Depression, anxiety and obsessive–compulsive symptoms and quality of life in children with attention-deficit hyperactivity disorder (ADHD) during three-month methylphenidate treatment

Kagan Gurkan¹, Ayhan Bilgic², Serhat Turkoglu², Birim G Kilic¹, Ayla Aysev¹ and Runa Uslu¹

Abstract
The current study was designed to investigate the changes that occur in depression, anxiety, obsessive–compulsive symptoms and health-related quality of life during methylphenidate (MPH) treatment in children with attention-deficit hyperactivity disorder (ADHD). Forty-five treatment naive children with ADHD, aged 8–14, were assessed based on self, parent and teacher reports at the baseline and at the end of the first and third month of MPH treatment regarding changes in inattention, hyperactivity, impulsivity, depression, anxiety and obsessive–compulsive symptoms. Changes in the quality of life were also noted. Repeated measures of analysis of variance (ANOVA) tests with Bonferroni corrections were conducted in order to evaluate the data. Symptoms of inattention, hyperactivity and impulsivity were significantly reduced (p < 0.017) following a three-month MPH treatment. There were significant decreases in depression (p = 0.004), trait anxiety (p = 0.000) and checking compulsion symptom scores (p = 0.001). Moreover, parents reported significant improvements in psychosocial (p = 0.001) and total scores (p = 0.009) of quality of life, despite no change in physical health scores (p > 0.05). Children's ratings of quality of life measures showed no significant changes in physical health and psychosocial scores (p > 0.05), while total scores significantly improved (p = 0.001) after the treatment. Over a three-month MPH treatment, depression, trait anxiety and checking compulsion symptoms decreased and quality of life seemed to improve along with those of inattention, hyperactivity and impulsivity.

Keywords
anxiety, attention-deficit hyperactivity disorder (ADHD), children, depression, health-related quality of life, methylphenidate, obsessive–compulsive symptoms

Introduction
Attention-deficit hyperactivity disorder (ADHD) is an early onset neuropsychiatric disorder that is characterized by hyperactivity, impulsivity and attention deficit (AD) (APA, 2000). It is a highly prevalent mental disorder of childhood which affects 3–7% of school children. It continues during adolescence and adulthood and is associated with loss of functioning throughout the entire lifespan (Cantwell, 1996).

In children with ADHD, social and emotional problems frequently emerge along with the core symptoms of the disorder. AD causes organization difficulties and academic underachievement and hyperactive/impulsive features and mood lability may result in poor peer relationships (Weiss and Weiss, 2002). Moreover, depression, anxiety disorders and obsessive-compulsive disorder (OCD) coexist with ADHD and may cause additional impairment (Gillberg et al., 2004). Whether or not co-existing symptoms reach a level that is severe enough to constitute a comorbid disorder, it is important to document these symptoms, as they may influence the clinician’s treatment choice.

Psychostimulants are the first line choices among the drugs for ADHD treatment and methylphenidate (MPH) is one of the most commonly used psychostimulant drugs (Biederman and Faraone, 2005). The main targets of MPH treatment are symptoms of AD, behavioural control and impulsivity; however, some evidence suggests that it may also affect co-existing symptoms. There are some reports that MPH may induce depression and anxiety (Barkley et al., 1990; Swanson et al., 1978). Moreover, it is reported that MPH may worsen the symptoms if there are comorbid mood and anxiety symptoms (DuPaul et al., 1994; Goez et al., 2007). On the other hand, some studies documented that MPH may improve the anxiety itself (The MTA Cooperative Group, 1999) or may be efficient in the presence of ADHD with comorbid anxiety (Diamond et al., 1999). Similarly, some of the investigators studied MPH alone (Fernandez et al., 1995; Lee et al., 2005)
and others in combination with antidepressants as an augmentation (Gwirtsman et al., 1994) for the treatment of depression and MPH was shown to be efficient in this respect in adult patients.

Conflicting results are also reported for obsessive-compulsive (OC) behaviours associated with MPH. Some of the authors suggested OC symptoms may emerge during the MPH treatment (Kotsopoulos and Spivak, 2001). Conversely, it was also observed that MPH may alleviate the OC symptoms (Joffe and Swinson, 1987).

