The Effect of Sertraline on the Quality of Life for Children and Adolescents with Anxiety Disorder

Anksiyete Bozukluğu Olan Çocuk ve Ergenlerde Sertralin Tedavisinin Yaşam Kalitesi Üzerine Etkisi

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ABSTRACT

Introduction: In this study, we aimed to determine the changes in quality of life of children/adolescents with anxiety disorders during six months of sertraline treatment, to investigate parent-child/adolescent concordance in perception of quality of life and to examine the effect of treatment on children/adolescents.

Methods: In this study, 30 patients with anxiety disorders according to criteria specified in Diagnostic and Statistical Manual of Mental Disorders, 4th. Edition (DSM-IV) were assigned to sertraline treatment. The patients were evaluated using the Pediatric Quality of Life Inventory (PedsQL), State-Trait Anxiety Inventory for Children, Clinical Global Impression Scale (CGI) and the Children's Global Assessment Scale (CGAS) at 0th, 2nd and 6th months.

Results: PedsQL total scores increased significantly with the treatment in children and adolescents ($p<.001$), however, no differences were observed in parent proxy report ($p=.326$). The mean CGAS score was 59.85 ± 7.73 at the beginning of treatment and 73.70 ± 7.01 at the end of treatment ($p<.001$). The average CGI score decreased from $4.68\pm.96$ to $2.27\pm.84$.

Conclusion: It was observed that perception of quality of life in children and adolescents with anxiety disorders increased with the treatment. (*Archives of Neuropsychiatry 2014; 51: 30-39*)

Key words: Anxiety disorders, child, adolescents, quality of life

Conflict of interest: The authors reported no conflict of interest related to this article.

ÖZET

Amaç: Bu çalışmada, anksiyete bozukluğu olan çocuk ve ergenlerin tedavi ile altı ay boyunca yaşam kalitesi alanında yaşanan değişikliğin, yaşam kalitesi algısı yönünden ebeveyn çocuk/ergen uyumunun ve tedavinin çocuk ve ergen üzerine etkisinin incelenmesi amaçlanmıştır.

Yöntem: Mental Bozuklukların Tanısal ve İstatistiksel El Kitabı 4. Baskı, (DSM-IV) tanı ölçütlerine göre anksiyete bozukluğu olan 30 hasta çalışmaya alınmış, izlem boyunca sertralin tedavisi uygulanmıştır. Her bir hasta 0., 2. ve 6. aylarda Çocuklar için Yaşam Kalitesi Ölçeği, Çocuklar için Durumluk-Süreklilik Kaygı Envanteri, Klinik Global İzlem Ölçeği ve Çocuklar için Genel Değerlendirme Ölçeği ile hastalar değerlendirilmiştir.

Bulgular: Çocuklar için Yaşam Kalitesi Ölçeği-ölçek toplam puanı çocuk ve ergenlerde tedavi ile istatistiksel olarak anlamlı düzeyde artmış ($p<.001$), ebeveynlerde fark görülmemiştir ($p=.326$). Çocuklar için genel değerlendirme ölçeğinden elde edilen puan ortalaması tedavinin başında 59.85 ± 7.73 iken, tedavi sonunda 73.70 ± 7.01 olmuştur ($p<.001$). Klinik global izlem ölçeğinden alınan puan ortalaması $4.68\pm.96$ 'dan $2.27\pm.84$ 'e düşmüştür.

Sonuç: Bu çalışma ile anksiyete bozukluğu olan çocuk ve ergenlerin yaşam kalitesi algılarının tedavi ile arttığı görülmüştür. (*Nöropsikiyatri Arşivi 2014; 51: 30-39*)

Anahtar kelimeler: Anksiyete bozukluğu, çocuk, ergen, yaşam kalitesi

Çıkar çatışması: Yazarlar bu makale ile ilgili olarak herhangi bir çıkar çatışması bildirmemişlerdir.

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Introduction

The most common psychiatric disorders in children and adolescents have been found to be anxiety disorders (1,2,3,4). In epidemiological studies, the prevalence of anxiety disorders has been reported to be 8-17.3% (5,6,7,8). Social withdrawal that affects functionality negatively was detected in 10-20% of school-age children with anxiety disorders (9). It is known that children with anxiety disorder experience difficulties, such as low self-esteem, social isolation, poor social skills and difficulties in academic areas (10,11). In addition to social difficulties, physical symptoms, such as headache, abdominal pain and irritable bowel syndrome are also seen frequently (12). All these symptoms clearly influence physical, social, spiritual, and emotional well-being of a person. It was determined that the quality of life of people with mental disorders is affected adversely and also their life quality is lower than that of healthy ones, and even sometimes than in individuals with physical diseases (13,14,15,16,17). The quality of life in internalizing disorders is reported to be perceived worse than that in externalizing disorders, generally (18).

In many adult studies, it was stated that perceptions of quality of life in anxiety disorders, such as obsessive-compulsive disorder, social phobia and panic disorder were lower than in healthy individuals (15,19,20,21,22,23,24,25,26,27,28,29). In a study by Saarni et al. (14), it was found that chronic anxiety disorders affect the quality of life negatively. Compared to other anxiety disorders, social phobia and generalized anxiety disorder were found to reduce the quality of life mostly. In a review by Mendlowicz et al., including the presence of sub threshold symptoms as well, it was reported that quality of life was affected adversely in anxiety disorders (30). Quality of life, school, social and academic functionality in individuals with anxiety disorders are known to be impaired significantly (28,31,32). Although there have been numerous studies on adults with anxiety disorders and the effects of treatments on quality of life, no study on children and adolescents could be found in this area. In the treatment of anxiety disorders in children, it is known that serotonin reuptake inhibitors are effective, safe and suitable as the psychopharmacological agents of first choice. (32,33,34,35,36,37,38). Sertraline, a serotonin reuptake inhibitor, was found to be effective in the treatment of various anxiety disorders, such as obsessive-compulsive disorder (39,40), panic disorder (41,42), post-traumatic stress disorder (43), social anxiety disorder (44,45), and generalized anxiety disorder (46). Sertraline was found to be effective on both psychological and somatic symptoms in a placebo-controlled study that has been performed on children with anxiety disorder (47). In an adult study done by Allgulander et al. (46), it was reported that significant improvements in the quality of life and in the productivity as well as mental and physical symptoms of patients with generalized anxiety disorder were seen after 12 weeks of sertraline treatment. Several publications (39,48) indicated that sertraline was superior to placebo in the treatment of

