e-ISSN 2757-5195

Çanakkale Onsekiz Mart University

Journal of Advanced Research in Natural and Applied Sciences

Open Access

doi.org/10.28979/jarnas.1147207 2023, Vol. 9, Issue 3, Pages: 606-614 dergipark.org.tr/tr/pub/jarnas

Effect of Atypical Antipsychotic Usage at Therapeutic Doses on Daytime Sleepiness

Meltem Alan [1], Tugba Nurcan Yuksel [2,*], Birol Topcu [3]

[1] Department of Neurology Intensive Care, Tekirdağ Namık Kemal University Education and Research Hospital, Tekirdağ, Türkiye
[2] Department of Pharmacology, Faculty of Medicine, Tekirdağ Namık Kemal University, Tekirdağ, Türkiye
[3]Department of Biostatistic, Faculty of Medicine, Tekirdağ Namık Kemal University, Tekirdağ, Türkiye

Article History

Received: 22.07.2022
Accepted: 09.03.2023
Published: 20.09.2023

Research Article

Abstract − The aim of this study is to determine the effect of using atypical antipsychotic drug usage at therapeutic doses on daytime sleepiness. One hundred twenty volunteers who met the inclusion-exclusion criteria were divided into two equal groups. Group 1: patient group (60 patients volunteers used atypical antipsychotic in therapeutic doses and hospitalized in the psychiatry clinic of Tekirdağ Namık Kemal University Hospital and Group 2: control group (60 control volunteers). Socio-demographic and Clinical Information Form consist of 14 questions was administration all volunteers. Also, Epworth Sleepiness Scale which is a survey that determines the degree of sleepiness in eight different situations during the day was administered to all volunteers. Atypical antipsychotic drug usage at therapeutic doses significantly increased patients' daytime sleepiness compared to the control group. Among the atypical antipsychotic drugs usage in therapeutic dose, the drug that caused the most daytime sleepiness was clozapine. Also, using of atypical antipsychotic drugs in therapeutic doses markedly decreased patients' life quality compared to the control group. Atypical antipsychotic drug usage at therapeutic doses could cause daytime sleepiness and reduce patients' quality of life.

Keywords − *Atypical antipsychotic, daytime sleepiness, epworth sleepiness scale, life quality, sedation*

1. Introduction

Atypical antipsychotics is used in the treatment of many diseases such as bipolar disorder-mania, psychotic depression, resistant depression, schizophrenia, anxiety disorder, organic mental disorders, borderline personality disorder, antisocial personality disorder, and post-traumatic stress disorder. It exerts its effects by selectively blocking dopaminergic D2 receptors and serotonergic 5-HT2A receptors in A 10 neurons in the limbic system (Çetin & Turgay 2002).

Antipsychotic drugs cause extrapyramidal syndrome symptoms such as parkinsonism, muscle rigidity, bradykinesia, akinesia, dystonia, akathisia and tardive dyskinesia (Weiden, 2007). Atypical antipsychotic drugs can cause cognitive disorders such as psychomotor slowdown, impaired attention and memory (Cankorur, 2013), sedation and daytime sleepiness (Ahnaou, Megens & Drinkenburg, 2003). Sedation causes hypersomnia, wich is a sleep disorder characterized by daytime sleepiness / excessive daytime sleepiness (Ak et al., 2022).
Daytime sleepiness is defined as the inability to stay awake or wake up during the daytime (Selvi, Kandeğer & Sayın et al. 2016). An individual's daytime sleepiness may be mild only during rest; it can also be seen during driving, eating and other daily activities (Sürücü & Özvurmaz 2020). People with daytime sleepiness may experience life-threatening road or work accidents, decrease in occupational performance, and social incompatibility. The use of drugs is among the most common causes of daytime sleepiness. Drugs cause sedation by antagonizing α1 adrenergic receptors, muscarinic cholinergic receptors, histamine H1 receptors or serotonin

[1] malan@nku.edu.tr
[2] tnyuksel@nku.edu.tr
[3] btopcu@nku.edu.tr
[*] Corresponding Author

5-HT2A receptors, inhibiting the wakefulness system or increasing the sleep-provoking system activity via GABA (Selvi, Kandeğer & Sayın et al. 2016).

