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ORIGINAL ARTICLE

Factors leading to Non-Compliance to Antidepressants Among Patients with Major Depressive Disorder: A Cohort Study from Pakistan

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ABSTRACT

Objectives: To determine and explore the factors that contribute towards non-compliance to antidepressants among patients with major depressive disorder.

Methodology: A longitudinal multicenter study was conducted from April to October 2019 to October 2020 in several psychiatric clinics in Pakistan. All patients with diagnosed depression as per ICD 10 Criteria, who were above the age 18 years, gave consent to take part in the study were eligible for the study. Patients with a history of traumatic brain injury, aged < 18 years were excluded from the study. Compliance to treatment was measured through self-report and prescription refill data.

Results: A total of 820 patients were included in this study. A median age of 33.0 (18-67) was observed with the majority of female patients. Out of the total study population of 820 patients, 284 (34.6%) reported non-compliance to the treatment. The cause of non-compliance was significantly associated with therapeutic management. The majority of the patients who were on tricyclic antidepressants (TCAs) stopped taking medication because of lack of improvement in their symptoms. About 100 (55.90%) patients on SSRis reported lack of efficacy for non-compliance however, when antidepressants were combined with cognitive behavioral therapy the reported rate of lack of efficacy reduced to 32.9%

Conclusion: The current study shows that the foremost reason for non-compliance was lack of efficacy among patients.

Keywords: anxiety, antidepressants, cognitive behavioral therapy, efficacy, depression, tricyclic antidepressants

INTRODUCTION

Major Depressive Disorder (MDD) is a widespread, recurrent, and debilitating psychological disorder that poses significant therapeutic obstacles for patients. The challenges in adherence to treatment regimens are the chief element that leads to poor treatment outcomes, frequent relapse, long-term recurrences, and higher chances of comorbidities and mortality [1]. Despite the availability of effective therapies, symptoms of depression in MDD and mood disorders constitute a huge fraction of time being spent afflicted [2]. Analyses of persistent depression and its symptoms demonstrate that initiation of disease at an earlier age is linked with extended symptom duration, especially in adolescents and young populations [3].

In pharmacological terms, treatment adherence has two main components: persistence and compliance. Completing the entire treatment regimen for the advised duration is defined as persistence while compliance refers to the level of conformity to medical directions [4]. Literature shows strong evidence regarding poor treatment adherence to prescribed doses of antidepressants in almost half of the patients receiving care from primary or psychiatric health care services [5]. Antidepressant nonadherence is a multifaceted process including both patient- (e.g., fears around adverse reactions, healthcare costs, fear of dependence, and sociocultural and behavioral challenges) and clinician-related elements (e.g., lack of appropriate patient and family counselling , and inadequate follow up mechanism) [5,6,7].

Patients' noncompliance with antidepressant drugs may also reflect providers' quality of healthcare services, thus interventions to improve treatment adherence should address concerns in prescribers' attitudes and training [6,8,9]

Nevertheless, provider-related issues such as compromised patient counseling, a lack of collective decision making, under-dosing of therapeutic agents, and a lack of follow-up plan are all aspects that health professionals must regulate to ensure better adherence, as they are some of the most significant barriers to efficient and accurate antidepressant treatment [10].

In Pakistan, the reported antidepressant compliance rates are outdated and unsatisfactory therefore, it is necessary to conduct comprehensive research on the factors associated with non-compliance to antidepressants among patients in our population to devise strategies to promote adherence. The primary objective of the study was to report the rate of non-compliance to antidepressants among patients who present to the psychiatry department,

Jinnah Postgraduate Medical Centre. The secondary objective is to determine and explore the factors (both patient- and physician-related) that contribute towards non-compliance to antidepressants among patients with major depressive disorder in our set up.

METHODS AND MATERIALS

A longitudinal study was conducted in several psychiatric clinics in Pakistan including the Department of Psychiatry and Behavioral Science, Jinnah Postgraduate Medical Centre between October 2019 to October 2020. A non-probability convenience sampling technique was employed to enroll participants in the study. Ethical approval was obtained from the ethics committee of Jinnah Postgraduate Medical Centre.

The estimated sample size calculated for the given prevalence at 95 percent confidence interval is 236. The frequency of depressed diagnosed individuals in Karachi was taken as 8.6% with a population of 10 million, the level of significance equal to 0.05, and the bound of error 5 percent (variance from the actual value). **All** Patients with diagnosed depression as per ICD 10 Criteria who were above the age of 18 and were newly diagnosed with depression were included in the study. All participants were requested to give full informed verbal and written consent before study was initiated. **All individuals with** a history of traumatic brain injury were below the age of 18, and those who did not give consent to take part in the study were excluded from the study.

All patients diagnosed with major depressive disorder according to the ICD 10 criteria were enrolled in the study. All patients were issued a prescription for antidepressants. The patients then were asked to visit on a regular basis. Compliance to treatment was measured through self-report and prescription refill data. Patients were asked to keep a note of all the side effects they experience and the dropout rate was also noted.

All the data were analyzed using Statistical Package for Social Sciences (SPSS) version 26. Results were presented via tables and graphs. Descriptive statistics were used to calculate mean and standard deviation (SD) for age of patients, depression severity scores, duration of illness, etc. Frequency (%) were calculated for severity of depression, gender, education, marital status, and job status, and comorbidities, etc. Association between different sociodemographic variables and adherence to medication were explored using chi square tests and an independent t test. A p-value of < 0.05 was considered as statistically significant.

