PALIPERIDONE PALIMITATE (PP3M- INVEGA TRINZA) IN THE TREATMENT OF SCHIZOPHRENIA AND ITS EFFECT ON THE IMPROVEMENT OF PSYCHOLOGICAL, SOCIAL AND OCCUPATIONAL FUNCTIONING: WITH CASE STUDY

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Abstract: Schizophrenia is a disabling brain disorder characterized by symptoms such as hallucinations, delusions, disorganized communication, poor planning, reduced motivation and blunted affect. Schizophrenia affects people from all around the world contributing significantly to the global burden of disease. Due to the complexities of the disorder, efficacy and adherence of treatment regimens are a top priority for both patients as well as health care providers. Consequences of non-adherence heavily influences overall quality of life by affecting patients psychosocial and occupational functioning. With the improvements in the formulations of long acting injectables, the onset of Paliperidone Palmitate (PP3M), also known as Invega Trinza, has promising potential in the maintenance treatment of Schizophrenia. Longer dosing intervals allow increased adherence and decrease risk of relapse. In this article, we will examine the value of switching patients who are already stable on Paliperidone Palmitate (PP1M- Invega Sustenna), monthly injections to the 3-month depot formulation of Paliperidone Palmitate (PP3M- Invega Trinza), to increase adherence and reduce relapse, in turn improving overall psychosocial functioning and quality of life for schizophrenic patients. We will also present 1 case study which highlights improvements on a psychosocial and occupational level of functioning of this patient.

Keywords- Schizophrenia; Invega Trinza; Paliperidone Palmitate PP3M; nonadherence; relapse

I. INTRODUCTION

Schizophrenia is a chronic mental illness known as one of the most complex and challenging psychiatric disorders to treat [1]. It is a combination of cognitive, behavioral and emotional dysfunctions [2]. Worldwide, Schizophrenia is listed as one of the top 20 causes of disability [3]. According to The World Health Organization (WHO), Schizophrenia is responsible for 1.1% of the total disability adjusted life years (DALYs) and 2.8% of the years lived with disability (YLDs) [4]. Finding an effective treatment regimen which improves overall quality of life is therefore the most profound aspect of dealing with Schizophrenic patients, as well as enhancing their overall ability to cope with the various aspects of their disorder [5].

II. PREVALENCE

Schizophrenia has a worldwide prevalence of 1% [6]. Schizophrenia is a debilitating, chronic mental illness that has a substantial economic burden on patients, family members, friends and society in general [7]; therefore, understanding the prevalence of schizophrenia has important implications for both health service planning and risk factor epidemiology [8]. It has been estimated that approximately 24 million people suffer from schizophrenia worldwide; annual incidence rates of 1-4 per 10000 adults aged 15 to 54 years of age are affected [9-11], and there is an average lifetime prevalence of between 0.5% to 1% [8,10]. The estimated number of persons with schizophrenia in Canada in 2004 was 234 305, of which 120401 are males and 113904 females [7]. When estimating the prevalence of schizophrenia, factors such as the age structure of the population, mortality rates and migration patterns can have an impact on these estimates [8].

III. MORTALITY

The most disturbing consequence of Schizophrenia is a higher than normal rate of premature mortality [7]. Schizophrenia contributed to excess mortality in mostly industrialized countries [12] which was due to higher than normal rates of suicide [7]. The lifetime risk of suicide in the general population is approximately 0.5%-1% [13-14], compared to persons with Schizophrenia which is approximately 15-25 times higher [14-18]. Evidence has shown that middle aged men are at higher risk when compared to middle aged females to having deaths from suicide attributable to Schizophrenia [19-20].

IV. SOCIOECONOMIC BURDEN

One of the major challenges faced when treating Schizophrenic patients is non-adherence to medication regimens, reports indicated non-adherence to be as high as 40% to 60% to antipsychotics [21]. Relapse, hospitalization,

exacerbation of symptoms, harmful behavior to self or others, and suicide are all recognized consequence of poor adherence, which in turn negatively impacts patients and their families [21-22]. Schizophrenia accounts for 1.5% to 3% of national health care expenditures among different countries worldwide, with relapses leading to high hospitalization rates and costs [23]; 30% of costs due to relapses while another study shows hospitalization cost range from 52.5% to 80.7% [24-25]. A 2005 Analysis demonstrated that health and non-health costs amount to over 2 billion dollars in Canada [26]. Of the 2 billion dollars, prescription medication costs were equal to approximately 150 million dollars [26]. Improvement in the formulations of LAI may lead to a decrease in economic burdens [27]. One study showed better cost effectiveness per month per patient when patients were switched from oral antipsychotics to LAI, this resulted in a decrease in hospitalizations and relapses [27].