The Epworth Sleepiness Scale was first defined by Murray W. Johns at Melbourne Epworth Hospital in Victoria, Australia in 1991 and its use became widespread worldwide (Borsini et al. 2019). Epworth Sleepiness Scale is an understandable, easy to apply, simple and validated and reliable scale to evaluate the general sleepiness level.

In the literature, there are studies investigating different side effects of atypical antipsychotic drugs such as extrapyramidal syndrome symptoms, metabolic, hematological and cardiovascular system symptoms. However, in the literature there is no study investigating the effects of atypical antipsychotic drug usage at therapeutic doses on daytime sleepiness with Epworth Sleepiness Scale and comparing multiple atypical antipsychotic drugs. In the light of this information, we aimed to investigate the effect of atypical antipsychotic drug usage at therapeutic doses on daytime sleepiness with Epworth Sleepiness Scale

2. Material and Methods

This study was approved by Tekirdağ Namık Kemal University Non-Interventional Clinical Research Ethics Committee with the decision dated 13.04.2021 and numbered 202192.04.10. Permission was granted by the chief physician of Tekirdağ Namık Kemal University Hospital. In addition, an informed consent form was obtained from all volunteers participating in the study.

2.1 Groups

Patient Group

In this study, the patient group was consisted of 60 volunteers, who were hospitalized in the psychiatry clinic of Tekirdağ Namık Kemal University Hospital between 03.05.2021 and 15.05.2022. The inclusion and exclusion criteria for patient group were determined accordance with DSM-IV diagnostic criteria.

Inclusion criteria for the patient group in accordance with DSM-IV diagnostic criteria; having one of the diagnoses of personality disorder including schizoaffective disorder schizophrenia/psychosis, bipolar disorder, major depressive disorder, to have been using one of the atypical antipsychotic drugs alone at therapeutic level for last one month being between the ages of 18-65.

Exclusion criteria for the patient group in accordance with DSM-IV diagnostic criteria; having used atypical antipsychotic drugs irregularly or discontinued for last one month, not using atypical antipsychotics in the therapeutic dose range, having one of the diagnosed sleep diseases such as narcolepsy, insomnia, having the use of drugs (antihistamines, benzodiazepines, etc.) whose side effects cause daytime sleepiness, having alcohol and/or substance use.

Control Group

In this study, the control group consisted of 60 volunteers meeting the inclusion and exclusion criteria, who were employees or patient relatives in the Tekirdağ Namık Kemal University Hospital between 03.05.2021 and 15.05.2022.

2.2 Data Collection Tools

Sociodemographic and Clinical Information Form and Epworth Sleepiness Scale were applied to the all volunteers by face-to-face interview method.

Sociodemographic and Clinical Information Form

A sociodemographic and clinical information form designed in accordance with the data obtained from the scanned sources and clinical experience was produced and administered to all volunteers. Furthermore, questions 12, 13 and 14 were designed to be asked only to the patient group in order to determine the relation between atypical antipsychotic drugs and quality of life in Table 1.

Table 1

Sociodemographic and Clinical Information Form

Question	Answer
1- Your Age?	
2- Your Gender?	( ) Female ( ) Male
3- Education Status?	( ) Illiterate ( ) Primary School ( ) High School ( ) Associate-Bachelor's Degree ( ) Post-Graduate
4- Who do you live with?	( ) Alone ( ) Family ( ) Housemate ( ) Other-Please explain:
5- Are you diagnosed with any chronic diseases other than psychiatry?	( ) No ( )Yes Please explain:
6- Are you using drugs due to chronic disease?	( ) No ( )Yes-Please explain:
7- Are you diagnosed with any psychiatric disease?	( ) No ( )Yes-Please explain:
8- Do you have any drug that you constantly use due to psychiatric disease?	( ) No ( )Yes-Please explain:
9- At nights, I sleep an average of ( ) hours.	( )
10-My sleep pattern is:	( ) Regular ( ) Irregular ( ) Difficulty in sleeping
11- I do following practices in order to facilitate falling asleep:	( )
12- Please score your quality of life before using atypical antipsychotic drug usage on a scale of 1 to 10.	Score ( )
13- Please score your current quality of life after atypical antipsychotic drug usage on a scale of 1 to 10.	Score ( )
14- Please score the degree to which quality of life due to the side effects of atypical antipsychotic drugs on a scale of 1 to 10.	Score ( )

