Efficacy of paliperidone palmitate in the treatment of schizophrenia and its effect on psychosocial and occupational functioning in patients: 2 Case studies

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Abstract

Schizophrenia is a chronic recurrent illness with positive, negative and cognitive symptoms, which can lead to severe impairment of psychosocial and occupational functioning. Antipsychotic medications have been available for decades in both oral (PO) and long-acting injectable (LAI) formulations, with demonstrated efficacy in treating positive symptoms of schizophrenia. Most antipsychotic medications, however, have only limited success in improving psychosocial and occupational functioning for patients. Paliperidone palmitate (PP) LAI has been available for the treatment of schizophrenia in Canada since 2010[1] and has shown some promising results in improving psychosocial and occupational functioning. In this article we examine the role of patient adherence to antipsychotic medication, the resulting effect on relapse, and the socioeconomic impact of schizophrenia. We also present 2 case studies where two adult female patients diagnosed with schizophrenia are examined in the context of economic, functional, cognitive and psychosocial outcomes, before and after treatment with PP LAI. Both patients and caregivers demonstrated an improvement in their quality of life over a relatively short period of time. This paper indicates that PP LAI has had great impact on patients' quality of life and further studies should be conducted to verify its effectiveness.

I. Introduction

A. Schizophrenia

Schizophrenia is a chronic disease characterized by positive, negative and cognitive symptoms.[2] These symptoms include delusions, hallucinations, disorganized speech and behaviour and/or other symptoms, which cause social and/or occupational dysfunction.[2] Approximately 1% of the world's population and 300,000 Canadians suffer from schizophrenia.[3] Every year, from a population of 100,000 people, 20-25 people will develop this illness for the first time.[4]

B. Psychosocial functioning of schizophrenia

Individuals with schizophrenia often have poor social interactions, poor work performance and difficulty maintaining meaningful relationships.[5] In one study, 72.9% of those with schizophrenia reported no employment activity.[6] Poor social functioning is one of the most debilitating features of schizophrenia, which reflects impairments in interpersonal relationships and communication.[7] Many patients with schizophrenia become dependent on their caregivers, typically family members, for support.[8] This results in social isolation for the patient aside from their caregivers.[8] Due to the chronic nature of the disease, caregivers become necessary lifetime support systems to the patients.[8] The caregivers are forced to change their life plans and they often experience emotional, social and financial burdens.[8,9]

C. Cost of schizophrenia

In 2004, the total economic burden of this disease in Canada was $6.85 billion of which $4.83 billion was due to decreased productivity associated with morbidity and premature mortality due to schizophrenia.[10] Treatment of schizophrenia consumed 1.7% of the Canadian healthcare budget, making schizophrenia a disproportionately expensive disease to treat.[10] Of the health care and non-health care related costs, 61% was due to hospitalization, making it the largest cost component of health and non-healthcare related

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costs.[10] High relapse rates are a significant contributor to these high hospitalization costs.

D. Relapses

Weiden and Olfson found in 1986 that the aggregate cost of readmission for approximately 260,000 patients with schizophrenia in the United States was nearly $2 billion.[11] As well, Haya et al. found that patients with prior relapses incur 3 times higher total annual direct mental health-care costs than those without prior relapses over a 1-year period. Those with prior relapses faced higher costs of medication and outpatient services.[12] Many of those who stop treatment and then relapse are unable to achieve prior levels of functioning. This may be due to multiple relapses leading to continuing neurodegeneration.[13] Compared to patients who have relapsed, first episode patients have higher rates of stabilization from acute symptoms, lower rates of symptom exacerbation over a 2-year follow up, and require lower doses of antipsychotics for acute and maintenance treatment.[13] As well, first-episode patients experienced reduced negative symptoms and deficit states.[13] In first-episode patients the greater increase in plasma homovanillic acid (pHVA) after the first week of treatment is associated with better treatment outcome.[13] Antipsychotic drug response is associated with pHVA levels, which acts as a peripheral marker for dopamine activity in the brain.[14] Those with higher pre-treatment levels experience more effective therapeutic response, whereas those with lower levels often experience Parkinsonism.[15,16]