RESULTS

A median age of 33.0 (18-67) was observed with the majority of female patients. Out of the total study population of 820 patients, 284 (34.6%) reported non-compliance to the treatment. The most common reason for non-compliance was the lack of efficacy i.e. 145 (51.05%) (Figure 1).

The cause of non-compliance was significantly associated with therapeutic management. The majority of the patients who were on tricyclic antidepressants (TCAs) stopped taking medication because of lack of improvement in their symptoms. About 100 (55.90%) patients on SSRis reported lack of efficacy for non-compliance however, when antidepressants were combined with cognitive behavioral therapy the reported rate of lack of efficacy reduced to 32.9% (Table 1).

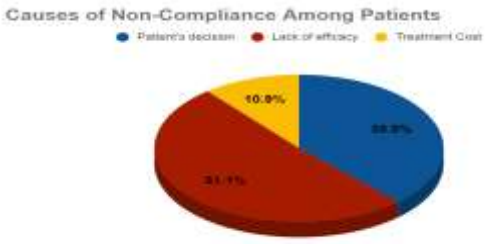

Figure 1: Causes of Non-Compliance Among Patients (n=284)

Table 1: Association Between Factors Causing Non-compliance and the Treatment Regime

Treatment	Patient's decision	Lack of efficacy	Treatment Cost	p-value
Antidepressants + Cognitive behavioral therapy	35 (46.10%)	25 (32.90%)	16 (21.10%)	0.001
Serotonin–norepinephrine reuptake inhibitor (SNRI)	0 (0.00%)	7 (100.00%)	0 (0.00%)	
Selective serotonin reuptake inhibitor (SSRi)	65 (36.30%)	100 (55.90%)	14 (7.80%)	
Tricyclic antidepressants (TCAs)	8 (36.40%)	13 (59.10%)	1 (4.50%)	

There was no significant difference in factors contributing towards non-compliance and geographical region of the patient (Table 2).

Table 2: Association Between Factors Causing Non-compliance and the Geographical Region

Geographical Region	Patient's decision	Lack of efficacy	Treatment Cost	p-value
Punjab	76 (41.10%)	88 (47.60%)	21 (11.40%)	0.294
Sindh	11 (39.30%)	14 (50.00%)	3 (10.70%)	
Balochistan	7 (19.40%)	25 (69.40%)	4 (11.10%)	
KPK	7 (30.40%)	14 (60.90%)	2 (8.70%)	
Azad Kashmir	7 (58.30%)	4 (33.30%)	1 (8.30%)	

DISCUSSION

The aim of our study was to identify the causes of non-compliance of patients to antidepressants in patients diagnosed with depression. When antidepressants and cognitive behavioural therapy were given together in our study, the most common cause of lack of compliance to this treatment was the patient's decision (46.10%), due to lack of efficacy (32.90%) and cost of treatment (21.10%). Lack of efficacy was seen to be highest in the groups of SNRIS (100%), SSRIS (55.90%) and TCAs (59.10%).

Similarly for patients who were on SSRIS, lack of efficacy was seen as the most common cause (55.90%) followed by the patient's decision (36.60%) and treatment cost (7.80%). The geographical region and cause of lack of compliance did not correlate with each other significantly in our study (p value < 0.294). Majority of patients in the provinces of Punjab (41.10%), Sindh (39.30%), Balochistan (19.10%) and KPK (30.40%) stopped taking their medicines on their own decisions, Azad Kashmir having the highest number (58.30%). Different medications worked differently on different ethnic groups. In patients who were not compliant with their medicines because of lack of efficacy of treatment, patients in Balochistan had the highest number of patients (69.90%), followed by KPK (60.90%), Sindh (50%), Punjab (47.60%) and Azad Kashmir (33.30%). Very minor number of patients left their medicines due to treatment cost, Punjab having the highest number (11.40%).

Semahegn et al. found an alarming 49% of psychiatric patients to be non-compliant to their prescribed medications [11]. The authors found the non-compliance to psychiatric medications to be influenced by a number of factors such as individual behaviour of patients, family support and the type of treatment being given. Khan et al. in their study found 57.3% of patients with migraines to discontinue the prescribed medication and persistence was higher in females ((58.8%) [12]. Similarly, Marasine et al. discussed factors leading to non-adherence to antidepressants such as misled conceptions about the disease, forgetfulness, adverse effects, treatment cost, cultural and religious beliefs, stigma, comorbidities and interactions between patients and physicians [13]. An older study by Jin et al. observed that non-compliance to medications leads to a burden in the healthcare system [14]. The authors suggested solutions that might be beneficial to increase patient compliance such as prescribing oral medication (non-invasive), shortening the duration of treatment for maximum efficacy and simplifying dosage regimens. Khan et al. in their study found patients who had other comorbidities such as Diabetes Mellitus, Hypothyroidism and Hypertension had higher adherence to psychiatric medications in comparison to those who had no comorbidities [15]. Similar results were found in studies conducted by Almas et al. and Naeem et al. [16], [17]. Furthermore, Kvarnström et al. discussed that patients were eager to discuss their reservations concerning psychiatric medications and more effective ways of communication should be established between patients and doctors to improve adherence to treatment [18].

We did not explore the adverse effects that the treatment might have on the patients. Also, we should have focused on patients who would have had complaints such as weight gain, agitation or insomnia which are some of the side effects that these medicines might have caused.

CONCLUSION

The current study shows that the foremost reason for non-compliance was lack of efficacy among patients. Future studies should explore factors of genetics and ethnicities leading to non-compliance of medications. More efforts are needed to strengthen doctor to patient interactions and clarify myths and misconceptions that are held by patients to increase adherence to medications.

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