Gastrointestinal and Sleep Problems in Children with Autism Spectrum Disorder: Their Relationship with Problematic Behavior

Otizm Spektrum Bozukluğu Olan Çocuklarda Gastrointestinal Sistem ve Uyku Sorunları: Bunların Problemli Davranışlarla İlişkisi

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ABSTRACT

Objective: The purpose of this research is to investigate sleep and gastrointestinal problems in children with autism spectrum disorder (ASD) and their relationship with each other, autism severity and problematic behavior.

Material and Methods: The children who were admitted to outpatient clinics of child psychiatry at our hospital in a 3-months period and had diagnosis of ASD according to DSM-5 were included. The parents filled Aberrant Behavior Checklist (AbBC), Rome-3 Diagnostic Questionnaire for Pediatric Functional Gastrointestinal Disorders Parent Report Form (QPGS-RIII), Children's Sleep Habits Questionnaire (CSHQ), Autism Behavior Checklist (ABC) and sociodemographic data form. The clinician applied Childhood Autism Rating Scale (CARS).

Results: Ninety-seven children with ASD were included. According to QPGS-RIII, 38.1% of the cases had probable functional gastrointestinal problems. Those were 26.8% (n=26) functional constipation, 8.2% (n=8) nonretentive fecal incontinence, 2.1% (n=2) aerofaji, 3.1% (n=3) rumination syndrome, 4.1% (n=4) irritable bowel syndrome, 1% (n=1) functional abdominal pain syndrome, 1% (n=1) functional dyspepsia, 3.1% (n=3) functional abdominal pain, 1% cyclic vomiting and 1% (n=1) abdominal migraine. According to CSHQ 58.8% of the cases had sleep problems. ASD patients with functional gastrointestinal problems, had higher total scores of CSHQ, ABC and AbBC, compared to children with no functional gastrointestinal problems.

Conclusion: Our findings revealed that frequency of gastrointestinal and sleep problems were high in children with ASD. It is appropriate to evaluate patients with ASD in terms of gastrointestinal and sleep problems especially if behavioral problems accompanies. And treating gastrointestinal and sleep problems might decrease challenging behaviors that seen in ASD.

Key Words: Autism, Gastrointestinal diseases, Sleep, Problem behavior

ÖΖ

Amaç: Bu araştırmanın amacı, otizm spektrum bozukluğu (OSB) olan çocuklarda uyku ve gastrointestinal sorunları ve bunların birbirleriyle, otizm şiddeti ve problemli davranışlarla olan ilişkisini incelemektir.

Gereç ve Yöntemler: Hastanemizde 3 aylık bir sure içinde çocuk psikiyatrisi polikliniklerine başvuran ve DSM-5'e göre OSB tanısı alan çocuklar çalışmaya alındı. Ebeveynler tarafından Sorun Davranış Kontrol Listesi (SDKL), Pediatrik

Conflict of Interest / Çıkar Çatışması: On behalf of all authors, the corresponding author states that there is no conflict of interest

Ethics Committee Approval / Etik Kurul Onayı: This study was conducted in accordance with the Helsinki Declaration Principles. Our study was approved by Ankara Children Hematology and Oncology Hospital Clinical Research Ethics Committee (2018-186 protocol number).

Contribution of the Authors / Yazarların katkısı: AKBAL BAĞCI K: Constructing the hypothesis or idea of research and/or article, Planning methodology to reach the Conclusions, Taking responsibility in patient follow-up, collection of relevant biological materials, data management and reporting, execution of the experiments, Taking responsibility in necessary literature review for the study, Taking responsibility in the whole or important parts of the study, Reviewing the article before submission scientifically besides spelling and grammar. **PARLAK GÖZÜKARA** Ö: Taking responsibility in patient follow-up, collection of relevant biological materials, data management and reporting, execution of the experiments, Reviewing the article before submission scientifically besides spelling and grammar. **CÖRE E:** Organizing, supervising the course of progress and taking the responsibility of the research/ study, Taking responsibility in logical interpretation and conclusion of the results, Reviewing the article before submission scientifically besides spelling and grammar. **CÖKER 2:** Taking responsibility in logical interpretation and conclusion of the results, Reviewing the article before submission scientifically besides spelling and grammar. **CÖKER 2:** Taking responsibility in logical interpretation and conclusion of the results, Reviewing the article before submission scientifically besides spelling and grammar. **CÖKER 2:** Taking responsibility in logical interpretation and conclusion of the results, Reviewing the article before submission scientifically besides spelling and grammar.