obsessive-compulsive disorder in children. In the literature, we could not find any study investigating the effect of anxiety disorders on quality of life in children and on the nature of changes of the treatment process. In this study, we aimed to explore the effect of anxiety disorders and sertraline treatment on quality of life in children and adolescents as well as the concordance between children's/adolescents' and parents' perception of quality of life.

Method

Participants

Thirty children/adolescents between the ages of 8 and 18 years, diagnosed with panic disorder, separation anxiety disorder, social phobia, obsessive-compulsive disorder, generalized anxiety disorder, and specific phobia were included in the study in the Child and Adolescents Psychiatry Clinic at Kocaeli University Medical School between March 2008 and October 2008. Patients who have been treated for anxiety disorders and children/adolescents with psychotic disorders or mental retardation, a neurological disorder or chronic disease and physical disabilities were excluded from the study.

Procedure

The study was approved by the University Ethics Committee. The children/adolescents and their parents were informed about the study by giving forms providing information about the planned research; volunteers were taken to the study. An interview that was a diagnostic interview and the Schedule for Affective Disorders and Schizophrenia for School age Children-Present and Lifetime version-Turkish version (K-SADS-PL-TR) were administered to both the parents and the children/adolescents in order to confirm the diagnosis that was given by a child and adolescent psychiatrist according to criteria specified in the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV). After the definitive diagnosis, the patients and their parents were asked to fill the State-Trait Anxiety Inventory for Children (STAIC) and the Pediatric Quality of Life Inventory (PedsQL). After the first meeting at the beginning of the research, the patients and their parents were given the forms to fill out again at the 2nd and 6th months in order to evaluate the concordance between the children/adolescents and parents and to evaluate the efficacy of the treatment.

Intervention

Sertraline treatment was started at a dose of 25 mg/day per oral after the diagnosis. Then according to the patient's response, the dose was increased up to a maximum of 150 mg/day. Interviews were conducted with 2-3 weeks intervals to evaluate anxiety level, overall functionality and medication management; the dose was increased depending on clinical response and side effects. During the interviews, a structured psychotherapeutic approach was not applied.

Measurements

Pediatric Quality of Life Inventory (PedsQL)

The PedsQL is designed by Varni et al. to measure health-related quality of life of children and adolescents

between the ages of 2 and 18 years (49,50). The validity and reliability study of the Turkish version of the PedsQL for the ages between 8 and 18 years is done by Cakin Memik et al. (51,52). Scores are given as total scale score (TSS), physical health summary score (PSS), psychosocial health summary score (PsychoSS). The PSS score (eight items) is the same as that for the physical functioning subscale. The PsychoSS score (15 items) is created by computing the mean of the emotional (EFS), social (SFS), and school (SchFS) functioning subscale scores (50).

State-Trait Anxiety Inventory for Children (STAIC)

It is a self-report scale to measure state and trait anxiety and it consists of two twenty-item scales, developed by Spielberger et al. (1973) (53). The validity and reliability study of the Turkish version was made by Ozusta (1995) (54). Although the validity and reliability of the study has been done in children aged 9-12 years, it is used until the age of 17 (55).

Schedule for Affective Disorders and Schizophrenia for School-Age

Children-Present and Lifetime Version-Turkish version (K-SADS-PL-TR)

The K-SADS, which is the one of the scales of structured or semi-structured interviews used in children or adolescents, has two different forms. The reliability and validity of the Schedule for Affective Disorders and Schizophrenia for Adults Present Episode Version was developed by Endicott and Spitzer (56). The epidemiological version of K-SADS was developed to assess psychopathology that has occurred over the course of the subject's entire life (57). Evaluation of the reliability and validity of the K-SADS-Present and Lifetime-Turkish Version was made by Gokler et al. (58).

Children's Global Assessment Scale (CGAS)

This scale that was adapted from the Global Assessment Scale for adults, is a pointbased measurement used during follow-up observations of children. CGAS is a scale evaluating the patient's overall well-being and functioning by using symptoms, social and school functions as well as variables in dealing with problems. The CGAS scores on information from the child interview and, the scores range from 100 (excellent function) to 0 (severe malfunction) (59). This scale has been adapted to Turkish (58).

Clinical Global Impression Scale (CGI)

The Clinical Global Impression rating scale is a research rating tool applicable to all psychiatric disorders. CGI measures the symptom severity, treatment response and the efficacy of treatments in treatment studies of patients by physicians. The CGI has two components: the CGI-Severity (CGI-S), which rates illness severity, and the CGI-Improvement (CGI-I), which rates change from the baseline of treatment (60).