In children with ADHD, health-related quality of life (HRQL) was also investigated and worse HRQL scores were documented compared to normal children (Hakkarta-van Roijen et al., 2007; Klassen et al., 2004). However, there are few studies with regard to the effects of MPH on HRQL (Flapper and Schoemaker, 2008; Yang et al., 2007). In the only prospective study evaluating HRQL after MPH treatment in children with ADHD plus developmental coordination disorder, Flapper and Schoemaker (2008) reported an improvement in HRQL scores. Yang et al. (2007) documented poorer HRQL in MPH-using children with ADHD compared to normal controls in a cross-sectional study.

Given the presence of comorbid anxiety, depression and OC symptoms and the lower HRQL in children with ADHD and the widespread use of MPH in treatment of the condition, it is important to know how this medication affects these symptoms and HRQL. We hypothesized that depression, anxiety and OC symptoms that were caused by the core features of ADHD would decrease related to improved organization after MPH treatment, and also that HRQL would improve during the MPH trial as well. Therefore, in the present study, we aimed to define whether there was a change in anxiety, depression, OC symptoms and HRQL scores in children with ADHD following MPH treatment.

Methods and materials

Subjects

Forty-five children with ADHD who were consecutively referred to the outpatient clinic of the Ankara University Department of Child and Adolescent Psychiatry were included in the study. The mean age of the children in the sample was 10.09 ± 1.80 years (range, 8–14 years), which consisted of 34 (75.6%) boys and 11 (24.4%) girls. All of the children were treatment naïve and were at their first psychiatric referral. Exclusion criteria included the presence of a major physical/neurologic illness (e.g. cardiac illness, epilepsy, etc.), pervasive developmental disorder, substance abuse and an intelligence quotient (IQ) score below 80 according to the Weschler Intelligence Scale for Children – Revised (WISC-R) (Wechsler, 1974). Children who took any medication for ADHD symptoms in the past and have any current or past comorbid psychiatric disorder warranting the use of a medication other than MPH were also excluded. At first, 53 consecutively referred families were approached for the study. Two parents refused to participate, whereas six children were excluded based on the exclusion/inclusion criteria.

Evaluation measures

Kiddie Schedule for Affective Disorders and Schizophrenia – Present and Lifetime version (K-SADS-PL): K-SADS-PL is a widely used semi-structured diagnostic interview tool (Kaufman et al., 1997). It inquires about current and past episodes of child and adolescent psychiatric disorders and allows a diagnosis to be made. The Turkish version of the K-SADS-PL was reported to have good test-retest and inter-rater reliability (Gokler et al., 2004). In the current study, the ADHD module of K-SADS-PL was used to make the diagnosis of ADHD.

Conners Parent Rating Scale – Revised (CPRS-R): The Conners Rating Scales are among the most popular rating scales in ADHD field. The revision of these scales was conducted by Conners et al. (1998a,b). The 80-item Turkish Form of CPRS-R was translated and adapted by Kaner et al. (2006a). The Turkish version of the scale was reported to be valid and reliable and suitable for using in research and clinical purposes. In rating their child’s behaviour, the parents respond to each item on a four-point Likert type scale: 0 = never, 1 = rarely, 2 = often and 3 = always. In this study, DSM-IV symptoms subscale (inattention, hyperactivity/impulsivity (H/I) and total) scores of the CPRS-R were utilized in order to determine the severity of the ADHD symptoms.

Conners Teacher Rating Scale – Revised (CTRS-R): The reliability and validity study of the Turkish version of the CTRS-R was completed by Kaner et al. (2006b). The scale consists of 59 items and allows screening of ADHD symptoms by teachers in school settings. The teacher ratings are scored on a four-point Likert-type scale, the same as the parent ratings (0 = never, 1 = rarely, 2 = often and 3 = always). The DSM-IV symptoms subscales (inattention, H/I and total) of the CTRS-R were used.

Children’s Depression Inventory (CDI): This is a self-report depression scale for children between six and 17 years old that was developed by Kovacs (1985). It is composed of 27 items and each item is scored as 0, 1, or 2 according to the severity of the symptom. The items assess the severity for the previous two weeks. The reliability and validity study of the scale for the Turkish population was conducted by Oy (1991).

