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Cost-effectiveness analysis of olanzapine and risperidone in schizophrenic patients in the Indian healthcare settings of Andhra Pradesh, India

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Abstract

Objectives The prevalence of schizophrenia in Andhra Pradesh, India is 279, and the crude disability-adjusted life year is 177 per 100 thousand people. It is one of the major mental health problems of the state. However, there is a dearth of information regarding the pharmacoeconomics of schizophrenia treatment. The purpose of this study was to evaluate the cost and effectiveness of the two most commonly used drugs olanzapine and risperidone for schizophrenia.

Methods A prospective observational study was carried out in a tertiary care teaching hospital (Department of psychiatry) for a period of 1 year among 124 schizophrenia patients. The data were collected in a specially designed patient data form, and the cost and effectiveness of the treatment were evaluated. Then, the ICER for olanzapine 71 and risperidone 53 users were calculated. Sensitivity analysis was run creating a model to identify uncertainties and its effect on the results.

Key findings The mean cost per patient for olanzapine was 89.96 USD, and risperidone was 85.56 USD for 8 weeks from the start of the treatment. The incremental effects and value of the treatment score with the Positive and Negative Syndrome Scale (PANSS) for olanzapine (27.33) were greater than that of risperidone (20.38). The cost (USD) per PANSS reduction for olanzapine was 3.29 and risperidone was 4.20. The overall incremental cost-effectiveness ratio (ICER) of olanzapine compared to risperidone was 0.63 USD/PANSS.

Conclusion The results showed that olanzapine was a cost-effective drug and an alternative to risperidone in the Indian healthcare settings. With further revision and validation, the cost-effectiveness outcome of olanzapine and risperidone can be used to inform any comprehensive healthcare financing mechanism in Indian healthcare settings.

Keywords Andhra Pradesh; cost-effectiveness analysis; olanzapine; pharmacoeconomics; risperidone; schizophrenia

Introduction

Schizophrenia is a mental disorder characterized by disruptions in thought processes, perceptions, emotional responsiveness and social interactions.[1] Schizophrenia causes huge economic burden to the individual patient, families and communities as a whole and affects the overall societal productivity.[2,3] The global prevalence of schizophrenia approaches one per cent, and the incidence is about 1.5 per 10 000 people.[4] In India, as per the Rangaswamy Thara et al. study, among the population of 100 000, the age-corrected prevalence rate of schizophrenia was 3.87/1000.[5] Other studies in India have reported prevalence of 0.7/1000 to 14.2/1000. There exists some variability in prevalence of schizophrenia in India as the studies are carried out in different geographical locations using different diagnostic criterion. A study by ICMR, SOFPUC, reported high prevalence of the illness among people who were living along, living in urban slums and unemployed.[6] The study also reported higher illness among male when compared to female.[7]

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Schizophrenia has a multifactorial aetiology. Multiple susceptible gene interacts with environmental insults, giving rise to a range of schizophrenia spectrum. The abnormalities in the neurotransmission are the basic element in the pathophysiology of schizophrenia. Excess or deficiency of neurotransmitters such as dopamine, serotonin and glutamate as well as aspartate, glycine and gamma-aminobutyric acid (GABA) forms the basic theories for schizophrenia.[8] Two classes of medication are available for the treatment of schizophrenia. Typical antipsychotics such as chlorpromazine, haloperidol and fluphenazine and/or atypical antipsychotics such as quetiapine, risperidone and olanzapine and their newer generation such as clozapine, olanzapine, risperidone, ziprasidone and risperidone are used for the treatment of schizophrenia.[9] The effectiveness, safety profile and treatment outcomes of antipsychotics vary between and within the different drug classes. As per the American Psychiatric Association, second-generation (atypical) antipsychotics (SGAs) (exception for clozapine) are considered the agents of choice for first-line treatment of schizophrenia.[9,10]