Epworth Sleepiness Scale

With the Epworth Sleepiness Scale (Table 2), the rate of falling asleep in different situations in daily life of individuals with daytime sleepiness is determined. Epworth Sleepiness Scale is a questionnaire that determines the degree of falling asleep/snoozing in 8 different situations during the day. Each question is asked to give a score between 0 and 3 according to the frequency of the last two weeks (Kendirli et al. 2016).

In the Epworth Sleepiness Scale;

1. While sitting and reading,
2. While watching TV,
3. While sitting still in a community (such as meeting and theatre),
4. On a car journey that takes at least an hour without a break,
5. Lying down for an afternoon rest when conditions are right,
6. When you sit and talk to someone,
7. Sitting calmly after a non-alcoholic lunch
8. When the car has to stop for a few minutes due to traffic on the journey; to your questions;

Scoring:

0. I never sleep

1. I rarely sleep

2. I sleep moderately,

3. I sleep very often; the appropriate answer is given (Karakoç et al. 2007).

Table 2
Scoring of the Epworth Sleepiness Scale

Score	Degree of sleepiness
<10 points	Normal sleepiness level
10-15 points	Increased sleepiness level
>16 points	Dangerous sleepiness level

2.3 Statistical analysis

The findings were statistically evaluated using the SPSS 25.0 software program. By testing the conformity of the data for normal distribution, one-way analysis of variance ANOVA and Independent Samples T Test in pairwise comparison group analysis showing normal distribution, and Tukey and Tamhane Tests, one of the Post Hoc tests, were applied for multiple comparisons. In the presentation of the variables, mean±standard deviation (mean±sd), median (min-max), number (n), percentage (%) values were used. According to the analysis results, $p \leq 0.05$ was considered significant.

3. Results and Discussion

The Epworth Sleepiness Scale is one of the routinely used questionnaires to assess subjective experience of sleepiness in clinical setting. It evaluates sleepiness by asking patients to grade their propensity to fall asleep in eight everyday scenarios with good test–retest reliability. The ESS is currently used as a screening tool to determine patients that require further evaluation by sleep testing, to evaluate alterations in severity of daytime symptoms linked to effectiveness of treatment (Packard et al. 2021).

In this study, we investigated the effect on daytime sleepiness of atypical antipsychotic drug usage at therapeutic doses with Epworth Sleepiness Scale. To this end, the findings of the Sociodemographic and Clinical Information Form administered to all volunteers are presented in Table 3. In addition, psychiatric diseases and atypical antipsychotic drugs used in the treatment of these diseases as a result of the findings of the Sociodemographic and Clinical Information Form administered to the patient group, are listed in Table 4.

Table 3
Sociodemographic and Clinical Information Form Results

Questions	Frequency (f)	Percent (%)
Gender		
Woman	70	58,3
Male	50	41,7
Education status		
Primary school	39	32,5
High school	33	27,5
Associate degree-license	47	39,2
Graduate	1	0,8
With whom does he/she live?		
Alone	18	15,0
Family	89	74,2
Roommate	10	8,3
Other	3	2,5
Chronic disease state diagnosed outside of psychiatry		
No	98	81,7
Yes	22	18,3
Drug use related to chronic disease diagnosed other than psychiatry		
No	104	86,7
Yes	16	13,3
The state of having a psychiatric illness		
No	60	50
Yes	60	50
Drug use due to psychiatric illness		
No	60	50
Yes	60	50
Sleep patterns		
Tidy	58	48,3
Irregular	62	51,7
The presence of applications that facilitate		
No	75	62,5
Yes	45	37,5