Statistical Analysis

Study data were analyzed using SPSS (Statistical Package for Social Sciences) 10.0 for Windows. Last Observation Carried Forward (LOCF) technique was used for the analysis of the data. For the LOCF analysis, the rating for a patient who missed a scheduled evaluation or who withdrew before scheduled study completion was carried forward into all

subsequent time slots for which actual (observed) rating results were not available. After the descriptive statistical analysis (mean, standard deviation), the Mann Whitney-U test was used for comparison of two groups. During the comparison of repeated measurements, the Friedman test is applied for data that not conform to normal distribution. When a significant difference was detected, the Bonferroni correction was used on the results of the Wilcoxon test used as a post-hoc test. The Bonferroni correction paired sample t-test was applied for the data fitting the normal distribution. Correlations were determined by Pearson's correlation coefficient. The results were evaluated at the level of significance $p \leq 0.05$.

Table 1. Sociodemographic variables and distribution of diagnosis of the patients

	Number (n)	Percentage (%)
Gender		
Female	25	83.3
Male	5	16.7
Class		
3 th -5 th	11	36.7
6 th -8 th	8	26.7
9 th -12 th	11	36.7
Mother's education level		
Primary education	24	80
High-school	6	20
University	-	-
Father's education level		
Primary education	13	43.3
High-school	14	46.7
University	3	10
Anxiety disorder diagnoses		
Panic disorder	3	10
Separation anxiety disorder	6	20
Social phobia	4	13.3
Specific phobia	2	6.7
Generalized anxiety disorder	13	43.3
Obsessive-compulsive disorder	11	36.7
Anxiety disorder not otherwise specified	1	3.3
Comorbidities		
Major depressive disorder	4	13.3
Enuresis nocturna	4	13.3
Attention deficit hyperactivity disorder	3	10
Oppositional defiant disorder	3	10
Conversion disorder	4	13.3
Dysthymic disorder	4	13.3

Results

Of the 30 (56.7%), 17 patients who were continued the treatment for 6 months, completed the study. After the 2th month, 5 patients (16.7%) did not continue the treatment, 2 patients (6.7%) after the 3th month, 3 patients (10.0%) after the 4th month, and 3 patients after the 5th month

did not attend the appointment without any notification. Sertraline was used at the dose of 25-150 mg/day and the mean daily dose was 64.65±29.51 mg. Sertraline was well tolerated. Only 2 patients reported nausea and one reported mild drowsiness in the first two weeks. No patient terminated the treatment because of adverse medication events.

Table 2. Mean PedsQL, STAIC and CGAS scores

mean SD		Baseline n=30		2 th month n=25		6 th month n=17		Statistical analysis				
		mean	SD	mean	SD	Test Statistics	fd	p	Post hoc test (between months)			
PedsQL	Child self-report	PSS	57.49	23.27	67.60	22.36	69.17	20.75	11.327	2	.03	0 th <2 nd 0 th <6 th 2 nd =6 th
		EFS	55.83	27.07	63.33	29.16	64.66	29.53	2.374	1.69	.186	-
		SFS	81.83	21.79	84.83	22.34	86.16	22.54	5.559	2	.062	-
		SchFS	62.16	24.02	64.66	21.16	66.16	21.48	1.580	2	.454	-
		PsychoSS	64.99	21.50	70.16	22.47	71.66	22.15	6.911	2	.032	0 th =2 nd 0 th <6 th 2 nd =6 th
	TSS	64.21	19.05	70.14	19.60	71.58	19.34	15.380	2	.00	0 th <2 nd 0 th <6 th 2 nd =6 th	
	Parent proxy report	PSS	63.33	20.51	60.00	18.86	64.57	17.47	0.680	1.70	.369	-
		EFS	57.00	19.10	60.83	19.43	63.33	19.31	2.350	1.99	.119	-
		SFS	78.50	24.11	77.00	19.72	77.83	22.50	1.055	2	.590	-
		SchFS	63.50	19.57	66.83	16.10	68.33	17.33	3.055	2	.217	-
		PsychoSS	66.44	15.31	68.44	14.52	69.63	14.83	0.978	1.79	.482	-
		TSS	65.10	15.77	65.50	13.61	68.37	12.75	1.093	1.78	.326	-
		State**	37.26	8.65	34.20	8.36	35.70	8.317	3.479	1.88	.043	0 th <2 nd 0 th =6 th 2 nd =6 th
	CGAS*	42.10	8.01	37.66	10.40	37.13	79.01	10.300	1.46	0.006	0 th <2 nd 0 th <6 th 2 nd =6 th	
		59.85	7.73	70.00	8.43	73.70	7.01	38.868	2	.000	0 th <2 nd 0 th <6 th 2 nd <6 th	

*Friedman test, Bonferroni correction Wilcoxon test

**Repeated Measure variance analysis, Bonferroni correction paired sample t test

PSS: Physical health summary score, EFS: Emotional functioning subscale score, SFS: Social functioning subscale score

SchFS: School functioning subscale score, PsychoSS: Psychosocial health summary score, TSS: Total scale score

Thirty children and adolescents aged between 8 and 17 years (mean age: 12.37 ± 2.52) were evaluated and 25 (83.3%) of them were female.

Sociodemographic variables and diagnostic data of the patients were presented in Table 1. It was seen that there was more than one anxiety disorders in 10 (33.3%) and a mental disorder without comorbid anxiety disorders in 17 (56.7%) patients.

In PedsQL child self-report, a statistically significant difference was observed in PSS, PsychoSS and TSS ($p < .03$, $p < .03$, $p < .001$, respectively). In PedsQL parent proxy report, there was no statistically significant difference between TSS and subscale scores (Table 2).

As seen in Tables 3 and 4, there were statistically significant and positive correlations except the subscale scores of SFS at baseline and 6th month and SchFS at baseline. When the children's and adolescents' self-reports were compared with their parents' proxy reports for the PedsQL, it was found that

there was no statistically significant difference between the TSS and subscale scores ($p > .05$).

