A One-Year Health Economics Study Before and After Switching from Oral Antipsychotics to Once-Monthly Paliperidone Palmitate in Patients with Schizophrenia, A Retrospective, Prospective, Mirror-Image Study

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Research Article

Keywords: schizophrenia, direct costs, indirect costs, oral antipsychotics, once-monthly paliperidone palmitate

Posted Date: July 8th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-620450/v1>

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Abstract

Background: Schizophrenia is ranked among the top 25 leading causes of disability worldwide in 2013 which resulting in social and economic burden. By observing patients with schizophrenia one year before and after switching from oral antipsychotics (OAPs) to once-monthly paliperidone palmitate (PP1M), we can better understand the change of total costs in schizophrenic patients, including direct costs and indirect costs, after switching treatment patterns.

Methods: A total of 100 schizophrenic (ICD-10) outpatient and inpatient patients from Shandong Mental Health Center were collected from December 2016 to June 2019. Treatment modalities, health care resource utilization and costs were compared before and after switching directly from oral antipsychotics to PP1M.

Results: Of the 82 patients included in the main analyses, hospitalization costs decreased was partly offset by the increase of medical costs, which causing direct costs slightly increased ($t=-1.81$, $P=0.05$). The reduction of productivity costs ($t=2.06$, $P=0.05$) and caregiver care costs ($t=1.99$, $P\leq 0.05$) was seen at post-PP1M switch, therefore the indirect costs also obviously reduced ($t=2.31$, $P=0.05$). Total costs slightly increased ($t=-0.05$, $P=0.05$) compared to pre-PP1M period. For patients with ≥ 1 all-cause inpatient stay in the baseline period ($n=32$), compared with pre-PP1M, a fewer number of inpatient stays ($t=1.73$, $P=0.05$) and hospitalizations ($t=2.56$, $P\leq 0.01$) were observed and a significant reduction in direct costs ($t=2.20$, $P=0.01$) was observed post-transition to PP1M.

Conclusions: Switching to PP1M from OAPs can improve adherence to therapy and not increase the costs of health care in the clinical. Patients with ≥ 1 recent all-cause inpatient stay had a significant reduction in direct costs after switching from oral antipsychotics to PP1M, suggesting that patients with ≥ 1 all-cause inpatient stay may benefit after switching to PP1M. Indirect costs decrease from OAPs to PP1M, suggesting that reduce the burden of the family labor after switch to PP1M.

Introduction

Schizophrenia is a remitting and relapsing psychiatric disorder, characterized by profound disruptions in thinking, language, perception, and self-perception¹. Schizophrenia is ranked among the top 25 leading causes of disability worldwide in 2013². The average age of onset of the disease is between 15 and 35 years, usually in late adolescence or in the early 20s in men and later in women¹. Despite its low prevalence, its social and economic burden remains substantial, not only for patients, but also for families, and more broadly for society. Economic burden studies often incorporate both direct and indirect costs. Direct costs are costs associated with hospital inpatient treatment, prescription medications, long-term institutional care, and treatment costs associated with psychological and physical complications³. Indirect costs are defined as morbidity, premature mortality, and productivity losses related to informal care provided by caregivers with schizophrenia⁴⁻⁷. There are two main reasons causing the high economic burden of schizophrenia. First, non-adherence to antipsychotic use is a serious contributor to

the economic burden of schizophrenia. Approximately one-third of patients with schizophrenia have poor adherence to treatment with OAPs². Non-adherence to treatment can hinder the success of treatment and may lead to poor clinical outcomes and a higher risk of relapse and rehospitalization⁸⁻¹¹, which is also associated with increased direct cost. Second, the impairment of physical function and quality of life in schizophrenia, which often leads many nursing responsibilities for family members¹² and increases indirect burden. In fact, one study has shown that between 50%-80% of schizophrenic patients live closely with family members¹². Furthermore, there is a third type of costs is referred to as an intangible fee. These are associated with decreased quality of life of patients, families, and caregivers due to other factors such as pain or distress¹³. But these costs are extremely difficult to quantify and are therefore often ignored in economic research¹⁴.

In addition, long-acting injectable antipsychotics (LAIs) have been shown to increase medication adherence^{15,16}, reduce relapse and rehospitalization¹⁶⁻¹⁸, and are even more cost-effective than OAPs. Although there is much strong evidence recommending the use of LAIs, it remains underutilized in clinical practice^{19,20} due to the so-called high costs²¹. Therefore, we believe that the following question remains: which clinical treatment is more economical between OAPs and LAIs. Based on which treatment is more cost-effective, the goal of our study is understanding the change of total costs in schizophrenic patients, including direct costs and indirect costs, after switching treatment from PP1M to OAPs. We hope to provide data support for the efficient and reasonable utilization of social health resources and for the reduction of social medical treatment costs.

