, Methylphenidate hydrochloride, Aripiprazole
Primary Outcome Measures:

- Child Behavior Checklist (CBCL) total and subscale scores [Time Frame: six weeks]

Secondary Outcome Measures:

- Beck Youth Inventories-II total and subscale scores [Time Frame: six weeks]
  An self-reported inventory to evaluate children's and adolescents' emotional and social impairment. It includes five subscales: depression, anxiety, anger, disruptive behaviour, and self-concept.

- Conner's Continuous Performance Test [Time Frame: six weeks]
  A task-based computerized assessment of attention problems and neurological functioning

- Children Color Trail Test (CCTT) [Time Frame: six weeks]
  The CCTT assesses sustained attention, sequencing, and other executive functions.

- Resting state functional magnetic resonance imaging [Time Frame: six weeks]
  A method of functional brain imaging that can be used to evaluate regional interactions that occur when a subject is not performing an explicit task.

- Swanson, Nolan, and Pelham Scale—version IV (SNAP-IV) total and subscale scores [Time Frame: six weeks]
  The items from the DSM-IV (1994) criteria for Attention-Deficit/Hyperactivity Disorder (ADHD) are included for the two subsets of symptoms: inattention (items #1-#9) and hyperactivity/impulsivity (items #11-#19). Also, items are included from the DSM-IV criteria for Oppositional Defiant Disorder (items #21-#28) since it often is present in children with ADHD.

Enrollment: 58

Actual Study Start Date: November 19, 2014

Study Completion Date: August 12, 2017

Primary Completion Date: August 12, 2017 (Final data collection date for primary outcome measure)

<table>
<thead>
<tr>
<th>Arms</th>
<th>Assigned Interventions</th>
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</thead>
<tbody>
<tr>
<td>Experimental: ADHD+DMDD Group</td>
<td>Drug: MPH + APZ</td>
</tr>
<tr>
<td>The subjects with comorbid ADHD and</td>
<td>MPH was administered with either Ritalin (from 10mg/day to</td>
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<tr>
<td>DMDD received pharmacological</td>
<td>40mg/day) or Concerta (from 18mg/day to 36mg/day) according</td>
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<tr>
<td>intervention with combination</td>
<td>clinical judgement for six weeks. APZ was</td>
</tr>
<tr>
<td>treatment of MPH+ APZ with</td>
<td>administered with dose from 2.5mg/day to 5mg/day</td>
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<tr>
<td>flexible dosage according to</td>
<td>according to clinical judgement for six weeks.</td>
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<tr>
<td>clinical judgment for six weeks.</td>
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</tbody>
</table>
**Detailed Description:**

**Background:**
Disruptive mood dysregulation disorder (DMDD) in children and adolescents with attention-deficit/hyperactivity disorder (ADHD) is a common clinical challenge and leads to severe impact and burden on both the patients and their family. Although methylphenidate (MPH) showed good efficacy in the treatment of ADHD, there is still lack of well-established pharmacological treatment for DMDD. Furthermore, little research focuses on the effect of pharmacological treatment on neural correlates of chronic irritability. Previous literature suggested the potential role of atypical antipsychotics in the treatment of DMDD. Therefore, this study aimed to investigate the effectiveness of adjuvant of aripiprazole (APZ) to MPH in patients with comorbid ADHD and DMDD. In addition, we explored the clinical manifestation and neural basis of DMDD using inventories, neuropsychological tests and neuroimaging studies.

**Methods:**
We enrolled patients with ADHD+DMDD (n = 31) and ADHD only (n = 27). Those subjects were evaluated with inventories of emotional and behavioral problems, neuropsychological tests, as well as fMRI with challenging tests which aimed to induce frustration at baseline assessment. Then, subjects of ADHD+DMDD group received 6 weeks' combination treatment of MPH+APZ with flexible dosage according to clinical judgment. All the initial evaluations were administered again after treatment. The comparison of clinical characteristics and neuroimaging findings between ADHD+DMDD group and ADHD only group will be conducted. In addition, the effectiveness of treatment will be analyzed. The effects of pharmacological treatment on neural correlates of chronic irritability will also be investigated.

**Eligibility**

**Information from the National Library of Medicine**

*Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the contacts provided below. For general information, Learn About Clinical Studies.*

**Ages Eligible for Study:** 7 Years to 17 Years (Child)
**Sexes Eligible for Study:** All
**Accepts Healthy Volunteers:** No

**Criteria**

**Inclusion Criteria:**
For subjects with comorbid ADHD and DMDD:
- Subject meets the DSM-5 criteria for ADHD and DMDD
- Subject is free from prior psychotropic medication for at least one year
For subjects with ADHD only:
- Subject meets the DSM-5 criteria for ADHD and DMDD
- Subject is free from prior psychotropic medication for at least one year

**Exclusion Criteria:**
- Patients not willing to participate in the study after detailed explanation
- Patients who could not follow the investigator's instructions
- Patients with severe neurological or mental illness such as epileptic disorder, schizophrenia, bipolar disorder, mental retardation or uncontrolled suicide risk
- Patients with severe medical illness or surgical conditions which were judged by investigators for safety concerns as inappropriate for this study, such as uncontrolled abnormal thyroid function, history of heart attack, uncontrolled hypertension.
- Patients taking psychotropic medication within one year prior to the evaluation for entering our study
- Patients being allergic to methylphenidate or aripiprazole
- Female patients being pregnant, nursing, or lactating

**Contacts and Locations**

Information from the National Library of Medicine

To learn more about this study, you or your doctor may contact the study research staff using the contact information provided by the sponsor.

Please refer to this study by its ClinicalTrials.gov identifier (NCT number): **NCT03358277**

**Sponsors and Collaborators**

Tri-Service General Hospital
Ministry of Science and Technology, Taiwan

**Investigators**

Principal Investigator: Chin-Bin Yeh, MD, PhD
Tri-Service General Hospital, National Defense Medical Center

**More Information**

Responsible Party: Chin-Bin Yeh, MD, PhD, Director of Department of Psychiatry, Tri-Service General Hospital

ClinicalTrials.gov Identifier: **NCT03358277**
History of Changes

Other Study ID Numbers: TSGH 099-05-159
First Submitted: November 24, 2017
First Posted: November 30, 2017
Last Update Posted: November 30, 2017
Last Verified: November 2017

Individual Participant Data (IPD) Sharing Statement:

Plan to Share IPD: No

Studies a U.S. FDA-regulated Drug Product: No
Studies a U.S. FDA-regulated Device Product: No

Additional relevant MeSH terms:
- Aripiprazole
- Methylphenidate
- Antipsychotic Agents
- Tranquilizing Agents
- Central Nervous System Depressants
- Physiological Effects of Drugs
- Psychotropic Drugs
- Central Nervous System Stimulants
- Dopamine Uptake Inhibitors
- Neurotransmitter Uptake Inhibitors
- Membrane Transport Modulators
- Molecular Mechanisms of Pharmacological Action
- Dopamine Agents
- Neurotransmitter Agents