Second-generation antipsychotics (SGAs) because of their lesser extrapyramidal symptoms are preferred over their predecessor first-generation antipsychotics (FGAs).[11] However, these SGAs too have side effects such as hyperlipidemia, weight gain and diabetes mellitus that can contribute to the increased risk of cardiovascular mortality in schizophrenic patients.[12] The focus of schizophrenia treatment includes targeting the symptoms, preventing relapse and improving the adaptive functioning of the patient so that they can live with their families and community.[11] Treatment of schizophrenia incurs huge cost to the family as well as society as the cost includes treatment cost, cost of looking after the person, resources for looking after the patient and providing them with a suitable environment in family and society. Therefore, the intervention both (pharmacological and non-pharmacological) has to be both effective and cost-effective.[13]

Main outcome of any pharmacoeconomic evaluation is the incremental cost-effectiveness ratio (ICER). ICER is obtained by first calculating incremental cost and incremental change in outcome and dividing incremental cost by incremental health outcome. ICER provides information for the health economic evaluation of medicines. Medicines with greater ICERs are selected to maximize health until the resources are exhausted.[15,16,17] Several studies have been carried out comparing cost-effectiveness of different atypical antipsychotics using different pharmacoeconomic models and methodologies.[15,16,17]

A meta-analysis of randomized controlled trials to compare the effects of first-generation vs second-generation antipsychotics in patients with schizophrenia by Stefan Leucht et al. showed that only four of the second-generation antipsychotic medicines (amisulpride, clozapine, olanzapine and risperidone) were better than first-generation antipsychotic in terms of overall efficacy.[14] The study also showed other second-generation antipsychotic medicines to be more efficacious than their predecessor, even for negative symptoms.[14] A study by De Hert M et al. to estimate the cost-effectiveness of two atypical antipsychotics, that is olanzapine and risperidone, and one typical antipsychotic haloperidol for schizophrenia showed olanzapine and risperidone to be more cost-effective than haloperidol. The study also showed risperidone to be more cost-effective among the two atypical antipsychotics.[15] Likewise, another cost-effectiveness analysis study by André Soares Santos et al. in Brazil on second-generation antipsychotics reported olanzapine to be more cost-effective than risperidone, quetiapine and ziprasidone in Brazil.[16] Furthermore, another study by J John et at. on olanzapine and risperidone showed olanzapine to be more cost-effective than risperidone. It reported a high Brief Psychiatric Rating Scale (BPRS) and effective schizophrenia reduction for olanzapine despite low cost.[17] This study uses Positive and Negative Syndrome Scale (PANSS) score for the estimation of outcome of treatment in the patient as it is one of the most popular rating scale for schizophrenia and has been reported to have been widely used in clinical pharmaceutical trials.[18] In the Indian context, as per the Indian Psychiatric Association, factors other than effectiveness that need to be considered for the treatment of schizophrenia are past treatment, cost of treatment, affordability, psychiatric comorbidity, side effects, patient and family preference, nonadherence, etc.[19]

According to a WHO survey, five of the ten leading causes of disability were in the category of mental illnesses: major depression, alcohol dependence, schizophrenia, bipolar affective disorder and obsessive–compulsive disorder.[20]

As per the India State-Level Disease Burden Initiative Mental Disorders Collaborators study, 3.5 million people had schizophrenia in India in 2017.[21] The contribution of mental disorder to DALYs was 4.7 (2017) while the contribution of schizophrenia to mental disorder DALYs was 9.8%.[21] Andhra Pradesh is a state of India, located in the southeastern part with a population of about 50 million.[22] The prevalence of schizophrenia per 100 000 populations in Andhra Pradesh India is 279, and the crude DALY (disability-adjusted life year) rate per 100 000 populations is 177 (132-219). Schizophrenia is one of the pressing mental health problems and causes significant financial burden to the people in Andhra Pradesh, India.[21] However, there is dearth of information regarding the pharmacoeconomic aspects of schizophrenia treatment in Andhra Pradesh. Moreover, the huge interstate variability in India in terms of socioeconomic status, sociocultural background, economic development, poverty and access to resources shows the need to carry cost-effectiveness studies on schizophrenia at local/ regional level. Risperidone and olanzapine are among the most commonly used antipsychotics in India. However, studies on efficacy, effectiveness, tolerability and side effects are lacking in India. Therefore, this study aims to evaluate the cost and effectiveness of two most commonly used drugs, that is olanzapine and risperidone, for schizophrenia in a tertiary care teaching hospital of Nellore, Andhra Pradesh, India.