The average CGAS score was 59.85 ± 7.73 at baseline and it was found to be 73.70 ± 7.01 at the 6th month. When it was considered statistically, the average scores of CGAS increased significantly at the end of the treatment ($p < .001$) (Table 2).

The average CGI-S score of the patients was found to be $4.68 \pm .96$ at baseline. The average CGI-I score was 2.79 ± 10.81 after two months and 2.79 ± 10.81 after 6 months of treatment. According to CGI-I, patients with a score of 3 or less were considered to respond the treatment. 80% ($n=24$) of patient in the 2nd month and 90% ($n=27$) in the 6th month showed signs of improvement.

Whether comorbidity and anxiety disorder were more than one or not, score averages of PedsQL, STAIC, CGAS and CGI are shown in Table 5, and no statistically significant difference was found.

Table 3. The correlation among child and parent's PedsQL scores at baseline

Items PSS	Child self-report				
	EFS	SFS	SchFS	PsychoSS	TSS
PSS	.494**				
EFS		.430*			
SFS			.142		
SchFS				.310	
PsychoSS					.494**
TSS					.435**

Pearson correlation test * $p < .05$, ** $p < .001$
PSS: Physical health summary score, EFS: Emotional functioning subscale score, SFS: Social functioning subscale score, SchFS: School functioning subscale score, PsychoSS: Psychosocial health summary score, TSS: Total scale score

Table 4. The correlation among patients and parent's PedsQL scores at 6th month

Items PSS	Child self-report				
	EFS	SFS	SchFS	PsychoSS	TSS
PSS	.478*				
EFS		.670*			
SFS			.313		
SchFS				.656*	
PsychoSS					.589*
TSS					.597*

Pearson correlation test * $p < .001$
PSS: Physical health summary score, EFS: Emotional functioning subscale score, SFS: Social functioning subscale score, SchFS: School functioning subscale score, PsychoSS: Psychosocial health summary score, TSS: Total scale score

Table 5. Mean scores of PedsQL, STAIC, CGAS and CGI

	No comorbidity	Comorbidity exist	Statistical test*		One anxiety disorder	More than one anxiety disorder	Statistical test*	
			Z	p			Z	p
PedsQL child self-report/TSS								
Baseline	63.03±17.56	65.12±20.61	-.25	.80	61.43±19.73	69.78±17.23	-1.08	.28
6 th month	70.40±23.75	72.48±15.91	-.06	.95	73.41±16.50	67.92±24.67	-.19	.84
PedsQL parent proxy report/TSS								
Baseline	63.95±14.76	65.98±16.89	-.29	.76	66.79±15.70	61.73±16.16	-.94	.34
6 th month	65.99±14.79	70.20±11.07	-.60	.54	68.87±13.27	67.38±12.27	-.70	.48
STAIC/state								
Baseline	38.23±7.74	36.52±9.46	-.83	.40	37.35±9.18	37.10±7.95	-.26	.79
6 th month	34.53±8.88	36.58±8.01	-.52	.60	36.55±8.75	34.00±7.51	-1.03	.30
STAIC/trate								
Baseline	41.00±9.06	42.94±7.27	-.60	.54	41.85±8.15	42.60±8.11	-.37	.70
6 th month	35.84±11.15	38.11±9.86	-.58	.55	37.65±10.12	36.10±11.17	-.44	.65
CGAS								
Baseline	50.45±8.50	59.43±7.42	-.82	.41	60.61±7.17	58.33±9.01	-.59	.55
6 th month	72.72±5.17	74.37±8.13	-1.10	.27	74.44±7.04	72.22±7.12	-.90	.36
CGI								
CGI-S								
Baseline	4.50±0.90	4.82±1.01	-.84	.39	4.60±0.88	4.88±1.16	-.70	.48
CGI-I								
6 th month	2.33±0.77	2.23±0.90	-.21	.83	2.20±0.83	2.44±0.88	-.68	.49

* Mann-Whitney U test

Discussion

Knowing a person's perception of quality of life is important. It helps us know the functional impact of diseases and observation of the effectiveness of different treatment methods. In addition, better understanding of the disorder in the quality of life assessment in anxiety disorders and to recognize the load on patients will be useful in developing ways of coping and methods of treatment. In addition to their ease of use and safety, anxiolytic effects of serotonin reuptake inhibitors lead to widespread use. Many serotonin

reuptake inhibitors e. g. sertraline are used in a safe manner for anxiety disorders, such as obsessive compulsive disorders, separation anxiety disorders and generalized anxiety disorder in children and adolescents (61). In the literature, there are many studies investigating the quality of life in adults with anxiety disorders. When considering studies on the quality of life in panic disorder, it was found that psychopharmacological agents, such as imipramine, clonazepam and clomipramine besides cognitive behavioral therapy lead to an increase in the quality of life (62,63,64,65).