V. CAREGIVER BURDEN

Not only do Schizophrenic patients feel the impacts of the illness, but so do their families, friends and caregivers. Schizophrenia affects the physical, psychological, emotional, social and financial life of patients' caregivers [28]. According to a 2012 survey that was conducted in Ontario Canada, caregivers of Schizophrenic patients report that it affects their careers (34%), relationships with family and friends (54%), personal health (50%) and that it leads to feelings of frustration (61%), sadness (49%) and inadequacy (43%) [29]. The same study indicated that upward of 30% of caregivers in Ontario report missing a total of 30 days of work due to Schizophrenia-related responsibilities [29]. The cumulative burden on the caregiver is significant and often underestimated [30]. The burden may be exacerbated by limited financial and healthcare resources [30]. The most overwhelming emotion felt by 90% of caregivers was worry for the future of their child or loved one suffering from Schizophrenia, and more than 70% of caregivers reported feeling sad, protective and even frustrated when they overheard comments being made about the person they were caring for [31].

VI. RELAPSE RATES

Patients with Schizophrenia often lack insight into their disease and the importance of medication, compromising treatment adherence and increasing relapse frequency [32]. Relapses frequently lead to hospitalizations, poor treatment response, and further worsening of functioning [33]. Following relapse, 1 in 6 patients fails to respond to treatment and 1 in 10 commits suicide [34]. It is thought that the length of time between relapses is associated with loss of grey matter and white matter in the brain [35] while consecutive relapses are related to progressive loss in brain volume [36]. There is also a hypothesis that states, active psychosis reflects a period of disease progression to the extent that patients may not come back to their previous level of functioning and can be more resistant to treatment [37-38]. Therefore, prevention of relapse is a fundamental target in treatment of Schizophrenia [39].

VII. PALIPERIDONE PALMITATE (PP3M-INVEGA TRINZA)

A new formulation of Paliperidone Palmitate (PP3M) has been approved for the maintenance treatment of Schizophrenia [40]. It offers a considerably longer dosing interval (3months), which shows to be beneficial for patients suffering from Schizophrenia [40]. Studies have shown that approximately 93% of patients who were adequately stabilized with PP1M for at least 4 months, and subsequently treated with PP3M, did not experience a significant return of Schizophrenic symptoms [41]. Another study also showed superiority of PP3M over placebo in delaying time to relapse, 29% on placebo were relapsing compared to 9% of patients taking PP3M [39]. When compared at the 36-week mark post study, 92% of subjects receiving PP3M were still in remission compared to 58.3% of patients in the placebo group [39].

VIII. ADHERENCE

Risk of relapse is approximately 5 times higher among patients who discontinue their treatment, which is a major consequence of non-adherence [42]. Therefore, addressing non-adherence is key in diminishing the risk of relapse. The most effective approach to combat non-adherence is the use of LAI's [43-44]. With respect to preventing severe relapses requiring hospitalizations, studies show that LAI antipsychotics demonstrate superiority over oral medications [41]. There is evidence which shows PP3M delays time to relapse [45]. This 3-month injection would further mitigate the low treatment adherence and improve patients quality of life, by increasing time between visits to the physician or clinic for these injections [32]. PP3M would further decrease the burden placed on family members or friends who bear the responsibility of taking care of schizophrenic patients [32]. One of the major factors in adherence is coordination of transportation for more frequent injection visits, due to many patients living in under-serviced rural areas or inner-city settings [32]. Studies have shown individuals strongly prefer receiving LAI's once every 3 months as opposed to receiving injections every 2 weeks or 4 weeks [46]. According to Joshi et al. patients who were initiated on PP3M utilized fewer health care resources and proved to be more adherent to their PP3M treatment plan [47].

IX. HEALTH RELATED QUALITY OF LIFE

For the past 20 years, there has been a heightened interest in Quality of Life for Schizophrenic patients, due to the complexities of the disorder, which are associated with severe social and occupational dysfunction [48]. The development of atypical antipsychotics with broader efficacy and lower incidences of extrapyramidal side effects, compared to typical neuroleptics, has promoted greater interest from a patient-centered perspective [49]. In a study conducted by Norman et al. showed that negative symptoms, level of functioning and positive symptoms were all related to the Quality of Life Scale ratings [50]. Research on psychosocial influences of Quality of Life among inpatients with Schizophrenia suggests social support and self esteem may have a significant influence on Quality of Life for Schizophrenic patients [51-52].

