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The influence of antipsychotic type (typical vs. atypical) on quality of life among individuals with schizophrenia

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ABSTRACT

Introduction. Schizophrenia is a severe mental health disorder affecting almost 0.5% of the global population. Despite decades of research, it remains a debilitating condition that significantly impacts individuals' quality of life (QoL) in aspects such as physical health, psychological well-being, independence, social relationships, beliefs, and environment. Current pharmacological treatment for schizophrenia consists of typical and atypical antipsychotics.

Objective and methods. We conducted a cross-sectional study on a population of 109 patients who met the DSM-IV-TR or ICD-10 criteria for schizophrenia, aiming to assess their QoL, depending on the type of antipsychotic used (typical or atypical). Descriptive statistics were used to characterize the sample, and simple linear regression was used to evaluate the impact of the type of antipsychotic on the QoL. In addition, educational level, pathology, and previous treatment were considered as controlling factors. QoL was assessed using the EuroQol EQ-5D Quality of Life Scale (EQ-5D-3L) and the abbreviated version of the World Health Organization Quality-of-Life (WHO-QOL-BREF) Scale.

Results. Patients treated with atypical antipsychotics (AA) presented higher overall scores on the EQ-5D-3L, indicating better QoL. In addition, there were significant associations between treatment type and gender, as well as employment status. However, no significant differences were observed in treatment history, marital status, educational level, or Positive And Negative Syndrome Scale (PANSS) results between the two groups.

Conclusion. These findings highlight the need for individualized considerations of QoL when selecting the most suitable treatment approach for patients with schizophrenia. Further studies are warranted to provide precise guidance in tailoring treatments for these patients. Additionally, it is essential to conduct studies focusing on specific antipsychotic medications rather than broad categories to understand their distinct impacts on QoL and explore the complex relationships between antipsychotics and various influential factors in schizophrenia treatment.

Keywords: schizophrenia, quality of life, typical antipsychotic, atypical antipsychotic

INTRODUCTION

Schizophrenia is a chronic, debilitating psychiatric disorder which commonly impacts various crucial domains of life, including personal, familial, social, educational, occupational, and others [1]. It affects an estimated population of around 24-million, with a prevalence rate of approximately 1 in 300 people (0.32%) globally. Among adults, this rate rises to 1 in 222 people (0.45%) [1,2]. The magnitude of the global burden of schizophrenia persists at a significant level and shows a continuous upward trajectory. [3]

Prioritizing the improvement of quality of life (QoL) is crucial in managing patients with schizophrenia, as it constitutes a fundamental aspect influencing their overall psychosocial functioning and subjective well-being. The World Health Organization (WHO) defined QoL as "individuals" perceptions of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns" [4]. This broad concept incorporates not only the person's physical health and psychological state but also their level of independence, social relationships, beliefs, and relationship to the environment [4].

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According to the Fifth Edition of the Diagnostic and Statistical Manual of Mental Disorders 5 (DSM-5), schizophrenia is characterized by at least two of the following symptoms: hallucinations, delusions, disorganized speech, grossly disorganized or catatonic behavior, or negative symptoms, such as reduced emotional expression or motivation, which must be present for a significant period, resulting in a noticeable decline in the person's overall functioning in various aspects of life, such as work, relationships, or self-care. The disturbance should persist for a minimum of six months, with at least one month of active symptoms [5].

Typically, the onset of the disorder occurs during early adulthood, and it is frequently preceded by a prodromal period characterized by early signs and symptoms. Positive symptoms, such as delusions and hallucinations, are often the primary reason for patient presentation in clinical settings. However, schizophrenia is also characterized by negative symptoms, including avolition and social withdrawal, and cognitive symptoms, such as deficits in working memory, executive function, and processing speed. The long-term burden associated with schizophrenia is significantly influenced by the presence of negative and cognitive symptoms [6]. When assessing QoL in patients with schizophrenia, several factors must be evaluated, such as symptom control, functionality, and, most importantly, the patient's subjective well-being. For patients with predominant negative and cognitive symptoms, the perception of QoL is challenging to evaluate [7].

Despite more than a century of continuous medical research, this disorder remains one of the most severe, debilitating medical conditions. Clinicians and researchers are united in a global effort to identify biomarkers and other tools to detect subtle features in patients at risk or in the prodromal stage of the disorder. Schizophrenia leads to loss of function, leaving patients in a state of chronic disability, isolated from family and society, and has an unquestionable effect on their quality of life. [8] Data show that in Europe, less than 20% of people with schizophrenia are employed [9] and in the United States, almost 20% are homeless [10].

