Assessment of the quality of Life, Adherence and side effects of Pharmacotherapy in Bipolar Patients being managed in a specialist Hospital in Nigeria.

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ABSTRACT

Background: Advances in pharmacotherapy alongside psychotherapy enablesbipolardisorder (BPD) to become a manageable chronic mental condition. BPD has a major deleterious impact on many aspects of a patient's functioning and quality of life (QoL).

Objectives: To assess theprescribed medication, QoL of patients, medication adherence, treatment cost and side effects.

Methods: Adescriptive cross sectional study involving 46 BPD patients. A structured questionnaire was used to obtain data on sociodemographic, treatment variables and cost of treatment. WHOQoL-Bref was used to assessQoL of the patients. Clinical diagnosis and side effects were obtained from the patients'medical record. Adherencewas assessed using tablet counting and side effects were also obtained from the patient.Data obtained were analysed using Systat for Windows, version 10.2 (Systat Software Inc., USA

Results: All the 46 questionnaires were valid for analysis, 35(76%) of the patients were 18-39 years old and 20(54%) were females. A total of 34(74%)f participants scored above 50% overall average values for QoL. There was no significant difference ($p > 0.05$) between QoL reported in correlation with treatment variables.

Conclusion: Patient reported QoL was good and was independent of psychotropic drug regimen prescribed. The medication used are few conventional ones, adherence was high for most patients. Side effects reported received adequate interventions from the hospital staff. The average cost of treatment is not affordable by most of the respondents. Further studies are required in pharmacotherapyofBPD.

Keywords: Bipolar disorder, quality of life, adherence, side effects, treatment cost.

Evaluation De La Qualite De Vie, Adherence Et Effets Secondaires De La Pharmacotherapie Chez Les Patients Bipolaires Geres Dans Un Hopital Specialise Au Nigeria.

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RESUME

Contexte - Les progrès de la pharmacothérapie aux côtés de la psychothérapie permettent au trouble bipolaire (BPD) de devenir un état mental chronique gérable. BPD a un impact délétère majeur sur de nombreux aspects du fonctionnement du patient et de la qualité de vie (QoL).

Objectifs - Évaluer la médication prescrite, la qualité de vie des patients, l'observance du traitement, le coût du traitement et les effets secondaires.

Méthodes – Une étude transversale descriptive impliquant 46 patients bipolaires. Un questionnaire structuré a été utilisé pour obtenir des données sur les variables sociodémographiques, les variables de traitement et le coût du traitement. WHOQoL-Bref a été utilisé pour évaluer la qualité de vie des patients. Le diagnostic clinique et les effets secondaires ont été obtenus à partir du dossier médical des patients. L'adhésion a été évaluée à l'aide du comptage des comprimés et des effets secondaires ont également été obtenus chez le patient. Les résultats obtenus ont été analysés à l'aide SystatTM pour Windows, version 10.2 (Systat Software Inc., USA

Résultats - Tous les 46 questionnaires étaient valables pour l'analyse, 35 (76%) des patients avaient entre 18 et 39 ans et 20 (54%) étaient des femmes. Au total, 34 (74% des) participants ont obtenu des résultats moyens supérieurs à 50% pour la qualité de vie. Il n'y avait pas de différence significative ($p > 0,05$) entre QoL rapportée en corrélation avec les variables de traitement.

Conclusion - La qualité de vie rapportée par le patient était bonne et indépendante du régime thérapeutique psychotrope prescrit. Les médicaments utilisés sont quelques-uns parmi les conventionnels, l'observance était élevée pour la plupart des patients. Les effets secondaires rapportés ont reçu des interventions adéquates de la part du personnel hospitalier. Le coût moyen du traitement n'est pas abordable pour la plupart des répondants. D'autres études sont nécessaires en pharmacothérapie des bipolaires (BPD).

Mots clés : Trouble bipolaire, qualité de vie, observance, effets secondaires, coût du traitement.

