

We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

5,200

Open access books available

129,000

International authors and editors

150M

Downloads

Our authors are among the

154

Countries delivered to

TOP 1%

most cited scientists

12.2%

Contributors from top 500 universities



WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com



A Comparison Between Life Quality and Weight-Height Measurements of Patients, Under Stimulant and Non-Stimulant Treatment due to Attention-Deficit and Hyperactivity Disorder, and Healthy Population

Esra Ozdemir Demirci, Merve Cikili Uytun,
Rabia Durmus and Didem Behice Oztop

Additional information is available at the end of the chapter

<http://dx.doi.org/10.5772/53790>

1. Introduction

Attention Deficit and Hyperactivity Disorder (ADHD) comprises a disorder which is characterized with inattention, hyperactivity and impulsivity, seen in 3-7% of school-age children. Boys are two to nine times more often affected than girls [1]. Twin, adoption, and molecular genetic studies show ADHD to be highly heritable. Evidence from animal and human studies implicates the dysregulation of frontal-subcortical-cerebellar catecholaminergic circuits in the pathophysiology of ADHD. Imaging studies suggest that abnormalities of the dopaminergic and adrenergic transmitter systems lead to impaired neurotransmission [2].

The main course of ADHD is a persistent pattern of inattention and/or hyperactivity-impulsivity that may be seen more frequently and/or severely compared to individuals with the same level of development. Its pathophysiology appears to involve different alterations in dopaminergic and noradrenergic pathways related to the control of attention and impulsivity [1,3,4].

ADHD is associated with important deterioration at numerous fields such as developmental, cognitive, emotional, social and academical, and also associated with personal time for parents because of affecting several health risks and academic performance. Deterioration in these fields based on basic symptoms of ADHD: hyperactivity, inattention and impulsivity [5]. In case of ADHD, as a result of inadequacies any time in the life of the child, reduction in self-confidence, misery, failure and thus reduced quality of life; deterioration of interpersonal and

intra-family relations, being affected adversely of psychological well-being could be seen. Therefore, it is reported that “psychosocial dimension” gains importance gradually besides clinical parameters in multidimensional monitoring of disease and adequacy and inadequacy in this dimension could be explained with “life quality” concept [6]. Because of difficulties in academical, social and emotional fields, the effects of deterioration over life quality came into discussion in the context of the recent literature [7,8,9]. This level of interest is not surprising due to the complexity of the relationships; QoL(Quality of life) is not only influenced by the disorder itself, but also by many proximal (i.e. family, friendship) and distal (socioeconomic and cultural) factors. In addition to its core symptoms of attention deficit, hyperactivity and impulsivity, ADHD is associated with numerous developmental, cognitive, emotional, social and academic impairments [10,11].

The psychostimulants (e.g., methylphenidate) are considered the first-line of therapy for ADHD, relieving symptoms by increasing intrasynaptic dopamine, norepinephrine, and serotonin [12]. Nevertheless, some patients fail to respond to stimulants or are unable to tolerate them, and the stimulants such as methylphenidate are contraindicated for some children and adolescents including those with Tourette’s disorder. Nonstimulant agents used in ADHD include tricyclic antidepressants, bupropion, clonidine, guanfacine, selective serotonin reuptake inhibitors, and newer atypical antidepressants [13,14]. But their current use is limited, because these agents do not improve impulsive behavior and cognitive impairments and also they have serious adverse effects [15].

On the other hand, atomoxetine, a highly selective inhibitor of the noradrenergic transporter, is the first non-psychostimulant agent approved by the Food and Drug Administration (FDA) for ADHD. Compared to its effect on the norepinephrine transporter, atomoxetine has very little affinity for the dopamine or serotonin transporter. As a result of the central role of CYP2D6 in metabolism of atomoxetine, the activity of this enzyme plays a significant role in its pharmacokinetics. The majority of people ([90%]), who metabolise atomoxetine and other CYP2D6 substrates relatively rapidly, are designated as CYP2D6 extensive metaboliser. Its efficacy in children with ADHD has been demonstrated in three double-blind, placebo-controlled trials [16].

Commonly used drugs for ADHD are shown in table 1.

| Drug | Dosage | Dosage range | Time of Maximum plasma concentration (hour) | FDA approval year |
|-------------|----------------|--------------|---|-------------------|
| Concerta | 18,27,36,54,72 | 18-72 | 8 | 2000 |
| Metadate CD | 10,20,30 | 20-60 | 5 | 2001 |
| Ritalin LA | 10,20,30,40 | 20-60 | 5 | 2002 |
| Adderall XR | 10,20,30 | 10-40 | 1-4 | 2001 |
| Ritalin | 5,10,20 | 10-60 | 0.3-4 | 2000 |
| Atomoksetin | 10,18,25,40,60 | 10-60 | 1-2,3-4 | 2002 |

Table 1. Commonly used drugs for ADHD

Consequently, methylphenidate for stimulant group and atomoxetine for nonstimulant group are in primer use for ADHD treatment. The use of these medications becomes widespread gradually. It is reported that both medications are effective on treatment of ADHD's basic symptoms in children and adolescents. Thus, significant improvement could be seen in life quality [9,17,18]. When comparing with normal population, difficulties in academical, social and emotional fields could be developed more frequently.

The side effects on weight and height of these medications which are used considerably in child psychiatry are in discussion over a long time. Although a few studies defend inefficiency over weight and height, some studies show arrest in height development and shortness in ultimate height [19]. Current studies in this content on children and adolescents are subjects of only a few studies specially in our country [20].

In our study, we aimed to compare the effect of long acting methylphenidatefor and/or atomoxetine usage due to ADHD, weight-height measurements, and comparison of life quality between children and adolescents, and healthy population.

