

Tropical Journal of Pharmaceutical Research February 2018; 17 (2): 339-344

ISSN: 1596-5996 (print); 1596-9827 (electronic)

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Available online at <http://www.tjpr.org><http://dx.doi.org/10.4314/tjpr.v17i2.20>

Original Research Article

Antipsychotic prescription patterns and treatment costs of schizophrenia in northwestern Pakistan: A one-year observational study

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Sent for review: 16 September 2017

Revised accepted: 18 January 2018

Abstract

Purpose: To evaluate the antipsychotic drugs most commonly prescribed for schizophrenia patients in Peshawar, Pakistan and to analyze the treatment costs associated with these drugs.

Methods: One hundred patients diagnosed with schizophrenia were recruited from outpatient psychiatry departments in Peshawar, Pakistan and followed for one year. Demographic data were collected for each patient at the beginning of the study. A questionnaire was used to collect antipsychotic prescription information at 4, 8 and 12 months. The cost of antipsychotics was obtained from PharmaGuide, Pakistan. The cost associated with antipsychotic drug use was statistically analyzed using post hoc tests.

Results: Of the patients who completed this study, 68.1 % were prescribed second-generation antipsychotic (SGA) drugs, 6.9 % first-generation antipsychotic (FGA) drugs, and 25.0 % a combination of SGAs and FGAs. Furthermore, 40.3 % of the patients who completed the study received antipsychotic monotherapy and 34.7 % antipsychotic polytherapy. In monotherapy, risperidone was the most commonly prescribed antipsychotic drug, used by 44.8 % of patients while in polytherapy, risperidone plus olanzapine was the most commonly prescribed combination, used by 32 % of patients. Switching of antipsychotic drugs was observed in 25 % of patients. The mean annual cost of antipsychotic therapy was US\$79.90 (8079 Pakistani rupees). Risperidone treatment cost was US\$60.30 (PakRs 6095), constituting 52 % of the total monotherapy cost. The cost of SGAs was significantly higher than the cost of FGAs ($p < 0.05$).

Conclusion: The results provide policymakers with appropriate information necessary for managing pharmacotherapy plans for the treatment of schizophrenia.

Keywords: Schizophrenia, Prescribing pattern, Antipsychotics, Cost analysis, Pharmacotherapy

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INTRODUCTION

Schizophrenia is a severe mental disorder that affects the patient's perceptions, language,

behavior, and thinking [1]. A prolonged course of therapy is required to treat this disease, which can impose a significant financial burden on the patient and their family [2,3]. This is especially

true in low and middle income countries that lack treatment facilities such as nursing homes and community rehabilitation centers [4,5].

Antipsychotic drugs account for much of the cost of schizophrenia treatment. The older, first-generation antipsychotic (FGA) drugs are efficacious in treating the positive symptoms of schizophrenia and are relatively inexpensive. However, these drugs can cause serious side effects, such as extrapyramidal symptoms and tardive dyskinesia, which can lead to irreversible damage and non-compliance by the patient [1,6]. The newer, second-generation antipsychotic (SGA) drugs cause fewer side effects, are helpful in reducing the negative symptoms of schizophrenia, and are well tolerated by patients [7] but are costly compared to FGAs [8]. Schizophrenia may be treated with a single drug or a drug combination [9,10]. FGAs and SGAs are commonly co-prescribed [10], and this combination therapy has been shown to be effective in the treatment of acute psychotic symptoms.

Antipsychotic drugs may be administered orally or via long-acting antipsychotic injection (LAI). LAIs have been shown to help prevent relapse and reduce hospitalizations [9,11] and are particularly useful in the 50–60% of schizophrenic patients who are noncompliant [12,13]. Combined oral administration of SGAs and LAI administration of FGAs has been shown to be particularly effective [13,14].

Variations in the prescribing pattern of antipsychotics exists among different countries due to factors including drug availability, efficacy, adverse effects, cost, and local prescription guidelines [15]. To date, no detailed study regarding antipsychotic use and its associated cost has been conducted in Pakistan. Therefore, this study will provide new insight into the antipsychotic prescribing practices in Pakistan and the costs associated with the use of antipsychotic drugs.

METHODS

This descriptive study was conducted in three major hospitals in the city of Peshawar, Khyber Pakhtun Khwa, Pakistan: the Sarhad Hospital for Psychiatric Diseases, Khyber Teaching Hospital, and Lady Reading Hospital. The study was approved by the ethical committee of Khyber Medical College, Peshawar (ref no. 19/RD/Cell/KMC) and was conducted in accordance with the 1964 Helsinki declaration. Informed consent to participate in the study was

obtained from all patients, and patient data were coded for confidentiality [16].