Pharmacological options for schizophrenia consist in antipsychotic drugs, which are first-generation antipsychotics (FGA), also known as conventional or typical antipsychotics (TA) and newer, second-generation antipsychotics (SGA), also called atypical antipsychotics (AA). The FGAs are high-affinity antagonists of dopamine D2 receptors, and their effectiveness among psychotic symptoms has been shadowed by their neurological side effects, such as debilitating extrapyramidal symptoms (EPS). SGAs have a lower affinity for D2 receptors and a higher affinity for serotonin (5-HT1A,2A,2C,3,6,7) and norepinephrine (α1, α2) receptors. Various studies indicate that SGAs are similar to FGAs in reducing positive symptoms but have an increased efficacy on negative symptoms, probably due to multiple mechanisms. Regarding the treatment effects on cognitive symptoms, studies have shown inconclusive results. There is continuous research regarding the impact of antipsychotics on functionality, long-term outcome and QoL [11]. Despite the pharmacological variations among available antipsychotic drugs, their common mechanism of action involves the blockade of postsynaptic dopamine receptors in the brain. This association between dopamine and QoL is mediated through the brain's reward system. Therefore, when assessing QoL, it is crucial to consider the specific antipsychotic medication used, as it may influence outcomes despite the shared final target of these drugs [12,13].

Since the introduction of atypical antipsychotic medication, there has been an increased interest in studying the QoL in patients with schizophrenia, given the different side effect profiles of these drugs [14]. Voruganti et al. conducted a study comparing the effectiveness of TA and AA from the patient's perspective, and they found that patients on TA had significantly lower QoL compared to the group receiving AA [15]. Mortimer and Al-Agib also concluded that QoL was superior for patients treated with AA, however mentioning that there was an important age difference between the patients in the two groups, with the patients within the AA group having a younger age and a shorter duration since the onset of the disorder [16]. In another study by Ritsner et al., QoL scores of outpatients with schizophrenia stabilized on risperidone or olanzapine (AA) and TA were compared. Both self-report and observer-rated QoL outcomes were evaluated, considering demographic, illness-related, and treatment-related factors. The results consistently demonstrated that AA outperformed TA in terms of QoL, even after adjusting for daily doses, treatment duration, subjective tolerability, and the use of adjuvant antidepressants. Factors such as gender, marital status, age, education, living arrangement, employment status, age of onset, duration of illness, symptom severity, emotional distress, subtypes of schizophrenia, and treatment adverse reactions did not significantly affect QoL outcomes in either group [17]. A meta-analysis by Leucht et al., published in 2009, compared various factors (including QoL) between patients treated with AA vs. TA. Among the 17 studies reporting QoL results, only amisulpride, clozapine, and sertindole demonstrated better effects compared to TA [18]. A prospective study conducted by Killian and Angermeyer assessing health-related QoL could not confirm the superiority of AA. [19] The Cost Utility of the Latest Antipsychotic Drugs in Schizophrenia Study (CUtLASS1) tested the hypothesis that AA (other than clozapine)

are associated with an increased QoL compared to TA. They performed a randomized controlled trial on 227 patients with schizophrenia and applied the Quality-of-Life Scale (QLS) to verify their hypothesis. However, the results showed that using non-clozapine AA is not superior to using TA regarding QoL at one year [20].

OBJECTIVE

The aim of our study was to assess and compare the differences in QoL between patients receiving typical antipsychotics and those treated with atypical antipsychotics. Educational level, pathology, and previous treatment were considered as controlling factors. Our purpose was to obtain results that would provide valuable insights into the potential benefits of the pharmacological approach on the patients' overall well-being.

METHODS

Participants

We conducted a cross-sectional study on a population of 109 patients who met the DSM-IV-TR [21] or ICD-10 [22] criteria for schizophrenia and who were admitted to the "Prof. Dr Alexandru Obregia" Clinical Psychiatry Hospital in Bucharest, Romania, between October 1, 2009, and October 1, 2012.

The inclusion criteria consisted in having a schizophrenia diagnosis according to DSM-IV-TR or ICD-10 criteria in patients aged between 18 and 65 years old, that have been voluntarily admitted to the hospital and who have been treated with antipsychotics for at least four weeks before inclusion in the study.

Patients with a diagnosis of mental retardation, those under legal guardianship or who have been involuntarily admitted to hospital according to the Mental Health Law were excluded. Moreover, patients with a psychiatric history of other mental health disorders (bipolar disorder, schizo-affective disorder, persistent delusional disorder, substance abuse/addiction and others) did not meet the criteria for the study. All patients offered informed consent for participating in this research study. All the scales used in this study were translated into the Romanian language, and the evaluator obtained approval for their application. The study was authorized by the Ethics Committee of "Prof. Dr. Alexandru Obregia" Clinical Psychiatry Hospital in Romania [12].