Methods

Subjects

A total of 100 schizophrenic (ICD-10) outpatient and inpatient patients from Shandong Mental Health Center were collected from December 2016 to June 2019. The inclusion criteria were as follows: (a) the date of the first observation of a diagnosis of schizophrenia during this period was identified as the initial date; (b) subjects with the course of the disease ≥ 1 year; (c) subjects with at least one illness exacerbation or hospitalization (PANSS score ≥ 70) in the year prior to enrollment; (d) between 18 and 65 years old. The exclusion criteria were as follows: (a) pregnant or lactating women; (b) alcoholism or substance abuse; (c) patients with severe physical diseases and organic brain disease.

Design and Variables

This was a retrospective, prospective, mirror-image study. The day on which PP1M commenced was set as the "mirror point". The study compared the number of days of health care use and costs during the 1-year period before and after PP1M implementation between December 2016 and June 2019.

In this study, Economic burden scale assessed economic indicators, in which direct costs included medication and hospital costs, and indirect costs included productivity costs and caregiver care costs.

Statistical methods

Statistical analyses were performed using 23.0 SPSS software. Demographic characteristics were described during the baseline period including age, gender and duration of disease. Means, medians, and standard deviations (SDs) were used for continuous variables, while counts and percentages were used for categorical variables. Significant differences between pre- and post-PP1M switch values were identified using P values < 0.05 . All study indicators were reassessed as part of the subgroup analysis, which included only patients with ≥ 1 all-cause hospitalization during baseline period.

Results

A total 100 patients with schizophrenia who transitioned from oral risperidone or oral paliperidone to PP1M were included in the study. Patients with ≥ 1 all-cause inpatient stay were 32.

Demographic Before Transition to PP1M

Of the 82 patients included in the main analyses, the average age was 32.2 (SD = 1.2) years old and the mean disease course of schizophrenia was 57.5 months (SD = 40.6). 53.66% of the patients were female.

Direct Costs Before and After Transition to PP1M

Compared with pre-PP1M, medical costs increased significantly post-PP1M ($t = -12.09$, $P < 0.01$), while the hospitalization costs decreased from ¥9,155 to ¥2,915 ($t = 1.91$, $P > 0.05$). To sum up, direct costs slightly increased ($t = -1.81$, $P > 0.05$), as shown in Table 1.

Table 1
Comparison of Direct Costs Before and After Conversion to PP1M

	Medical costs	Hospitalization costs	Direct costs
pre-PP1M (¥)	8302 ± 4156	9155 ± 18816	17457 ± 17414
Post-PP1M (¥)	20121 ± 4580	2915 ± 8466	23030 ± 8648
T	-12.09	1.91	-1.81
P	<0.01	0.074	0.07

Direct Costs for Patients ≥ 1 All-Cause Inpatient Stay Before and After Transition to PP1M

Compared with pre-PP1M, medical costs in all-cause inpatient stay costs increased post-PP1M ($t = -11.91$, $P < 0.01$), and the hospital costs decreased significantly from ¥25,656 to ¥7,179 ($t = 5.02$, $P < 0.01$). An obvious decrease in direct costs of ≥ 1 all-cause inpatient stay during the transition to PP1M were observed ($t = 2.71$, $P < 0.05$)

Table 2
Comparison of Direct Cost of ≥ 1 All-Cause Hospitalizations Before and After Transition to PP1M

	Medical costs	Hospitalization costs	Direct costs
pre-PP1M (¥)	8992 $\pm$ 3414	25656 $\pm$ 18756	34700 $\pm$ 18044
Post-PP1M (¥)	21961 $\pm$ 5492	7179 $\pm$ 10552	27705 $\pm$ 8266
T	-11.91	5.02	2.20
P	<0.01	<0.01	<0.01

Inpatient Stays and Number of Hospitalizations after Transition to PP1M

After transition to PP1M, patients had a shorter inpatient length of stay ($t = 1.73$, $P > 0.05$) and a fewer number of hospitalizations ($t = 1.04$, $P > 0.05$) (Table 3). Furthermore, as shown in Table 4, the number of ≥ 1 all-cause inpatient stays ($t = 1.73$, $P < 0.01$) and hospitalizations ($t = 2.56$, $P < 0.05$) also decreased from pre- to post-PP1M period.

