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EFFECT OF VORTIOXETINE ON THE QUALITY OF LIFE IN PATIENTS WITH SCHIZOPHRENIA

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Summary

Background: *Quality of life is a multidimensional concept that includes both positive and negative aspects of well-being and life, as well as social, psychological and physical health. It is related to health and refers to the optimal level of mental, physical and social functioning.The aim of the research was to examine the effects of vortioxetine on the quality of life in patients with schizophrenia.*

Subjects and methods: *Overall 120 stable patients with schizophrenia were randomly divided into two groups (treatment and control). All subjects were on antipsychotic therapy (olanzapine or risperidone or aripiprazole). Vortioxetine was given to subjects in the treatment group at a dose of 10 mg. The study lasted twelve weeks. The quality of life was measured by the The World Health Organisation Quality of Life Assessment measuring scale (WHOQOL-BREF).*

Results: *Patients treated with additional therapy with vortioxetine showed a statistically significantly higher assessment of all aspects of quality of life compared to control group. Mild effects of vortioxetine on general life satisfaction, health satisfaction, social and environmental domains, and moderate effects of vortioxetine on physical and mental quality of life domains were demonstrated. Patients taking olanzapine and vortioxetine showed the largest increase in quality of life in the treatment group. Patients treated with risperidone or aripiprazole with vortioxetine showed equal improvements in the quality of life.*

Conclusion: *Given that quality of life is an important target for the treatment of schizophrenia, our results encourage future studies on the comparison between vortioxetine and other antidepressants on this patient-centered outcome. Given that quality of life is an important target for the treatment of schizophrenia, our results encourage future studies on the comparison between vortioxetine and other antidepressants on this patient-centered outcome.*

Keywords: *Schizophrenia, Quality of Life, Vortioxetine, Antipsychotics, Outcome*

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INTRODUCTION

„We suffer more often in imagination than in reality“
-Seneca

Schizophrenia is one of the most severe psychiatric disorders, which according to The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM 5) (American Psychiatric Association, 2014) is classified as a disorder from the spectrum of schizophrenia and other psychotic disorders (Lieberman et al. 2020). The most prominent symptoms include: disturbance of perception, thinking, affective modulation, behavior, as well as the development of negative symptoms (Šagud et al. 2021). There is a clear link between negative symptoms and functional incapacity of patients (Karlović et al. 2019).

Antipsychotics are the cornerstone for the treatment of schizophrenia. (Ceraso et al. 2022, Schneider et al. 2022). However, they have a number of limitations, including their poor efficacy against negative and cognitive symptoms as well as different adverse events, which may impact the quality of life. Prevailing view is that a combination of antipsychotics and psychosocial treatments can contribute most to functional recovery (Sadock et al. 2017).

Quality of life

According to the definition of health of the World Health Organization, health is a state of good physical, mental and wellbeing. Health is the mostly used as a term for absence from illness. Some of the health conditions are a balanced diet, physical activity and hygiene (WHO, 2012).

Quality of life refers to a satisfactory level of psychological, social, physical and functioning in certain social roles (eg. employee, parent, partner, spouse, friend). It includs both sexual and other relationships and the perception of health, abilities, self-satisfaction, life and well-being (Bowling et al. 2001). It is a multidimensional construct that measures overall life satisfaction and health satisfaction and four additional domains: physical, mental, social, and environmental (Revicki et al. 2016).

Aversive influences,such as disease, can disrupt the homeostasis of quality of life. Patients can no longer maintain the usual level of subjective quality of life and it falls (Cummins et al. 2003) There is meta-analytic evidence on the impaired quality of life in patients with schizophrenia compared to healthy controls (Dong et al. 2019).

Factors associated with the quality of life in patients with schizophrenia should be considered. While antipsychotics improved quality of life in patients with schizophrenia (Ceraso et al. 2022), severity of psychotic symptoms was not associated with any of quality life domains in this population (Dong et al. 2019). In agreement, in the absence of significant symptoms, including depression, patients may still present with poor quality of life and there may be the room for improvement. Concomitant treatment with antidepressants improved the majority of quality of life domains patients with schizophrenia who were in stable clinical condition (Ritsner & Gibel 2006). Those findings suggest that quality of life in schizophrenia is a distinct concept, which is highly subjective and not closely related to disease severity. It may be rather associated with other factors, such as low levels of physical activity, social isolation, insufficient support and stimulation, poor nutrition, stigmatisation and somatic comorbidities.