Assessment tools

We collected data by conducting semi-structured interviews and reviewing previous medical records. Moreover, family members or caregivers offered additional data whenever possible. Demographical data such as age, gender, rural or urban environment, educational and professional level and occupational status was collected. Additionally, we inserted data from the medical history, such as the total number of hospitalizations in our clinic, age at the onset of the first psychotic episode, the total number of years of the disease, and previous treatment with a typical or atypical antipsychotic.

We applied the Positive and Negative Syndrome Scale (PANSS) to assess the positive and negative symptoms of schizophrenia and also general psychopathology. It combines 18 items of the Brief Psychiatric Rating Scale and 12 items of the Psychopathology Rating Schedule. The 30 resulting items were offered a detailed definition and criteria for rating, with higher total scores indicating more severe symptomatology [23,24].

We used The European Quality of Life Quality of Life Scale – 5 Dimensions (EQ-5D) to assess the QoL among patients. It is a generic, short, and easy-to-administer instrument designed for self-evaluation of the QoL concerning one's health status that takes approximately 90 seconds to complete. It consists of two sections: one covering five dimensions - mobility, self-care, usual activities, pain/discomfort, anxiety/depression - and for each dimension, in the 3L version, three elements describe the condition: no problems, moderate problems, or severe problems. The respondent chooses the closest description to their state, resulting in a five-digit profile indicating the score on the dimensions. The second section allows for self-evaluation of the overall health status on a 20 cm analogue scale, anchored from 0 (worst state) to 100 (best health state), and patients are required to indicate the score that best represents their current health status [25,26].

Another tool that we used was The World Health Organization Quality-of-Life (WHO-QOL) scale. It denotes the person's perception of QoL in the following domains: physical, psychological, level of independence, social relationships, environment, and spirituality. It involves 24 specific facet scores and one general facet score that measures overall QoL and general health. In our study, we used the WHOQOL-BREF, which maintained the comprehensiveness of the WHOQOL in an abbreviated version. We evaluated four domains (physical, psychological, social, and living environment) and two other items were examined separately – one about the overall perception of QoL and one about the general perception of health. Domain scores are scaled in a positive direction, meaning that higher scores denote a higher satisfaction regarding QoL. A 5-point Likert scale was utilized to quantify the patients' responses [4].

We also scored the Global Assessment of Functioning (GAF) Scale, a scoring system which quanti-

fies the severity of the disorder, broadly used for its dual invaluable contribution to clinical practice and research studies. It measures the patients' general status as a mirror of the diagnosis burden and offers a quick, reliable, valid evaluation of overall psychological disturbance. Higher scores indicate better functionality [27,28].

The World Health Organization Disability Assessment Schedule (WHODAS 2.0) was also used as an effective and versatile evaluation tool to measure the level of functioning across six domains, namely cognition, mobility, self-care, interpersonal relationships, life activities, and participation in social activities. It offers a dependable and universally applicable measurement of functioning and disability in all adult populations across various cultures while providing a comprehensive profile and a reliable summary of functioning and disability [29].

In addition, we considered the patients' medical history regarding the type of antipsychotic used (typical or atypical). In the typical antipsychotic group, we included antipsychotics like haloperidol, and for the atypical antipsychotic group, we included patients who underwent treatment with risperidone, olanzapine, aripiprazole, clozapine and cariprazine.

Statistical analysis

The Statistical Package for Social Sciences (SPSS) 26 was used to analyze the available data. Descriptive statistics were used to characterize the sample using the mean (standard deviation, SD) for continuous variables and the number of cases (percentage) for categorical variables.

RESULTS

Out of all the patients we included in the current study (n=109), 64 participants (58.7%) were female, and 45 (41.3%) were male.

The patients were divided into two groups based on the type of antipsychotic treatment. There were 15 patients (13.8%) treated with a typical antipsychotic and 94 (86.2%) treated with an atypical antipsychotic. The mean age was 39.67 (SD=11.12) in the patients treated with TA and 40.29 (SD=10.36) in the AA group.

We ran a logistic regression comparing the means of several parameters between AA and TA use among our participants (Table 1).