E. Adherence

Following a psychotic episode, non-adherence to antipsychotic (AP) medication is common, with non-adherence rates reaching as high as 50% after 1 year and 75% within 2 years.[17] This poses a significant concern since adherence to antipsychotic medication appears to be protective against relapse. Brief periods of partial adherence also lead to higher relapse rates.[17] Patients who adhere to medication have a first, second and third year relapse rate of 18%, 29% and 36% respectively.[17] Comparatively, patients who do not comply with their antipsychotic medication have first, second and third year relapse rates of 29%, 42% and 57%.[17] As well, those who are non-adherent to medication spend an average of 38.1 days in hospitalization compared to those who are adherent who spent an average of 14.3 days.[17] It should be noted that small deviations in medication could have a significant effect on relapse. Missing only 25% of the medication dose for more than 2 weeks results in increased risk of relapse.[17] The average number of days from the beginning of non-adherence to relapse is 72 days.[17] Furthermore, even partial adherence over a short period of time can result in increased risk of hospitalization.[17] Subotnik's group observed that patients who were partially adherent for less than 10 days results in an increased odds of hospitalization with an odds ratio of 1.98; for partial adherence for 11-30 days, the odds ratio was 2.81, and for over 30 days, the odds ratio was 3.96.[18] It was also found that partial adherence increased the risk of hospitalization in the long-term treatment of chronic schizophrenia.[17] In addition to the personal suffering caused by psychotic relapse, medication non-adherence has a tremendous financial cost.[17] The cost of non-adherence is high, with as much as 50% of the direct medical costs attributed to non-adherence to medication.[11]

F. Long-acting injectable vs oral medication

A systematic review done by Leucht et al. on antipsychotic medication identified that 33.3% of participants on PO relapsed compared to 21.6% of participants on LAI.[19] As well, Subotnik et al. found that the 12-month relapse rate for participants on risperidone PO (RisO) was 33% compared to those on risperidone LAI (RLAI) of only 5%.[17] This was associated with a relative risk reduction for RLAI over RisO by 84.7%.[17] Cost calculations done by Koczerginski and Arshoff demonstrated that patients treated with RLAI in injection clinics saved $17,355 per patient annually in hospital and medication costs, when compared with PO medications.[20] The authors stated that this was due to reduced relapse rates associated LAI, which reduces hospital stays and emergency room visits through increased effectiveness of treatment.[20]

When comparing long-acting injectable (LAI) to oral medication (PO), early episode patients receiving risperidone LAI have higher adherence and symptom control resulting in a non-significant increase of white matter volume (WMV) in the frontal lobe compared to patients receiving oral risperidone.[21,22] WMV increase is the result of increased myelination, which results in faster conduction in neurons.[22] Bartzokis et al. conducted an MRI study where WMV remained stable in RLAI participants but

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decreased in RisO groups.[22] The effects of AP medication do not directly induce myelination.[22] Instead, AP medications that block dopamine receptors promote increased intracortical myelination, and in rodent models this exposure to AP medications promotes oligodendrocyte differentiation and myelin repair.[22] Patients on RLAI had faster reaction times involving frontal lobe function and had faster reaction time on working memory and mental flexibility tasks.[22]

G. Paliperidone palmitate

PP is an atypical long-acting injectable antipsychotic therapy (LAI) designed for once monthly intramuscular (IM) injection and is indicated for acute and maintenance treatment of adult patients with schizophrenia and schizoaffective disorder.[1]