State/Trait Anxiety Inventory for Children (STAIC): The STAIC is composed of two subscales each containing 20 items that assess state and trait anxiety (Spielberger et al., 1983). The scale is a widely used self-report instrument. It has demonstrated good concurrent validity and reliability in Turkish children and adolescents (Ozusta, 1995). The Cronbach alpha for the scale was reported to be between 0.83 and 0.86.
Maudsley Obsessive–Compulsive Questionnaire (MOCQ): This questionnaire is a 30 item self-report questionnaire in true–false item format, developed to measure OC symptoms (Hodgson and Rachman, 1977). The scale yields a maximum score of 30, with a higher score indicating greater obsessive compulsiveness. It has four subscales: cleanliness, checking, slowness and doubt. The MOCQ is widely used in children and adolescents to evaluate OC symptoms. The validity and reliability of the Turkish version of MOCQ was conducted by Erol and Savaşır (1988). Internal consistency analyses revealed Cronbach alpha scores as 0.86 for the full scale, and between 0.61 and 0.65 for the subscales.

Paediatric Quality of Life Inventory: Parent and child version (PedsQL-P and C): This scale was developed by Varni et al. (1999) in order to evaluate HRQL in children. The reliability and validity study of the scale for 8–12-year-old and 13–18-year-old Turkish children was conducted by Çakan Memik et al. (2007, 2008). It is short and easy-to-apply instrument which is scored on a five-point Likert-type scale. The scale has parent and child versions that investigate physical and psychosocial functioning.

Wechsler Intelligence Scale for Children – Revised (WISC-R): The WISC-R was designed to measure the IQ of the children between the ages of 6 and 16 (Wechsler, 1974). The standardization of the WISC-R for Turkish children was conducted by Savaşır and Şahin (1995). In the present study, it is used to ensure that participants had an IQ of 80 or higher.

Procedure
The study was approved by the Ankara University Ethical Committee. An education session about ADHD and the targets of the treatment regarding effects on attention and behavioural control, and a detailed description of the study and effects/side effects of the medications was given to all of the children and parents. Parents of children who agreed to participate in the study signed a written informed consent. At first, parents and teachers completed the CPRS-R and the CTRS-R. Then all children were interviewed using the K-SADS-PL and ADHD diagnoses were made according to the (DSM-IV-TR). Children were administered to the CDI, PedQL, STAI-C and MOCQ at the baseline. The parents also completed the PedsQL. All of the cases commenced treatment of short-acting MPH at a dose of 5mg twice a day. The dose of medication was gradually increased based on therapeutic response and adjusted by a child and adolescent psychiatrist during the study, considering the response and side effects. The mean MPH dose was 24.2mg/day. At the end of the first and third months, all self-report measures were re-administered. Patients who missed 30% of the total prescribed dose or above were accepted as non-compliant.

Statistical analysis
The analysis of the data was performed by Statistical Package for the Social Sciences (SPSS) 11.5 statistical software. Repeated measures of analysis of variance (ANOVA) tests were used in order to compare the symptom scores at three different points. Bonferroni correction was used as a post-hoc test. Analyses were repeated by controlling the change in the ADHD symptom scores, which were thought to affect the change in quality of life, the depressive, anxiety and OC symptoms. To measure the co-variation of ADHD and the depressive and anxiety symptoms during the treatment response, a canonical correlation was performed. Significance was set at a level of 0.05 (two tailed).

Results
Two subjects discontinued treatment during the first month because of the side effects (i.e. decreased appetite and headache). Two subjects dropped out before the visit at the third month and another four were excluded because of non-compliance to the medication. Thirty-seven (82.2%) participants completed the three-month study.