Furthermore, we examined the differences in various domains of well-being based on the responses to the WHOQOL-BREF questionnaire between the two groups (Table 2). The domains analyzed were physical health (D1), psychological well-being (D2), social relationships (D3), and environmental factors (D4). Statistically significant differences were found in the D3 domain regarding social relationships, meaning that participants treated with AA reported significantly higher scores (M = 41.73, SD = 19.69), indicating better social relationship quality (p-value = 0.010).

Moreover, we compared the impact of TA versus AA on functional impairment measured by the WHODAS 2.0 total score in the unemployed group (Table 3). Regression analysis was performed to examine the relationships between the variables, revealing significant findings regarding the impact of antipsychotic medications on functional impairment. The results suggest that treatment with AA was associated with lower levels of functional impairment compared to TA. These findings support the potential advantages of AA in managing functional impairment in this patient population.

DISCUSSION

The results demonstrated statistically significant differences in the impact of different treatments on various factors. Patients treated with AA exhibited higher overall scores on the EQ-5D-3L, indicating better QoL. The study also identified significant associations between treatment type and gender, as well as employment status.

Based on the detailed results in Table 1, our analysis revealed several influential factors associated with the overall outcome when stratifying the study participants into two groups based on the antipsychotic drug administered.

Notably, the mean EQ-5D-3L score presented a significant difference between these groups, suggesting a correlation between the type of antipsychotic drug and quality of life (QoL). Specifically, patients receiving an AA treatment have shown a higher mean score of 71.09 (SD 20.52) than those treated with a TA, with a lower mean score of 55.27 (SD 17.93). These findings suggest that patients treated with an AA generally experience a higher QoL. The potential correlation between AA and improved QoL could be attributed to the fact that AA have a broader pharmacological profile, targeting multiple neurotransmitter systems, which effectively alleviates not only positive but also negative and cognitive symptoms of schizophrenia. Moreover, AA have a lower risk of inducing extrapyramidal symptomatology, such as parkinsonism, dystonia, and tardive dyskinesia, symptoms which can have detrimental effects on QoL and may result in noncompliance with treatment [30]. However, individual responses to antipsychotics may vary, and treatment decisions should consider each patient's specific needs. Recognizing the disparity in QoL between treatment groups is important, as it can influence treatment adherence and long-term outcomes.

After controlling for variables such as pathology, educational level and treatment history, the p-value of 0.032 in relation to occupational status indicates a statistically significant association between the type of antipsychotic treatment (TA vs AA) and employment status. A systematic review published by Bouwmans et al. in 2015 demonstrated a general positive correlation between being employed

TABLE 1. Results of logistic regression

	Variable	Group I (TA) n=15		Group II (AA) n=94		P value (Sig.)
Psychiatric history	Mean age at the first episode (SD)	23.33	(3.47)	24.04	(4.94)	0.503
	Mean duration of disorder in years (SD)	16.47	(9.48)	16.23	(9.88)	0.14
	Number of hospital admissions (SD)	2.83	(1.11)	2.19	(3.68)	0.93
EQ-5D-3L	Mean score (SD)	55.27	(17.93)	71.09	(20.52)	**0.016**
Occupational status	Employed	6	40%	28	29.8%	**0.032**
	Unemployed	9	60%	66	70.2%	
PANSS	Positive score (SD)	23.20	(3.14)	21.19	(3.79)	0.338
	Negative score (SD)	26.07	(3.28)	23.8	(4.55)	0.284
	General pathology score (SD)	49.47	(5.27)	46.45	(7.19)	0.915
Marital status	Single	8	53.3%	46	48.9%	0.234
	Married	2	13.3%	19	20.2%	
	Divorced	5	33.3%	21	22.3%	
Educational level	Low	8	53.3%	52	55.3%	0.096
	Medium	7	46.7%	29	30.9%	
	High	0	0%	13	13.8%	
Gender	Women	7	46.7%	57	60.6%	**0.036**
	Men	8	53.3%	37	39.4%	
Treatment history	History of TA treatment	9	81.8%	33	56.9%	0.699
	No history of TA treatment	2	18.2%	25	43.1%	

TA – typical antipsychotic, AA – atypical antipsychotic, SD – standard deviation, PANSS – Positive and Negative Symptom Scale, EQ-5D-3L – European Quality of Life 5 Dimensions 3 Level Version

TABLE 2. WHOQOL-BREF mean scores in participants for the current study

	Variable	Group I (TA) Mean (SD)		Group II (AA) n=94		P-value (Sig.)
WHOQOL-BREF	Domain 1	49.47	(13.13)	53.63	14.65	0.276
	Domain 2	45.4	13.44	49.39	13.36	0.299
	Domain 3	27.87	17.17	41.73	19.69	**0.010**
	Domain 4	42.13	19.38	50.97	13.95	0.109