II. Case Study 1: Patient NB

The following is a case study for a female, aged 26, who had been diagnosed in 2007 and 2008 with Obsessive Compulsive Disorder (OCD) and paranoid schizophrenia respectively. Patient NB is single female with normal weight, unemployed, and living with her parents. From 2005-2006 she repeatedly dropped out of school and refused to leave the house. She was not very communicative, stopped eating for several weeks and lost a significant amount of weight. In 2007, the year NB was diagnosed with OCD, she started to exhibit bizarre behaviour, such as putting on and removing clothes, shoes, etc.; she would walk back and forth in a room, pull out tissues from tissue boxes continuously until the box was empty, and walk the streets to pick up cigarettes butts to smoke. Self- harm led to hospitalization: in 2008, the patient was non-adherent to medication and attempted to commit suicide by jumping from the roof of her family home. This led to a 3-week hospital stay, during which time NB was diagnosed with schizophrenia. In 2009, she was hospitalized again for 3 weeks. In 2011, the patient stopped taking her medication and increased her recreational drug use. The family then took the patient to India to seek treatment. Upon returning to Canada in 2013, the patient had aggressive violent behaviour and used abusive language. She would laugh to herself and was withdrawn. The patient refused to sleep in her bedroom opting instead for the couch. She was not eating, would not shower for days, and maintained poor hygiene. She would stay up nights, just sitting on the couch, not doing anything. In 2014, the patient was admitted to the Centre for Addiction and Mental Health (CAMH). Her medical, family and social history were unremarkable. The patient was on sertraline HCL and zuclopenthixol decanoate depot. On February 20, 2014, the medication was switched to PP 150 mg. This dose was reduced to 100 mg but then was subsequently increased to 150 mg on May 22, 2014. This change in treatment, given as LAI, was effective with a 100% compliance. The patient started to show reduction in her positive, negative and cognitive symptoms. NB had an improvement in her family interactions, started social activities, her speech improved spontaneously, her social and emotional isolation was reduced and she became less suspicious. After the switch to PP, the patient was able to maintain good eye contact and her personal hygiene improved, even going as far as the application of makeup. Furthermore, she was able to watch television with her parents, ask her parents questions, talk to her grandparents in India, clean her room, talk to people if they initiated the conversation and eat regular meals. NB now wants to volunteer and take a reintegration course at George Brown College. In the future she wishes to attend university and get a job in management. Prior to PP treatment, the patient had three hospitalizations, cumulating in a 59-day length of stay. She also had 3 ER visits. After switching, the patient had no hospitalizations and no ER visits. NB's caregiver was interviewed and a Zarit Burden Caregiver score was determined. Prior to treatment, the caregiver's interview was ranked at a score of 88, the highest possible score and considered a severe burden (61-88).[23] However, after one year of treatment the family reported an improvement in her psychosocial function and after 2 years of treatment the total score was reduced to 36, which is considered a mild to moderate burden (21-40).[23] The patient was ranked on a Personal and Social Performance scale (PSP), which is considered to be one of the most effective scales for assessing changes in functionality in a clinical setting due to its sensitivity to change and brevity.[24] Before starting treatment with PP, NB was ranked at 20 out of 100: she had very severe difficulties in aggressive behaviour and severe impairment of personal and social functioning. After taking PP, her score increased to 70, which indicates manifest but not marked difficulties. She also took a Medication Satisfaction Questionnaire,

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where the patient identified that she was very satisfied with the medication with a score of 6 out of 7. The patient stated that she is now "more happy". To measure the quality of life, patient NB took the S-QoL questionnaire. The S-QoL is a self-administrated questionnaire used to measure the quality of life of those suffering from schizophrenia.[25,26] This multidimensional instrument has been demonstrated by Auquier et al. to be effective in measuring a patients perspective of their psychological well-being, self-esteem, family relationships, relationships with friends, resilience, physical well-being, autonomy and sentimental life.[26] This scale has been shown to be sensitive to change, reproducible, responsive and has high construct validity and internal consistency reliability.[26] Prior to LAI treatment, NB marked 95% of the 41 items as "much less" to "less" than she preferred. After the treatment with LAI, she marked only 15% of the items, as "much less" to "less" than she preferred.

