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BRIEF REPORT

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# Effectiveness and adverse effects of methylphenidate treatment in children diagnosed with disruptive mood dysregulation disorder and attention-deficit hyperactivity disorder: a preliminary report

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**ABSTRACT**

**Objective:** Comorbidity with attention deficit hyperactivity disorder (ADHD) and disruptive mood dysregulation disorders (DMDD) is very common in children and adolescents In this study, we aimed to present a retrospective study of methylphenidate (MPH) treatment in 12 cases who were diagnosed with DMDD and ADHD.

**Method:** All patients were followed-up in our outpatient clinic and the effectiveness and side effects of MPH were explored. Mood Symptom Questionnaire (MSQ-7) and Clinical Global Impression-Severity (CGI-S) were used for assessing the mood symptoms and their severity.

**Results:** The differences between initiation time and the end-point time in CGI-S and MSQ-7 scores were statistically significant.

**Conclusion:** In this present study, the usage of MPH was found to lead to an increase in irritability in children with ADHD and DMDD evidently.

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**KEYWORDS**
Adverse effect; attention-deficit hyperactivity disorder; disruptive mood dysregulation disorder; methylphenidate

## Introduction

Attention-deficit hyperactivity disorder (ADHD) is one of the most common childhood neurodevelopmental disorders, the worldwide prevalence rate of ADHD is 5% and MPH is frequently the first choice treatment of ADHD [1]. Comorbidity with ADHD and disruptive mood dysregulation disorders (DMDD) is very common in children and adolescents [2]. It is little known how DMDD symptoms affect ADHD treatment. In this study, a retrospective analysis of MPH treatment in 12 cases who were diagnosed with DMDD and ADHD was presented; they were followed-up in outpatient clinic and the effectiveness and side effects of MPH were evaluated.

## Method

All included cases were presented to the Outpatient Clinic of Dokuz Eylul University School of Medicine's Department of Child and Adolescent Psychiatry. Their diagnostic confirmation of ADHD and DMDD was provided according to the Kiddie-Sads-Present and Lifetime Version (K-SADS-PL). Their sociodemographic data, treatments, medication times, doses and adverse effects of MPH were evaluated retrospectively by experienced child psychiatrists. The Mood Symptom Questionnaire (MSQ-7) and The Clinical Global Impression-Severity (CGI-S) were used for assessing the mood symptoms, irritability and their severity. We analyzed some of patients' follow-up data retrospectively from the study of Pervasive Developmental Disorder traits of DMMD and bipolar disorder. The research protocol was approved by the Dokuz Eylul University of Medical Sciences Research Ethics Committee (Date:12.05.2011; No:2011/16-23). *Post hoc* analysis with Wilcoxon signed-rank tests was conducted. MSQ and CGI scores with a Bonferroni correction were performed, resulting in a significance level set at $p < .017$ (Tables 1–3).

## Results

There were 12 cases and all of them were male. The median of their ages was 13 (min = 8, max = 17). The median of CGI-S score was 5 (min = 3, max = 6) and MSQ-7 score was 36.5 (min = 33.5, max = 43.5) at the beginning. The median follow-up period was 51 months and the range was 2–86 months. Eleven of 12 cases had reported adverse effects with MPH use. Increasing irritability had been seen in all cases and increasing tantrums had been observed in five cases. The median of CGI-S score was 6 (min = 5, max = 7) and MSQ-7 score was 39 (min = 35, max = 45) when irritability occurred and were statistically significantly higher compared to the beginning scores ($p = .001$ and $p = .002$) (Table 1). $p$ Values of CGI-S and MSQ

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**Table 1.** CGI-S and MSQ scores at the beginning of treatment, at the time when MPH treatment discontinued and last visits.

| Agemedian (min–max) | CGI-S T1 median (min–max) | CGI-S T2 median (min–max) | CGI-S T3 median (min–max) | MSQ T1 median (min–max) | MSQ T2 median (min–max) | MSQ T3 median (min–max) |
|---|---|---|---|---|---|---|
| 13 (8–17) | 5 (3–6) | 6 (5–7) | 2.5 (1–3) | 36.5 (33–43) | 39.0 (35–45) | 21 (15–25) |

Note: CGI-S, clinical global impression-severity scale MSQ-7: mood symptom questionnaire; T1, the beginning of treatment; T2, the time when MPH treatment was discontinued; T3, last visit.

**Table 2.** *p* Values of CGI-S and MSQ scores at the beginning of treatment, at the time when MPH treatment discontinued and last visits.

| *p* | T1–T2 | T1–T3 | T2–T3 |
|---|---|---|---|
| CGI-S | 0.001 | 0.002 | 0.002 |
| MSQ | 0.002 | 0.002 | 0.002 |

Note: CGI-S, clinical global impression-severity scale MSQ-7: mood symptom questionnaire; T1, the beginning of treatment; T2, the time when MPH treatment stopped; T3, last visit. $p < .017$ was used for statistical significance.

**Table 3.** Concomittant, additional therapies and MPH doses during treatment.

| Cases | Concomittant therapy | Additional therapy | MET dosage and type |
|---|---|---|---|
| 1st | Aripiprazole 10 mg | | 54-MET OROS |
| 2nd | | Quetiapine 25 mg | 18-MET OROS |
| 3rd | | Aripiprazole 5 mg | 18-MET OROS |
| 4th | Aripiprazole 10 mg | | 15-MET |
| 5th | Aripiprazole 5 mg | | 10-MET |
| 6th | | | 18-MET OROS |
| 7th | | Aripiprazole 10 mg | 36-MET OROS |
| 8th | Valproic acid 1000 mg | | 20-MET |
| 9th | | Risperidone 0.5 mg | 20-MET |
| 10th | | Aripiprazole 5 mg | 27 MET |
| 11th | | Risperidone 0.5 mg | 10 MET |
| 12th | Risperidone 0.75 mg | | 18 MET |

scores at the beginning of treatment, at the time when MPH treatment discontinued and last visits were shown in Table 2. MPH treatment was tried once in 11 of 12 cases but only one of them used MPH twice and irritability was seen for two times during the period of MPH use (Table 3).

The mean MPH dose was 18 mg/day (min = 10, max = 54). Four of the cases had already taken antipsychotics together with MPH; one of them had already taken valproic acid and six of the cases began to use antipsychotics after MPH was discontinued.

## Discussion

In this present study, the use of MPH increased the irritability clearly in children diagnosed with ADHD and DMDD. However, irritability and temper tantrums are among core features of DMDD; due to reports from the mothers and information provided by the clinician, children's irritability increased after MPH usage. Clinical severity and the MSQ scores which are very sensitive to mood symptoms also increased. In recent studies stimulant treatment should be considered as a first-line treatment for ADHD with or without irritability [3,4]; however, MPH can increase irritability when ADHD occurs comorbid with mood or anxiety disorders [5]. The underlying mechanism, which causes increased irritability in comorbid situations with MPH, is still largely unknown.

The evidence-based knowledge is insufficient for clinicians on the question whether children with DMDD and ADHD should first receive stimulants and behavior therapy for ADHD or mood stabilizers for mood dysregulation. Further studies are needed to determine initial treatment for children who are diagnosed with comorbid DMDD and ADHD.

## Disclosure statement

No potential conflict of interest was reported by the authors.

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