X. PSYCHOLOGICAL AND SOCIAL IMPAIRMENT

When compared to the general population, Schizophrenic patients have a shorter life expectancy [53-55]. They are at an increased risk of physical illnesses, such as cardiovascular diseases, higher rates of suicide or accidental injury [53-55]. Attempted suicide rates for Schizophrenic patients range between 40% to 60%; this population is 15 times more likely than the general population to die from a suicide attempt [56], while 10% of Schizophrenic patients complete their suicide attempt successfully [5].

Most patients are unable to have stable relationships, or have a full time competitive employment, or even experience self-supported independent living [57]. Many Schizophrenic patients have limited social contacts [58]. 60% to 70% of Schizophrenic patients do not marry [58]. Contrary to popular belief, they also tend to be more withdrawn than aggressive [5].

Due to the chronic course of their disorder, Schizophrenic patients have ongoing social problems [5]. Some of the many aspects of daily life affected for Schizophrenic patients include self-care, family, relationships, income, education, employment, housing, community and social life [59]. Schizophrenic patients lose their ability to relax, concentrate or sleep and they may withdraw from friends or family in the early stages of the disease [5]. Performance declines if working or at school [5]. Early and effective treatment to control symptoms is essential to optimize chances of leading a productive life [5]. At a point in time where individuals should be most productive, young and middle aged Schizophrenic men and women experience high rates of hospitalizations due to the various symptoms they experience [5]. As a direct result, instead of forming families, establishing careers and building equity in their lives, these options become compromised or even non-existent [5].

11. CASE STUDY- X.X. 1

Mr. X.X.1 is a 25-year old single male who has a history of Schizophrenia. He was first diagnosed when he was 19 years old. During that time, he was having delusions that his roommates were poisoning him, and also having auditory hallucinations. He was also exhibiting bizarre behaviour, such as hitting his head, jumping out of moving cars, banging his head on the wall, tapping on walls, sitting on the balcony with his leg out, asking for his father to stay with him until he fell asleep, walking around the house repeatedly, violent outbursts when he did not get his way, etc. He was admitted to the hospital twice. He was treated with various antipsychotic medications of typical and atypical classes. He was treated with Clopixol (Zuclopentixol, Acuphase, and Depo) injections, and he was also treated with Olanzapine previously. During his stay at the hospital, he was also treated with antidepressant medication (Escitalopram). He did not show any improvement of his symptoms with the Clopixol Acuphase. Later, he was treated with Risperidone Consta, with limited success. His medication was changed to Paliperidone Invega 150mg IM, and a week later, he started to receive the Paliperidone Invega IM 150mg injection monthly. He started to show some improvement of his symptoms. His psychosocial functioning was severely impaired when he was on Clopixol and Risperidone Consta. After several months on Paliperidone Invega 150mg IM monthly, he was started on Paliperidone Trinza. Since Trinza was started, he began to show more improvement of his residual symptoms, and his psychological, social, and occupational functioning started to improve considerably. He was able to go out and make friends, and he was able to lead a normal life. His insight improved, and he has decided to “become normal.” He started to look for jobs. He had a few jobs, but he wanted to advance himself to find a better job. Currently, he is working as a mortgage broker. He stated that he is quite happy with the Paliperidone Trinza, and he is able to function “normally.” His parents stated that no bizarre behaviour has been noted. During his last visit, his Sheehan Disability Scale combined score on work, social life, and family life was 4 (mild disruptions). This score was a reduction from his combined score of 25 (markedly to extremely disrupted) that was assessed four years ago. He and his family are content with his current status of his illness, and with his psychological, social, and occupational improvement.

DISCUSSION

It is evident that the disruptions suffered from Schizophrenia have a substantial impact on patients, their families, friends and society on a whole. Non-

adherence reduces the effectiveness of treatment plans resulting in relapse of Schizophrenic symptoms, re- hospitalization and in turn prolonging recovery or maintenance of the disorder. This further worsens psychosocial functioning and lowers Quality of Life for Schizophrenic patients. LAIs have proven to be of utmost benefit for maintenance treatment of Schizophrenia and with the onset of newly developed formulations, there is optimism that such a debilitating disorder may finally be maintained and restore a better Quality of Life for Schizophrenic patients. Paliperidone Palmitate (PP3M-Invega Trinza) has demonstrated its effectiveness in reducing risk of relapse, and due to the reduced dosing frequencies, has also increased adherence. Addressing these two very key factors are directly related to the overall improvement of psychosocial, occupational functioning and Quality of Life which was demonstrated in the case presented.

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