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DEVELOPMENT

Comparison of Oral and Depot Antipsychotic Medications in Perspective of Relapse Rates in Patients with Schizophrenia

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1 INTRODUCTION

Schizophrenia is a chronic and disabling mental illness with a major impact on social and occupational functioning of a person. Approximately 1% of the global population is affected by the disease (Tiihonen *et al.,* 2011). Relapses and remissions of the illness are commonly observed. A relapse is described as the exacerbation or re-emergence of symptoms which may or may not result in hospitalization (Olivares *et al.,* 2013). The majority of patients reported experiencing multiple relapses during the course of their illness (Emsley *et al.,* 2013). Unfortunately, nearly 40% of all patients suffer their first relapse within the first year of diagnosis (Hogarty and Ulrich, 1998). Most patients (81.9%) would have experienced a relapse within five years of the initial episode (Robinson *et al.,* 1999).

Relapse prevention is the most important aspect of managing schizophrenia once the diagnosis is established. Improving medication adherence is a key factor in relapse prevention (Kane, 2007). Further, it is the best known predictor for decreasing the chance of relapse in schizophrenia (Ahmadkhaniha *et al.,* 2014) which is known to be 2–6 times higher without medication (Robinson *et al.,* 1999).

In order to improve adherence to psychotropic medication, it is essential to choose an effective and safe antipsychotic agent and optimize treatment according to the response and tolerability of the individual (Lamberti, 2001). However, the choice of medication is usually complicated due to variety of available pharmaceuticals, specific considerations for unique differences in patient's individualized response to the same medication and side effects (Tavcar *et al.,* 2000). Once an antipsychotic medication is selected the challenge is the mode of delivery and effective dose for this individual patient. There are two main routes of administering antipsychotic medications namely oral (tablets) and intramuscular (depot/ long acting injectable preparations).

Though results of previous research suggest that depot antipsychotics are more effective in reducing relapses in schizophrenia (Rauch and Fleischhacker, 2013) some meta-analysis of Randomized Controlled Trials showed no significance between the two treatment formulations

in reducing relapse (Kishimoto *et al.,* 2013). The aim of this study is to assess the effectiveness of oral and depot antipsychotic medications in reducing relapse rates of patients with schizophrenia.

2 METHODOLOGY

2.1 Experimental design

This is a retrospective comparative study carried out at the two mental health clinics coming under the purview of Top End Mental Health Service, Darwin in the Northern Territory of Australia. All patients diagnosed with schizophrenia during the period of 2010.01.01-2014.12.31(5 years) and on a particular oral or depot medication continuously at least for 3 months while remaining under the care of the service for a minimum period of one year were included in this study. Patients who dropped the treatment in less than 12 months, whom the diagnosis was subsequently changed from schizophrenia to other psychotic disorders, patients who received combination therapy (i.e. both oral and depot medication simultaneously) and patients who changed the treatment modality from oral to depot of a particular medication or vice versa in less than 3 months were excluded.

Patients' past medical records in the electronic record system were reviewed and data were collected according to a data record sheet. In the instances where patients have been treated with more than one drug during the study period with no overlap of medication, each medication trial was considered as a separate 'case' in data analysis.

Ethical approval was obtained from the Ethics Review Committee of the Menzies School of Health Research, Darwin, Australia. All patient records in the sample were de-identified before enrolling into the study.

2.2 Calculation of MRM index

The mean relapse per month (MRM) index was calculated as below (Ahmadkhaniha *et al.*, 2014). The lowest numerical value that could be obtained for MRM is 0 and it is assigned when there is no relapse recorded. A lower MRM value implies low relapse rates and vice versa.

$$\text{MRM index} = \frac{\text{Number of relapses}}{\text{Follow up time (month)}}$$

2.2 Statistical analysis

Data were analyzed by using SPSS version 23. Descriptive statistics including frequencies, means and standard deviations (SD) were studied in variables. Associations of oral and depot antipsychotics with the relapse rate were evaluated by an independent t-test. $P<0.05$ was considered as statistically significant.

3 RESULTS AND DISCUSSION

The study sample represented participants between 19 and 69 years of age. Among 193 patients 137 were males. Alcohol and substance consumption were respectively 56.48% and 27.46%.

Eight Second Generation antipsychotics (SGAs) and five First Generation Antipsychotics (FGAs) have been used to treat patients with schizophrenia. The SGAs used were Aripiprazole, Paliperidone, Risperidone, Olanzapine, Quetiapine, Ziprasidone, Amisulpride and Clozapine. Of these, Aripiprazole, Paliperidone and Risperidone had been used in both oral and depot preparations. The FGAs used were Chlorpromazine, Haloperidol, Fluphenazine, Flupenthixol and Zuclopenthixol. Haloperidol was used in both oral and depot preparations. Fluphenazine, Flupenthixol and Zuclopenthixol were used only as depot preparations.

The mean MRM of total oral medications was significantly higher ($p=4.0577$ E-19) compared to total depot medications

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(Table 1). It reveals that overall oral antipsychotics are less effective than depot antipsychotics in controlling relapses in patients with schizophrenia.

Table 1: Descriptive statistics of oral and depot antipsychotic medications

Medication type	Frequency	Mean MRM	SD
Oral	188	0.1003	0.0495
Depot	237	0.0557	0.048
Oral FGA	10	0.0542	0.0519
Depot FGA	94	0.057	0.0506
Oral SGA	178	0.1029	0.0482
Depot SGA	143	0.0549	0.0464

There were a total of 321 cases reported for second generation antipsychotic therapy and among them, 178 were for oral medications while 143 were for depot preparations. The effectiveness of SGA oral and depot antipsychotic drugs was assessed by independent sample t-test. Results indicate that depot SGA medications significantly reduced (p=1.8507E-17) MRM compared to oral SGA medications in patients with schizophrenia (table 1). Though depot FGAs are used widely (n=94), the use of oral FGAs were very limited and only ten cases were reported. This is mainly due to side effects caused by oral FGA antipsychotics.

Further, the sample contained 114 patients who have been treated with both oral and depot medications at different times during the study period. The MRM of these patients were compared using the paired sample t-test. The mean MRM of depot antipsychotic medications (0.0441 ± 0.0366) was significantly lower than oral antipsychotic medications (0.1048 ± 0.0459, p=3.1777E-20). This further reveals the effectiveness of depot antipsychotics over orals.

Patient adherence in taking prescribed medications is extremely important in obtaining a maximum therapeutic outcome. Side effects and lack of insight are the two main factors contributing to medication non-compliance in patients with schizophrenia. Depot formulations are considered the most successful pharmacological intervention that addresses the non-adherence problems in schizophrenia. The reason is that depot preparations are administered by a health care professional (doctor or a nurse) and therefore, missing an appointment for their injection is easily noticeable.

In contrast, compliance with oral medication is erratic because they are usually taken at home and not well monitored. Furthermore, parenteral preparations are not influenced by first-pass metabolism, and efficient in maintaining optimum plasma levels.

4 CONCLUSIONS AND RECOMMENDATIONS

Depot antipsychotics are superior to oral antipsychotics in reducing relapses in patients with schizophrenia. Further, the second generation depot preparations are more effective than the second generation orals. The use of depot antipsychotic medications could be considered as a more reliable and effective tool to ensure patient compliance with treatment. This in turn could prove cost effective by preventing relapses and potential hospital admissions.

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