ADHD symptoms
Changes in the CPRS-R and the CTRS-R scores are summarized in Table 1. The decrease in subscale scores of the CPRS-R and the CTRS-R are shown in Figures 1 and 2. Symptoms of inattention reduced significantly during the three-month MPH therapy as measured by both parent (F(2,72) = 11.67, p = 0.000) and teacher ratings (F(2,72) = 24.60, p = 0.000). A significant reduction in AD scores was achieved in all levels of the visits according to teacher ratings. With regard to parent ratings, a significant improvement in AD scores was observed over visit 1 to 3. H/I scores significantly decreased according to parent (F(1,80,64.72) = 9.20, p = 0.000, with the Huynh–Feldt correction) and teacher ratings (F(2,72) = 11.64, p = 0.000). The reduction in H/I scores of the CPRS-R was significant over visit 1 through 3, while the reduction in the CTRS-R scores was significant during the first month and visit 1 through 3. Finally, the total DSM-IV symptoms scores decreased significantly both in ratings of the CPRS-R (F(2,72) = 13.17, p = 0.000) and the CTRS-R (F(2,72) = 22.04, p = 0.000). According to pairwise comparisons the decrease in total Diagnostic and Statistical Manual of Mental Disorders (DSM) symptoms scores of the CPRS-R was significant over visit 1 through visit 3. In the CTRS-R, reductions were significant during the first month and from the baseline to the third month.

Depressive symptoms
Depressive symptom scores according to the CDI (F(1,64,59.18) = 9.47, p = 0.001, with the Huynh–Feldt correction) significantly decreased during the treatment. The decrease in the CDI score was significant over visit 1 to visit 2 and visit 1 to visit 3. The summary of change in the CDI score is given in Table 3 and the decrease was shown in Figure 6.
Anxiety symptoms

The state \(F(1.66, 59.88) = 5.26, p = 0.011\), with the Huynh–Feldt correction) and the trait anxiety \(F(1.73, 62.13) = 11.30, p = 0.000\), with the Huynh–Feldt correction) scores according to the children’s self report also significantly decreased. However, reductions in state anxiety scores were not significant after the Bonferroni correction. Trait anxiety scores did not significantly reduce during the first month of MPH therapy, however the reductions were significant over visit 2 to 3 and 1 to 3. The summary of changes in the state and trait anxiety scores are presented in Table 3 and the decrease in these scores is demonstrated in Figure 7.

OC Symptoms

The results of changes in the MOCQ subscale scores are summarized in Table 3. The decrease in the checking subscale of the MOCQ is demonstrated in Figure 5. The total \(F(2,72) = 2.52, p = 0.088\), cleanliness \(F(1.63, 58.74) = 0.428, p = 0.613\), with the Huynh–Feldt correction), slowness \(F(2,72) = 0.346, p = 0.708\) and doubt \(F(2,72) = 1.68, p = 0.193\) subscale scores of the MOCQ did not change significantly during the three-month MPH treatment according to the children’s self reports. However, there was a significant change in the checking subscale \(F(2,72) = 6.78, p = 0.002\) of the MOCQ. In pairwise comparisons, the decrease in checking compulsions was significant from the baseline to the third-month ratings.

Paediatric quality of life scores

The summary of changes in the quality of life scores is shown in Table 2. The subscale scores of the PedsQL-C and the PedsQL-P that improved during the MPH therapy are shown in Figures 3 and 4. The increases in physical health scores were not significant neither in child \(F(1.78, 64.11) = 1.24, p = 0.272\), with the Huynh–Feldt correction), the psychosocial subscale scores of the PedsQL-P improved significantly \(F(2,72) = 6.69, p = 0.002\) during the three-month MPH therapy, while there were no significant changes in the psychosocial subscale scores of the PedsQL-C \(F(2,72) = 2.44, p = 0.094\). The increase in the psychosocial subscale score of the PedsQL-P was significant over visit 1 through 3. The total scores of both the PedsQL-C \(F(2,72) = 6.70, p = 0.002\) and the PedsQL-P \(F(2,72) = 8.39, p = 0.001\) increased

Table 1. Change in AD, H/I and total DSM symptom scores of the CPRS-R and the CTRS-R during MPH therapy