Vortioxetine is a multimodal serotonergic antidepressant (Chen et al. 2018); 5-HT3, 5-HT1D and 5-HT7 antagonist, 5-HT1A agonist and 5-HT1B partial agonist, and also a 5-HT transporter inhibitor depending on the dose (Jakovljević 2016, Dvojković et al. 2021). It is also demonstrated improvements in both depression and cognitive symptoms (Salagre et al. 2018)

To best of our knowledge, there is no data on the effects of vortioxetine on the quality of life in patients with schizophrenia. The aim of the present research is to examine the effects of vortioxetine on the quality of life in patients with schizophrenia.

SUBJECTS AND METHODS

This study enrolled 120 patients diagnosed with schizophrenia according to DSM 5 (American Psychiatric Association, 2014) who were randomized on a 1:1 basis in the treatment or control group.

Included were patients who were in stable condition, which was defined as having Positive and Negative Syndrome Scale (PANSS) total score ≤ 70 (Kay et al. 1987), and also did not present wih significant depressive symptoms, as reflected from their The Calgary Depression Scale (CDSS) scores ≤6 (Addington et al. 1994). The patients were enrolled after they provided the written informed consent, approved by the Local Ethics Committee. Patients were excluded if they were receiving diazepam or diazepam equivalent in doses ≥ 10 mg daily, mood stabilizers, any antidepressants in the past 3 months, abused substances in the past three months, attempted suicide in the past 6 months, or presented with suicidal, heteroaggressive, or other similar behavior in the past 6 months, or had somatic comorbidities (such as intellectual disabilities, significant neurological disease or head trauma). Pregnant or lactating individuals were also excluded.

Both groups, which were consisted of 60 patients, were divided into three subgroups, according to the antipsychotic monotherapy: 20 patients were on olanzapine, 20 patients on risperidone and 20 patients were on aripiprazole. In a treatment group, patients were prescribed vortioxetine in a fixed dose of 10 mg.

The study lasted 12 weeks, and patients were tested at baseline, and at the end of the study (month 3). The quality of life was measured by the The World Health Organisation Quality of Life Assessment measuring scale (WHOQOL-BREF) (World Health Organisation, 1992). There were no adverse events during the study. Six patients were no longer willing to participate.

The study is registered in ClinicalTrials.gov. Identifier: NCT04456777

Statistical analysis

The statistical methods used for data analysis of this prospective study were descriptive statistical methods (frequencies, percentages, arithmetic mean, standard deviations, minimum, maximum, skewness/curvature, kurtosis/flatness), general linear models, factorial analysis of covariance, 2 x 3 plus covariate. The SPSS21 program was used for data analysis. Graphs were created in MS Excel. Initially, the descriptive characteristics of the included scales were calculated. Due to the small sample, the normality of the distributions was checked using skewness and kurtosis statistics, and it turned out that most of the results do not deviate significantly from the normal distribution.

RESULTS

Sociodemography: The study enrolled 70 (58%) of men and 50 (42%) women. The age range of the respondents was from 21 to 50 years old, with an average of 37 years (sd=7.88). The average age of the disease onset was M=21.8 years (sd=3.54), and all subjects were diagnosed with schizophrenia between the ages of 15 and 33. The subjects were hospitalized between 1 and 11 times and the

average number of hospitalizations per subject was M=5 (sd=2.25). The majority of subjects (63%) completed secondary education. 26% had a college or university degree, while the remaining 12% have completed primary school or lower. moreover, 63% of subjects were unemployed, 74% not married and 77% had no children. In addition, 61% of participants had positive family history for psychiatric disorders, while, and a total of 22% of subjects have had at least one previous suicide attempt.

Descriptive statistics: All subscales are presented of the WHOQOL-BREF questionnaire that include two items representing general quality of life and health satisfaction and four domains of quality of life: physical, mental, social and environmental. The results on the scale are adjusted in such a way that they are comparable to the results on the extended version of the 100-degree scale.

Descriptive statistics of all subscales of quality of life shows that the arithmetic means of the four domains of quality of life range from 2.14 to 3.31. On all subscales and individual particles there is an increase in the average quality of life in the third dimension. None of the subscales deviated from the normal distribution (Table 1).