In two studies (41,42) investigating the effect of sertraline on quality of life of in panic disorder, a statistically significant increase was seen in quality of life compared to placebo. Fluvoxamine treatment and quality of life were assessed in a study (66) which was done in adult patients with social phobia; a significant improvement was observed in family functioning in patients receiving fluvoxamine compared to that in patients receiving placebo. In a research (23) that cognitive behavioral therapy was administered to patients with social phobia, perceptions of quality of life increased at the end of treatment, but the received scores were still lower compared to that of healthy subjects. After escitalopram treatment, quality of life of patients with generalized social anxiety disorder was found to be increased (67). In a study on patients with generalized anxiety disorder (68), quality of life score was reported to reach the normal range in 51% of the sertraline treatment group and 35% of placebo recipients after 12 weeks of sertraline and placebo treatment. It was investigated in a study (69) whether venlafaxine and paroxetine can cause a change in quality of life in adults with obsessive-compulsive disorder, or not. It was observed that serotonin reuptake inhibitors led to improvement in quality of life perception, and venlafaxine and paroxetine were found to have similar efficacy. In a study done by Lochner et al. (31), perceptions of quality of life of patients having obsessive compulsive disorder, panic disorder and social anxiety disorder were compared and it was seen that they perceived quality of life negatively in similar rates. However, a similar study on children could not be found in the literature. In our study, when TSS and all sub-scale scores in PedsQL child self-report were evaluated, scores increased during the treatment; also a statistically significant difference was seen in PSS, PsychoSS and TSS. These results suggest that the treatment in children and adolescents had a positive effect on quality of life. However, there was no statistically significant difference between TSS and subscale scores in PedsQL parent proxy report. Some previous studies have reported that perception of quality of life in parents and children could be different (70,71) while in some studies parent and adolescent reports were compatible with each other (72,73). Parents can perceive quality of life of their children to be lower than it can be with their expectations, hopes or being effected by their current stress and mental conditions or by comparing the quality of life of their children with that of other children they know. In general, the use of self-report scale is recommended since in the assessment of quality of life of children could give direct information regarding the effect of mental disorders on the children's own lives (74,75). In our study, we observed a significant increase in child self-reported quality of life, however, this condition was not noticed in parent proxy reports, and this emphasizes the importance of self-report scales.

In our study, there was a statistically significant correlation between PedsQL scores of the children and parents. Parent proxy report is needed in cases of too young age, low mental capacity or when the child does not want to answer the questions. However, it has been emphasized

that self-report scales should be preferable during treatment, follow-up or in research studies as children reflect their own subjective perceptions. While parent and child forms are generally concordance in the physical functioning area, this concordance was reported to decrease in the emotional and social functioning areas (76). When the concordance between PedsQL of parent and child forms was evaluated at baseline and after six months of treatment, no significant correlation in the field of SFS was seen also in our study. When social functioning is considered, using the questions such as "trouble getting along with other children, other children do not want to be friend, other children are teasing, not doing things that other children at the same age can do, hard to keep up with peers" and considering that these questions can be more accurately assessed by subjective assessments, not having a correlation in between is an expected result. In the light of all this information, to obtain the best information on PedsQL, parent proxy reports and child self-reports are used together. Perception of quality of life was assessed in patients with obsessive-compulsive disorder, panic disorder and social anxiety disorder in a study (31) and it was determined that people who have comorbidity perceived the quality of life lower. In other studies, it has been reported that comorbidity and severity of symptoms affect anxiety disorders adversely (14,77,78,79). Perceptions of quality of life were found to be lower in those who have social phobia comorbid with a mental disorder (27). It has been reported that half of patients seeking treatment meet the criteria for more than one anxiety disorder and one-third meets the criteria for a secondary depressive disorder (80). Quality of life was perceived negatively by patients with anxiety disorders compared to healthy subjects in a study by Norberg et al. (81). In addition to the study of anxiety disorders in the same study, the patients who meet criteria for major depressive disorder were found to have more negative perceptions of quality of life than the patients who did not meet criteria for major depressive disorder. However, it was reported that there was not an additional negative impact on the quality of life of patients having more than one anxiety disorders. In our study, the existence of comorbidity or more than one anxiety disorder did not affect the quality of life in children/adolescents or parents' perception about their child. Because of the small number of patients in our study, the effect of comorbidity might not be evaluated reliably.

The most important limitation of our study is that all patients did not complete the six-month study for unknown reasons. Not to be blinded to the patients and the absence of placebo control group are the major constraints in the study we have done. On the other hand, under the category of anxiety disorders, the effect of each disorder on the quality of life and how the treatment improves the quality of life have not been evaluated, and the comparison of each disorder and the others in the category has not been done. It prevents the generalization of the results for all anxiety disorders due to the small number of patients.

It is thought that by understanding the effect of anxiety disorders on the quality of life, the awareness and the

interest towards research will increase against these disorders, and it is expected to focus on prevention and treatment modalities. Therefore, evaluating the quality of life in anxiety disorders will give important information related to the severity and the level of disorders. When considering that internalizing disorders such as anxiety disorders is difficult to be noticed by the family, more emphasis should be placed on this topic.