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Department of Child and Adolescent Psychiatry, Ankara Bilkent City Hospital, Ankara, Türkiye E-posta: drkardelenakbal@gmail.com Received / Geliş tarihi : 25.05.2023 Accepted / Kabul tarihi : 11.08.2023 Online published : 27.09.2023 Elektronik yayın tarihi DOI: 10.12956/tchd.1302455 Gastrointestinal Semptomlar Ölçeği- Ebeveyn Rapor Formu, Çocuk Uyku Alışkanlıkları Anketi (ÇUAA), Otizm Davranış Kontrol Listesi (ODKL) ve sosyodemografik veri formu dolduruldu. Klinisyen tarafından Çocukluk Otizm Derecelendirme Ölçeği (ÇODÖ) uygulandı.

Bulgular: Çalışmaya 97 OSB hastası dahil edildi. Pediatrik Gastrointestinal Semptomlar Ölçeği- Ebeveyn Rapor Formuna göre vakaların %38.1'inde olası fonksiyonel gastrointestinal problem saptandı. Bunlardan %26.8'i (n=26) fonksiyonel konstipasyon, %8.2'si (n=8) retansif olmayan fekal inkontinans, %2.1'i (n=2) aerofaji, %3.1'i (n=3) ruminasyon sendromu, %4.1'i (n=4) irritabl bağırsak sendromu, %1'i (n=1) fonksiyonel karın ağrısı sendromu, %1'i (n=1) fonksiyonel dispepsi, %3.1'i (n=3) fonksiyonel karın ağrısı, %1'i siklik kusma ve %1'i (n=1) abdominal migrendi. ÇUAA'ya göre vakaların %58.8'inde uyku problemi vardı. Fonksiyonel gastrointestinal problemi olan OSB hastalarının, fonksiyonel gastrointestinal problemi olmayan hastalara göre ÇUAA, ODKL ve SDKL toplam puanları daha yüksek saptandı.

Sonuç: Bulgularımız OSB'li çocuklara gastrointestinal ve uyku sorunlarının sıkça eşlik ettiğini göstermiştir. Özellikle davranış sorunları eşlik eden OSB'li hastaların, altta yatan gastrointestinal ve uyku sorunları açısından değerlendirilmesi önemli görünmektedir. Gastrointestinal hastalıkları ve uyku problemlerini tedavi etmek, OSB'ye sık eşlik eden davranış sorunlarını azaltabilir.

Anahtar Sözcükler: Otizm, Gastrointestinal Hastalıklar, Uyku, Sorunlu Davranış

INTRODUCTION

Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by deficits in social communication, stereotypical repetitive behaviors and restricted interests (1). Recent studies estimated that 1 in 54 children has been identified with ASD and prevalence is increasing (2).

ASD develops from interaction of genetic, environmental and neurobiological factors (3). Although the pathophysiology of ASD is not fully known, gut and brain interaction has taken attention in recent years. In addition to neurological symptoms, ASD subjects frequently suffer from gastrointestinal (GIS) symptoms including constipation, encopresis, diarrhea, flatulence, gastroesophageal reflux and abdominal pain (4-6). Frequency of GIS symptoms in ASD children is 9 to 91% (5). Increased problematic behavior has been demonstrated in individuals with ASD and GIS symptoms. It has been observed that GIS symptoms trigger self-harm, aggression and anxiety behavior in children with autism (6).

Also, it has been indicated that sleep problems are highly common in ASD, with rates ranging from 40% to 80% (7). It was observed that impaired sleep leads to irritability and tendency to violence and causes emotional disregulation in ASD (8).

The purpose of this research is to investigate sleep and gastrointestinal problems in children with autism spectrum disorder (ASD) and their relationship with autism severity, problematic behavior and each other. We also aimed to drew attention to possible gastrointestinal and sleep problems that may be the underlying reasons for behavioral problems in ASDs. Unlike other studies we investigate all these factors in a single study.

MATERIALS and METHODS

Ninety-seven ASD patients aged 3-12 years who applied to the child and adolescent psychiatry outpatient clinics of Ankara Children Hematology and Oncology Hospital, in a 3 months period, were included in the study. Patients who had history of organic gastrointestinal disorder were excluded.

Clinical interview based on DSM-5 was conducted and Childhood Autism Rating Scale (CARS) was performed by the clinicians. Autism Behavior Checklist (ABC), Children's Sleep Habits Questionnaire (CSHQ), Aberrant Behavior Checklist (AbBC), Diagnostic Questionnaire For Pediatric Functional Gastrointestinal Disorders Parent Report Form (QPGS-RIII) and sociodemographic data form were filled by the parents and checked by the clinician. Clinician also questioned clinical features such as medical condition, drug use, family history of chronic diseases.