Table 1. Descriptive statistics of all subscales of quality of life

		N	Min	Maks	M	SD	Skewness	Kurtosis
General quality of life	baseline	119	1	5	2.90	1.092	.124	-.692
	3. m.	114	1	5	3.32	1.117	-.402	-.280
Health satisfaction	baseline	119	1	5	3.11	1.007	-.020	-.426
	3. m.	114	1	5	3.48	.952	-.105	-.366
Physical domain	baseline	119	7	20	13.2	2.33	-.116	.090
	3. m.	114	8	19	14.3	2.32	-.158	-.173
Mental domain	baseline	119	7	20	12.7	2.53	.025	-.202
	3. m.	114	9	19	14.5	2.14	-.261	-.417
Social domain	baseline	119	4	20	11.1	3.31	.413	-.266
	3. m.	114	7	20	12.4	2.94	.444	-.402
Enviroment domain	baseline	119	7	20	13.1	2.51	.001	.031
	3. m.	114	8	20	14.1	2.45	-.026	-.598

Table 2. Descriptive statistics of all quality of life subscales, depending on group and measurement

	N		M		SD	
	Treatment	Control	Treatment	Control	Treatment	Control
Quality of life, baseline	60	59	3.0	2.8	0.90	1.26
Quality of life, 3rd month	57	57	3.7	3.0	0.74	1.31
Satisfaction with health, baseline	60	59	3.0	3.2	0.94	1.07
Satisfaction with health, 3rd month	57	57	3.8	3.1	0.80	0.96
Physical domain, baseline	60	59	13.2	13.3	2.50	2.16
Physical domain, 3rd month	57	57	15.3	13.4	2.24	2.00
Mental domain, baseline	60	59	12.3	13.2	2.70	2.29
Mental domain, 3rd month	57	57	15.4	13.6	1.81	2.08
Social domain, baseline	60	59	11.2	10.9	3.46	3.16
Social domain, 3rd month	57	57	13.5	11.3	2.77	2.69
Environmental domain, baseline	60	59	13.6	12.7	2.69	2.24
Environmental domain, 3rd month	57	57	15.3	13.0	2.18	2.16

Descriptive statistics of all quality of life subscales, depending on group and measurement shows that the treatment group has higher arithmetic means in the third measurement than the control group on all subscales of quality of life. We also see that in the treatment group there was an increase in arithmetic means in all domains of quality of life, which is not the case in the control group (Table 2).

Arithmetic means and standard deviations to the first two particles of the quality of life scale depending on the group and antipsychotic used (third measurement) is shown in (Table 3) and (Table 4) shows the arithmetic means and standard deviations measured in the third measurement, for all quality of life subscales, depending on group and antipsychotic which participants take.

Table 3. Arithmetic means and standard deviations to the first two particles of the quality of life scale depending on the group and antipsychotic used (third measurement)

Group		General quality of life			Health satisfaction		
		M	SD	N	M	SD	N
Treatment	Olanzapine	3.7	0.56	19	3.7	0.73	19
	Risperidone	3.7	0.89	18	4.0	0.91	18
	Aripiprazole	3.6	0.75	20	3.8	0.77	20
	Total	3.7	0.74	57	3.8	0.80	57
Control	Olanzapine	2.4	1.29	18	3.2	1.15	18
	Risperidone	3.3	1.63	19	3.1	1.08	19
	Aripiprazole	3.2	0.71	19	3.2	0.69	19
	Total	3.0	1.31	56	3.1	0.97	56
Total	Olanzapine	3.1	1.19	37	3.5	0.99	37
	Risperidone	3.5	1.33	37	3.5	1.10	37
	Aripiprazole	3.4	0.75	39	3.5	0.79	39
	Total	3.3	1.11	113	3.5	0.96	113

Table 4. Arithmetic means and standard deviations on quality of life subscales depending on the group and antipsychotic used (third measurement)

