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THE EFFECT OF METHYLPHENIDATE ON OPPOSITIONAL DEFIANT DISORDER COMORBID WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER

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ABSTRACT - *Objective:* To assess the effect of methylphenidate on the diagnosis of oppositional-defiant disorder (ODD) comorbid with attention-deficit hyperactivity disorder (ADHD). *Method*: We conducted an open-label study in which 10 children and adolescents with a dual diagnosis of ODD and ADHD were assessed for their ODD symptoms and treated with methylphenidate. At least one month after ADHD symptoms were under control, ODD symptoms were reevaluated with the Parent form of the Children Interview for Psychiatric Syndromes (P-ChIPS). *Results:* Nine of the 10 patients no longer fulfilled diagnostic criteria for ODD after they were treated with methylphenidate for ADHD. *Conclusion*: Methylphenidate seems to be an effective treatment for ODD, as well as for ADHD itself. The implications for the treatment of patients with ODD not comorbid with ADHD needs further investigation.

KEY WORDS: oppositional-defiant disorder, attention-deficit hyperactivity disorder, methylphenidate, treatment, comorbidity.

O efeito do metilfenidato sobre o transtorno opositivo-desafiador comórbido com transtorno do déficit de atenção e hiperatividade

RESUMO - *Objetivo*: Avaliar o efeito do metilfenidato sobre o diagnóstico de transtorno opositivo-desafiador (TOD) comórbido com transtorno do déficit de atenção e Hiperatividade (TDAH). *Método*: Conduzimos um estudo aberto em que 10 crianças e adolescentes com diagnóstico de TOD e TDAH foram avaliados para seus sintomas de TOD e tratados com metilfenidato. Pelo menos um mês após os sintomas e TDAH estarem controlados, os sintomas de TOD foram reavaliados com a entrevista P-ChIPS (Children Interview for Psychiatric Syndromes-Parent form). *Resultados*: Nove dos dez pacientes não preenchiam mais critérios diagnósticos para TOD após serem tratados com metilfenidato para TDAH. *Conclusão*: Metilfenidato parece ser um tratamento eficaz para TOD, além de para TDAH. As implicações para o tratamento de pacientes com TOD não comórbido com TDAH necessita mais investigação.

PALAVRAS-CHAVE: transtorno opositivo-desafiador, transtorno do déficit de atenção e hiperatividade, metilfenidato, tratamento, comorbidade.

The efficacy of stimulants on the core symptoms of attention-deficit disorder (ADHD) is solidly established in the literature[1,2]. However, ADHD is commonly comorbid[3] in many cultures, including Brazil[4,5]. Of the psychiatric diagnoses associated to ADHD, oppositional defiant disorder (ODD) is the most common occurrence and is found in at least 35% of patients[3]. There is no firmly established treatment for ODD. There have been positive trials with cognitive-behavioral therapy[6] and risperidone[7]. Lithium[8], typical anti-psychotics[9], anticonvulsants[10] and clonidine[11] have also been studied and occasionally found effective for aggression and typical ODD behaviors such as noncompliance and temper outbursts. However, to our knowledge, these drugs have not been systematically tested for their effect on a diagnosis of ODD.

The effect of stimulants on ODD is not as clearly documented as its effects on the core symptoms of ADHD. A study conducted with patients with ODD and conduct disorder (CD) comorbid with ADHD shows the increase of positive mood/behavioral ratings and the reduction of oppositional defiant and peer conflicts ratings with the use of methylphenidate, but not in all settings[12]. Twenty-eight other studies were reviewed in a meta-analysis[13] and found to demonstrate a

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robust effect of stimulants on aggression. However, the presence of a diagnosis of ODD or CD diminished the effect size of the drug. Klein et al.[14] have reported the efficacy of methylphenidate for CD symptoms of patients with ADHD comorbid with CD. However, they did not assess oppositional-defiant symptoms in particular.

The purpose of this study is to evaluate if methylphenidate induces remission of ODD comorbid with ADHD.

METHOD

Subjects were drawn from the population who sought care at the ADHD Program (GEDA) at the Institute of Psychiatry of the Federal University at Rio de Janeiro. A written Informed Consent approved by the Ethics Committee of the Institute of Psychiatry – UFRJ was signed by the parents or the guardian of the children.

The sample consisted of 12 consecutively referred children and adolescents who had a diagnosis of ADHD and ODD, according to the Parent Form of the Child Interview for Psychiatric Syndromes (P-ChIPS)[15], which is based on the DSM-IV criteria. Patients had to be between 6 and 18 years old. They were excluded if they had a diagnosis of a mood disorder, mental retardation, pervasive developmental disorder or schizophrenia. These patients were screened at GEDA, where they were first interviewed along with their parents or guardians by a trained psychiatrist or neurologist and then referred to a second interview for further assessment, which included neuropsychological testing and a semi-structured interview.

This was an open–label, flexible-dose escalating trial. Short-acting methylphenidate in two daily doses was prescribed for all patients. The initial dosage was 5 mg twice a day. The dosage was increased at intervals no shorter than two weeks by 10mg daily according to the evaluation on the ADHD Rating Scale. When their ADHD symptomatology was considered under remission, defined by fulfillment of less than 5 criteria of hyperactivity/impulsivity or inattention (i.e., patients did not attend DSM-IV criterion for ADHD anymore), the dosage was then stabilized for at least a month. At that point, they were reassessed for their ODD symptoms.