INTRODUCTION

Bipolar affective (BPD) disorder has a major deleterious impact on many aspects of a patient's functioning and quality of life (QoL).Studies conducted in Nigeria and Ethiopia indicated a life time prevalence estimate of 0.1- 1.83% for bipolar disorder and 36% missed diagnosis rate for BPD.[1]This fact delays the onset of mental health care for affected patients. South Africa has an estimated prevalence rate of 9.6% for mood disorders which includes BPA while poorer countries like Kenya has a prevalence rate of 10.8% for mental illness.[2] Mental illness which is poorly diagnosed in developing countries like Nigeria (prevalence of 20%)suffers serious institutional and normative neglect.[3] BPDis a common severe chronic psychiatric disease characterized by the recurrence of mania, depression or mixed episodes. Depression is currently more frequent in Nigeria and is associated with suicidal tendencies.[4] The World Health Organization's report in 2017 showed that there are 7,079,815 Nigerians suffering from depression which may include Patients at the depressive pole of BPD.[5] Treatment of mental disorders goes beyond control of presenting symptoms to restoring patients to their normal daily life and improving their overall QoL. This involves a person's physical, social, emotional and environmental wellbeing.[6] BPD is a mental disorder that requires both pharmacotherapy and psychotherapy. The major classes of medicines used for managing bipolar mania are antipsychotic medicines and mood stabilizers, these medicines have given hope to families with relatives affected by this mental disorder. Studies have reported that atypical antipsychotics show an improved safety and tolerability profile compared to typical anti-psychotics but the effectiveness of these two classes of psychotherapeutic medicines are clinically the same.[7] Adherence to therapy may be a challenge to the patients and their care giver but is a necessity to achieving desired goals of therapy.

QoL and adherence are major consideration for choice of antipsychotic medication and is affected by cost of treatment, effectiveness and side effects.

Psychiatric diseases and affective disorders are present in our community and need the attention of Pharmacists in the hospital setting and in other Public health facilities. These patients though a small fraction of the medical cases in the health facilities are a major public health concern in our society.This study will assess some important aspects of pharmacotherapy of BPD patients who have come to a Federal neuropsychiatric hospital, a tertiary health facility with highly qualified professionals, services and infrastructure available to treat these patients and help incorporate back to the society.

Main objective of this study was to assess thequality of life, adherence and side effects of pharmacotherapy in bipolar patients managed with psychotropic medicines.

METHODS

Study Site

The study was carried out in the Pharmacy department of Federal Neuro Psychiatric hospital Uselu (FPHU), Benin City, Edo state, Nigeria. The FPHU is located in the Uselu district of Egor local Government area of Edo state with an out station at Idunwowina. It is a 267-bedded tertiary healthcare facility with a service catchment area that extends to neighboring states like Ondo, Ekiti, Kogi, Delta and Bayelsa.

The hospital is equipped with modern equipment and infrastructure and staffed with Administrators, Consultants, Clinicians, Pharmacists, psychiatric nurses, laboratory scientists, social workers/public health extension workers etc.[3]

As at the time of recruitment of participants for this study, the enrolment of bipolar affective disorder patients receiving mental health care was 173. A sample size of 46 was consecutively recruited.

Study design

This was a descriptive cross sectional study of BPD patients receiving medicine therapy in a specialist hospital in Nigeria.

Study population and sample size

The study population as at the commencement of this work was 173 patients, the sample size calculation was then determined as described by Araoye (2004) using the equations:[8]

$$n_f = \frac{n}{1 + n/N} \quad \text{and} \quad n = z^2 pq / d^2 \quad \text{where}$$

n_f = desired sample size when population is less than 10,000 as in this case

N = estimate of the population size (173)

n = desired sample size when population is greater than 10,000

z = standard normal deviate (1.96) corresponding to 95% confidence level

p = proportion in the target population estimated to have a particular characteristic (mania); estimated to be 0.99 since all patients are diagnosed with Bipolar mania

q = proportion in the target population estimated not to be having the particular characteristics (mentally stable); estimated to be 0.01 (1-p)

d = degree of accuracy at the 0.02 level

The calculated sample size was ten but a total of 46 patients diagnosed with BPD receiving treatment in the study site who agreed to participate in this study were recruited. The inclusion criteria included adult BPDout-patients that were attending outpatient clinic and refilled their prescription in the pharmacy department of the FPHU. Only patients who had been on medication for at least three months prior to the study and consented to participate in the study were recruited.