Group		Physical domain			Mental domain			Social domain			Environmental domain		
		M	SD	N	M	SD	N	M	SD	N	M	SD	N
Treatment	Olanzapine	15.6	2.06	19	15.3	1.76	19	13.2	2.88	19	15.1	2.54	19
	Risperidone	15.1	2.65	18	15.1	2.11	18	13.9	3.11	18	15.1	2.19	18
	Aripiprazole	15.1	2.08	20	15.7	1.62	20	13.5	2.40	20	15.6	1.86	20
	Total	15.3	2.24	57	15.4	1.81	57	13.5	2.77	57	15.3	2.18	57
Control	Olanzapine	13.4	2.30	18	14.2	2.03	18	11.4	2.79	18	13.1	1.85	18
	Risperidone	13.1	1.81	19	13.6	2.10	19	11.2	2.09	19	13.3	2.46	19
	Aripiprazole	13.6	2.01	19	13.1	2.14	19	11.4	3.25	19	12.6	2.24	19
	Total	13.3	2.01	56	13.6	2.10	56	11.3	2.70	56	13.0	2.18	56
Total	Olanzapine	14.5	2.41	37	14.8	1.95	37	12.3	2.94	37	14.1	2.43	37
	Risperidone	14.1	2.45	37	14.3	2.22	37	12.5	2.95	37	14.2	2.48	37
	Aripiprazole	14.4	2.17	39	14.4	2.30	39	12.4	3.00	39	14.1	2.53	39
	Total	14.3	2.33	113	14.5	2.15	113	12.4	2.94	113	14.1	2.46	113

General quality of life

To check whether there is a main effect of vortioxetine treatment, the main effect of antipsychotics and their interaction on the general quality of life, as in previous problems, a factorial analysis of covariance was performed with the results of the first measurement as a covariate.

There is a statistically significant effect of treatment with vortioxetine (F = 32.333 , p <, 001) while the type of antipsychotic that participants take has no statistically significant effect on overall quality of life (F = 0 , 633 , p>, 05). The main effect of vortioxetine treatment is low to moderate (η^2 = .234). According to the arithmetic means in Table 4, we see that the treatment group, in the third measurement (M = 3.7) achieves higher results on the particle measuring the general quality of life than the control group (M = 3.0). In other words, participants who received vortioxetine reported a higher level of general quality of life in the third measurement than participants who were not treated. The interaction between the treatment and the type of antipsychotic was statistically significant, but with a very mild effect (F = 3.358, p <.. 05 ; η^2 = .06). Although the effect of interaction of treatment and type antipsychotic is low. Namely, we see that participants taking olanzapine have the largest increase in quality of life in the treatment group (while at the same time reporting the lowest quality of life). Participants taking risperidone and aripiprazole report an equal increase in quality of life if further treated with vortioxetine (Table 5).

Health satisfaction

The same analysis was performed to determine whether there was a major effect of vortioxetine treatment, a major effect of antipsychotic types as well as their interaction on health satisfaction.

When it comes to health satisfaction, we see that only the main effect of vortioxetine treatment was statistically significant (F = 42,256 , p < , 001) while the main effect of the antipsychotic used and the interaction of antipsychotics and vortioxetine treatment were not statistically significant in table 5. The effect is mild to moderate (η^2 = , 285). According to the arithmetic means in table 3, we see that the treatment group (M = 3.8) achieved significantly higher results on the particle measuring health satisfaction than the control group (M = 3.1), which indicates that taking vortioxetine with regular therapy associated with greater health satisfaction in participants (Table 6).

Table 5. Covariance analysis – testing the main effects of vortioxetine treatment, types of antipsychotics and their interactions on general quality of life

	SS	df	MS	F	p	Parc. This square
General quality of life, baseline	78,613	1	78,613	225,074	.000	.680
Group	11,293	1	11,293	32,333	.000	.234
Antipsychotics	.442	2	.221	.633	.533	.012
Group * Antipsychotic	2,346	2	1,173	3,358	.039	.060
Error	37,023	106	.349			
Total	1397.00	113				
Corrected total	139,221	112				

Table 6. Covariance analysis – testing the main effects of vortioxetine treatment, types of antipsychotics, and their interactions on health satisfaction

	SS	df	MS	F	p	Parc. This square
Satisfaction with health, baseline	39,146	1	39,146	86,968	.000	.451
Group	19,020	1	19,020	42,256	.000	.285
Antipsychotics	.020	2	.010	.022	.979	.000
Group * Antipsychotic	1,052	2	.526	1,169	.315	.022
Error	47,712	106	.450			
Total	1476.00	113				
Corrected total	102,230	112				

Domains of quality of life

Analysis of covariance that test the main effects of vorioxetine treatment and types of antipsychotics and their interactions in four different domains of quality of life (Table 7) show that when it comes to the physical domain of quality of life, there is a statistically significant main effect of vortioxetine treatment (F = 71,999 , p <, 001) while the main effect of the antipsychotic used and the interaction of antipsychotics and vortioxetine treatment statistically significant. The effect is of moderate intensity (η^2 = .404), and according to the arithmetic means in table 4. it can be seen that the treatment group (M = 15.3) achieves significantly higher results on the subscale measuring the physical domain of quality of life than the control group (M = 13.3). Such results suggest that participants taking vortioxetine are more satisfied with the physical domain of their lives .