Our study was approved by Ankara Children Hematology and Oncology Hospital Clinical Research Ethics Committee (2018-186 protocol number). The research was conducted according to the Helsinki Declaration rules of good clinical practice and ethics.

Written and verbal informed consent was obtained from the parents.

CARS: The scale has 15 items. It was developed to diagnose ASD and to distinguish children with developmental delays from children with autism spectrum disorders. It categorizes autism severity from mild to moderate to severe.

ABC: The scale has 57 items and 5 subscales. Those are; sensory, relating, body and object use, language, and social and self-help. It evaluates autistic children's symptoms and behaviors.

AbBC: It has 58 items and five subscales. Those are irritability, lethargy/social withdrawal, stereotypic behavior, hyperactivity/ noncompliance and inappropriate speech.

QPGS-RIII: The scale has 71 items. It evaluates GIS symptoms, categorize functional GIS disorders (FGIDs) due to Rome-III criteria.

CSHQ: It has 33 items and investigates children's sleep habits and sleep-related problems. The cut off point off the scale is 41.

Statistical analysis, Continuous variables were expressed as arithmetic mean, standard deviation, median, minimum-

maximum values, and categorical variables were expressed as frequency (n) and percentage (%). Conformity of continuous variables to normal distribution was evaluated with Kolmogorov-Smirnov test. Age; Problematic Behavior Checklist (PBCL)'s sub-scores of latergy-social withdrawal, stereotypical behaviors, hyperactivity and speech; and all sub-scores of the Childhood Autism Rating Scale (CARS) did not show normal distribution. On the other hand, parental age, Problematic Behavior Checklist (PBCL)'s other scores, Childhood Autism Rating Scale (CARS) total score, Autism Behavior Checklist (ABC) total score and all sub-scores, Child Sleeping Habits questionnaire-total score distribution was found as normal. Mann-Whitney U test was used to compare the measurement variables that did not show normal distribution. Pearson Chi-square and Fisher's exact test were used in the analysis of categorical variables. Spearman correlation test was used in the correlation analysis of the variables. p<0.050 was accepted as the significance level.

RESULT

Ninety-seven ASD patients were included the study. 84.5% of the cases were male (n=82). The median age of the patients were 6.0 years (min-max: 3-12 years). 19.6% (n=19) of the cases had at least one physical diseases. 52.6% (n=51) of the cases

Table I: Demographic and clinical characteristics of	1
patients with ASD	

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Variables	
Age (year)*	6 (3-12)
Gender [†] Boys Girls	82 (84.5) 15 (15.5)
Sibling [†] Yes	78 (80.4)
Birth order [†] First Second Third Fourth Fifth	41 (42.3) 38 (39.2) 12 (12.4) 5 (5.2) 1 (1.0)
Medical disease [†] Yes Epilepsia Cerebralpalsy Asthma Cardiomyopathy Nephroticsyndrome Brain tumor Nistagmus Fragil X syndrome	19 (19.6) 9 (9.3) 3 (3.2) 2 (2.1) 1 (1.0) 1 (1.0) 1 (1.0) 1 (1.0) 1 (1.0)
At least one psychiatric disorder [†] Yes Attention deficit hyperactivity disorder Intellectual disability Generalised anxiety disorder	51 (52.6) 40 (41.2) 22 (22.7) 1 (1.0)

Variables	
Psychotropic medication use [†] No Yes	54 (55.7) 43 (44.3)
Mother'sage (years) [*]	37 (29-55)
Father'sage (years)*	32 (24-50)
Mothers' education [†] Primary Secondary College University	36 (37.1) 24 (24.7) 27 (27.8) 10 (10.3)
Fathers' education [†] Primary Secondary College University	28 (28.9) 15 (15.5) 33 (34.0) 21 (21.6)
History of miscarriage [†]	11 (11.3)
Smoking during pregnancy [†]	14 (14.4)
History of prematurity [†]	24 (24.7)
History of regression [†]	41 (42.3)

*: Median (minimum-maximum), †:n(%)