Study Instruments

A structured questionnaire was used to collect sociodemographic, treatment variables and adherence status. The World Health Organization quality of life assessment questionnaire (WHOQoL- BREF) was used to assess the patient's QoL.WHOQoL Bref health survey form is one of the most widely used QoL instruments and has demonstrated high levels of reliability and validity in diverse patient populations. The summary scores have been shown to be responsive to psychiatric disease progression. WHOQoL- Bref contains 26 items divided into four domains. domain one which is aimed at assessing physical health examines the following; activities of daily living, dependence on medicinal substances and medical aids, energy and fatigue, mobility pain and discomfort, sleep and rest, work capacity. Domain two assesses psychological functioning and the key points are; Bodily image and appearance, negative and/ or Positive feelings, Self-esteem, Spirituality / Religion / Personal beliefs, thinking, learning, memory and concentration.

Domain three assesses social functioning and the major factors are; Personal relationships, social support and sexual activity.

Domain four assesses Environmental factors which include; Financial resources, Home environment, freedom, physical safety and security, accessibility and quality of Health and social care.[9,10]

In this study, poor Qol was set at below 50% and good Qol was above 50%.

Data collection

Socio-demographic characteristics, treatment variables and adherence to medication were obtained by the researcher. The WHOQoL Bref questionnaires were completed by the patient or with assistance from their care giver. Some patients detected to have inconsistent responses were interviewed and the appropriate corrections made during the period of data collection.

Data quality and reliability

For the health outcomes survey form, the percentage of patients with all items within each health survey form domain completed was found to be consistently 100%. The proportion of completed items was uniformly high for items in the structured questionnaire with the minimum being 96%.

The response consistency for WHOQOL- Bref was higher than 97%.The internal-consistency reliability coefficients (Cronbach's alpha) for the data were consistently high and ranged from 0.78 to 0.86 for the structured questionnaire and 0.75 to 0.92 for the WHOQOL- Bref.

Clinical variables including patients' diagnosis, prescribed medications and side effects were also obtained from patients' medical records. The respondents and their care givers were interviewed in the Pharmacy department during prescription refill and counseling. The pharmacist interviewed the patients about any side effect, how they have been taking their prescribed drugs and if they were taking other medications which were not in their medical records as well as their self reported medication-related problems. Physical examination (observation) was also done to identify extra pyramidal side effects.

Adherence to medication and clinic appointment was assessed using both tablet counting,

non-adherence was set as patients that stopped their medications for a period of 3 days to 2 weeks and reasons for their non-adherence were sought.[11]

Data analysis

Data obtained were entered into Microsoft excel spread sheet and double checked. Data quality and reliability were calculated using internal-consistency reliability coefficients (Cronbach's alpha). Each domain in the WHOQoL- Bref was transformed and the percentage scores calculated as specified by WHOQoL- Bref procedures manual.

Table 1: Number of items in the domains of the WHOQOL- BREF

Domain	WHOQOL-BREF
Physical functioning	Q3, Q4, Q1 0, Q15, Q16 Q17 Q18
Psychological functioning	Q5, Q6, Q7, Q11, Q19 ,Q26
Social functioning	Q5, Q6, Q7, Q11, Q19 ,Q26
Environmental	Q8 + Q9 + Q12 + Q13 + Q14 + Q23 + Q24 + Q25

Each domain in the WHOQOL- BREF was transformed and the percentage scores calculated as specified by WHOQOL- BREF procedures manual. The domain scores were derived by averaging the recorded raw scores for corresponding items of each domain Statistical calculations were performed with the assistance of the personal computer program Systat for Windows, version 10.2 (Systat Software Inc., USA). Descriptive (frequency and percentages), correlation and nonparametric statistics were performed to determine association of the QoL scores with sociodemographic and treatment variables. Proportional data were compared using chi-square test or Fisher's exact test, as appropriate. The criterion for statistical significance was 95% confidence interval and $p < 0.05$.