Using a convenience sampling method, 100 patients were recruited into this study between July 2014 and June 2015. This sample size, calculated using the World Health Organization sample size calculator, takes into account the high dropout rate expected to occur over the 1-year course of the study [17]. All patients included in the study were between 18 and 80 years old, had a diagnosis of schizophrenia (ICD-10 in the World Health Organization International Statistical Classification of Diseases and Related Health Problems classification system), and had at least one attendant. Patients with a co-morbid illness or with demographic data that were not credible were excluded from the study sample. As electronic patient medical records were not available in all of the selected hospitals, a questionnaire was developed to collect sociodemographic information and to record prescriptions of antipsychotics and other drugs. Patients and attendants were required to keep complete medical records during the 1-year course of the study and to complete the questionnaire at 4, 8 and 12 months, for a total of three assessments. Drug prices were obtained from Pharma-Guide Pakistan.

Data analysis

Patients were placed in three groups depending on the antipsychotic treatment regimen they received. Patients in Group I received antipsychotic monotherapy for the entire year. Patients in Group II received antipsychotic polytherapy. Patients in Group III switched from one treatment regimen to another during the course of the year.

The type of antipsychotic drug or drug combination prescribed for each patient was assessed. Within each group, the number of patients receiving a particular type of antipsychotic treatment was measured, and the percentage of patients receiving that treatment was calculated based on the total number of patients in that group. The annual antipsychotic cost was calculated as the mean cost per day multiplied by the number of days the antipsychotic was used. Statistical Package for Social Sciences (SPSS version 20, Chicago IL-USA) software was used calculates the mean annual antipsychotic prescription drug cost for all patients receiving a particular type of therapy using one-way ANOVA (post hoc analysis). For this study, a p -value of ≤ 0.05 was considered statistically significant.

RESULTS

Demographic and clinical variables

Twenty-eight patients failed to return for follow-up appointments and were excluded from the study, leaving 72 patients in the final study population. Demographic and clinical variables for patients in the final study population are shown in Table 1. In the final population, 67.7 % of patients were male. The majority of patients (63.9 %) were young adults between 18 and 38 years of age. More than half of the patients (54.2 %) were married, and most (62.5 %) were educated. At the time of enrollment in the study, the mean duration of illness was 2.8 years, and the mean positive and negative syndrome scale score was 77.6.

Table 1: Demographic and clinical variables (N = 72)

Variable	N (%)
Sex	
Female	24 (33.3)
Male	48 (67.7)
Age, years	
18-38	46 (63.9)
39-59	24 (33.3)
60-80	2 (2.8)
Mean \pm SD	33.6 \pm 11
Marital status	
Unmarried	33 (45.8)
Married	39 (54.2)
Education	
Uneducated	27 (37.5)
Educated	45 (62.5)
Duration of illness, years (mean \pm SD)	2.8 \pm 1.3
Monotherapy	29 (40.3)
Polytherapy	25 (34.7)
Switching of Antipsychotics	18 (25)
Antipsychotic Type	
SGA	49 (68.1)
FGA	5 (6.9)
SGA + FGA	18 (25.0)

A slight majority of patients (40.3 %) received monotherapy. The remaining patients (34.7 %) received polytherapy. SGAs alone were prescribed to 68.1 % of patients, FGAs alone were prescribed to 6.9 % of patients, and a combination of SGAs and FGA was prescribed to 25 % of patients.

Drug prescription patterns and associated costs

The mean number of antipsychotics prescribed per patient was 1.4. Among the three study centers participating in this study, Khyber Teaching Hospital prescribed the lowest number

of antipsychotics per patient (1.07). Lady Reading Hospital prescribed an average of 1.3 antipsychotics per patient, and Sarhad Hospital for Psychiatric Diseases prescribed 1.8 antipsychotics per patient.

Table 2 shows the drug prescription pattern and average annual drug cost for patients receiving antipsychotic monotherapy (Group I). This group represents 40.3 % of the population. In this group, risperidone was the most commonly prescribed antipsychotic, used by 44.8 % of patients. The remaining patients were prescribed olanzapine (34.5 %), aripiprazole (10.3 %), haloperidol (6.9 %), and prochlorperazine (3.4 %). The mean cost of antipsychotic monotherapy was \$ 52 USD (Rs. 5255). Risperidone treatment was the most expensive, costing \$ 60.30 USD (Rs. 6095) and constituting 52 % of the total monotherapy cost. Olanzapine treatment was the second most expensive, costing \$ 59.70 USD (Rs. 6039).