Similar results were obtained when it comes to the psychological domain of quality of life. Here, too, there is a statistically significant main effect of vortioxetine treatment (F = 102,343 , p < .001) while the main effect of the antipsychotic used, and the interaction of the antipsychotic type and vortioxetine treatment did not prove statistically significant. The effect is of moderate intensity (η^2 = .491), and according to the arithmetic means

Table 7. Covariance analysis – testing the main effects of vortioxetine treatment, types of antipsychotics, and their interactions in the four domains of quality of life

		SS	df	MS	F	p	Parc. This square
Physical domain	Physical domain, baseline	338,221	1	338,221	223,527	.000	.678
	Group	108,942	1	108,942	71,999	.000	.404
	Antipsychotics	3,358	2	1,679	1,110 c	.333	.021
	Group * Antipsychotic	1,569	2	.785	.519	.597	.010
	Error	160,390	106	1,513			
	Total	23767.184	113				
	Corrected total	607,896	112				
Mental domain	Mental domain, baseline	248,199	1	248,199	160,707	.000	.603
	Group	158,061	1	158,061	102,343	.000	.491
	Antipsychotic	4,567	2	2,284	1,479	.233	.027
	Group * Antipsychotic	.874	2	.437	.283	.754	.005
	Error	163,708	106	1,544			
	Total	24285.351	113				
	Corrected total	518,400	112				
Social domain	Social domain, baseline	531,669	1	531,669	192,625	.000	.645
	Group	94,579	1	94,579	34,266	.000	.244
	Antipsychotics	1,694	2	.847	.307	.736	.006
	Group * Antipsychotic	6,865	2	3,432	1,244 th	.293	.023
	Error	292,573	106	2,760			
	Total	18412.444	113				
	Corrected total	968,055	112				
Envirom. domain	Environmental domain, baseline	320,036	1	320,036	170,066	.000	.616
	Group	73,885	1	73,885	39,262	.000	.270
	Antipsychotics	3,771	2	1,886	1,002	.371	.019
	Group * Antipsychotic	1,423	2	.711	.378	.686	.007
	Error	199,475	106	1,882			
	Total	23275.000	113				
	Corrected total	676,735	112				

in table 5, it can be seen that the treatment group (M = 15.4) achieves significantly higher results on the subscale measuring the physical domain of quality of life than the control group (M = 13.6). Such results suggest that participants taking vortioxetine show higher levels of psychological wellbeing in life .

Participants in vortioxetine treatment are also more satisfied with the social domain of their lives. In table 7, we see that there is a statistically significant main effect of vortioxetine treatment (F = 34,266 , p <.001), and the main effect of the antipsychotic used, and the interaction of antipsychotic type and vortioxetine treatment are not statistically significant. The effect is weaker (η^2 = , 244). According to the arithmetic means in table 5, we see that the treatment group (M = 13.5) achieves significantly higher results on the subscale that measures the physical domain of quality of life than the control group (M = 11.3). In other words, the results show that participants taking vortioxetine are more satisfied with the social domain of their lives.

Finally, similar results were obtained when it comes to the environmental domain of quality of life. There is also a statistically significant main effect of vortioxetine treatment (F = 39.262 , p < .001), and the main effect of the antipsychotic used, nor the interaction of antipsychotic type and vortioxetine treatment are not statistically significant. The effect is slightly lower (η^2 = , 270), and according to the arithmetic means in table 3. we see that the treatment group (M = 15.3) achieves significantly higher results on the subscale that measures the physical domain of quality of life than the control group (M = 13.0). While it may seem that environmental satisfaction is not related to the treatment participants receive, it is not uncommon for higher levels of quality of life in some domains to increase participant satisfaction and thus quality of life in other domains.