Methods

Study design and setting

It is a prospective observational study. Data were collected on a patient data collection form, and cost-effectiveness

analysis of olanzapine and risperidone was carried out by comparing the relative costs and outcomes, following a health decision strategic model. The study was conducted at Narayana Medical College and Hospital in Nellore, Andhra Pradesh, India. It is a privately managed teaching hospital that provides affordable health care to the people of Nellore district and also many people from various areas of Andhra Pradesh. It is a major healthcare provider in this region.

Population and sample

The study population included 124 schizophrenic patients that were receiving treatment for schizophrenia at Narayana Medical College and Hospital, Nellore district, Andhra Pradesh, India. These patient were treated for a period of 1 year in the Department of Psychiatry.

Data collection

Data were collected using standard form that included demographic data such as age, sex, education status, employment, marital status, residence, family and income. Treatment chart (medical files) was reviewed. The PANSS scores before the treatment and after the treatment were calculated. For those cases, where information was not available on the patient treatment, chart information was obtained from the patients or their caregiver. Patients were briefed about the study, following a verbal consent was obtained from the patient or caregiver and the required information was obtained from them by interviewing them.

Costs

Costs calculated in this study include the direct cost for medication cost and laboratory charges and the indirect cost for loss of productivity and other costs (maintenance cost). All costs were calculated in Indian Rupee (INR) and converted to the United States Dollar (USD). The Positive and Negative Syndrome Scale (PANSS) were noted before the treatment and after eight weeks of course of the treatment. The incremental cost-effectiveness ratio (ICER) values of drugs were also calculated and analysed graphically using Online CEA Software.

Outcomes

This study compared two antipsychotic medicines olanzapine and risperidone. These were the commonly used second-generation antipsychotics for the treatment of schizophrenia in Andhra Pradesh, India. The optimal dose for the treatment of schizophrenia patients was 4.5 mg/day of risperidone and 12.7 mg/day of olanzapine in India.[23] The average scores noted before the treatment and after 8 weeks of course for olanzapine were 92.33 $\pm$ 8.99 and 65.114 $\pm$ 8.48 and for risperidone were 91.442 $\pm$ 10.211 and 70.884 $\pm$ 7.26, respectively.

Data analysis

The collected data were arranged in the Excel sheet and also used GraphPad Prism for data analysis. The data were tested for incremental costs and incremental effects for both drugs. Health Decision Strategies Software, LLC under formulary choices, was used for calculation of incremental cost-effectiveness ratio (ICER).

Ethical considerations

Ethical approval for the study was obtained from the Institutional Ethical Committee of the Narayana Pharmacy College and Narayana Medical College & Hospital, Nellore, Andhra Pradesh, India, prior to the commencement of the study, on July 2018. Information was obtained from the patient or caregiver following written consent. For the patient who did not have formal education, verbal consent was obtained.

Sensitivity analysis

Sensitivity analysis was conducted for two different scenarios (as depicted in Table 1).

Scenario 1: Cost was assumed to be constant, sensitivity analysis due to uncertainties in outcomes estimation was calculated. Scenario 1 had three models (base model was created for average cost per patient, model with lower assumption was average −SD, and higher assumption was average +SD).

Scenario 2: Outcome was assumed to be constant, sensitivity analysis due to uncertainties in cost estimation was calculated. Scenario 2 had three models (base model was created for average cost per patient, model with lower assumption was average −SD, and higher assumption was average +SD).

A sensitivity analysis was performed in order to determine the robustness of the result. The results of N number of one-way and N number of multi-way analyses conducted on different assumptions related to uncertainties in cost, and outcomes are presented in Figures 1 and 2.

Results

Demographic characteristics

Table 2 contains the demographic details of 124 schizophrenia patients interviewed. As per the Indian economic survey (2019), an annual income of less than 943.42 USD is considered as lower class.