Table 3
Comparison of Length of Stay and Number of Hospitalizations After Conversion to PP1M

	Number of hospitalizations	Inpatient stays (days)
pre-PP1M	0.38 $\pm$ 0.71	27.27 $\pm$ 49.71
Post-PP1M	0.23 $\pm$ 0.58	10.17 $\pm$ 21.84
T	1.04	1.73
P	0.3	0.09

Table 4
Comparison of Length of Inpatient Stay and Number of Hospitalizations After Switching to PP1M in Patients with ≥ 1 Recent All-Cause Hospitalizations

	Number of hospitalizations	Inpatient stays (days)
pre-PP1M	0.67 $\pm$ 0.96	52.80 $\pm$ 60.54
Post-PP1M	0.22 $\pm$ 0.42	16.33 $\pm$ 29.48
T	2.56	1.73
P	≤ 0.01	<0.05

Indirect Costs Before and After Transition to PP1M

Compared with pre-PP1M, productivity costs ($t = 2.06$, $P \leq 0.05$) and caregiver care costs ($t = 1.99$, $P \leq 0.05$) reduced post-PP1M. Consequently, indirect costs also significantly reduced ($t = 2.31$, $P < 0.05$) (Table 5).

Table 5
Comparison of Indirect Costs Before and After Transition to PP1M

	Caregiver care costs	Productivity costs	Indirect costs
pre-PP1M (¥)	3830 ± 3260	11767 ± 8133	15967 ± 10128
Post-PP1M (¥)	2141 ± 4044	8137 ± 8150	10279 ± 11878
T	2.06	1.99	2.31
P	≤ 0.05	≤ 0.05	<0.05

Total Costs Before and After Transition to PP1M

The direct costs of the patients increased ($t = -1.81$, $P > 0.05$), while the indirect costs decreased significantly ($t = 2.31$, $P < 0.05$) after the switch of PP1M, by the comparison of the pre-PP1M period. Overall, the total cost to patients increased only slightly ($t = -0.05$, $P > 0.05$), as shown in Table 6. Furthermore, as shown in Table 7. An obvious decrease in indirect, direct and the total costs of ≥ 1 all-cause inpatient stay during the transition to PP1M were observed.

Table 6
Comparison of Direct Costs, Indirect Costs and Total Costs Before and After Transition to PP1M

	Direct costs	Indirect costs	Total costs
pre-PP1M (¥)	17457 ± 17414	15967 ± 10128	33095 ± 21984
Post-PP1M (¥)	23030 ± 8648	10279 ± 11878	33309 ± 15254
T	-1.81	2.31	-0.05
P	0.07	<0.05	0.96

Table 7
Comparison of Direct Cost, Indirect Costs and Total Costs of ≥ 1 All-Cause Hospitalizations Before and After Transition to PP1M

	Direct costs	Indirect costs	Total costs
pre-PP1M (¥)	34700 $\pm$ 18044	21718 $\pm$ 11246	56418 $\pm$ 28020
Post-PP1M (¥)	27705 $\pm$ 8266	15023 $\pm$ 10875	42728 $\pm$ 15307
T	2.20	2.67	2.68
P	<0.01	<0.01	<0.01

Discussion

Nowadays, oral antipsychotics remain the first-line pharmacologic treatment option for patients with schizophrenia, but a high discontinuation rate is a known problem with oral antipsychotic treatment²². LAIs are generally indicated in patients who are considered non-adherent to oral therapy. In this real-world retrospective and prospective study, all patients improved adherence after switching to PP1M. After switching patients from OAPs to PP1M, there were not only fewer hospitalizations but also fewer days spent in an inpatient setting. This finding has been replicated in other studies^{23,24}. More importantly, changes in pharmacoeconomics were also found after switching to PP1M, in addition to improvements in adherence. There was no increase in total all-cause costs (direct and indirect costs) after patients switching from OAPs to PP1M in the study. The increase in medical costs was offset in part by lower hospitalization costs, resulting in no significant increase in direct costs (¥17,457 *versus* ¥23,030). For the treatment of schizophrenia, most of the cost of treatment does come from hospitalization^{25,26}, thus finding that the use of PP1M partially reduces the economic burden of the disease. The results of this study are consistent with the findings of others^{27,28}. In a true observational study, treatment with LAIs was associated with fewer hospitalizations and fewer days of hospitalization, thus significantly reducing monthly hospitalization costs (\$4,007 for LAIs and \$8,769 for oral AP cohort). In a retrospective longitudinal study of US veterans, the average annual all-cause health care costs for U.S. veterans with schizophrenia treated with PP1M and oral AP were \$78,589 and \$82,895, respectively²⁹.