Ethical consideration

Prior to the commencement of this study, appropriate approval was obtained from the Ethics committee of FNPH, Benin City and informed consent was obtained from the patients and their care givers before they were included in this study.

RESULTS

All 46 questionnaires were valid for analysis, the sociodemographic characteristics of the patients are given in Table 1. Age range of respondents was 18-65 years, 35 of them (76%) were between 18-39 years and 20 (23%) were females. About 28 (61%) of those that took part in the study were single , while 3065% were married)only a few of them were divorced or widowed. A total of 21 (46%) of the patients had no source of income while the others were self employed or worked for the government.Majority of patients had obtained above secondary education (40, 87%).Most of the patients 32, 70%) reported not to have any history of substance use (alcohol and or tobacco, Indian hemp) but five patients who reported to have history of substance use claimed to have stopped.

Table 2: Sociodemographic characteristics of BPD patients receiving treatment in FPHU Benin City, Nigeria.

Characteristics	Frequency n=46	%
Sex		
Female	20	43
Male	26	57
Age(years)		
18-28	21	46
29-39	14	30
40-50	4	9
≥ 50	7	15
Marital status		
Single	28	60.9
Married	14	30.4
Widowed	2	4.3
Divorced	2	4.3
Level of education		
No formal education	2	4.3
Primary	4	8.7
Secondary	26	56.5
Tertiary	14	30.4
Occupation		
Self employed	17	36.9
Civil servant	7	15.2
Private sector	1	2.2
Not employed	21	45.7
Substance hab its		
Prior alcohol	6	13.0
Prior smoking	2	4.3
Current alcohol	5	10.9
Current smoking	0	
Nil	33	71.1

Patients included in this study were being managed with atypical antipsychotic medicines either as monotherapy or as combination therapy with other antipsychotic medicines i.e typical antipsychotics and/or with mood stabilizers etc. Olanzapine and risperidone were the only atypicals prescribed during the study.

Treatment variables

All patients received treatment for their BPD and refilled their prescriptions at the pharmacy department of FPHU. Most of the psychotropic medicines and other classes of medicines needed for other possible co morbidities were in stock for dispensing and sale to patients managed by the health facility. Patients purchased most of their medicines from the Pharmacy Department of the hospital but sourced the other medicines which were not immediately available in private Pharmacies. Majority of the patients (31,68%) in this study were being treated with Olanzapine as a monotherapy or as adjunct to typical antipsychotic medicines and mood stabilizers. About 12(26%) of the

study participants were on combination therapy of atypical and typical antipsychotics, 5 (11%) were on atypicals and mood stabilizers. Four major categories of medication combinations were used. These were Olanzapine/I.M. Fluphenzine , Olanzapine/ Sodium valporate, Risperidone / I.M. Flupenthixol, Olanzapine/ Benzhexol, Olanzapine/ I.M. Fluphenazine / Sodium valporate, and Olanzapine / I.M Fluphenazine / I.M. Haloperidol/ Sodium valporate combinations. The other patients were on combination therapy with other classes of medicines e.g antibiotics, antihypertensives and antimalarial medicines

The average monthly cost of treatment per patient was N5,840 (US$36). Most of the patients (67%) spent less than N10, 000.00 (US $62) monthly. Amount spent on treatment here included cost of medicines (antipsychotic medicines and other medicines prescribed to treat acute infections or chronic co morbidities), hospital charges for clinics and transportation cost.

Assessment of side effects showed that only 8 (17%) of the patients reported to be experiencing extra pyramidal side effects, they already had Benzhexol in their therapy. Two females reported significant weight gain which was their reason for skipping doses of their medication and 5(11%) of the respondents reported sexual dysfunction.