References

1. Schniering CA, Hudson JL, Rapee RM. Issues in the diagnosis and assessment of anxiety disorders in children and adolescents. *Clin Psychol Rev*. 2000;20:453-478.
2. Fergusson DM, Horwood LJ, Lynskey MT. Prevalence and comorbidity of DSM-III-R diagnoses in a birth cohort of 15 year olds. *J Am Acad Child Adolesc Psychiatry*. 1993;32:1127-1134.
3. Verhulst FC, Ende J, Ferdinand RF, Kasius MC. The prevalence of DSM-III-R diagnoses in a national sample of dutch adolescents. *Arch Gen Psychiatry*. 1997;54:329-336.
4. McGee R, Feehan M, Williams S, Partridge F. DSM-III disorders in a large sample of adolescents. *J Am Acad Child Adolesc Psychiatry*. 1990;29:611-619.
5. Anderson JC, Williams S, McGee R, Silva PA. DSM-III disorders in preadolescent children. Prevalence in a large sample from the general population. *Arch Gen Psychiatry*. 1987;44:69-76.
6. Bernstein GA, Borchardt CM, Perwien AR. Anxiety disorders in children and adolescents: A review of the past 10 years. *J Am Acad Child Adolesc Psychiatry*. 1996;35:1110-1119.
7. Costello EJ. Child psychiatric disorders and their correlates: a primary care pediatric sample. *J Am Acad Child Adolesc Psychiatry*. 1989;28:851-855.
8. Kashani JH, Orvaschel H. Anxiety disorders in mid-adolescence: a community sample. *Am J Psychiatry*. 1988;145:960-964.
9. Orvaschel H, Weissman M. Epidemiology of anxiety in children. In: Gittelman R, eds. *Anxiety Disorders of Childhood*. New York, Guilford Press; 1986; p. 58-72.
10. Strauss CC. Behavioral assessment and treatment of overanxious disorder in children and adolescents. *Behav Modif*. 1988;12:234-251.
11. Dweck C, Wortman C. Learned helplessness, anxiety and achievement. In: Krone H, Laux L, editors. *Achievement, Stress and Anxiety*. New York: Hemisphere; 1982; p. 87-89.
12. Livingston R, Taylor JL, Crawford SL. A study of somatic complaints and psychiatric diagnosis in children. *J Am Acad Child Adolesc Psychiatry*. 1988;27:185-187.
13. Cook EL, Harman JS. A comparison of health-related quality of life for individuals with mental health disorders and common chronic medical conditions. *Public Health Rep*. 2008;123:45-51.
14. Saarni SI, Suvisaari J, Sintonen H, Pirkola S, Koskinen S, Aromaa A, Lonnqvist J. Impact of psychiatric disorders on health-related quality of life: general population survey. *Br J Psychiatry*. 2007;90:326-332.
15. Koran LM, Thienemann ML, Davenport R. Quality of life for patients with obsessive-compulsive disorder. *Am J Psychiatry*. 1996;153:783-788.
16. Spitzer RL, Kroenke K, Linzer M, Hahn SR, Williams JB, deGruy FV III, Brody D, Davies M. Health-related quality of life in primary care patients with mental disorders: results from the PRIME-MD 1000 Study. *JAMA*. 1995;274:1511-1517.
17. Sherbourne CD, Wells KB, Judd LL. Functioning and well-being of patients with panic disorder. *Am J Psychiatry*. 1996;153:213-218.
18. Bastiaansen D, Koot HM, Ferdinand RF, Verhulst FC. Quality of life in children with psychiatric disorders: Self, parent, and clinician report. *J Am Acad Child Adolesc Psychiatry*. 2004;43:221-230.
19. Stengler-Wenzke K, Kroll M, Matschinger H, Angermeyer MC. Subjective quality of life of patients with obsessive-compulsive disorder compared to the general population. *Psychiatr Prax*. 2006;33:350-352.
20. Eisen JL, Mancebo MA, Pinto A, Coles ME, Pagano ME, Stout R, Rasmussen SA. Impact of obsessive-compulsive disorder on quality of life. *Compr Psychiatry*. 2006;47:270-275.
21. Carrera M, Herran A, Ayuso-Mateos JL, Sierra-Biddle D, Ramirez ML, Ayestaran A, Hoyuela F, Rodriguez-Cabo B, Vazquez-Barquero JL. Quality of life in early phases of panic disorder: predictive factors. *J Affect Disord*. 2006;94:127-134.
22. Mogotsi M, Kaminer D, Stein DJ. Quality of life in the anxiety disorders. *Harv Rev Psychiatry*. 2000;8:273-282.
23. Safren SA, Heimberg RG, Brown EJ, Holle C. Quality of life in social phobia. *Depress Anxiety*. 1996-1997;4:126-133.
24. Stein MB, Barrett-Connor E. Quality of life in older adults receiving medications for anxiety, depression, or insomnia: findings from a community-based study. *Am J Geriatr Psychiatry*. 2002;10:568-574.
25. Lane D, Carroll D, Ring C, Beevers DG, Lip GY. Mortality and quality of life 12 months after myocardial infarction: effects of depression and anxiety. *Psychosom Med*. 2001;63:221-230.
26. Cass AR, Volk RJ, Nease DE Jr. Health-related quality of life in primary care patients with recognized and unrecognized mood and anxiety disorders. *Int J Psychiatry Med*. 1999;29:293-309.
27. Wittchen HU, Fuetsch M, Sonntag H, Müller N, Liebowitz M. Disability and quality of life in pure and comorbid social phobia. Findings from a controlled study. *Eur Psychiatry*. 2000;15:46-58.
28. Rapaport MH, Clary C, Fayyad R, Endicott J. Quality-of-life impairment in depressive and anxiety disorders. *Am J Psychiatry*. 2005;162:1171-1178.
29. Stein MB, Kean YM. Disability and quality of life in social phobia: epidemiologic findings. *Am J Psychiatry*. 2000;157:1606-1613.
30. Mendlowicz MV, Stein MB. Quality of life in individuals with anxiety disorders. *Am J Psychiatry*. 2000;157:669-682.
31. Lochner C, Mogotsi M, du Toit PL, Kaminer D, Niehaus DJ, Stein DJ. Quality of life in anxiety disorders: a comparison of obsessive-compulsive disorder, social anxiety disorder, and panic disorder. *Psychopathology*. 2003;36:255-262.
32. Reinblatt SP, Riddle MA. Selective serotonin reuptake inhibitor-induced apathy: a pediatric case series. *J Child Adolesc Psychopharmacol*. 2006;16:227-233.
33. Williams TR, Miller BD. Pharmacologic management of anxiety disorders in children and adolescents. *Curr Opin Pediatr*. 2003;15:483-490.
34. Labellarte MJ, Walkup JT, Riddle MA. The new antidepressants. Selective serotonin reuptake inhibitors. *Pediatr Clin North Am*. 1998;45:1137-1155.
35. Emslie GJ, Weinberg WA, Mayes TL. Treatment of children with antidepressants: focus on selective serotonin reuptake inhibitors. *Depression Anxiety*. 1998;8:13-17.
36. Stein MB, Seedat S. Pharmacotherapy. In: Morris TL, March JS, eds. *Anxiety Disorders in Children and Adolescents*. New York London: The Guilford Press; 2004; p. 329-355.
37. Compton SN, Grant PJ, Chrisman AK, Gammon PJ, Brown VL, March JS. Sertraline in children and adolescents with social anxiety disorder: an open trial. *J Am Acad Child Adolesc Psychiatry*. 2001;40:564-571.
38. Fairbanks JM, Pine DS, Tancer NK, Dummit ES 3rd, Kentgen LM, Martin J, Asche BK, Klein RG. Open fluoxetine treatment of mixed anxiety disorders in children and adolescents. *J Child Adolesc Psychopharmacol*. 1997;7:17-29.
39. March JS, Biederman J, Wolkow R, Safferman A, Mardekian J, Cook EH, Cutler NR, Dominguez R, Ferguson J, Muller B, Riesenberger R, Rosenthal M, Sallee FR, Wagner KD, Steiner H. Sertraline in children and adolescents with obsessive-compulsive disorder: a multicenter randomized controlled trial. *JAMA*. 1998;280:1752-1756.