Table 4

Percentile distribution of psychiatric diseases and drugs used in the treatment of these diseases

Psychiatric Diseases	Frequency (f)	Percent (%)
Bipolar Disorder	26	21,7
Major Depressive Disorder	5	4,3
Schizophrenia	15	12,6
Non-Organic Psychosis	5	4,3
Borderline Personality Disorder	1	0,8
Obsessive-compulsive disorder	1	0,8
Transient Psychotic Disorder	1	0,8
Depression with Psychotic Features	2	1,7
Schizoaffective Disorder	1	0,8
Anxiety Disorder	3	2,5
Drugs used due to psychiatric diseases		
Paliperidone	17	14,1
Aripiprazole	7	5,8
Quetiapine	18	15,0
Clozapine	5	4,1
Olanzapine	10	8,3
Risperidone	3	2,5

Daytime sleepiness can impair cognition, including concentration and alertness, and may interfere with daily work and task performance. In addition, daytime sleepiness may impair driving skills and increase risk for accidents (Loebel et al. 2013). In a randomized, double-blind, placebo-controlled study conducted by Loebel et al. (2013), it was demonstrated that quetiapine led to daytime sleepiness. Koller et al (2021).carried out a study evaluating the adverse events and safety of aripiprazole and olanzapine treatment and showed that these antipsychotics caused insomnia and somnolence. Reeve et al (2021) ,in a study conducted patients with psychosis, reported that both antipsychotic drug usage and low levels of activity caused excessive sleepiness. In a study of Deest et al (2022) carried out on aripiprazole treatment, the major adverse effect observed was the increased daytime sleepiness. Gómez-Revuelta et al (2020) investigated the antipsychotic treatment efficacy in their study involving olanzapine, risperidone, aripiprazole, quetiapine and reported that these drugs affected sleep duration at different levels. Consistent with the previous studies, although the daytime sleepiness of the patient group was at the normal level of sleepiness in this study, there was a statistically significant difference when compared to the daytime sleepiness of the control group (Table 5).

Table 5
The average of Epworth Sleepiness Scale scores of all volunteers

Groups	x
Patient group	6,83
Control group	4,78

($p \leq 0{,}000$, n=120)

Daytime sleepiness associated with antipsychotic treatment may adversely impact functional performance and quality of life (Loebel et al. 2013). Quality of life is defined as the subjective self-evaluation of a person's current state of life in relation to his or her self-constructed expectations and standards (Ong WJ et al. 2020). Quality of life and sleep are important outcomes to assess the effectiveness of treatment in patients with mental disorders, and they are highly correlated (Wang et al. 2020). In the study of Takenoshita et al (2020) investigating the pharmacological management of daytime sleepiness, it was shown that daytime sleepiness reduced quality of life, causing medical and social problems. Earlier studies indicated that extreme daytime sleepiness had negative influences on the quality of life ((Perotta B. et al. (2021), Lal C. et al. (2021) Amaral et al. (2017)). Also, in this study, there was a statistically significant difference between the effects of atypical antipsychotic drugs on daytime sleepiness and relevant quality of life according to the Sociodemographic and Clinical Information Form data (Table 6). In concordance with the previous studies, our results show that the quality of life of patients decreases with the effect of daytime sleepiness caused by the use of atypical antipsychotic drugs (Table 6).