Costs

Table 3 shows the base model and cost input for olanzapine and risperidone. For olanzapine and risperidone, the cost was calculated for 12.7 mg/day and 4.5 mg/day, respectively. This study accounts for direct cost of medication, laboratory charges and indirect cost for loss of productivity (of caregiver) and other costs (transportation charge, daily expenses and food charge). Here, we had observed the total cost for olanzapine was greater than the risperidone, it was about 4.40 USD.

Outcomes

Table 3 shows the PANSS scores for olanzapine and risperidone, before and after treatment. Treatment outcomes

Table 1 Model input and sources

Cost inputs (in INR)		Olanzapine (n = 71)	Risperidone (n = 53)	Source
SN	**Type of cost**			
1	Total direct medical cost	88023.6	79308.79	Trial
2	Total indirect medical cost	328100.0	218200	Trial
3	Total laboratory cost	71350.0	48580	Trial
4	Total cost	487473.6	346088.79	#1 + #2 + #3
5	Mean cost per patient	6865.8	6529.98	#4/n
Outcome outputs				
1	Total PANN score before medicine	6553.0	4835	Trial
2	Total PANN score after medicine	4613.0	3755	Trial
3	Total outcomes gained	1940.0	1080	Assumed each unit of decrease in PANN score as unit gained in outcomes
4	Mean outcomes gained	27.3	20.38	#3/n
	Cost (INR)/PANSS reduction	251.28	320.45	
	ICER = 48.35/PANSS (Olanzapine)			

were analysed by using scoring scales such as PANSS which describes nature before and after the treatment and the difference reported statistically significant by using *Z*-test scoring.

As shown in Table 1, cost (USD) per PANSS reduction for olanzapine and risperidone was 3.29 USD and 4.20 USD, respectively. Incremental cost-effectiveness ratio per patient was calculated to be 0.63 USD per PANSS reduction and showed olanzapine to be more cost-effective compared to risperidone.

Discussion

This study compares cost-effectiveness of olanzapine and risperidone using a PANSS score in the regional Indian healthcare settings of Andhra Pradesh. The previous study on cost-effectiveness of olanzapine and risperidone in Kerala, India used Brief Psychiatric Rating Scale score. One advantage of using PANSS score is that it can be converted into utility score using algorithms.[24] These utility score will help in cost–utility analysis in the clinical settings when EQ-5D and SF-6D are not available.[24] Furthermore, another study by Nemeth B et al. used a previously made algorithm for converting PANSS scores to utility value for the calculation of QALYs.[25] Using the Health decision strategic model for cost-effectiveness evaluation, this study finds out that olanzapine is more cost-effective than risperidone.[17] A study from Spain also reports olanzapine as a more effective and less costly option than risperidone. However, the Spanish study used discrete event simulation (DES) model that was developed specifically for the Spanish healthcare settings.[26] Olanzapine and risperidone were among the most commonly prescribed medicines in India and causes considerable financial burden to the patients. This study shows that male patient in the working group was mostly affected by schizophrenia. Likewise, it also showed that the patients were poor, lacking formal education and from a rural background. A study by Saeed Shoja Shafti and Mahsa Gilanipoor in Tehran too had patients who were mostly on similar age groups.[27]

Schizophrenia can occur to anyone irrespective of class or socioeconomic background; however, the rural working age patients from this study showed that the diseases can have significant financial burden to the family and further impoverish them. It also shows the need to have a comprehensive effort for mental health problems with financial protection mechanism. The Andhra Pradesh state has Aarogyasri Scheme which is a community health insurance scheme that provides financial cushioning to poor families (below poverty line) with an annual income up to USD 2600 (approx.).[28,29] The scheme covers treatment of serious health problems that requires hospitalization and surgery, and at present, 949 treatments are covered under the scheme.[28,29] However, this scheme does not cover outpatient treatment and mental health problems are mostly treated as outpatients in India hospitals.[30] Individuals can suffer from multiple mental disorders concurrently for which they need both hospitalizations and outpatient treatment for long time. Thus, schemes from the government such as the Aarogyasri Scheme need to provide proper adequate coverage for both outpatient and inpatient treatment of mental health problems. Studies assessing the willingness to pay for mental health services are required. Such studies are needed to examine how much people are willing to pay and afford for health insurance schemes that cover mental health problems. It will also assess the amount they are willing to pay for mental health services if they have to pay it on their own.