DISCUSSION

The main finding of the present trial is that add on treatment with vortioxetine significantly affected all aspects of quality of life in patients with schizophrenia. While the effects of vortioxetine on quality in life in schizophrenia were never tested, we have found three studies which focused on vortioxetine treatment in schizophrenia. In general, our results agree with findings of other beneficial effects on vortioxetine in schizophrenia patients. More specifically, in a retrospective study, almost half of patients with schizophrenia or schizoaffective disorder have improved three months after vortioxetine was added to their current antipsychotic regimen (Redaelli et al. 2022). Another study demonstrated improvement in cognitive functions in patients with schizophrenia who had vortioxetine augmentation on their clozapine treatment, along with the improvement of psychotic and depressive symptoms (Bruno et al. 2020). In a third trial in patients with schizophrenia, greater improvement of negative symptoms was observed 8 after weeks in participants who were receiving vortioxetine in addition to risperidone, compared to those who were treated with placebo and risperidone (Moazen-Zadeh et al. 2020). In agreement with our findings, excellent vortioxetine tolerability was reported across those studies (Bruno et al. 2020; Moazen-Zadeh et al. 2020; Redaelli et al. 2022), but similar findings were also observed in the majority of studies with other antidepressants (Helfer et al. 2016). Retention rate of 75% after three months of vortioxetine treatment was lower compared to our results (Redaelli et al. 2022), but the latter study included patients with more severe disease presentation, given that majority of them were hospitalized, and more than half treatment-resistant. Moreover, in Bruno et al. 2020, who included stabilized patients on clozapine treatment, with a baseline PANSS score of 68, retention rate was 90% after three months of vortioxetine application, which is similar to our findings.

When it comes to general life satisfaction, a mild but significant main effect of vortioxetine treatment was found, with subjects using vortioxetine reporting more general satisfaction. The findings are similar with health satisfaction – a mild main effect was found, which can be explained by treatment with vortioxetine. The subjects from the treatment group reported on average higher health satisfaction (Brief et al. 1993).

It is interesting to note that approximately similar main effects were found in all four domains of quality of life: a moderate effect on the physical and mental domains and mild significant effects on the social and environmental domains of quality of life. Subjects who used vortioxetine showed more positive assessments in all domains of quality of life than subjects who were only on conventional antipsychotic treatment. Such results are interesting because the physical, mental, and consequently social domains are directly related to better mental functioning, while the environmental domain actually represents a person's satisfaction with the environment in which he lives and is not necessarily related to the person's functioning. Nevertheless, such results suggest a close link between personal wellbeing and perception of the environment in which a person lives. Due to improved general health and mental functioning, people will often perceive their environment more positively (Leendertse et al. 2018).

Recently, it has been recognized how important the quality of life is as a component of treatment, as well as

health assessments in general. Quality of life in patients with schizophrenia is impaired relative to healthy individuals including the physical, psychological, social, and environmental domains. Interestingly, according to this meta-analysis, quality of life was not related to the severity of psychotic symptoms, but was related to some other variables, such as age, gender, and length of illness (Dong et al. 2019). Nevertheless, some studies have found an association between schizophrenia symptoms and quality of life (Ueka et al. 2011). We found only one study that measured the effect of anhedonia on quality of life in patients with schizophrenia. This paper found an association between the severity of physical and social anhedonia and poorer quality of life in multiple domains, regardless of the symptoms of schizophrenia as well as drug side effects (Ritsner et al. 2011). Furthermore, cognitive dysfunction (Ueka et al. 2011, Kadakia et al. 2022); and according to one study especially verbal memory (Sigaudo et al. 2014); have an adverse effect on the quality of life in patients with schizophrenia. All of this, research suggests that the subjective sense of wellbeing and life satisfaction in patients with schizophrenia depends not so much on the psychotic symptoms themselves as on other factors, including physical and social anhedonia, and cognition. Therefore, the effective effect of vortioxetine on all domains of quality of life in our study may be mediated by both effects on cognitive symptoms and on physical and social anhedonia.

There is no research to test the effects of vortioxetine on the quality of life of people with schizophrenia. The results to date in the literature confirm the positive effects of vortioxetine use on quality of life in people with depressive disorder (Florea et al. 2015); but not in general anxiety disorder, where it has shown no effect at all (Qin et al. 2019). However, it is reasonable to expect that the improvement of cognitive functioning, depressive symptoms and anhedonia, consequently leads to an increased quality of life, which our results confirm.