Domain 1 – Physical health, Domain 2 – Psychological, Domain 3 – Social relationship, Domain 4 – Environment

TABLE 3. WHODAS 2.0 total score in the unemployed group

	Variable	Group I (TA) Mean (SD)		Group II (AA) n=94		P-value (Sig.)
WHODAS 2.0F	Unemployed	96.53	(15.95)	82.56	(19.02)	0.008

and health-related QoL in patients with schizophrenia. However, the type of treatment was not included among the considered associated factors [31]. One possible explanation for this association, as indicated by Brekke et al. [32], is the mediating role of self-esteem between employment and QoL. An alternative explanation suggests that a larger social network due to employment may also contribute to improved QoL [33].

The difference in the distribution of gender between the two groups was also found to hold statistically significant power (p-value = 0.036), meaning that gender could influence the relationship between medication type and QoL. Literature data suggest that women have certain advantages over men. Specifically, women tend to experience a later onset of illness, and their symptoms show faster and better response to available treatments [34]. Additionally, previous studies have shown that women also experience shorter hospital stays and are less frequently readmitted [35]. Our findings may be relevant and warrant further investigation or consideration.

No statistically significant differences were observed between the two treatment groups regarding the psychiatric history (including treatment history), marital status, educational level, and PANSS results. The lack of difference between the two groups regarding the PANSS score reveals that symptom severity does not significantly influence the type of antipsychotic used, results that are supported by more extensive studies. The fact that the psychotic symptomatology does not correlate with the QoL in those patients needs further assessments and a closer look at the overall functionality of patients with schizophrenia [36].

One noteworthy aspect concerning antipsychotic medications is that research outcomes may be influenced by the fact that patients are more prone to maintain their adherence to the novel antipsychotic treatment [37,38]. This has been linked to an increased QoL in numerous studies [39-41].

Moreover, based on the analysis of the WHODAS 2.0 scale among unemployed patients, treatment with AA was associated with lower levels of functional impairment compared to TA, supporting the potential advantages of AA in managing functional impairment in patients with schizophrenia. In addition, the WHOQOL-BREF questionnaire revealed statistically significant differences in the domain of social relationships (D3), indicating that participants treated with AA reported better social relationship quality than those receiving TA.

These results emphasize the importance of considering various factors, such as gender, medication type, and employment status when making medical decisions in order to optimize outcomes and enhance the well-being of individuals with schizophrenia. Further studies incorporating larger sample sizes and evaluating additional variables are warranted to provide more comprehensive guidance in tailoring treatments for this patient population.

In addition, it is crucial to conduct studies focusing on specific antipsychotic medications rather than solely examining the broad categories of typical or atypical antipsychotics. Different medications within these classes may have varying effects on QoL outcomes and other factors. Investigating individual antipsychotic agents in well-designed studies will enable a more precise understanding of their impact on patients' QoL, thereby facilitating evidence-based treatment decisions. Furthermore, such research can shed light on the nuanced relationships between specific antipsychotics, gender disparities, employment status, and other influential factors, providing valuable insights for personalized treatment approaches in schizophrenia.

Limitations

Our study has several limitations. Firstly, the relatively low number of patients included in the study may impact the broader applicability of our findings. Additionally, there was an imbalance in gender distribution, with a slightly higher proportion of women than men. These factors could contribute to inconsistencies between our results and existing literature and limit our ability to draw conclusions that apply to the larger population. Furthermore, our sample consisted of patients who were already stable on medication, and we did not assess the dynamics of switching from a TA to an AA. This limitation prevents us from capturing the potential impact of medication changes on the observed outcomes. Moreover, our study lacked a control group, which limits our ability to compare the effects of different antipsychotic types on QoL outcomes. A control group would have provided a reference point for comparison and enhanced the validity of our findings. Lastly, it is essential to note that our study was cross-sectional, assessing data at a single point in time. This limits our ability to establish causal relationships and track changes in QoL over time.

These limitations highlight the need for future research with a larger sample of patients, balanced gender distribution, inclusion of longitudinal designs, assessment of medication dynamics, and incorporation of control groups to provide more robust and comprehensive insights into the relationship between antipsychotic type and QoL outcomes in patients with schizophrenia.

CONCLUSION

In conclusion, our study focused on patients diagnosed with schizophrenia treated with typical and atypical antipsychotics. The results revealed no significant variations in the severity of symptoms between the two groups. However, it is worth noting that patients receiving atypical antipsychotics consistently reported a higher quality of life compared to those on typical antipsychotics.

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