Table 2: Type of antipsychotic used and annual drug cost for patients in Group I^a

Antipsychotic	n (%) ^b	Average annual cost ^c (US\$, mean \pm SD)	Annual cost (%)
Single antipsychotic			
Risperidone	13 (44.8)	60.3 \pm 32	52.0
Olanzapine	10 (34.5)	59.7 \pm 34	39.6
Aripiprazole	3 (10.3)	29.2 \pm 7.1	5.8
Haloperidol	2 (6.9)	15 \pm 3.3	2.0
Prochlorperazine	1 (3.4)	8.4	0.6
Sub-total	29 (100)	52.0 (33)	100

^aIncludes patients prescribed a single antipsychotic; ^bPercent of the 29 patients in Group I who were prescribed a particular drug; ^cCost in USD (\$1 USD = 101 Pak Rs.)

Table 3 shows the drug prescription pattern and average annual drug cost for patients receiving antipsychotic polytherapy (Group II). This group represents 48.5 % of the final population. In this group, oral risperidone and oral olanzapine was the mostly prescribed drug combination (32 %), followed by oral risperidone and LAI fluphenazine (24 %). The mean cost of antipsychotic polytherapy was \$103.20 USD (Rs. 10427). The most expensive polytherapy treatment, a combination of oral risperidone and oral olanzapine, cost \$ 126.70 USD (Rs. 12797), or 39 % of the mean polytherapy cost.

Table 3: Types of antipsychotic used and annual drug cost for patients in Group II^a

Antipsychotic	Combination	n (%) ^b	Average annual cost ^c (US\$, mean ± SD)	Annual cost (%)
Two antipsychotics				
Risperidone + ^d	Olanzapine	8 (32)	126.7 ± 54.6	39.3
	LAI Fluphenazine	6 (24)	84 ± 28	19.5
	Quetiapine	1 (4)	141.3	5.5
	Aripiprazole	1 (4)	135	5.2
Olanzapine + ^d	LAI Fluphenazine	3 (12)	107 ± 46.6	12.5
	Aripiprazole	4 (16)	91.2 ± 12.3	14.1
	Prochlorperazine	1 (4)	62.3	2.4
Haloperidol + ^d	LAI Fluphenazine	1 (4)	35.8	1.4
Subtotal		25(100)	103.2 ± 43.9	100

^a Includes patients prescribed a combination of antipsychotics; ^b Percent of the 25 patients in Group II prescribed a particular drug; ^c Cost in USD; ^d + indicate a combination of antidepressant drugs.

Table 4 shows the drug prescription pattern and average annual drug cost for patients who switched antipsychotic medications during the course of the study (Group III). Of the patients in this group, 22.2 % switched from a combination of oral risperidone and LAI fluphenazine to oral risperidone alone, and 22.2 % switched from a combination of oral olanzapine and LAI fluphenazine to a combination of oral olanzapine and oral haloperidol. Switching of other drug combinations occurred less frequently. The mean cost of antipsychotic therapy in patients who switched drugs was \$ 92.70 USD (Rs. 9366). The highest cost was incurred by patients initially treated with an oral risperidone and LAI fluphenazine combination who then switched to oral risperidone monotherapy. Treatment for these patients cost an average of \$ 77.50 USD

(Rs. 7836), about 18.6 % of the antipsychotic cost for this group.

Antipsychotic treatment patterns and cost analysis

For the entire sample population, the mean annual cost of antipsychotics prescribed was US\$79.90 (Pakistani rupees (Rs.) 8079). For SGAs used alone, the mean annual cost was US\$ 80.29 (Rs. 8110). For FGAs used alone, the annual cost was \$ 25.20 USD (Rs. 2554). For a combination of SGAs and FGAs, the mean annual cost was US\$94.30 (Rs. 9528).

Post hoc LSD analysis using one-way ANOVA was used to assess whether various treatment regimens differed significantly in cost.

Table 4: Type of antipsychotic used and annual drug cost for patients in Group III^a

Antipsychotic	Switch to	n (%) ^b	Average cost ^c (mean ± SD)	Annual cost (%)
Risperidone + ^d LAI Fluphenazine	Risperidone	4 (22.2)	77.5 (13.8)	18.6
Olanzapine + LAI Fluphenazine	Olanzapine + Haloperidol	4 (22.2)	65 (18.7)	15.6
Risperidone	Risperidone + LAI Fluphenazine	1 (5.6)	64.3	3.9
Risperidone + Olanzapine + LAI Fluphenazine	Risperidone + Olanzapine	1(5.6)	148.8	8.9
Risperidone + Olanzapine	Olanzapine + LAI Fluphenazine	1 (5.6)	241	14.4
Olanzapine	Olanzapine + LAI Fluphenazine	1 (5.6)	106.6	6.4
Olanzapine + Haloperidol	Olanzapine	1 (5.6)	78	4.7
Risperidone	Olanzapine	1 (5.6)	172.2	10.3
Aripiprazole	Risperidone	1 (5.6)	63	3.8
Olanzapine	Risperidone	2 (11.1)	86 (30.7)	10.3
Olanzapine + Haloperidol	Haloperidol	1 (5.6)	52	3.1
Sub Total		18 (100)	92.7 (49.6)	100