Table II: The score distributions of the scales		
AbBC – Total Score* Irritability Lethargy/social withdrawal Stereotypic behavior Hyperactivity/noncompliance Inappropriate speech CARS – Total Score	56 (1-163) 14 (0-40) 15 (0-42) 7 (0-21) 21 (1-48) 3 (0-12) 34 (19-48)	
Nonautistic (CARS – TS = $15-29.5$) [†]	24 (24.7)	
Mild-Moderate (CARS – TS = $30-36.5$) ⁺	40 (41.2)	
Severe (CARS – TS = $37-60$) ⁺	32 (33.0)	
ABC – Total Score* Sensory stimuli Relating Body and Object Use Language Social and Self-Help skills	62 (3-120) 8 (0-23) 16 (0-32) 14 (0-36) 12 (0-34) 12 (0-25)	
ABC – Total skor ≤39 [†]	27 (27.8)	
ABC – Total skor >39 ⁺	70 (72.2)	

*: Median (Min-max), †: n (%), **AbBC**: Aberrant Behavior Checklist, **CARS**: Childhood Autism Rating Scale, **ABC**: Autism Behavior Checklist

 Table III: Children's Sleep Habits Questionnaire (CSHQ)
 Results

CSHQ-Total Score*	47 (34-68)
Presence of clinically significant sleep problems [†]	57 (58.8)
Amount of sleep (hours) (night+day)*	9.3 (5-12)
Time spent awake at night (minutes)*	10 (1-240)
Child's bedtime*	22.15 (20:00-02-30)

*: median (min-max), *n (%): CSHQ -total score>41

	Functional GIS Disease Yes (n = 37)	Functional GIS Disease No (n = 60)	Statistics zorx ²	р
Age (years)*	7 (3-12)	6 (3-12)	-1.88	0.060
Gender [†] Boys Girls	36 (97.3) 1 (2.7)	46 (76.7) 14 (23.3)	7.45	0.008
MR [†]	11 (29.7)	11 (18.3)	1.69	0.190
ABC scores* Total Score Sensory behavior Relating Body and Object Use Language Social and Self-Help skills	79 (16-110) 11 (3-22) 18 (0-31) 15 (0-34) 14 (0-34) 14 (4-21)	51 (3-109) 7 (0-19) 14.5 (0-30) 13 (0-29) 11 (0-27) 9 (0-25)	-2.60 -2.69 -1.82 -1.35 -1.45 -3.00	0.009 0.007 0.070 0.180 0.150 0.003
AbBC scores* Total Score Irritability Lethargy/social withdrawal Stereotypies Hyperactivity Inappropriate speech	75 (2-122) 17 (0-31) 16 (0-32) 7 (0-21) 23 (2-46) 3 (0-10)	46 (1-123) 10 (0-40) 14 (0-27) 4 (0-20) 15.5 (0-40) 2.5 (0-12)	-2.10 -2.73 -1.22 -1.88 -1.70 -0.71	0.040 0.006 0.220 0.060 0.090 0.480
CARS Total Score	37.5 (19-45.5)	33 (19-44.5)	-1.30	0.200
CSHQ Total Score*	47 (35-68)	43 (32-68)	-1.88	0.060
Sleep problems (CSHQ scores) [†] No [‡] Yes [§]	7 (20.6) 27 (79.4)	26 (46.4) 30 (53.6)	6.08	0.010

Table IV: The relationship between functional GIS disease and autism symptom severity, problematic behavior and sleep problems

*:Median(minimum-maximum), †: n (%), ‡:No (CSHQ score ≤41), ^{\$}:Yes (CSHQ score>41), **AbBC:** Aberrant Behavior Checklist, **CARS:** Childhood Autism Rating Scale, **ABC:** Autism Behavior Checklist, **CSHQ:** Children's Sleep Habits Questionnaire

Table V: Correlation between sleep problems, autism symptom severity and behavioral problems			
	CARS	ABC	AbBC
CSHQ-Total			
Rho	.227*	.273**	.479**
р	.032	.010	.000

CSHQ: Children's Sleep Habits Questionnaire, **CARS:** Childhood Autism Rating Scale, **ABC:** Autism Behavior Checklist, **AbBC:** Aberrant Behavior Checklist, ******: p = .010, ***:** p = .050

had at least one psychiatric comorbidities. The most common psychiatric comorbidities were attention deficit hyperactivity disorder (ADHD) (41.2%, n=40) and intellectual disability (ID) (22.7%, n=22). 33% (n=32) of the cases had severe (CARS total score= 37-60), 41.2% (n=40) had mild-moderate (CARS total score= 30-36.5) autistic symptoms according to CARS score. 72.2% (n=70) of the cases had a score above 39 according to the ABC (Tables I and II).

The median total score of CSHQ was 47 points (34-68). 58.8% of the subjects had clinically significant sleep problems (CSHQ total score >41). The median amount of the daily sleep of was 9.3 hours (min-max=5-12 hours). The median duration of waking up at night was 10 minutes (min-max: 1- 240 minutes) (Table III).