In addition to the main effects of vortioxetine treatment on quality of life, there is a very mild effect of antipsychotic interactions and vortioxetine use on general life satisfaction (6% of the explained variance), indicating that the greatest difference between treatment and control groups occurs in olanzapine. In other aspects of quality of life (WHOQOL-BREF 1996); we do not find significant interactions between the use of vortioxetine and various antipsychotics. Differences among antipsychotics in quality of life may, as in their effect on other factors, arise from their mechanism of action. Namely, it was found that high occupancy of D2 receptors in striatum may be associated with poorer quality of life (Veselinović et al. 2019). Therefore, all antipsychotics act on these receptors, minor differences between them that exist in this effect may affect some components of quality of life.

Also, the main effects of treatment with various antipsychotics on the quality of life of patients with schizophrenia have not been found.

The effects of vortioxetine on quality of life in schizophreia may be attributed to its unique mechanism of action. For example, there is evidence that partial agonism on 5HT1A receptors may strenghten the inhibitory control on behavior, and therefore reduce the impulsivity and promote decision-making (Pattij et al. 2015) and decrease impulsive aggression (Popova et al. 2022), which may improve social relationship. Moreover, 5HT3 antagonism may reduce anxiety and therefore contribute to the improvement of social behavior (Bhatt et al. 2021), while 5HT7 antagonism may ameliorate cognitive dysfunction, social withdrawal and anxiety (Okubo et al. 2021). Vortioxetine was also reported to increase peripheral brain-derived neurotrophic factor (BDNF) expression in hippocampus in preclinical studies and peripheral BDNF levels, at least in patients with major depression (Sun et al. 2020). While BDNF is a key player in neuroplasticty, which profoundly affects different aspects of cognition and behavior we can speculate that effects on BDNF may also have contribute to effects of vortioxetine (Dvojković et al. 2021). While BDNF levels were not measured in the present trial, it would be intriguing to investigate if improvements of different domains observed with vortioxetine treatment in schizophrenia, the present trial are accompanied by the changes in BDNF indices (Bruno et al. 2020, Moazen-Zadeh et al. 2020, Redaelli et al. 2022).

Scientific Contribution and Implications for Practice

The most significant scientific contribution of the conducted research is related to the fact that the effects of vortioxetine use in patients with schizophrenia have been so far very little clinically examined, especially on a wide range of accompanying symptoms that come with the disease. Therefore, this research is a pioneer in describing, predicting and understanding the effects of vortioxetine on the quality of life in patients with schizophrenia. This creates a basis for upgrading knowledge about the effect of vortioxetine in future researches.

From a practical point of view, it is indisputable that the knowledge about the existence of additional medication that can reduce symptoms resulting from schizophrenia, as well as improve the quality of life of patients, has high value for clinicians and patients themselves.

Limitations

The present study is limited by the open design and small sample size. Due to the absence of active control, it is impossible to ascertain whether the effects of vortioxetine on quality of life was different from drugs from the same class. However, the data on the impact of other antidepressants on quality of life is scarce. For example, meta-analysis reported that given that other antidepressants also improved the qualitiy of life in schizophrenia, but the only two studies were included (Helfer et al. 2016). Moreover, patients were not checked for treatment adherence. Although participants remained in remission during follow-up, occasional non-compliance cannot be excluded. Levels of physical activity, anhedonia, eating habits, loneliness, stigmatisation and support, were not measured. Therefore, it cannot be concluded whether vortioxetine treatment contributed to changes in any of those variables, which in turn may had impact on quality of life.

CONCLUSION

Patients with schizophrenia treated with additional therapy with vortioxetine showed a statistically significantly higher ratings of all aspects of quality of life: general life satisfaction and health satisfaction, and higher results in the physical, mental, social and environmental domains of quality of life. While effects of vortioxetine were mild on general life satisfaction, health satisfaction, social and environmental domains, and moderate on physical and mental quality of life domains, such changes may be important for patients on their long way to recovery from the psychotic illness. Given that quality of life is an important target for the treatment of schizophrenia, our results encourage future studies on the comparison between vortioxetine and other antidepressants on this patient-centered outcome.

Ethical Considerations: Does this study include human subjects? YES
Authors confirmed the compliance with all relevant ethical regulations.
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