<table>
<thead>
<tr>
<th>Symptom scores (mean ± SD)</th>
<th>Baseline (visit 1)</th>
<th>First month (visit 2)</th>
<th>Third month (visit 3)</th>
<th>1–2</th>
<th>2–3</th>
<th>1–3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CPRS-R</strong></td>
<td></td>
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</tr>
<tr>
<td>AD</td>
<td>15.96 ± 5.40</td>
<td>13.37 ± 4.99</td>
<td>11.16 ± 5.09</td>
<td>2.41*(0.038)</td>
<td>1.92(0.103)</td>
<td>4.32*(0.000)</td>
</tr>
<tr>
<td>H/I</td>
<td>14.87 ± 5.60</td>
<td>12.16 ± 5.45</td>
<td>10.81 ± 5.04</td>
<td>2.73(0.062)</td>
<td>1.46(0.204)</td>
<td>4.19*(0.001)</td>
</tr>
<tr>
<td>Total</td>
<td>30.82 ± 9.68</td>
<td>25.53 ± 8.80</td>
<td>21.97 ± 9.21</td>
<td>5.14*(0.027)</td>
<td>3.38(0.060)</td>
<td>8.51*(0.000)</td>
</tr>
<tr>
<td><strong>CTRS-R</strong></td>
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<tr>
<td>AD</td>
<td>15.98 ± 5.16</td>
<td>12.98 ± 6.48</td>
<td>10.00 ± 4.81</td>
<td>3.24*(0.001)</td>
<td>2.78*(0.009)</td>
<td>6.03*(0.000)</td>
</tr>
<tr>
<td>H/I</td>
<td>12.87 ± 6.70</td>
<td>9.67 ± 5.72</td>
<td>9.05 ± 5.76</td>
<td>3.03*(0.004)</td>
<td>0.89(0.645)</td>
<td>3.92*(0.001)</td>
</tr>
<tr>
<td>Total</td>
<td>28.84 ± 9.80</td>
<td>22.60 ± 10.32</td>
<td>19.05 ± 9.46</td>
<td>6.32*(0.001)</td>
<td>3.62(0.054)</td>
<td>9.95*(0.000)</td>
</tr>
</tbody>
</table>

*p < 0.017 (with the Bonferroni correction); #p < 0.05.

Figure 1. Improvement in the CPRS-R subscale scores during the three-month MPH therapy.

Figure 2. Improvement in the CTRS-R subscale scores during the three-month MPH therapy.

Anxiety symptoms

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significantly during the trial. According to post-hoc tests, child ratings differed significantly between the visit 1 and 3, and parent ratings were significantly different between visit 1 and 2 and visit 1 and 3.

However, when we controlled the change in any subscale scores of ADHD symptoms from visit 1 through 3 and repeated the analyses, the reduction in checking compulsions, depression, anxiety scores and the improvement in the PedsQL scores during treatment were no longer significant ($p > 0.05$).

**Covariance of ADHD symptoms and depression and anxiety symptoms during the treatment response**

To measure the covariance of ADHD and depression and anxiety symptoms during the treatment response, a canonical correlation analysis was conducted. The improvement in ADHD symptoms during the three-month MPH treatment according to the CPRS-R and the CTRS-R subscales were defined as a set, while the improvement in depression, state and trait anxiety symptoms during the treatment were taken as another set. The correlation between the two sets of symptoms was calculated by canonical correlation analysis and it was revealed that there was no significant correlation ($r_c = 0.47, p = 0.82$).
Discussion

This open-label study showed that depressive, trait anxiety and checking compulsions and quality of life scores improved along with parent and teacher ratings of AD, hyperactivity and impulsivity symptoms during the three-month MPH therapy. The results suggested that improvements in quality of life, depression, anxiety and OC symptoms could be secondary to the effects of MPH on the core features of ADHD. Contrary to concerns in some of the previous reports (Barkley et al., 1990; Kotsopoulos and Spivak, 2001; Swanson et al., 1978), MPH treatment in moderate doses did not cause increments in anxiety, depression and OC symptoms. Our results showed that depression scores significantly decreased during MPH treatment in children with ADHD. This finding was interpreted as compatible with previous reports that suggested an antidepressant effect of MPH (Buhagiar and Cassar, 2007; Fernandez et al., 1995; Lee et al., 2005; Rickels et al., 1972). MPH treatment in moderate doses did not cause increments in anxiety, depression and OC symptoms.