According to the QPGS-RIII, 38.1% of the cases had probable functional gastrointestinal disease: 26.8% (n=26) functional constipation, 2.1% (n=2) aerophagia, 8.2% (n=8) nonretensive fecal-incontinence (NFI), 4.1% (n=4) irritable bowel syndrome (IBS), 3.1% (n=3) adolescent rumination syndrome, 1% (n=1) functional abdominal pain syndrome and 1% abdominal migraine.

ASD group was divided into two subgroups according to having GIS disease: ASD +functional GIS disease and ASD without any GIS disease. And it was found that ABC total, sensory behavior, social and adaptive skills subscales and AbBC total and irritability subscale scores were statistically significantly higher in those with GIS disease comorbidity. In addition, it was demonstrated that children with functional GIS disease had a statistically significant higher clinical level of sleep problems than those without (Table IV).

A statistically significant positive correlation was found between the total CSHQ and the total scores of ABC, CARS and AbBC. No significant correlation was found between the children's night time awakening duration (minutes) and total daily sleep duration (hours) variables to the total scores of CARS, ABC and AbBC (p>0.050 for all) (Table V).

DISCUSSION

In our study, the frequency of functional gastrointestinal disorders and sleep problems and their relationship with each others, ASD severity and problematic behaviors were evaluated. ASD patients frequently have problematic behaviors. Oftenly clinicians overlook GIS and sleep problems that may be the underlying reasons for behavioral problems. Furthermore GIS symptoms might cause sleep disturbance and both aggravate problematic behaviors. It was thought that GIS dysfunction and sleep disturbance might increased ASD symptoms. And treating GIS and sleep problems might decrease ASD symptoms and challenging behaviors.

Among the many medical comorbidities associated with ASD, GIS symptoms drew considerable attention due to its prevalence and association with symptom severity (9). Studies has shown that GIS symptoms such as abdominal pain, constipation, diarrhea and flatulence are very common in children with ASD (6). Gorrindo et al. (10) identified constipation as the most common symptom (85%) in children with ASD. ASD children, who suffer from abdominal pain, gaseousness, diarrhea, constipation or pain on stooling have higher scores at AbBC subscales such as Irritability, Social Withdrawal, Stereotypy and Hyperactivity compared with children who don't have frequent GIS symptoms (11).

We demonstrated that functional gastrointestinal disorders are common in ASD patients and there is a positive correlation between autism severity and GIS problems. Most frequent GIS symptom was functional constipation according to our findings. GIS disorders might emerge as non-gastrointestinal symptoms especially with nonverbal patients such as sleep problems or challenging behavior. GIS symptoms might induce pain and inconvenience and lead to aggression and self harm behavior and sleep problems (12,13). According to our findings problematic behaviors such as irritability and sleep problems found more common in ASD patients who have GIS problems. Sometimes clinicians might consider problematic behaviors and sleep problems are occur due to autism itself. Yet, treating GIS disorder may decrease irritability, aggressive behavior and sleep problems. In our study increased/decreased sensory sensitivity was found higher in ASD with GIS disorder. Mazurek et al. (14) research the relationship between sensory hypersensitivity and GIS symptoms at ASD patients. They demonstrated that, autistic children who have chronic GIS problems had higher levels of sensory hypersensitivity. Sensory hypersensitivity might cause food selectivity which is a common problem in ASD. And food selectivity may give rise to constipation.

Sleep problems frequently accompanies ASD and increase the severity of behavioral and social skills problems and stereotypes (15,16). In a study conducted with a group of children, has shown that chronic sleep problems increase hyperactivity and impulsivity during school periods and predict poor performance

in learning and neurodevelopmental tests (17). A positive correlation was found between autism severity and sleep problems in our study. Our findings revealed that, those who has sleep problems were more likely to demonstrated problematic behaviors than who hasn't. Therefore, treating sleep problems may reduce autistic symptoms, learning difficulties and problematic behaviours.

Limitations;

- 1. The mean age of the participants was young and some of them didn't developed language yet and they couldn't able to describe their symptoms well enough.
- 2. Some of the ASD patients were using medicine that was a confounding factor for the results.
- 3. Diet might affect GIS symptoms and we didn't use dietary dairy.

CONLUSION

In our study, it was shown that sleep problems and GI symptoms frequently accompany children with ASD, in line with the literature. It is appropriate to routinely evaluate patients with ASD in terms of gastrointestinal and sleep problems especially if behavioral problems accompanies. And treating GIS and sleep problems might decrease challenging behaviors that seen in ASD.

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