2. Material and methods

This study was conducted in Department of Child and Adolescent Pscyhiatry, Erciyes University Faculty of Medicine in the period from September 2011 to May 2012. Study population consists of 52 patients with ADHD based on DSM-IV and these patients were pharmacologically treated for at least 12 months and sypmtom severity is consistent with Scanning and Evaluation Scale based on DSM-IV for Behavioral Disorders in Children and Adolescents. Coexisting psychiatric disorders were accepted as exclusion criteria. Children with no previous history of psychopharmalogical treatment except ADHD and simultaneously no previous history of epilepsy and other medical disease was examined. Control group was selected randomly between patients of social pediatriac clinical and specified as 25 healthy children in physical and psychological way. Smilarity between control and patient group from the point of gender and age avaragewas noticed. Parents of children with ADHD filled sociodemographic data form, The Pediatric Quality of Life Inventory(PedsQL), Atilla Turgay Scanning and Evaluation Scale based on DSM-IV for Behavioral Disorders in Children and Adolescents. Weight and height measurements were performed by our nurse specialist. Parents of control group also filled the same tests. Parents of both group signed informed consent and ethics committee approval was obtained.

3. Scales used in this study

The Pediatric Quality of Life Inventory(PedsQL): Developed for psychosocial and physcial life quality measurement of children and adolescent between 2-18 age interval by Varni and et all. and adapted into Turkish for 8-18 age interval was carried out by Çakın Memik et al. [21,22]. It is obtained that Cronbach Alfa coefficients vary between 0.80 and 0.88. PedsQL between the

ages of 8-18 children / adolescents, there are forms for both self-report and parent and consists of 23 articles. The scale of physical health, emotional functioning, social functioning, and school functioning challenged areas. Scoring, scale total score (CAP), physical health score (FSTP), emotional, social and school functioning scores evaluating the substance of the calculation of the total score of psychosocial health (PSTP) to be carried out in three areas. This is the last month of children and adolescents with the scale in question. Substances "never", "rarely", "sometimes", "often" or "always" in the form of, and in turn responded, 100, 75, 50, 25, 0 points are given. Points total score is obtained by dividing the number of items collected and replenished. As a result the higher the PedsQL total score, the better the perceived health-related quality of life [20].

Thus fields of physical health, emotional functioning, social functioning and school functioning as features of well-being, identified by WHO, was examined.

Turgay DSM-IV Based Child and Adolescent Behavior Disorders Screening and Rating Scale: This scale was developed by Turgay [23], based on DSM-IV diagnosis criteria. This scale consists of 41 questions; 9 of them for attention deficit, 9 of them for mobility and impulsivity, 8 of them for comorbid oppositional defiant disorder (ODD), and 15 of them for behavioral disorder. Each question has 4 choices: 0 for strongly disagree, 1 for somewhat, 2 for agree, 3 for strongly agree. For ADHD diagnosis, min 6 of 9 questions that examine attention deficit should have 2 or 3 scoring, min 6 of 9 questions that examine hyperactivity or impulsivity should have 2 or 3 scoring. For ODD, min 4 of 8 questions should have 2 or 3 scoring; for BD diagnosis, min 2 of 25 questions should exist for 6 months or 1 year. Confidence validity test was conducted by Ercan et al. in Turkey [24].

4. Statistical evaluation

The statistics software SPSS 17.0 is utilized in this study. The data obtained through measurement is indicated as arithmetic mean (\bar{X}) and standard deviation (SD); the data obtained through census is indicated as percentages (%). The significance level in the evaluations is determined as $p < 0.05$. One-Sample Kolmogorov-Smirnov Test is used for control if variables are normal distribution or not. The grading differences between the groups (children-adolescents with ADHD diagnoses and healthy children-adolescents) are compared by using the "Student t test" for the measuremental variables that conform to the normal distribution and "Mann Whitney-U test" for the measuremental variables that do not conform to the normal distribution. Tukey and Dunnett post hoc tests are also used for varyans analyze. Spearman correlation test is used for showing correlations.

5. Results

Forty two of patients who admitted into study were men (80.8%) and ten were women (19.2%). The average age of children was 10.42 ± 2.136 . Control group was similar to patient

group in terms of average age and sex ratio. Socio-demographic characteristics of the group with ADHD and the control group are shown in tables (Table 2 and table 3). Socio-demographic differences between the two groups are outstanding.

| | Mean | Standart deviation/Percent |
|-----------------------------------|----------|----------------------------|
| Age | 10,57 | 2,17 |
| Mother age | 36,03 | 5,87 |
| Father Age | 40,44 | 6,16 |
| Education | n | % |
| The First 5 years | 32 | 61,5 |
| 6th-10th.years | 20 | 38,5 |
| Number of siblings | n | % |
| 2 and under 2 | 46 | 93,9 |
| 2- 4 siblings | 3 | 6,1 |
| Mother's Educational level | n | % |
| Not education | 2 | 3,8 |
| Primary school | 20 | 38,5 |
| Secondary high school | 4 | 7,7 |
| High school | 16 | 30,8 |
| University | 10 | 19,2 |
| Father's Educational level | n | % |
| Not education | 0 | 0 |
| Primary school | 15 | 28,8 |
| Secondary high school | 6 | 11,5 |
| High school | 14 | 26,9 |
| University | 17 | 32,7 |
| Location | n | % |
| Metropolitan | 43 | 82,7 |
| City | 3 | 5,8 |
| Town | 5 | 9,6 |
| Village | 1 | 1,9 |
| Monthly Income | n | % |
| Under 1000 TL | 18 | 34,6 |
| 1000-3000 TL | 27 | 51,9 |
| 4000-10000 TL | 6 | 11,5 |
| up to 10000 | 1 | 1,9 |
| Father Occupation | n | % |
| Employee | 16 | 30,8 |
| Civil servant | 11 | 21,2 |
| Tradesman | 3 | 5,8 |

| | Mean | Standart deviation/Percent |
|-----------------------------|--|----------------------------|
| Retired | 5 | 9,6 |
| Other | 17 | 32,7 |
| Mother Occupation | n | % |
| Housewife | 41 | 78,8 |
| Civil servant | 6 | 11,6 |
| Nurse | 2 | 3,8 |
| Other | 3 | 5,8 |
| Psychopathology in family | n | % |
| Psychopathology in mother | 3(ADHD,depression) | 5,7 |
| Psychopathology in father | 3(ADHD,depression ,psychotic disorder) | 5,7 |
| Psychopathology in siblings | 5(DEHB) | 9,6 |