Table 6
The effect of atypical antipsychotic drug usage at therapeutic doses on quality of life (n=60)

	Scale Score Averages X±SS	Minimum Values	Maximum Values
Quality of life before using of atypical antipsychotic drug	3,25±1	0	7
Quality of life after atypical antipsychotic drug usage	6,79±1	3	9
Quality of life due to the side effects of atypical antipsychotic drugs	4,95±1	1	7

Moreover, the effects of atypical antipsychotic drugs usage by the patient group on their daytime sleepiness were compared in this study. When the Epworth Sleepiness Scale score was evaluated, the drug that caused the most daytime sleepiness was clozapine Table 7. Clozapine, considered the first atypical or second-generation antipsychotic, has a differential pharmacological profile. It is known for its superiority over other antipsychotics in patients with schizophrenia, especially in those with resistant psychotic symptoms, and is the gold standard of efficacy in non-responders to trials with other treatments Rey Souto et al. (2021). Sharma et al. (2021) performed the perspective cluster analysis of patients using clozapine and compared with patients using other antipsychotics, one of the most common side effects was sedation. In an analysis study of Imazu et al. (2021) investigating the safety profile of Clozapine using national registry data in Japan, it was reported that the sedation/sleepiness side effect of clozapine was one of the reasons for drug discontinuation.
Our findings are consistent with the outcomes of previous studies as well.

Table 7
Evaluation of the Epworth Sleepiness Scale of patient groups

Drugs	n	Scale Score Averages X±SS	Minimum Values	Maximum Values
Olanzapine	10	6,70±3,683	1	13
Quetiapine	18	6,06±3,134	0	12
Paliperidone	17	6,00±4,062	0	13
Clozapine	5	12,00±1,000	11	13
Risperidone	3	6,33±1,528	5	8
Aripiprazole	7	9,00±4,830	4	18
Total	60	6,83±3,923	0	18

As part of this study, it was determined that atypical antipsychotic drug usage at therapeutic doses can increase daytime sleepiness, and that atypical antipsychotic drug usage may decrease quality of life due to increased daytime sleepiness.

4. Conclusion

Atypical antipsychotic drug usage at therapeutic doses increases daytime sleepiness. Among the atypical antipsychotic drugs used at therapeutic doses within the scope of the study, clozapine stands out as the drug that causes the most daytime sleepiness. Use of atypical antipsychotic drug may decrease the quality of life due to increased daytime sleepiness. This shows that side effects in question should be carefully monitored in the early stages of atypical antipsychotic therapy. The data obtained in our study could lead to the optimal and safe use of atypical antipsychotic drugs for therapy purposes. Further studies are needed in order to determine the effect of these drugs on daytime sleepiness and quality of life in patients using atypical antipsychotic drugs.

Acknowledgement

We would like to thank Asst. Prof. Elmas Beyazyüz, Prof. Dr. Murat Beyazyüz and Prof. Dr. Yakup Albayrak, Department of Mental Health and Diseases and Chief Physician of Tekirdağ Namık Kemal University Hospital and the organizers of the congress.

Author Contributions

Meltem Alan: Collected data and performed the analysis, wrote the paper.

Tugba Nurcan Yuksel: Conceived and designed the analysis, wrote the paper

Birol Topcu: Performed statistical analysis and wrote the paper

Conflicts of Interest

All author report that there are no competing interests to declare.

References

Ahnaou A., Megens A.H.P., Drınkenburg W.H.I.M. (2003). The Atypical Antipsychotics Risperidone, Clozapine and Olanzapine Differ Regarding Their Sedative Potency in Rats *Neuropsychobiology*. 48:47–54 https://doi.org/10.1159/000071829

Amaral MO, de Almeida Garrido AJ, de Figueiredo Pereira C, Master NV, de Rosário Delgado Nunes C, Sakellarides CT. (2017) Quality of life, sleepiness and depressive symptoms in adolescents with insomnia: A cross-sectional study. Aten Primaria. Jan;49(1):35-41. https:// doi: 10.1016/j.aprim.2016.03.004. Epub 2016 Jul 15.

Borsini E., Blanco M., Ernst G., Schonfeld S., Salvado A. (2019). Performance of Epworth Sleepiness Scale and Tiredness Symptom Used With Simplified Diagnostic Tests for the Identification of Sleep *Apnea Sleep Science.* 12(4):287-294 https://doi: 10.5935/1984-0063.20190095.