Quality of Life (QoL)

The average QoL was 63%, for this study good QoL was set at 50% and above while values belowwere referred to as poor QoL. Seven of the patients had mean QoL values in domain one (physical health) below 50% while 74% of the patients scored above 50% in domain two (psychological function). Only three patients scored below 50% in domain three (social functioning). Majority of the patients, 42 (91%) scored above 50% in domain four (environment).

The mean QoL values for the domains were in the following descending order: psychological functioning >Physical function > Social function > Environment. The best quality of life functioning for the patients was with domain four, environment i.e. financial resources, home environment, freedom, physical safety and security, accessibility and quality of Health and social care. While the worst quality of life functioning were in domain two, psychological function i.e. bodily image and appearance, negative and/ or Positive feelings, Self-esteem, Spirituality / Religion / Personal beliefs, thinking, learning, memory and concentration.

One way analysis of variance (ANOVA) shows that there is no significant difference between QoL of respondents and their demographic characteristics, Tables 2 shows the p values against the four domains of WHOQoL questionnaire.There was no significant difference between the QoL values for the patients and their monthly health care cost or psychotropic medicine ($p > 0.05$).

Table 3: The relationship between variables and WHOQoL domains of BPD patients receiving treatment in FPHU Benin City.

Variable	Freq	WHOQ OL Scores ± SD			
		D1	D2	D3	D4
Sex					
Female	20	62.05 ± 10.61	57.85 ± 11.35	67.45 ± 12.6	71.0 ± 10.198
Male	26	58.96 ± 17.56	55.64 ± 15.78	67.0 ± 17.33	66.95 ± 17.29
p-value		0.493	0.6014	0.923	0.618
Self employed	17	63.76 ± 16.20	57.76 ± 12.99	66.18 ± 16.28	71.76 ± 15.12
Civil servant	8	54.71 ± 14.45	57.29 ± 11.16	63.29 ± 19.57	67.0 ± 10.80
Nil source of income	21	59.43 ± 13.69	55.48 ± 15.77	69.33 ± 13.22	69.14 ± 14.99
p-value		0.3767	0.8776	0.6342	0.7219
Monthly cost					
5000=		61.48 ± 15.67	58.13 ± 12.97	67.71 ± 15.66	71.87 ± 14.01
5000=	32	57.78 ± 12.86	53.29 ± 15.70	66.07 ± 14.87	65.21 ± 14.08
p-value	14	0.4453	0.2839	0.7429	0.1477
Olanzapine		58.84 ± 14.83	54.51 ± 14.44	65.10 ± 16.74	68.23 ± 15.48
Risperidone	31	63.64 ± 14.73	61.28 ± 11.70	71.86 ± 10.43	73.29 ± 10.61
p-value	15	0.4453	0.2839	0.7429	0.1477

There was no significant difference between the QoL values in all the domains for the Olanzapine and Risperidone. Most of these patients on pharmacotherapy had good QoL in the different domains and there was no significant difference between the different regimens used ($p > 0.05$). All the respondents reported to have good family support in relation to adhering to their medications.

Adherence to medication

The patients were assessed by the pharmacist for adherence to their medication using tablet count, 34(74%) patients were adherent to their medications. Some of them, 26(56%) did not miss any doses since the last refill. However, 6(12%) had not taken any of their medications for at least 7 days. Side effect to the prescribed drugs was a major reason for skipping doses which resulted to non adherence. Other reasons reported for non adherence werelack of moneyto attend clinic appointments or to refill their prescription and 'I don't think I need the dugs anymore'.