The incremental cost of olanzapine and risperidone were found to be 421.84 USD and 414.70 USD, respectively. The incremental effect was found to be 27.33 and 20.38 for olanzapine and risperidone. The incremental cost-effectiveness ratio (ICER) for olanzapine and risperidone were 1178 and 1553, respectively. This study shows that olanzapine was more cost-effective than risperidone by analysing the clinical data and values in outcome. Similar findings were reported by several other studies where olanzapine was

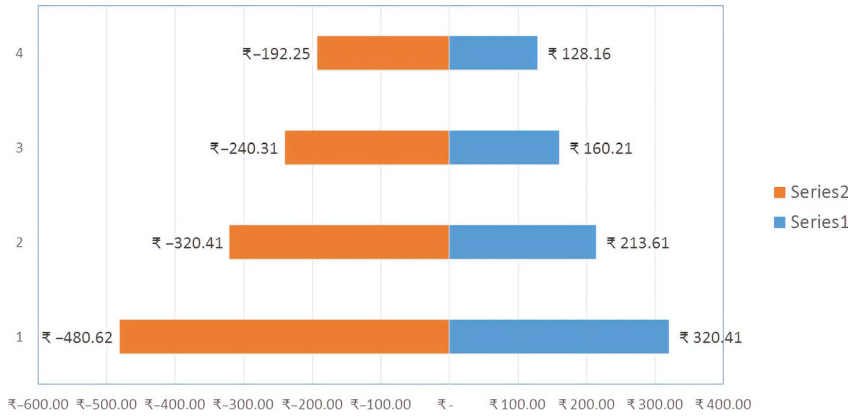

Figure 1 Tornado plot for risperidone multi-way sensitivity analysis.

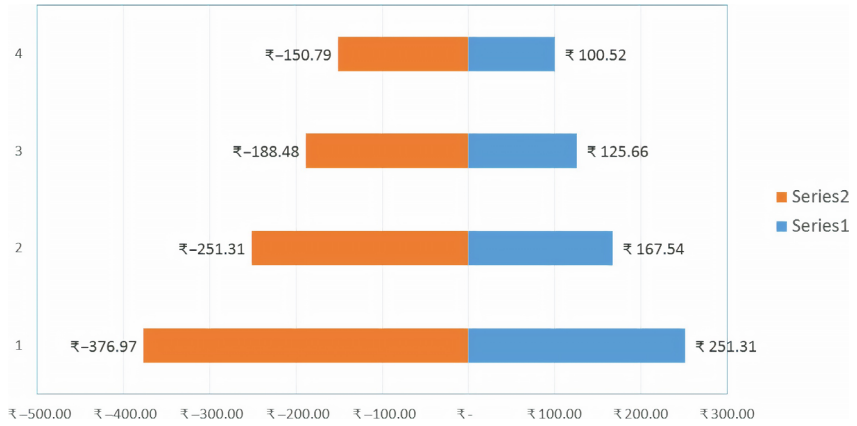

Figure 2 Tornado plot for olanzapine multi-way sensitivity analysis.

shown to be more effective and less costly alternative.[17,22] Nevertheless, Saeed Shoja Shafti and Mahsa Gilanipoor study reported olanzapine and risperidone to be equally effective for bringing out improvement in positive symptom while olanzapine to be better in terms of extrapyramidal side effects and negative effects.[27] Likewise, another study by Annemieke De Ridder and Diana De Graeve using net-benefit regression approach showed no significant monetary benefit between risperidone and olanzapine.[31] This study also showed that by using risperidone the patients were getting more drug-related complaints (based on observation) which resulted in more use of other supportive drugs and necessary laboratory investigations when compared to olanzapine. In line with the previous study from Kerala, this study demonstrates that olanzapine is more cost-effective drug than risperidone for the treatment of schizophrenia in the Indian healthcare settings.[17]

This study also shows a need to carry out larger scale cost-effectiveness analysis of various medicines for the treatment of schizophrenia and other mental illness across different states. State governments of India have rolled out health insurance schemes that are different from each other and the coverage of mental health illness by these schemes is not known. Thus, more studies on the pharmacoeconomic aspects of schizophrenia and other mental illness under different state-level health insurance schemes are needed. Such studies can guide comprehensive policies for the treatment of schizophrenia and other mental illness.