Cankorur V.S. (2013). İki Uçlu Bozukluk ve Bilişsel İşlevler *Journal of Mood Disorders* Volume: 3, Suppl: 1 https://dergipark.org.tr/en/pub/moodis/issue/10480/128303

Cohen D., Bonnot O., Bodeau N., Consolı A., Laurent C. (2012). Adverse effects of second-generation antipsychotics in children and adolescents: a Bayesian meta-analysis *J Clin Psychopharmacol.* Jun;32(3):309-16 http://dx.doi.org/10.1097/JCP.0b013e3182549259

Çetin M., Turgay A. (2002). Modern *Psikofarmakolojinin Ellinci Yılında Klorpromazinden Günümüze Antipsikotik Tedavinin Dünü, Bugünü* Klinik Psikofarmakoloji Bülteni. 12: 211-226 http://www.psikofarmakoloji.org

Deest M, Wieting J, Jakob MM, Deest-Gaubatz S, Groh A, Seifert J, Toto S, Bleich S, Frieling H, Eberlein CK. Aripiprazole treatment for temper outbursts in Prader-Willi syndrome. Orphanet J Rare Dis. 2022 Aug 26;17(1):324.https:// doi: 10.1186/s13023-022-02470-y.

Gómez-Revuelta M, Pelayo-Terán JM, Juncal-Ruiz M, Vázquez-Bourgon J, Suárez-Pinilla P, Romero-Jiménez R, Setién Suero E, Ayesa-Arriola R, Crespo-Facorro B. Antipsychotic Treatment Effectiveness in First Episode of Psychosis: PAFIP 3-Year Follow-Up Randomized Clinical Trials Comparing Haloperidol, Olanzapine, Risperidone, Aripiprazole, Quetiapine, and Ziprasidone. Int J Neuropsychopharmacol. 2020 Apr 23;23(4):217-229. https:// doi: 10.1093/ijnp/pyaa004.

Imazu S., Hata T., Toyodo K., Kubo Y., Yamauchı S., Kinoshita S., Nishihara M., Inada K., Kanazawa T. (2021). Safety profile of clozapine: Analysis using national registry data in Japan *J Psychiatr Res* Sep;141:116-123https://doi.org/10.1016/j.jpsychires.2021.06.041

Karakoç Ö., Akçam T., Gerek M., Birkent H. (2007). Horlama ve Obstüriktif Uyku Apneli Hastalarda Epworth Uykululuk Skalasının Güvenilirliği *Elektronik Kulak Burun Boğaz ve Baş Boyun Cerrahisi Dergisi.* Cilt 6, Sayı 3 http://www.kbb-forum.net

Kendirli M.T., Akgöz G., Özdağ M.F., Tekeli H., Yaşar H., Balıbey H., Kendirli N. (2016). Epworth Uykululuk Testinin Obstrüktif Uyku Apne Sendromu Tanısında Belirleyici Rolü Var mıdır? *Gülhane Tıp Dergisi.* 58: 161-164 https:// doi: 10.5455/gulhane. 178918

Koller D, Almenara S, Mejía G, Saiz-Rodríguez M, Zubiaur P, Román M, Ochoa D, Wojnicz A, Martín S, Romero-Palacián D, Navares-Gómez M, Abad-Santos F. Safety and cardiovascular effects of multiple-dose administration of aripiprazole and olanzapine in a randomised clinical trial. Hum Psychopharmacol. (2021) Jan;36(1):1-12. https://doi: 10.1002/hup.2761. Epub 2020 Sep 29.

Kutlu Y., Polat S. (2019). Ruhsal Bozukluklarda Hastalık Yönetimi ve İyileşme Programı *İzmir Kâtip Çelebi Üniversitesi Sağlık Bilimleri Fakültesi Dergisi.* 4(3): 111-115 https://dergipark.org.tr/en/pub/ikcusbfd/issue/51136/666491

Lal C, Weaver TE, Bae CJ, Strohl KP. (2021). Excessive Daytime Sleepiness in Obstructive Sleep Apnea. Mechanisms and Clinical Management. Ann Am Thorac Soc. May;18(5):757-768. https://doi: 10.1513/AnnalsATS.202006-696FR.