Our results showed that depression scores significantly decreased during MPH treatment in children with ADHD. This finding was interpreted as compatible with previous reports that suggested an antidepressant effect of MPH (Buhagiar and Cassar, 2007; Fernandez et al., 1995; Lee et al., 2005; Rickels et al., 1972). Similarly, some of the authors also reported an improvement in mood symptoms and emotional dysregulation with long-acting MPH in several studies conducted with adult ADHD patients by self-report instruments (Reimherr et al., 2007; Rösler et al., 2009). However, most of these studies included adult patients with major depression and in some of them MPH was used as an adjunctive treatment. To the best of our knowledge, there is no study examining the effect of MPH on depressive symptoms in children with pure ADHD. In the present study, the baseline scores of depressive symptoms were relatively low and these children did not have major depression. In addition, the CDI has a limitation in that it could not differentiate whether depressive symptoms reflect dysthymia or mood instability. Mood instability may represent an extended aspect of ADHD, whereas dysthymia is secondary to long-term poor function, and the nature of these symptoms is not clear. Nevertheless, it is important to see that symptoms of depression decreased during the MPH treatment in children with ADHD. The decrease in depression scores began within the first month and continued to a lesser degree until the end of the treatment.

Table 3. Change in OC, depressive, state and trait anxiety scores during the three-month MPH therapy

<table>
<thead>
<tr>
<th>Symptom scores</th>
<th>Baseline (visit 1)</th>
<th>First month (visit 2)</th>
<th>Third month (visit 3)</th>
<th>Pairwise comparisons (mean differences (p))</th>
</tr>
</thead>
<tbody>
<tr>
<td>MOCQ</td>
<td></td>
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<tr>
<td>Checking</td>
<td>3.82 ± 2.12</td>
<td>3.42 ± 2.56</td>
<td>2.57 ± 2.35</td>
<td>0.16(1.000) 1.08* (0.033) 1.24* (0.001)</td>
</tr>
<tr>
<td>Cleanliness</td>
<td>5.09 ± 2.01</td>
<td>4.37 ± 2.10</td>
<td>4.51 ± 3.70</td>
<td>0.41(0.787) 0.00(1.000) 0.41(0.001)</td>
</tr>
<tr>
<td>Slowness</td>
<td>2.76 ± 1.45</td>
<td>2.56 ± 1.69</td>
<td>2.89 ± 1.85</td>
<td>0.14(1.000) −0.22(1.000) −0.08(1.000)</td>
</tr>
<tr>
<td>Doubt</td>
<td>3.73 ± 1.53</td>
<td>3.44 ± 1.58</td>
<td>3.27 ± 1.71</td>
<td>0.32(0.676) 0.22(1.000) 0.54(0.345)</td>
</tr>
<tr>
<td>Total</td>
<td>14.02 ± 5.19</td>
<td>12.60 ± 6.09</td>
<td>11.89 ± 6.79</td>
<td>0.89(0.872) 1.19(1.000) 2.08(0.109)</td>
</tr>
<tr>
<td>CDI</td>
<td>11.80 ± 5.72</td>
<td>8.70 ± 5.43</td>
<td>8.27 ± 5.24</td>
<td>2.51* (0.001) 0.92(0.828) 3.43* (0.004)</td>
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<td>STAI</td>
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<tr>
<td>State</td>
<td>32.20 ± 6.38</td>
<td>30.02 ± 5.87</td>
<td>28.41 ± 6.60</td>
<td>1.92(0.257) 1.76(0.167) 3.68* (0.033)</td>
</tr>
<tr>
<td>Trait</td>
<td>36.36 ± 5.76</td>
<td>33.81 ± 7.42</td>
<td>31.14 ± 6.23</td>
<td>2.46(0.245) 3.05* (0.005) 5.51* (0.000)</td>
</tr>
</tbody>
</table>