Table 2. Socio-demographic characteristics of the group with ADHD

| | Mean | Standart deviation/Percent |
|-----------------------------------|----------|----------------------------|
| Age | 10,4 | 2,66 |
| Mother age | 37,7 | 5,28 |
| Father Age | 41,8 | 6,79 |
| Education | n | % |
| The First 5 years | 15 | 60 |
| 6th-10th.years | 10 | 40 |
| Number of siblings | n | % |
| 2 and under 2 | 22 | 88 |
| 2- 4 siblings | 3 | 12 |
| Mother's Educational level | n | % |
| Not education | 0 | 0 |
| Primary school | 0 | 0 |
| Secondary high school | 2 | 8 |
| High school | 8 | 32 |
| University | 15 | 60 |
| Father's Educational level | n | % |
| Not education | 0 | 0 |
| Primary school | 0 | 0 |
| Secondary high school | 0 | 0 |
| High school | 6 | 24 |
| University | 17 | 68 |
| Location | n | % |
| Metropolitan | 22 | 88 |
| City | 1 | 4 |

| | Mean | Standart deviation/Percent |
|-----------------------------|----------|----------------------------|
| Town | 2 | 8 |
| Village | 0 | 0 |
| Monthly Income | n | % |
| Under 1000 TL | 0 | 0 |
| 1000-3000 TL | 10 | 40 |
| 4000-10000 TL | 14 | 56 |
| up to 10000 | 1 | 4 |
| Father Occupation | n | % |
| Employee | 2 | 8 |
| Civil servant | 4 | 16 |
| Tradesman | 4 | 16 |
| Retired | 1 | 4 |
| Other | 9 | 36 |
| Mother Occupation | n | % |
| Housewife | 12 | 48 |
| Civil servant | 7 | 28 |
| Nurse | 6 | 24 |
| Other | 0 | 0 |
| Psychopathology in family | n | % |
| Psychopathology in mother | 0 | 0 |
| Psychopathology in father | 0 | 0 |
| Psychopathology in siblings | 0 | 0 |

Table 3. Socio-demographic characteristics of the control group

33 of patients (63.5%) were under long acting methylphenidate (OROS-MPH) therapy and 19 (36.5%) were under atomoxetine therapy. The medication use duration of first group was 18.54 ± 15.43 months and second group was 18.3 ± 14.8 months. No significant difference was found between these two groups in terms of duration ($p=0,958$, $t=0,52$).

Dose rate for OROS-MPH was averagely $29,4 \pm 7,88$ mg and for atomoxetine was averagely $45,42 \pm 12,36$ mg.

Height average in patient group was $141,4 \pm 13,8$ cm, weight average was $37,07 \pm 11,17$ kg and height average for control group was $145,6 \pm 17,9$ cm, weight average was $41,1 \pm 15,5$ kg ($p=0,251$). In terms of weight and height, there is no significant difference between atomoxetine users, MPH-OROS users and control group (Table 4 and 5).

When considered sub-group of life quality scale in patient group, physical sub-group was found as $80,8 \pm 15,27$, while emotional sub-group was $66,05 \pm 18,26$, life quality social was $76,15 \pm 22,28$ and sub-group associated with school was $66,25 \pm 18,86$. In control group, physical sub-group was found as $96,37 \pm 7,02$, while emotional sub-group was $90,2 \pm 13,5$, life quality social $97,4 \pm 7,92$ and sub-group associated with school was $91,6 \pm 10,19$. There is significant

difference between all fields of life quality in both groups ($p < 0.001^*$). When comparing life quality of atomoxetine and MPH users, no significant difference was found. But when comparing long acting MPH users and atomoxetine users with control group individually, significant difference was examined in life quality sub-groups between control group and other two groups (Table 4).

| | Patient group | Control group | Comparement of groups |
|---|---------------|---------------|-----------------------|
| Mean of ages | 10,42 ±2,136 | 10,4±2,66 | p= 0,970 t= 0,041 |
| Mean of height | 141,63 ±14,19 | 145,6±17,9 | p= 0,296 t= 1,051 |
| Mean of weight | 37,07±11,17 | 41,12±15,5 | p= 0,251 t= 1,166 |
| Mean of physical health field in PedsQL | 80,8 ±15,27 | 96,37±7,02 | p< 0,001* z= 4,845 |
| Mean of emotional functioning field in PedsQL | 66,05±18,26 | 90,2±13,5 | p< 0,001* t= 5,867 |
| Mean of , social functioning field in PedsQL | 76,15±22,28 | 97,4±7,92 | p<0,001* z=5,155 |
| Mean of shcool functioning field in PedsQL | 66,25±18,86 | 91,6±10,19 | P<0,001* t= 7,668 |

(p<0,05*)

Table 4. Comparement of Socialdemographic datas and life quality

In OROS-MPH user group, while score between age and life quality in school field was found significantly correlated; ($p < 0.05^*$, $r = 0.443$) in atomoxetine user group, no correlation was found. When considering changes in hand-writing and drug use, 20 patients of 52 parents showed recovery in hand writing after drug intake.

26 patients (50%) were applied before any other treatment of ADHD. However, several side effects, and due to non compliance of previously treatment patients couldn't maintain previous treatment is observed. 16 patients of the 26 patients, (20.8%), inability to benefit from treatment, 2 patients (2.6%), insomnia, and 2 (2.6%), loss of appetite, and 2 (2.6%), nervousness, 1 'patients (1.3%) hyperactivity, and 1 (1.3%), treatment noncompliance, and 1 (1.3%) increase in anxiety, and 1 (1.3%) were somnolence. The relationship between these side effects, drugs, the treatment of patients do not benefit from atomoxetine before 4 out, 11 patients are used long-or short-acting MPH, that 1 learned that used risperidone treatment. Insomnia, loss of appetite, and nervousness side effects was seen with all the OROS MPH. Increase in hyperactivity and

| | Comparement of patients under OROS-MPH treatment with atomoxetine treatment | Comparement of patients under OROS-MPH with control group | Comparement of patients under atomoxetine treatment with control group |
|---|---|---|--|
| Mean of ages | p= 0,586 | p= 0,933 | p= 0,806 |
| Mean of height | p= 0,294 | p= 0,336 | p= 1,00 |
| Mean of weight | p= 0,475 | p= 0,225 | p= 0,937 |
| Mean of physical health field in PedsQL | p= 0,991 | p<0,001* | p<0,005* |
| MMean of emotional functioning field in PPedsQL | p= 1,00 | p<0,001* | p<0,001* |
| MMean of , social functioning field in PedsQL | p= 0,821 | p<0,001* | p<0,005* |
| MMean of shcool functioning field in PedsQL | p= 0,683 | p<0,001* | p<0,001* |