40. Greist JH, Jefferson JW, Kobak KA, Chouinard G, DuBoff E, Halaris A, Kim SW, Koran L, Liebowitz MR, Lydiard B. A 1 year double-blind placebo-controlled fixed dose study of sertraline in the treatment of obsessive-compulsive disorder. *Int Clin Psychopharmacol*. 1995;10:57-65.
41. Pohl RB, Wolkow RM, Clary CM. Sertraline in the treatment of panic disorder: a double-blind multicenter trial. *Am J Psychiatry*. 1998;155:1189-1195.
42. Pollack MH, Otto MW, Worthington JJ, Manfro GG, Wolkow R. Sertraline in the treatment of panic disorder: a flexible-dose multicenter trial. *Arch Gen Psychiatry*. 1998;55:1010-1016.
43. Brady K, Pearlstein T, Asnis GM, Baker D, Rothbaum B, Sikes CR, Farfel GM. Efficacy and safety of sertraline treatment of posttraumatic stress disorder: a randomized controlled trial. *JAMA*. 2000;283:1837-1844.
44. Van Ameringen MA, Lane RM, Walker JR, Bowen RC, Chokka PR, Goldner EM, Johnston DG, Lavalley YJ, Nandy S, Pecknold JC, Hadrava V, Swinson RP. Sertraline treatment of generalized social phobia: a 20-week, double-blind, placebo-controlled study. *Am J Psychiatry*. 2001;158:275-281.
45. Liebowitz M, DeMartini N, Weihs K, Londeborg PD, Smith WT, Chung H, Fayyad R, Clary CM. Efficacy of sertraline in severe generalized social anxiety disorder: results of a double-blind, placebo-controlled study. *J Clin Psychiatry*. 2003;64:785-792.
46. Allgulander C, Dahl AA, Austin C, Morris PL, Sogaard JA, Fayyad R, Kutcher SP, Clary CM. Efficacy of sertraline in a 12-week trial for generalized anxiety disorder. *Am J Psychiatry*. 2004;161:1642-1649.
47. Rynn MA, Siqueland L, Rickels K. Placebo-controlled trial of sertraline in the treatment of children with generalized anxiety disorder. *Am J Psychiatry*. 2001;158:2008-2014.
48. Pediatric OCD Treatment Study (POTS) Team. Cognitive behavior therapy, sertraline, and their combination for children and adolescents with obsessive-compulsive disorder: the Pediatric OCD Treatment Study (POTS) randomized controlled trial. *JAMA*. 2004;292:1969-1976.
49. Varni JW, Seid M, Rode CA. The PedsQL: measurement model for the Pediatric Quality of Life Inventory. *Med Care*. 1999;37:126-139.
50. Varni JW, Seid M, Kurtin PS. The PedsQLTM 4.0: reliability and validity of the Pediatric Quality of Life Inventory TM version 4.0 generic core scales in healthy and patient populations. *Med Care*. 2001;39:800-812.
51. Çakın Memik N, Ağaoglu B, Coşkun A ve Karakaya I. Çocuklar için Yaşam Kalitesi Ölçeği'nin 8-12 yaş çocuk formunun geçerlik ve güvenilirliği [The validity and reliability of Pediatric Quality of Life Inventory in 8- 12 year old Turkish children]. *Çocuk ve Ergen Ruh Sağlığı Dergisi*. 2008;15:87-98 [Article in Turkish].
52. Çakın Memik N, Ağaoglu B, Coşkun A, Uneri OS, Karakaya I. The validity and reliability of the Turkish Pediatric Quality of Life Inventory for children 13-18 years old. *Türk Psikiyatri Derg*. 2007;18:353-363.
53. Spielberger CD. Preliminary Manual for the State-Trait Anxiety Inventory for children. Palo Alto: Consulting Psychologists Press;1973.
54. Ozusta S. Adaptation, validity and reliability of State-Trait Anxiety Inventory for children *Türk Psikoloji Dergisi*. 1995;10:32-44.
55. Öy B, İlgen R, Ekmekçi A, Türkmen M, Yılmaz N, Başoğlu N. The implementation of State-Trait Anxiety Inventory for children at elementary and secondary school students. *Çocuk ve Ergen Ruh Sağlığı Dergisi*. 1995;2:76-8.
56. Endicott J, Spitzer RL. A diagnostic interview: the schedule for affective disorders and schizophrenia. *Arch Gen Psychiatry*. 1978;35:837-844.
57. Orvaschel H, Puig-Antich J, Chambers W, Tabrizi MA, Johnson R. Retrospective assessment of prepubertal major depression with the Kiddie-SADS-E. *J Am Acad Child Adolesc Psychiatry*. 1982;21:392-397.
58. Gökler B, Ünal F, Pehlivan Türk B, Kültür EÇ, Akdemir D, Taner Y. Reliability and validity of schedule for affective disorders and schizophrenia for school age children-present and lifetime version-Turkish version (K-SADS-PL-T). *Çocuk ve Ergen Ruh Sağlığı Dergisi*. 2004;11:109-116.
59. Shaffer D, Gould MS, Brasic J, Ambrosini P, Fisher P, Bird H, Aluwahlia S. A children's global assessment scale (CGAS). *Arch Gen Psychiatry*. 1983;40:1228-1231.