Conclusions

This study shows that olanzapine is a more cost-effective drug when compared to risperidone. It supports olanzapine as a cost-effective drug and an alternative to risperidone in the Indian healthcare settings. This study also highlights the use of PANSS score as an outcomes measure for schizophrenia treatment. With further revision and validation, the cost-effectiveness outcome of olanzapine and risperidone can be used to inform any comprehensive healthcare financing mechanism in the Indian settings.

Declarations

Conflict of interest

The Author(s) declare(s) that they have no conflicts of interest to disclose.

Table 2 Socio-demographic characteristics of the schizophrenia patients (n = 124)

S. no.	Socio-demographic variables	Schizophrenia patients (n = 124)	
		Olanzapine users (n = 71) (%)	Risperidone users (n = 53) (%)
1.	Age (years)		
	18–28	18 (25.35%)	12 (22.64%)
	28–38	24 (33.80%)	21 (39.62%)
	38–48	15 (21.13%)	13 (24.53%)
	48–58	14 (19.72%)	07 (13.21%)
2.	Sex		
	Male	44 (61.972%)	28 (52.83%)
	Female	27 (38.028%)	25 (47.17%)
3.	Education status		
	Uneducated	22 (30.99%)	16 (30.19%)
	Primary	15 (21.13%)	11 (20.75%)
	Secondary	17 (23.94%)	13 (24.53%)
	Graduate	6 (8.45%)	7 (13.21%)
	Undergraduate	6 (8.45%)	5 (9.43%)
	Postgraduate	5 (7.04%)	1 (1.89%)
4.	Employment		
	Employed	41 (57.75%)	28 (52.83%)
	Unemployed	30 (42.25%)	25 (47.17%)
5.	Marital status		
	Married	45 (63.38%)	35 (66.04%)
	Unmarried	22 (30.99%)	14 (26.41%)
	Widow/Divorce	4 (5.63%)	4 (7.55%)
6.	Residence		
	Urban	32 (45.07%)	25 (47.17%)
	Rural	39 (54.93%)	28 (52.83%)
7.	Family		
	Nuclear family	58 (81.69%)	47 (88.68%)
	Joint/Extended family	13 (18.31%)	6 (11.32%)
8.	Income (Lakhs)		
	High class (>8.4)	0 (0)	0 (0)
	Upper Middle Class (5.4-8.4)	14 (19.72%)	18 (33.96%)
	Middle class (1.2–5.4)	39 (54.93%)	26 (49.06%)
	Below middle class (0.72–1.2)	16 (22.54%)	6 (11.32%)
	Lower class (<0.72)	2 (2.81%)	3 (5.66%)

Table 3 Statistical analysis of outcome scores between olanzapine and risperidone users

Drug users	PANSS scores	Mean	Median	Standard deviation
Olanzapine	Before treatment	92.33	91	8.67
	After treatment	65.12	65	8.48
	Mean difference between scoring	27.33	28	8.63
Risperidone	Before treatment	91.44	90	10.20
	After treatment	70.88	70	7.26
	Mean difference between scoring	20.38	18	7.65

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Authors' contributions

YP, KHS, GMR, KHB and KS conceptualized the study, performed analysis and interpretation of data. YP did the data collection. YP, KHS, GMR, KHB, KS and BKC drafted the manuscript. BKC and YP contributed in manuscript writing and review. All authors read and approved the final manuscript. All Authors state that they had complete access to the study data that support the publication

Ethical approval

Ethical approval to carry out the study was obtained from the Institutional Ethical Committee of the Narayana Pharmacy College and Narayana Medical College & Hospital, Nellore, Andhra Pradesh, India. Ethical approval was obtained on June 2019.

Consent for publication

Patients were briefed about the study, following which a written consent was taken from the patients. For those patient who could not read and write, a verbal consent was obtained from them following which data collection was carried out.

Data Availability Statement

The data sets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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