(p<0,05*)

Table 5. Comparement of patients under OROS-MPH, atomoxetine treatment with each others and control group

anxiety side effects could be showed with the use of OROS MPH. The side effects of somnolence and non-compliance with the development of atomoxetine (Table 6).

| Reason of finishing first treatment / First treatment | MPH | Atomoxetine | Risperidone |
|---|-----|-------------|-------------|
| Non effective | 11 | 4 | 1 |
| Insomnia | 2 | - | - |
| Loss of appetite | 2 | - | - |
| Nervousness | 2 | - | - |
| Non compliance of treatment | - | 1 | - |
| Hyperactivity | 1 | - | - |
| Increase in anxiety | 1 | - | - |
| Somnolence | - | 1 | - |

Table 6. Reason of finishing first treatment and relationship between drugs

6. Discussion — conclusions

Life quality measurement is a method that gains gradually importance in children and adolescent, mental health surveys and clinical practice. Investigators and practitioners supposed that important deterioration in psychosocial fields associated with ADHD based on basic symptoms of ADHD.

Children and adolescent with ADHD are at increased risk of academic failure, dropping out of school or college, teenage pregnancy, alcohol and substance use and criminal behaviour. Driving poses an additional risk. The emotional impairments of children and adolescents with ADHD may include poor self-regulation of emotion, greater excessive emotional expression, especially anger and aggression, greater problems coping with frustration, reduced empathy, and decreased arousal to stimulation [25]. Children and adolescents with ADHD have problems with peer relationships lack friendships, or have limitations in their activities with friends if they do have friends. More than half of these children and adolescents have serious problems with peer relationships [26]. Relationships and activities within the family can be impaired and in some cases family relationships can break down, bringing additional social and financial difficulties causing children to feel sad or show oppositional or aggressive behavior [27].

Specific academic difficulties noted in children with ADHD include slower reading fluency weaker reading comprehension (Ghelani and poor penmanship. Mastery of academic skills can also be hampered by the secondary effects (impulsivity, inattention, and disorganization) that ADHD can have upon a child's ability to practice newly learned skills or study recently presented material in the homework setting [28,29].

ADHD affects not only on the child, but also on parents and siblings, causing disturbances to family and marital functioning, increased healthcare costs for patients and their family. Children and their families changes from the preschool years to primary school and adolescence, with varying aspects of the disorder being more prominent at different stages. Also, ADHD had more parent-reported problems in terms of emotional-behavioral role function, behavior, mental health, and self-esteem. In addition, the problems of children with ADHD had a significant impact on the parents' emotional health and parents' time to meet their own needs, and they interfered with family activities and family cohesion[30].

ADHD is one of the most common psychiatric conditions estimated to affect 5-10% of all children and ADHD predisposes children to impaired academic, familial, social, vocational and emotional functioning if untreated. ADHD does not remit with the onset of puberty alone and teenagers and adults continue to have symptoms of the disorder that cause significant problems in their lives[31].

Children with attention-deficit and disruptive behavior disorder had, according to parent ratings, a better emotional functioning score than children with anxiety disorders. Their academic performance was significantly lower than for children with anxiety disorders and other disorders, but school functioning was reported as equal. Clinicians reported more problems in behavior toward others for this group compared to children with anxiety and

mood disorders. Comorbidity of attention-deficit disorder or disruptive behavior disorder with other psychiatric diagnoses did not influence overall Quality of Life. Also it had been found that children with ADHD were more limited in schoolwork and social functioning [32]. Danckaerts M. et al. showed that a robust negative effect on QoL was reported by the parents of children with ADHD across a broad range of psychopathology symptoms [33].

Because of difficulties in academical, social and emotional fields, the adverse effect of ADHD on life quality is in evidence in current studies. Numerous studies have shown significant recovery in life quality with medication use in case of ADHD [6,7,8]. The results of studies carried out in this content showed adverse effect on all fields of children with ADHD diagnosis and therapy requirement. Also, it is suggested that recovery attempts for children with ADHD diagnosis should include all fields of life [34]. In line with previous studies, our study showed that there is significantly difference in all sub-fields of life quality scale between control group and under ADHD treatment [6,7,8]. Among this, when comparing all sub-fields of life quality scale, there is no significant difference between atomoxetine and OROS-MPH users. This result is consistent with Leo Bastiaens's study [35] conducted in 75 children between 6-12 age interval, comparing the effects of atomoxetine and stimulant therapy over life quality, and there are further studies that suggests efficiency of OROS-MPH on life quality [36]. Also in another study of Leo Bastiaens, 84 patients (atomoxetine n = 39/stimulants n = 45), between the ages of 5 and 18, were treated for approximately 8 months. At end point, there were no significant differences in improvements of quality of life between the two groups [37].

However an interesting study is that; 977 Male and female patients aged 6-17 years seeking treatment for symptoms of ADHD were assessed, they were grouped according to whether they were prescribed psycho- and/or pharmacotherapy (treatment) or not (no/'other' treatment) Although both treatment and no/'other' treatment cohorts showed improvements in mean Quality of Life over 12 months, the difference was small and not statistically significant [38].