STAI: State Trait Anxiety Inventory.
*p < 0.017 (with the Bonferroni correction); *p < 0.05.
Initial studies regarding the effect of MPH on comorbid anxiety in children with ADHD reported increased placebo response rates (Pilzsk, 1992), worsening of symptoms (Dupaul et al., 1994) and greater side effects (Tannock et al., 1995). However, recent controlled studies have shown that anxiety may decrease with MPH (The MTA Cooperative Group, 1999) and may be efficient in the presence of anxiety (Diamond et al., 1999). Our results also suggest that with MPH treatment anxiety may decrease along with the core symptoms of ADHD. It is noteworthy that the decrease in anxiety occurred not within the first month but later in the treatment and only trait anxiety scores decreased significantly. Since our results lose their significance after controlling the change in ADHD symptoms, we considered that reductions in depressive and anxiety symptoms were secondary to the improvement in academic, social and behavioural areas. Another possibility is that decreases in depressive and anxiety symptoms might also reflect the improvement in mood lability, which is an extended aspect of ADHD, with MPH, as some of the authors reported in adult studies with ADHD (Reinherr et al., 2007; Rösler et al., 2009). However, the improvement in comorbid mood and anxiety symptoms was not correlated with the improvement in ADHD symptoms, and it is hard to conclude about the nature of these symptoms based on our findings.

Although OC symptoms are reported within the side effects of MPH (Borcherding et al., 1990; Greenhill et al., 2002; Kotsopoulos and Spivak, 2001; Kouris, 1998), OC symptom scores were not increased in our study. In an earlier study, Joffe and Swinson (1987) reported an improvement with MPH in OCD patients. However, in their later study, they failed to show such an effect with MPH compared to a placebo (Joffe et al., 1991). Although to our knowledge there is no clinical study in the literature about this observation, in our clinical experience, we observed that OC symptoms in some of the children with ADHD might develop as an effort to overcome organization difficulties associated with AD. Therefore, we expected an improvement in OC symptoms based on the improvement in AD. Although the decreases in most domains of OC symptoms were not significant, the checking behaviours were significantly reduced. This improvement occurred in the later stage of the MPH therapy. However, since this association disappeared when the change in AD or H/I scores were controlled, the improvement in checking behaviours were interpreted as a result of better organization of the child related to the MPH therapy. We should also note that none of the children with ADHD had an overt OCD warranting treatment of OC symptoms and we did not intend to treat OCD with MPH.

Although some of the authors documented that HRQL is poor in children with ADHD and emphasized the necessity of targeting HRQL in treatment, very few studies have investigated the effects of medications on HRQL changes. To the best of our knowledge, this is the second prospective study investigating the effect of MPH on the HRQL in children with ADHD. In a study, it is shown that MPH improved the HRQL scores during one month of treatment in 23 children with ADHD plus developmental coordination disorder (Flapper and Schoemaker, 2008). Similar to these findings, in the current study some aspects of the parent and child rated HRQL were improved during MPH treatment. However, there was no improvement in physical health scores according to both parent and child rated HRQLs. This may be the result of relatively higher physical health scores than psychosocial scores. Compatible with these findings, Hakkaart-van Roijen et al. (2007) documented that children with ADHD were not different from the normal school population in terms of physical health scores. It was also interesting that parents reported psychosocial improvement in their children during MPH treatment, while children did not. Since children’s psychosocial domain scores were higher than the parents’ in baseline, the improvement at the endpoint was not significant. Compatible findings with regard to the discrepancy between children’s and parents’ ratings of HRQL were also reported in the literature (Klassen et al., 2006). Nevertheless, the total scores of HRQL were significantly improved during the MPH treatment in both the parent and child ratings.

The main limitation of our study was the small sample size and lack of a placebo-controlled group. Nevertheless, the results of the study have an important clinical implication regarding clinical use of MPH. It seems reasonable to start treatment with MPH in children with ADHD who have mild depression, anxiety and OC symptoms. Decreases in depressive, anxiety and OC symptoms are noteworthy and warrant further exploration. A study with a larger sample size and a control group might help to elucidate to highlight these changes better. Differential responses to MPH in the presence of comorbid overt major depression, anxiety disorders and OCD should also be studied in children with ADHD.

In conclusion, symptoms of depression, trait anxiety, checking compulsions and quality of life along with those of inattention, hyperactivity and impulsivity seemed to improve over a three-month period of MPH treatment. These improvements were regarded as dependent upon change in the core symptoms of ADHD.

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