At the same time, Schizophrenia patients who can be effected by the mental symptom caused high productivity loss, which caused high productivity losses to patients and their families. In addition, the burden of schizophrenia also has a profound impact on caregivers and patient families in addition to direct medical costs³⁰. Currently, few studies have observed changes in indirect costs from OAPs to PP1M in patients with schizophrenia. In this study, it was found that indirect costs (productivity loss and informal care costs provided by caregivers) were effectively reduced when patients were switched from OAPs to PP1M ($P < 0.05$). In the meanwhile, the quality of life of the caregiver may also improve. In summary, in this study, it was found that after the transition from OAPs to PP1M, direct costs have

increased slightly and indirect costs have decreased, resulting in a further reduction in no difference in total costs ($t=-0.05$, $p = 0.96$) after from OAPs transition to PP1M.

A noteworthy finding in this study was patients with ≥ 1 all-cause hospitalization had lower costs before and after switching to PP1M. This subset consisted of patients with a recent hospitalization who were less likely to be fully compliant with treatment. These patients had lower direct costs, indirect costs, and total costs after the transition period compared to before the transition period with PP1M. Patients who ≥ 1 all-cause hospitalization may particularly benefit from switching from OAPs to PP1M, since it improves adherence and decreases the length of stay, thereby significantly reducing direct costs.

In contrast to prior studies that included a comparison of OAPs to PP1M using a cohort design, this study used a mirror-image design that compared patients before and after the initiation of PP1M. The advantage of the before-and-after design is that it describes the benefit of the same patients who switched from an oral regimen to PP1M over time. There are not many studies in this direction, and previous literature review studies have focused on summarizing direct costs associated with schizophrenia. There has been a lack of emphasis on indirect costs estimation. And China has no similar results at present. Therefore, this study focuses on the Chinese schizophrenia economic burden about direct and indirect costs when switching from OAPs to PP1M.

However, the finding of this study should be interpreted in the context of some limitations. First, part of our database was based on patient-provided data, and its accuracy cannot be guaranteed. The study is expected to obtain dates from the Chinese Medical Insurance Database. Second, the sample size is relatively small, so the data may not be representative of the entire Chinese population. Therefore, in the follow-up study, we will further cooperate with other regions in China to carry out follow-up research and evaluation.

Conclusions

Comparing patients one year before and after switching from OAPs to PP1M, the increase in medical costs in the post-PP1M period was partially offset by a decrease in hospital costs. Costs of production and caregiver care were also reduced, leading to a smaller difference in total costs after switching to PP1M. This suggests that patients switching from OAPs to PP1M can improve adherence to therapy and does not increase the costs of health care in the clinical. The Costs for patients with ≥ 1 recent all-cause inpatient stay prior to PP1M were associated with the reduction of the number of hospital stays and hospitalizations, resulting in pharmacy costs in the post-PP1M period being fully offset by lower hospital costs. Conversion to PP1M can reduce production costs and caregiver costs and therefore also save indirect costs.

Abbreviations

OAPs _ oral antipsychotics

LAIs_ long-acting injectable antipsychotics

PP1M _ once-monthly paliperidone palmitate

OAPs _ oral antipsychotics

ICD-10_ international classification of diseases, tenth revision

Declarations

Ethics Approval and Consent to Participate

Written consent was obtained from all subjects, and this study was approved by the Ethics Committee of Shandong Mental Health Center.

Consent for publication

The consent for publication is not applicable to this manuscript.

Availability of data and supporting materials

Data are available on request from the corresponding author.

Conflicts of interest

The author(s) declare that they have no conflicts of interest.

Funding

This study supported by grants from the Shandong Medical and Health Science and Technology Development project (Grant No.2017 WS792) and Shandong science and technology project of traditional Chinese medicine (Grant No.2020M053).

Authors' contributions

Ludong Bai designed the study, Jie Liu and Qian Wang performed the data analyses and wrote the manuscript, Jie Liu and Qian Wang contribute equally. Lei Su contributed significantly to analysis and manuscript preparation. Limin Yang and Lianyong Zou helped perform the analysis with constructive discussions.

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