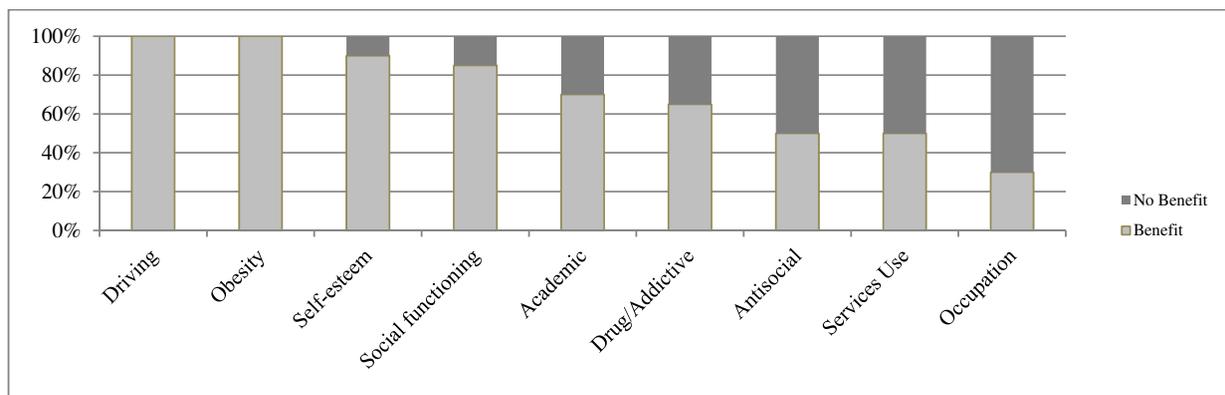
In our study, we found that confounding result, although patients with ADHD tend to show a decrease in school success with increase in age, patients who take OROS-MPH treatment show an increase in life quality school sub-score. This increase could be due to enhancement in OROS-MPH usage dose with age. Higher dose levels in OROS-MPH could be asserted as more effective for increase in academical success. Compared with the control group, decrease of life quality sub-areas is supported the view of pharmacotherapy alone not enough. However, further studies are needed to obtain certain data.

In this point; V A Harpin showed that the primary school children with ADHD frequently begins to be seen as being different as classmates start to develop the skills and maturity that enable them to learn successfully in school. ADHD to succeed, more frequently the child experiences academic failure, rejection by peers, and low self esteem. And This study suggested that assessment by an educational psychologist may help to unravel learning strengths and difficulties, and advise on necessary support in the classroom [39].

50 children and adolescents with ADHD diagnosis, 30 control group and both of their parents are examined. Rosenberg Self-Esteem Scale and Children's Quality of Life Scale are used. The

results of this study suggest that self-esteem in the children and adolescents with ADHD is not significantly high and that their quality of life is significantly low. This is noticeable for it draws attention to the psycho-social dimension in the clinical evaluation of the children with ADHD [40]. In this way, social support and motivational therapy may be needed.

From another study Figure 1 shows benefit (dark green bars) or no benefit (light green bars) by outcome group in treated participants with attention deficit hyperactivity disorder (ADHD) versus untreated ADHD. Improvement was reported most often in studies of driving and obesity outcomes (left side), with a greater proportion of outcomes reported to exhibit no benefit following treatment compared with no treatment in studies of occupation (right side). An intermediate proportion of studies of self-esteem, social functioning, academic, drug use/addictive behavior, antisocial behavior, and services use outcomes reported benefit with treatment [41].



*This figure is taken from "A systematic review and analysis of long-term outcomes in attention deficit hyperactivity disorder: effects of treatment and non-treatment"

Figure 1. Benefit and no benefit with treatment by outcome group

Treatment with OROS-MPH and atomoxetine also have side effects. Evidence shows that ADHD medications are safe and effective for children ages 6 and older. For children over the age of 6, long-term effectiveness and adverse effects are not well studied. More studies showed that psychostimulants and atomoxetine may cause insomnia, appetite loss, tiredness, social withdrawal, and abdominal pain. Psychostimulants and atomoxetine may also cause a modest increase in average blood pressure and average heart rate in some children and adolescents. Children or adolescents taking atomoxetine may be more likely to think about suicide than children who do not take it. More adverse effects were reported in preschoolers than in elementary school children. Moodiness and irritability often led to discontinuation of treatment with MPH. [42] In our study; 26 patients were applied before any other treatment of ADHD. However, several side effects, and due to non compliance of previously treatment patients couldn't maintain previous treatment is observed. Insomnia, loss of appetite, nervousness, hyperactivity, increase in anxiety, and somnolence are side effect which cause to stop first treatment. Insomnia, loss of appetite, and nervousness side

effects was seen with all the OROS MPH. Increase in hyperactivity and anxiety side effects could be showed with the use of OROS MPH. The side effects of somnolence and non-compliance with the development of atomoxetine. But our datas are limited about relationship of side effects and life quality. Further studies are needed side effects of OROS-MPH and atomoxetine on life quality.

Long-term effects of methylphenidate and atomoxsetine on growth rates of children with ADHD are the other size of the treatment which also effect the Quality of life. The effect of OROS-MPH and atomoxsetine over weight and height is still a subject of discussion. The final results, as to children with attention deficit who take stimulant medication grow slower than children with no treatment, verify the results of previous studies in 1972-1973. Recent study showed a decrease in expected weight and height growing in children who take stimulant therapy. In treatments continuing 2-3 years, the growing speed shows normalization tendency [43,44].

In the one of the review about effects of stimulants on height and weight; the quantitative analyses showed that treatment with stimulant medication led to statistically significant delays in height and weight. Treatment with stimulants in childhood reduced expected height and weight. This review also found statistically significant evidence of attenuation of these deficits over time. The qualitative review suggested that growth deficits may be dose dependent. Some data suggest that ultimate adult growth parameters are not affected [45].

Prolonged medication (data evaluated at 6 months - 5 years) with short-acting MPH has shown to have minimal impact on height only at the first 6 months; however, catch up growth was detected during adolescent period in 96 cases wo were treated with short-acting MPH 0.41-0.49 mg/kg/day [46]. In another research about the potential negative influence of methylphenidate on growth; mean value of height was lower than expected mean height for age by 0.42 cm at diagnosis. This difference increased to 2.69 cm (at 30 months of treatment), but it subsequently decreased to 0.83 cm (at 48 months of treatment). The relationship between nutritional status and the negative effects on the height curve in those patients would require nutritional optimization to return anthropometric variables to normal [47].

Two new researches was performed on the effect of amoxetine on growing patients with 5 year follow-up and long- time efficiency and reliability of atomoxetine. After a 5 year follow-up, it is suggested that while atomoxetine has no or a little effect on growing, in some cases could cause reduction in growing. Especially in 18 months, growing could be affected a little, however normal development could proceed in a period of 2-3 years [43,44]. Spencer et al present findings from an ongoing 5-year study of the efficacy and safety of treatment with atomoxetine. After 1 month's treatment,they found patients weighed less than expected from their starting percentiles relative to population norms, with a maximum shortfall at 15 months and a return to expected weight by 36 months. Patients were slightly shorter than expected after 12 months, reaching a maximum shortfall at 18 months and returning to expected height by 24 months. Patients in the top quartile for body mass index (BMI) or weight at baseline, and those in the third quartile for height, showed 5-year decreases from

expected values. Those below median height at baseline showed increases relative to expected values.[43]

In our study, we found no significant difference between both control group of OROS-MHP and atomoxetine in terms of weight and height. And also no significant difference were between treatment under OROS-MHP and atomoxetine. This result could be associated with time limitation. Further studies are needed if there are difference effects of between OROS-MPH and atomoxetine treatment on weight-height.