60. Guy W. ECDEU Assessment Manual for Psychopharmacology. Revised US Dept Health, Education and Welfare publication (ADM), Rockville, Md; National Institute of Mental Health 1976;76-338.
61. Labellarte MJ, Ginsburg G. Anxiety disorders. In: Martin A, Scahill L, Charney DS, Leckman JF, editors. *Pediatric psychopharmacology*. Oxford University Press; 2003; p. 497-511.
62. Jacobs RJ, Davidson JR, Gupta S, Meyerhoff AS. The effects of clonazepam on quality of life and work productivity in panic disorder. *Am J Manag Care*. 1997;3:1187-1196.
63. Mavissakalian MR, Perel JM, Talbott-Green M, Sloan C. Gauging the effectiveness of extended imipramine treatment for panic disorder with agoraphobia. *Biol Psychiatry*. 1998;43:848-854.
64. Lecrubier Y, Judge R. Long-term evaluation of paroxetine, clomipramine and placebo in panic disorder. Collaborative Paroxetine Panic Study Investigators. *Acta Psychiatr Scand*. 1997;95:153-160.
65. Telch MJ, Schmidt NB, Jaimez TL, Jacquin KM, Harrington PJ. Impact of cognitive-behavioral treatment on quality of life in panic disorder patients. *J Consult Clin Psychol*. 1995;63:823-830.
66. Stein MB, Fyer AJ, Davidson JRT, Pollack MH, Wiita B. Fluvoxamine treatment of social phobia (social anxiety disorder): a double-blind, placebo-controlled study. *Am J Psychiatry*. 1999;156:756-760.
67. François C, Montgomery SA, Despiegel N, Aballéa S, Roiz J, Auquier P. Analysis of health-related quality of life and costs based on a randomised clinical trial of escitalopram for relapse prevention in patients with generalised social anxiety disorder. *Int J Clin Pract*. 2008;62:1693-1702.
68. Dahl AA, Ravindran A, Allgulander C, Kutcher SP, Austin C, Burt T. Sertraline in generalized anxiety disorder: efficacy in treating the psychic and somatic anxiety factors. *Acta Psychiatr Scand*. 2005;111(6):429-35.
69. Tenney NH, Denys DA, van Megen HJ, Glas G, Westenberg HG. Effect of a pharmacological intervention on quality of life in patients with obsessive-compulsive disorder. *Int Clin Psychopharmacol*. 2003;18:29-33.
70. Sawyer M, Antoniou G, Toogood I, Rice M. A comparison of parent and adolescent reports describing the health-related quality of life of adolescents treated for cancer. *Int J Cancer*. 1999;12:39-45.
71. Danckaerts M, Sonuga-Barke EJ, Banaschewski T, Buitelaar J, Döpfner M, Hollis C, Santosh P, Rothenberger A, Sergeant J, Steinhausen HC, Taylor E, Zuddas A, Coghill D. The quality of life of children with attention deficit/hyperactivity disorder: a systematic review. *Eur Child Adolesc Psychiatry*. 2010;19:83-105.
72. Varni JW, Bruwinkle TM, Seid M, Skarr D. The PedsQLTM 4.0 as a pediatric population health measure: feasibility, reliability and validity. *Ambul Pediatr*. 2003;3:329-341.
73. Felder-Puig R, Frey E, Proksch K, Varni JW, Gadner H, Topf R. Validation of the German version of the Pediatric Quality of Life InventoryTM (PedsQLTM) in childhood cancer patients off treatment and children with epilepsy. *Qual Life Res*. 2004;13:223-234.
74. Eiser C, Morse R. Can parents rate their child's health-related quality of life? Results of a systematic review. *Qual Life Res*. 2001;10:347-357.
75. Varni JW, Katz ER, Seid M, Quiggin DJ, Friedman-Bender A, Castro CM. The Pediatric Cancer Quality of Life Inventory (PCQL): I. Instrument development, descriptive statistics, and cross-informant variance. *J Behav Med*. 1998;21:179-204.

76. Eiser C, Morse R. Quality-of-life measures in chronic diseases of childhood. *Health Technol Assess.* 2001;5:1-157.
77. Candilis PJ, McLean RY, Otto MW, Manfro GG, Worthington JJ 3rd, Penava SJ, Marzol PC, Pollack MH. Quality of life in patients with panic disorder. *J Nerv Ment Dis.* 1999;187:429-434.
78. Meltzer-Brody S, Davidson JR: Completeness of response and quality of life in mood and anxiety disorders. *Depression Anxiety.* 2000;12:95-101.
79. Strine TW, Chapman DP, Kobau R, Balluz L. Associations of self-reported anxiety symptoms with health-related quality of life and health behaviors. *Soc Psychiatry Psychiatr Epidemiol.* 2005;40:432-438.
80. Sanderson WC, DiNardo PA, Rapee RM, Barlow DH. Syndrome comorbidity in patients diagnosed with a DSM-III-R anxiety disorder. *J Abnorm Psychol.* 1990;99:308-312.
81. Norberg MM, DiefenbachGJ, Tolin DF. Quality of life and anxiety and depressive disorder comorbidity. *J Anxiety Disord.* 2008;22:1516-1522.