III. Case study 2: Patient XD

The following is a case study for a 30-year-old female (XD). In Grade 4 she was considered a gifted student. In 1998 she was diagnosed with a brain tumour. In the year 2000, the tumour was surgically removed. In 2002, XD attended the University of Toronto for English/Psychology. Two years later, she was hospitalized at Credit Valley Hospital (CVH) for 2 weeks, as a result of anxiety. XD's symptoms included paranoid ideation, losing concentration, an inability to complete assignments and she failed courses. In 2010, she was put on probation and later she was suspended from the University due to failing grades. In 2013, with worsening symptoms, the patient was found wandering the streets by police. She was subsequently admitted to CVH for 55 days with the diagnosis of schizophrenia. In July of that year, she was discharged with a prescription for RisO 2 mg per day. Due to lack of efficacy, in August 2013 she was started on PP 100 mg IM. In September of that year, she returned to school, gradually increasing the number of courses she was taking. In 2016, she successfully completed 4 courses with grades in the 80s, which, according to the University of Toronto, is considered to be an excellent academic standing.[27] Now she plans to pursue a master's degree. XD currently attends church and volunteers at the Acquired Brain Injury Association. She reports a "good relationship with people and classmates". Her family life has also "improved tremendously" and she is able to take her parents out. She started to trust her parents and is no longer fighting with them. They have stated that things are "very peaceful", that XD "involves in conversation" and that they have a "very good relationship". The family has even gone as far as to say, "With medication our daughter has no mental illness." These improvements were noticed within a year. This change was further exemplified by the change in her caregivers' Zarit Burden Caregiver score. Prior to treatment, her caregivers had a score of 73, which is classified as a severe burden (61-88). After two years of treatment her caregivers had a score of 24, which is classified as a mild to moderate burden (21-40).[23] As well, on the PSP, the patient showed major improvements. Prior to switching to PP 100 mg IM, XD scored only 15, due to very severe impairment in personal and social functioning; but after 2 years of treatment, this score rose to 90, which indicates almost no impairment. As well, based on the Medication Satisfaction Questionnaire, XD's caregivers reported a score of 6 indicating that they were very satisfied. Prior to treatment with LAI, out of the maximum 41 items of the S-QoL questionnaire, patient XD marked 100% as "much less" to "less" than she preferred. After the treatment with LAI, she marked only 2.5% as "much less" to "less" than she preferred.

IV. Discussion

Non-adherence limits the efficacy of pharmacotherapy resulting in recurrence of episodes of schizophrenia symptoms. These repeated episodes result in increased hospitalization, decreased effectiveness of treatment outcomes, worsening psychosocial functioning, and a lower quality of life. As a result, relapse prevention is critical. LAIs have been shown to be more cost-effective than other PO treatments. LAIs also improve clinical outcomes, decrease hospitalizations and maintain frontal lobe myelination. LAIs are associated with increased adherence, leading to greater relapse prevention, better psychotic symptom control and improved cognitive functioning. The cases presented here further demonstrate that the LAI PP significantly improved adherence, symptoms, and particularly improved psychosocial occupational functioning in the two adult patients described. Both patients and their families reported clinically significant

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improvements as a result of the medication. Simultaneously, both patients had a 100% adherence rate and neither experienced a relapse. The cases presented indicate promising results in improving psychosocial and occupational functioning associated with PP, however, further studies with larger sample sizes and robust methodologies are required.

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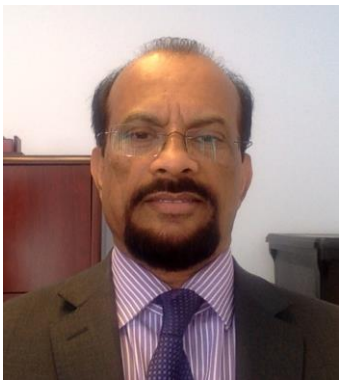
Authors' Profiles



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