Although one of the research children with ADHD who performed poorly on the neuropsychological battery had greater BMI z-scores, and were more likely to be classified as overweight/obese compared with children with ADHD who performed better on the neuropsychological battery. In addition, children with ADHD who were taking a stimulant medication had significantly lower BMI z-scores compared with children with ADHD who were not taking medication or who were taking a non-stimulant medication. They claimed that EF (Executive Function) is more impaired among children with ADHD and co-occurring weight problems, highlighting the importance of self-regulation as a link between pediatric obesity and ADHD [48].

An interesting point is that last studies reported an association between overweight and ADHD. Although a higher prevalence of overweight/obesity was reported in clinical samples of patients with ADHD, longitudinal studies are needed to better understand the mechanisms underlying the association between ADHD and overweight/obesity [49].

Current data suggests an association between growing and medical effect of stimulants. Also normal growing speeds have been shown in children who take no treatment with attention deficit hyperactivity disorder. Therefore, further studies should focus on fields as detailed definition of growing and development effects of stimulants in children with different ages, determining the growing deficiency mechanism up to stimulant [50].

Gender differences is another variability that may affect the quality of life. Children with high levels of ADHD symptoms have many associated behaviour problems, even in pre-school years, and boys with high levels of ADHD symptoms are more severely affected compared with girls. Datas of researches are not enough in this field.

Data from 5 clinical atomoxetine trials (4 from Europe and 1 from Canada) with similar inclusion and exclusion criteria and similar durations (8- to 12-week follow-up) were included in the pooled analysis. 136 girls and 658 boys were treated with atomoxetine. Atomoxetine was effective in improving some aspects of health-related quality of life (HR-QoL) in both genders without any significant differences across genders. Also, it was found that correlations between core symptoms of ADHD and HR-QoL were low to moderate in both boys and girls [51].

Also 6-17 aged of patients were treated with atomoxetine in two studies. ADHD-related difficulties were assessed after 8 and 24 weeks using the Global Impression of Perceived Difficulties (GIPD) instrument, which can be taken to reflect the patient's QoL from the three perspectives. The GIPD scores over time suggest that patients' QoL, as reflected by perceived

ADHD-related difficulties, improved with time on atomoxetine. The sexes did not differ significantly in mean GIPD total scores, and also improvement in ADHD-related difficulties did not differ significantly between boys and girls [52]. In the second step of our study; we aimed to compare effects of sex differences on response of treatment with both atomoxetine and OROS-MPH, also correlation with life quality, it is our limitation of this study.

Consequently, ADHD, which is a chronic neuropsychiatric disorder, is known as negatively effective on life quality perception in reports about children and it is suggested that evaluation of life quality in follow-up and treatment stages of ADHD and efficiency of pharmacological treatment on life quality of these patients could be a guide for determining the fields that children have difficulty on. Besides, when comparing with normal population, the difficulties in academical, social and emotional fields could be seen more frequently. Medical treatment of attention deficit and hyperactivity disorder alone could cause increasing in conceptualization tendency of problems and nondevelopment on problem solving skills. Therefore, it is suggested that recovery attempts for children with ADHD diagnosis should include all fields of life. Karabekiroğlu K. et al found that more than half of the teachers denoted that the medication used for ADHD would have serious side effects and even with treatment ADHD would not sufficiently improve, and the children diagnosed with ADHD or autism should be trained at separate classes. So that the parents and teachers may benefit from structured educative programs in order to get rid of wrong assumptions and stigma [53].

One of the important points is that further study is needed to understand the social and psychological processes that underlie stigmatization, how parents balance perceived benefits of treatment with mental health stigma concerns, and to determine how stigmatization affects quality of life of children with ADHD.

Although in our study, patients with ADHD tend to show a decrease in school success with increase in age, patients who take OROS-MPH treatment show an increase in life quality school sub-score. This information could be a guide for examining of detailed determining of OROS-MPH effects.

Limitations of our study are number of patients and time of treatments. Our data are not enough to show effects of socio-demographic differences, side effects, gender and stigma on life quality. Measurement of quality of life in attention-deficit-hyperactivity disorder (ADHD) gives a more complete picture of day-to-day functioning and treatment effects than behavioural rating alone. Quality of life is affected from numerous factors so that new measurement parameters should be developed.

In conclusion; there is a significant difference in all sub-fields of life quality scale between control group and under ADHD treatment. Treatment increases life quality of ADHD patients but only medical treatment is not enough. There is no significant difference between weight and height when comparing between control groups of OROS-MPH and atomoxetine. Further studies are needed to support the effects of OROS-MPH and atomoxetine on life quality and weight-height.

Acknowledgements

PubChem chemical substance (submitted) records that are classified under the same Medical Subject Headings (MeSH) controlled vocabulary as the current articles.

Author details

Esra Ozdemir Demirci, Merve Cikili Uytun, Rabia Durmus and Didem Behice Oztop

Department of Child and Adolescent Psychiatry, Erciyes University Medical Faculty, Kayseri, Turkey