Loebel A.D., Siu C.O., Cucchıaro J.B., Pikalov A.A., Harvey P.D. (2014). Daytime Sleepiness Associated with Lurasidone and Quetiapine XR: Results from a Randomized Double-Blind, Placebo-Controlled Trial in Patients with Schizophrenia Cns Spectrums. 19(2): 197–205pp https://doi.org/10.1017/S1092852913000904

Ong WJ, Tan XW, Shahwan S, Satghare P, Cetty L, Ng BT, Tang C, Verma S, Chong SA, Subramaniam M. (2020). Association between sleep quality and domains of quality of life amongst patients with first episode psychosis. Health Qual Life Outcomes 18, 114. https://hqlo.biomedcentral.com/articles/10.1186/s12955-020-01367-3

Packard A., Bautista R., Smotherman C., Gautham S. (2021). Gender differences in Epworth Sleepiness Scale revealed by paired patient–spouse scoring. Epilepsy Behav. Jan;114(Pt A):107272. https://doi: 10.1016/j.yebeh.2020.107272.

Perotta B, Arantes-Costa FM, Enns SC, Figueiro-Filho EA, Paro H, Santos IS, Lorenzi-Filho G, Martins MA, Tempski PZ. .(2021). Sleepiness, sleep deprivation, quality of life, mental symptoms and perception of academic environment in medical students. *BMC Med Educ.* Feb 17;21(1):111. https://doi: 10.1186/s12909-021-02544-8.

Reeve S., Sheaves B. Freeman D. (2021). Excessive Sleepiness in Patients with Psychosis: An Initial Investigation Plos One. 15;16(1)https://doi.org/10.1371/journal.pone.0245301

Rey Souto D, Pinzón Espinosa J, Vieta E, Benabarre Hernández A. (2021) Clozapine in patients with schizoaffective disorder: A systematic review. Rev Psiquiatr Salud Ment (Engl Ed). Jul-Sep;14(3):148-156. https:// doi: 10.1016/j.rpsmen.2021.07.001.

Selvi Y., Kandeğer A., Sayın A.A. (2016). *Gündüz Aşırı Uykululuğu Psikiyatride Güncel Yaklaşımlar.* 8(2):114-132 https://dergipark.org.tr

Sertöz *Ö.Ö., Akdeniz F., Vahip s.(2002). Bipolar bozukluk ve şizoaffektif bozukluk sağaltımında klozapinin yeri: Geriye dönük bir çalışma* Klinik Psikofarmokoloji Bülteni. 12:142-147 https://app.trdizin.gov.tr

Sharma S., Kopelovich S.L., Janjua A.U., Pritchett c., Broussard B., Dhır M., Wilson J.G., Goldsmıth D.R., O Cotes R. (2021). Cluster Analysis of Clozapine Consumer Perspectives and Comparison to Consumers on Other Antipsychotics Schizophr Bull Open. 28;2(1) https://doi.org/10.1093/schizbullopen/sgab043

Sürücü E. Özvurmaz S. (2020). Vardiyalı Sistemde Çalışanlarda Gündüz Uykululuğu *Halk Sağlığında Güncel Derlemeler*. 53-68 https://dergipark.org.tr

Takenoshita S, Nishino S. (2020) Pharmacologic Management of Excessive Daytime Sleepiness. Sleep Med Clin. Jun;15(2):177-194. https://doi: 10.1016/j.jsmc.2020.02.006.

Wang WL, Zhou YQ, Chai NN, Li GH.(2020). Sleep disturbance and quality of life in clinically stable inpatients with schizophrenia in rural China. Qual Life Res. 2020 Oct;29(10):2759-2768. https//doi: 10.1007/s11136-020-02541-2.

Weiden P. J. (2007). EPS Profiles: the Atypical Antipsychotics Are Not All the Same J*ournal of Psychiatric Practise*. J Psychiatr Pract. Jan;13(1):13-24. https://doi: 10.1097/00131746-200701000-00003.