A Portuguese language version of the P-ChIPS was used for the diagnosis of ODD and assessment of severity (attributing a point to each positive DSM-IV criteria).

ADHD was rated using the DuPaul ADHD Rating Scale[16] in a Portuguese version. Patients with no more than 4 positive criteria per subscale (inattention or hyperactivity/impulsivity) were considered asymptomatic. IQ was measured using the Vocabulary and Block Design subscales of the Wechsler Intelligence Scale for Children-III[17] in all the patients of the sample and clinical impression was used to exclude moderate cases.

Wilcoxon tests (one-tailed) were used to compare pre-treatment and post-treatment scores (P-ChIPS). Because one of the patients was undergoing psychotherapy, we applied the same test for the pre and post-treatment P-ChIPS scores excluding this patient.

RESULTS

Twelve patients were screened, assigned to the treatment group and initiated therapy.

Two patients (16%) dropped out of the study because of non-compliance with repeated medical appointments. The sample comprised 10 patients, six male patients, four female patients, aged 6 to 14 years. The mean time lag between first and last evaluation was 113.7 days. The mean daily dosage of methylphenidate was 23.5 mg.

Nine of the 10 patients who completed the protocol stopped fulfilling diagnostic criteria for ODD in their post-treatment evaluation a month or more after their ADHD symptoms were controlled. Table 1 shows the ADHD symptoms before and after treatment.

Patients fulfilled an average of 4.9 criteria in their pre-treatment evaluation, compared to 1.8 criteria in their post-treatment evaluation. The difference between these averages,

Table 1. Number of ADHD symptoms (inattention/ hyperactivity) fulfilled before and after treatment for each patient.

Patients	Before inattention	Treatment hyperactivity	After inattention	Treatment Hyperactivity
A	7	9	1	4
B	7	8	2	4
C	2	8	3	3
D	9	9	0	1
E	2	7	0	0
F	7	5	0	0
G	9	9	2	1
H	8	8	2	1
I	8	9	0	1
J	8	7	2	2

Table 2. Number of positive criteria for ODD on first and last evaluation of patients based on the P-ChIPS interview.

Patients	First P-ChIPS	Last P-ChIPS	Difference
A	5	3	-2
B	4	1	-3
C	5	6	1
D	4	3	-1
E	6	0	-6
F	4	2	-2
G	4	0	-4
H	4	3	-1
I	6	0	-6
J	7	0	-7
Mean	4,9	1,8	p=0.004

P-ChIPS; Children interview for psychiatric syndromes-parent form.

reached statistical significance (p=0.004). Since one of the patients was undergoing psychotherapy, we conducted the same analysis without this patient and it still reached statistical significance (p= 0.008). Table 2 shows the fulfillment of diagnostic criteria in baseline and end evaluations.

DISCUSSION

This study indicates that methylphenidate may be an effective anti-ODD agent in children with ADHD. Ninety percent of patients with ODD comorbid with ADHD underwent remission when treated with methylphenidate. This finding is in agreement with a number of studies that found a positive effect of stimulants on aggression or positive social behavior.

The present study differs from the ones already published evaluating the effect of methylphenidate on disruptive symptoms in a number of ways. Many of these studies used children with mental retardation[18], were conducted either in laboratory conditions[19] or very specific settings such as partial hospitalization programs[20] or strictly academic situations[21], so that the generalization of their findings does not necessarily extend to the home environment or more natural conditions. Hinshaw et al.[22] studied the effect of methylphenidate on an array of disruptive symptoms in boys with ADHD but the remission of an ODD diagnosis was not addressed. Our study, on the other hand, evaluated the effect of methylphenidate on children with a number of disruptive symptoms large enough to merit them the diagnosis of ODD and, to assess the effect of methylphenidate on these symptoms, used the parent or guardian's evaluation of the whole array of symptoms of the ODD diagnosis, which can manifest themselves in a number of settings. Additionally, children were evaluated at least a month after their methylphenidate dose was stabilized so that a more lasting effect was verified than in most studies. The most important finding, though, was that 90% of the patients not only had a decrease in their symptoms but also no longer fulfilled diagnostic criteria for ODD.

The sample was relatively small and, even though the findings reached statistical significance, they will need to be replicated in further larger-scale studied. We did not count with a placebo group and the assessments were, thus, not blinded. Finally, the Portuguese language version of the P-ChIPS and DuPaul scale have not been validated yet. However, it is our impression that this does not interfere with the results.

The positive effect of methylphenidate on ODD may mean that there is a sub-group of patients with ADHD and ODD in which the ODD symptoms are just a consequence of their ADHD or, alternatively, may mean that methylphenidate is directly effective for the control of ODD symptoms, possibly acting through the control of impulsivity. To properly answer this question a further study with ODD patients not comorbid with ADHD is necessary. For now, we can only state that methylphenidate seems to be effective for inducing remission in ODD comorbid with ADHD in a large percentage of patients.

If methylphenidate is effective for ODD comorbid with ADHD, the presence of this comorbidity should affect the choice of drug used for the treatment of ADHD in these patients and may also have implications for dose adjustments. Further studies should evaluate if the ODD symptoms respond solely to the control of ADHD or are impacted directly by different methylphenidate dosages.

The impact of methylphenidate on patients with ODD symptoms not comorbid with ADHD should also be promptly assessed.

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