References

- [1] American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, 4th edition, Text Revision (DSM-IV-TR). Washington, DC: American Psychiatric Association, 2000.
- [2] Biederman J, Faraone SV. Attention-deficit hyperactivity disorder. *Lancet* 2005;366:237–48.
- [3] Biederman J, Spencer TJ (1999) Attention-deficit/hyperactivity disorder (ADHD) as a noradrenergic disorder. *Biol Psychiatry* 46:1234–1242
- [4] Safer DJ (2000) Commentary: stimulant treatment in the community. *J Am Acad Child Adolesc Psychiatry* 39:989–992
- [5] Perwien AR, Faries DE, Kratochvil CJ, et al. Improvement in healthrelated quality of life in children with ADHD: An analysis of placebo controlled studies of atomoxetine. *J Dev Behav Pediatr* 2004;25:264–71
- [6] Güleç C, Köroğlu E. (1998) Psychiatry Text Book. in: Şenol Ü, Şener Ş (eds). Attention deficit hyperactivity disorder. Ankara, 2, 1119-1129.
- [7] Escobar R, Soutullo CS, Hervas AH ve ark. Worse quality of life for children with newly diagnosed attention-deficit/hyperactivity disorder, compared with asthmatic and healthy children. *Pediatrics* 2005; 116:364-9.
- [8] Bastiaansen D, Koot HM, Ferdinand RF ve ark. Quality of life in children with psychiatric disorders: self, parent, and clinician report. *J Am Acad Child Adolesc Psychiatry* 2004; 43:221-30.
- [9] Yıldız Ö, Çakın Memik N, Ağaoğlu B. Quality of Life in Children with (Attention-Deficit Hyperactivity Disorder): A Cross-Sectional Study. *Neuropsychiatry Archives* 2010; 47: 314-8

- [10] Raggi VL, Chronis AM (2006) Interventions to address the academic impairment of children and adolescents with ADHD. *Clin Child Fam Psychol Rev* 9:85–111
- [11] Wehmeier PM, Schacht A, Barkley RA (2010) Social and emotional impairment in children and adolescents with ADHD and the impact on quality of life. *J Adolesc Health* 46:209–217
- [12] Popper CW (2000) Pharmacological alternatives to psychostimulants for the treatment of attention deficit/hyperactivity disorder. *Child Adolesc Psychiatr Clin N Am* 9:605–646
- [13] Scahill L, Chappell PB, Kim YS, Katsovich L, Sheperd E et al (2001) A placebo-controlled study of guanfacine in the treatment of children with tic disorders and attention deficit hyperactivity disorder. *Am J Psychiatry* 158:1067–1074
- [14] Silver LB (1999) Alternative (nonstimulant) medications in the treatment of attention-deficit/hyperactivity disorder in children. *Pediatr Clin North Am* 46:965–975
- [15] Wilens TE, Biederman J, Baldessarini RJ, Geller B, Schleifer D, Spencer TJ et al (1996) Cardiovascular effects of therapeutic doses of tricyclic antidepressants in children and adolescents. *J Am Acad Child Adolesc Psychiatry* 35:1491–1501
- [16] Sauer JM, Ponsler GD, Mattiuz EL, Long AJ, Witcher JW, Thomasson HR et al (2003) Disposition and metabolic fate of atomoxetine hydrochloride: the role of CYP2D6 in human disposition and metabolism. *Drug Metab Dispos* 31:98–107
- [17] Hechtman A, Abikoff H, Klein RG, et al. Academic achievement and emotional status of children with ADHD treated with long-term methylphenidate and multimodal psychosocial treatment. *J Am Acad Child Adolesc Psychiatry* 2004;43:812–9.
- [18] Banaschewski T, Coghill D, Santosh P, et al. Long-acting medications for the hyperkinetic disorders. A systematic review and European treatment guidelines. *Eur Child Adolesc Psychiatry* 2006;15:476–95.
- [19] Zhang H, Du M, Zhuang S. Impact of long-term Treatment of Methylphenidate on Height and Weight of School Age Children with ADHD. *Neuropediatrics* 2010;41:55-59
- [20] Yıldız Ö, Ağaoğlu B, Karakaya I, Şahika G, Şişmanlar ŞG, Çakın Memik N, Efficiency and tolerability of OROS-methylphenidate in Turkish children and adolescents with attention-deficit/hyperactivity disorder, *Anatolian Journal of Psychiatry*, 2010; 11:44-50
- [21] Çakın Memik N, Ağaoğlu B, Coşkun A, et al. The validity and reliability of pediatric quality of life inventory in 8-12 year old turkish children. . *Turkish Journal of Child Adolesc Psychiatry* 2008; 15:87-98.
- [22] Çakın Memik N, Ağaoğlu B, Coşkun A ve ark. The validity and reliability of pediatric quality of life inventory in 13-18 year old turkish adolescents. *Turkish Journal of Psychiatry* 2007; 18:353-63
- [23] Turgay A. Turgay DSM-IV Based Child and Adolescent Behavior Disorders Screening and Rating Scale, Integrative Therapy Institute Toronto, Kanada 1995.

- [24] Ercan ES, Amado S, Somer O, et al. Development of A Test Battery for the Assessment of Attention Deficit Hyperactivity Disorder. *Turkish Journal of Child Adolesc Psychiatry* 2001; 8:132-42.
- [25] Barkley RA. *Attention-Deficit/Hyperactivity Disorder: A Handbook for Diagnosis and Treatment*. 3rd edition. New York, NY: Guilford Press, 2006
- [26] Escobar R, Soutullo CA, Hervas A, et al. Worse quality of life for children with newly diagnosed attention-deficit/hyperactivity disorder, compared with asthmatic and healthy children. *Pediatrics* 2005;116:e364–9.
- [27] Schreyer I, Hampel P. (ADHD among boys in childhood: quality of life and parenting behavior)(Article in German). *Z Kinder Jugendpsychiatr Psychother* 2009;37:69–75.
- [28] Ghelani K, Sidhu R, Jain U, Tannock R: Reading comprehension and reading related abilities in adolescents with reading disabilities and attention-deficit/hyperactivity disorder. *Dyslexia* 10:364–384, 2004.
- [29] Racine MB, Majnemer A, Shevell M, Snider L: Handwriting performance in children with attention deficit hyperactivity disorder (ADHD). *J Child Neurol* 23:399–406, 2008.
- [30] Anne F. Klassen, DPhil, Anton Miller, MB, ChB, FRCPC, Stuart Fine, MB, Health-Related Quality of Life in Children and Adolescents Who Have a Diagnosis of Attention-Deficit/Hyperactivity Disorder, *PEDIATRICS* Vol. 114 No. 5 November 1, 2004 pp. e541 -e547)
- [31] Pliszka S, AACAP Work Group on Quality Issues. Practice parameter for the assessment and treatment of children and adolescents with attention-deficit/hyperactivity disorder. *J Am Acad Child Adolescent Psychiatry* 2007; 46:894-921.)
- [32] Bastiaansen D, Koot MH, Ferdinand FR, Verhulst FR. Quality of Life in Children With Psychiatric Disorders: Self-, Parent, and Clinician Report *Journal of the American Academy of Child & Adolescent Psychiatry*, Volume 43, Issue 2, Pages 221-230
- [33] Danckaerts M, Sonuga-Barke EJ, Banaschewski T, Buitelaar J, Dopfner M, Hollis C, Santosh P, Rothenberger A, Sergeant J, Steinhausen HC, Taylor E, Zuddas A, Coghill D (2010) The quality of life of children with attention deficit/hyperactivity disorder: a systematic review. *Eur Child Adolesc Psychiatry* 19:83–105
- [34] Üneri ÖŞ, Turgut S, Öner P, Bodur Ş, Rezaki B, Quality of life in 8-12 years old children with attention deficit hyperactivity disorder *Turkish Journal of Child Adolesc Psychiatry*, 2010,17(1):27-31
- [35] Bastiaens L. Improvement in global psychopathology increases quality of life during treatment of ADHD with atomoxetine or stimulants. *Psychiatr Q.* 2011 Dec;82(4):303-8. doi: 10.1007/s11126-011-9172-4.
- [36] Niederkirchner K, Slawik L, Wermelskirchen D, Rettig K, Schäuble B. , Transitioning to OROS(®) methylphenidate from atomoxetine is effective in children and adolescents with ADHD. *Expert Rev Neurother.* 2011 Apr;11(4):499-508.