^a Includes patients switched from one antipsychotic treatment to another during the study period; ^b Percent of patients in Group III prescribed a particular drug out of a total of 18 patients; ^c Cost in USD; ^d + indicate a combination of antipsychotic drugs

All treatment regimens used by only one patient were excluded from this analysis. There was no statistically significant difference in the mean cost of the various antipsychotics used for monotherapy [$F(3, 24) = 1.9, p > 0.05$] or in the cost of various antipsychotics used for polytherapy [$F(3, 17) = 1.3, p > 0.05$]. There was also no statistically significant difference in the mean cost of various antipsychotic drug treatments that were switched in the course of the study [$F(2, 7) = 0.8, p > 0.05$]. However, a significant difference in treatment cost was observed for patients in group I compared with group II ($p < 0.05$) and for patients in group I compared with group III ($p < 0.05$). No statistically significant difference in treatment cost was observed for patients in group II compared with group III [$F(2, 69) = 11.47, p < 0.05$].

DISCUSSION

Antipsychotic monotherapy is recommended by most antipsychotic treatment guidelines [9,10]. In the present study, the percentage of patients receiving monotherapy was low compared with that in other countries [7,10,11]. The high incidence of polytherapy observed here may be due to the severity of symptoms; the patients from Sarhad Hospital for Psychiatrist Diseases who participated in this study were particularly unstable and may therefore have required more aggressive polytherapy treatment. Differences in study design may also account for the discrepancy in the number of patients receiving polytherapy. Tapp *et al*, for example, did not include drugs administered by LAI in the estimate of polytherapy treatment rates [10,18]. According to National Institute for Clinical Excellence, SGAs should be used as first-line antipsychotics in the treatment of schizophrenia. Clozapine, olanzapine, and risperidone are the most efficacious and well tolerated SGAs in most schizophrenic patients. In our study, the majority of patients were prescribed SGAs. These results are consistent with the results from similar studies conducted in Australia, Bahrain, Germany, and the United States, where most schizophrenic patients were treated with SGAs [7,10,11,19,20].

Our study indicates that the use of antipsychotic polytherapy is similar between Pakistan and Finland. Polytherapy is often used in the treatment of refractory schizophrenia. Polytherapy with FGAs and SGAs may be particularly effective because FGAs tend to act rapidly and may be able to quickly control psychotic symptoms until slower-acting SGAs become effective [10]. Polytherapy in which an

SGA is administered orally and an FGA is administered by LAI is often recommended for patients who resist treatment [21]. However, the literature suggests that patient non-compliance is mainly due to the belief that side effects associated with LAI are worse than side effects associated with oral therapy [13].

Polytherapy is also sometimes used early in treatment to manage the positive symptoms, and after these conditions are under control the patient is switched to SGA monotherapy. However a study conducted by Tapp *et al* [10] indicates that most psychiatrists found the FGA and SGA combination most effective and were therefore reluctant to switch from polytherapy to monotherapy. In this study, the rate of switching from one antipsychotic combination to another was 25 %. However, it is possible that some additional patients switched medications before the study began. The cost of SGAs in Pakistan is relatively low because most of the drugs are manufactured locally, although SGAs are still more expensive than FGAs [2,4,5]. Although SGA polytherapy, which typically combines an SGA and an FGA, can be considerably more expensive than monotherapy, the high cost of SGAs may be warranted, as it has been reported by Mauskopf and colleagues that treatment with SGAs reduces hospitalization and minimizes side effects, hence reducing overall medical cost and improving quality of life [22].

Limitations of the Study

The study enrolled only a small number of patients. However, in a developing country, conducting a 1-year follow-up study is challenging.

CONCLUSION

The present study assessed the economic cost of antipsychotics used in the treatment of schizophrenia in Pakistan. SGAs, which are the most frequently prescribed antipsychotic drugs, are costly compared to FGAs. The results of the present study can be used to assess the pharmacoeconomics of antipsychotic prescription practices and to afford policymakers with information necessary for developing successful pharmacotherapeutic plans for the treatment of schizophrenia.

DECLARATIONS

Acknowledgement

The authors are grateful to Dr. Abbas Ullah Jan, Professor of Economics, University of

Agriculture, Peshawar, Pakistan for his input into the statistical and cost analysis.

Conflict of interest

No conflict of interest is associated with this work.

Contribution of authors

The authors declare that this work was done by the author(s) named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors.

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