DISCUSSION

Health related quality of life studies in psychiatry is not so robust and majority of studies carried out are mainly focussed on patients diagnosed with schizophrenia, though there is now an upsurge in QoL studies relating to therapy, treatment cost and disabilities in BPD. QoL study is an important measure of mental health care for patients diagnosed with chronic psychiatric conditions such as bipolar affective disorder. The sample size recruited in this study is small but is a true representation of the total population of BPD patients currently being managed in FNPH Edo State. This is similar to the sample size of 49 BPD patients recruited in another study from FNPH Enugu State.[12] We obtained

more female respondents but they had a higher number of male BPD patients.In this study the average QoL was good with most patients scoring above average in all the domains, the highest QoL values were reported in relation to psychological function while the most affected aspect of QoL was the Environmental domain which include; financial resources, home environment, freedom, physical safety, accessibility to quality Health and social care. This finding is contrary to that reported by Arnold, et. al. (2000) where all the domains were compromised by BPA.[13] In a large study of QoL in BPA by Yatham*et. al*. (2004) using another validated questionnaire for QoL studies, patients reported physical function, vitality and social function as the most affected aspect of their QoL.[14] A study carried out in India with a sample size of 50 BPA patients reported a higher QoL when compared with another group of patients with schizophrenia.[15]The overall self reported high QoL is comparable with other QoL studiescarried on psychiatric outpatients.[9,16] However, the QoL value for respondents in this study was not associated with any of their demographic characteristics which is different from previous studies in other specialist hospitals in Nigeria which reported an association of QoL with the sex of the patients.[9,17] Also, we have observed that there was no significant difference in Qol of patients on different psychotropic drug therapy currently being used for treatment, this is similar to a previous study done in another FNPH in North East Nigeria.[9] Adherence to medication is very important in achieving desired clinical, economic and humanistic outcomes in psychiatry. For the patients in this study, most of the respondents were adherent to prescribed medication (74%) but the patients who defaulted in their use of medicines gave important excuses similar to findings reported by Garcia et.al. (2016) which require adequate patient focused intervention to resolve in order to improve their adherence status necessary to prevent a relapse in their mental condition.[18] This finding can be supported by the study carried out by Adelufosi and colleagues who identified medication nonadherence as an illness-related factor that significantly correlated with lower scores in all the domains of the WHOQOL-Bref.[19] The respondents in this study reported the psychological function as the best aspect of their health related quality of life, this domain 2 involves their bodily appearance, self image and reduction of clinical symptoms which can be attributed to the effective psychotropic medications and high adherence status of most of the respondents. However, this study has reported the lowest QoL scores in domain 4 which comprises of access to quality health care, social support and security. Poor social support has been identified as an important determinant of poor subjective Qol among psychiatric patients in Nigeria.[20] This shows that there is still a gap in the society in relation to stigmatization and inadequate support of the government and the private sector. Adequate social support has been identified as a positive indicator for good Qol in psychiatry in Nigeria.[21,22] The side effects to medication in this study were extra pyramidal side effects common with typical antipsychotics, significant weight gain common with atypical antipsychotics and sexual dysfunction, all these were reported to the Doctor and necessary interventions taken.The average monthly cost of treatment per patient wasabout one third of the Country's current minimum wage (N 18,000), which is not affordable by the respondents who were mainly unemployed therefore depend on care givers for support; this finding is similar to the study reported by Pan, et.al. (2016)[23]where the low income respondents were not able to afford their medication requiring support from family and friends. Only one typical antipsychotic medicine was on the essential drug list and National Health Insurance Scheme (NHIS) at the time of the study therefore patients/ care givers had to pay off their pockets every clinic day.

CONCLUSION

Patient reported QoL observed in this study was good and was independent of the psychotropic drug regimen prescribed. The medication used in this study site are few conventional ones, most of the patients were placed on atypical antipsychotics as a monotherapy or in combination with other psychotropic medicines. Adherence which is a desired outcome was high for most patients. Side effects of therapy reported which is an unwanted outcome were properly addressed by the hospital staff. The average monthly cost of treatment per patient is about one third of the Country's current minimum wage and about half of the respondents are unemployed therefore depend on care givers for support.

Improved government funding to FNPHs and social support for mentally ill patients is encouraged. These hospitals should explore more second generation antipsychotics which are better tolerated by patients.

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