- [37] Leo Bastiaens, Both Atomoxetine and Stimulants Improve Quality of Life in an ADHD Population Treated in a Community Clinic, *Psychiatr Q* (2008) 79:133–137)
- [38] Michal Goetz M. Yeh C.B, Ondrejka I, Akay A, et al A 12-Month Prospective, Observational Study of Treatment Regimen and Quality of Life Associated With ADHD in Central and Eastern Europe and Eastern Asia *J Atten Disord* 2012; 16:1 44-59
- [39] V A Harpin, The effect of ADHD on the life of an individual, their family, and community from preschool to adult life , *Arch Dis Child* 2005;90(Suppl I):i2–i7. doi: 10.1136/adc.2004.059006)
- [40] Zeynep Göker*, Evrim Aktepe**, Sema Kandil Self-esteem and Quality of Life in Children and Adolescents with Attention Deficit Hyperactivity Disorder *New/Yeni Symposium Journal* 2011 | 49 | 4
- [41] Shaw M, Hodgkins P, Caci H, Young S, Kahle J, Woods AG, Arnold LE. A systematic review and analysis of long-term outcomes in attention deficit hyperactivity disorder: effects of treatment and non-treatment. *BMC Medicine* 2012, 10:99
- [42] Eisenberg John M. Comparative Effectiveness Review Summary Guides for Clinicians (Internet). Rockville (MD): Agency for Healthcare Research and Quality (US); 2007-.AHRQ Comparative Effectiveness Reviews.2012 Jun 26.
- [43] Spencer TJ., Kratochvil JC, Sangal RB, Saylor KE, Bailey CE, Dunn DW, Geller DA, Casat CD, Lipetz RS, Jain R, Newcorn JH, Ruff DD, Feldman PD, Furr JA, and Allen JA. Effects of Atomoxetine on growth in children with Attention Deficit/hyperactivity disorder following up to five years of treatment. *J Child Adolesc Psychopharmacol* 17 (5): 689-699.
- [44] Kratochvil JC, Wilens ET, Greenhill LL ve ark (2006) Effects of long term Atomoxetine treatment for young children with Attention Deficit/hyperactivity disorder. *J Child Adolesc Psychiatry* 45 (8): 919-927.
- [45] Faraone VS, Biederman J, Morley PC, Thomas. Spencer JT, Effect of Stimulants on Height and Weight: A Review of the Literature *J. Am. Acad. Child Adolesc. Psychiatry*, 2008; 47(9):000–000.
- [46] Moungrnoi P, Maipang P. Long-term effects of short-acting methylphenidate on growth rates of children with attention deficit hyperactivity disorder at Queen Sirikit National Institute of Child Health. *J Med Assoc Thai*. 2011 Aug;94 Suppl 3:S158-63.
- [47] Durá-Travé T, Yoldi-Petri ME, Gallinas-Victoriano F, Zardoya-Santos P Effects of osmotic-release methylphenidate on height and weight in children with attention-deficit hyperactivity disorder (ADHD) following up to four years of treatment. *J Child Neurol*. 2012 May;27(5):604-9. Epub 2011 Dec 21.
- [48] Graziano PA, Bagner DM, Waxmonsky JG, Reid A, McNamara JP, Geffken GR Co-occurring weight problems among children with attention deficit/hyperactivity disorder: the role of executive functioning. *Int J Obes (Lond)*. 2012 Apr;36(4):567-72. doi: 10.1038/ijo.2011.245. Epub 2011 Dec 13.

- [49] Erhart M, Herpertz-Dahlmann B, Wille N, Sawitzky-Rose B, Hölling H, Ravens-Sieberer U. Examining the relationship between attention-deficit/hyperactivity disorder and overweight in children and adolescents. *Eur Child Adolesc Psychiatry*. 2012 Jan;21(1):39-49. Epub 2011 Nov 26
- [50] Poulton A. Growth and maturation in children and adolescents with attention deficit hyperactivity disorder *Current Opinion in Pediatrics* turkish edition, Vol 1, No 4, 2006.
- [51] Wehmeier PM, Schacht A, Escobar R, Hervas A, Dickson R. Health-related quality of life in ADHD: a pooled analysis of gender differences in five atomoxetine trials. *Atten Defic Hyperact Disord*. 2012 Mar;4(1):25-35.
- [52] Wehmeier PM, Schacht A, Dittmann RW, Banaschewski T. Minor differences in ADHD-related difficulties between boys and girls treated with atomoxetine for attention-deficit/hyperactivity disorder. *Atten Defic Hyperact Disord*. 2010 Jun;2(2):73-85
- [53] Karabekirođlu K, Memik NC, Özel ÖÖ, Toros F, Öztop D, Özbaran B et al.. Stigmatization and Misinterpretations on ADHD and Autism: A Multi-Central Study with Elementary School Teachers and Parents *Klinik Psikiyatri* 2009;12:79-89