



Original Article:

Prevalence & Prescription: Prescribing Practices of Clozapine in Australia between 2005 & 2010

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Abstract: Clozapine is an anti-psychotic used to treat refractory schizophrenia. This study reviews the rates of clozapine prescription for refractory schizophrenia in a region of Australia and compares the prescribing patterns to the estimated prevalence rates of refractory schizophrenia in the region. Utilising a pharmacoepidemiological approach; the results indicated that only 8.4% of the individuals estimated to be suffering from refractory schizophrenia in the region were prescribed clozapine between 2005 and 2010, with only 4.1% continuing clozapine to the conclusion of the study. In conclusion it is evident that clozapine is widely under-prescribed in this area of Australia.

Key Words: Clozapine; Treatment-resistant schizophrenia; Prevalence rates; Australia

Introduction:

Schizophrenia is a chronic and debilitating mental disorder that afflicts approximately 1% of the population worldwide.(1) Schizophrenia is primarily treated through the use of pharmacological treatments. However not all patients who suffer from schizophrenia respond well to pharmacological interventions. Approximately 30% of individuals who suffer from schizophrenia have a poor response to typical or novel atypical treatments.(2,3) That is these patients suffer from treatment-resistant or refractory schizophrenia.

Clozapine an atypical or second generation anti-psychotic treatment has been proven to be extremely effective in the treatment of refractory schizophrenia.(2,4,5) Moreover clozapine is the only anti-psychotic treatment that is endorsed to treat refractory schizophrenia.(6) Specifically Wheeler et al (5) in a large naturalistic study found that continued clozapine treatment lead to improved functional and clinical outcomes. That is patients made improvements in independent living and vocational activities coupled with a reduction in the need for compulsory treatment and hospitalisations. Additionally numerous studies have demonstrated a significant reduction in suicide rates and aggressive behaviour among those taking clozapine.(7) Furthermore clozapine has also been shown to be cost-effective in the treatment of refractory schizophrenia.(5)

However the benefits of clozapine therapy come at a high cost due to the drugs high side effect burden.(8) Some of the more significant side effects include weight gain, hypotension, tachycardia, agranulocytosis, myocarditis, cardiomyopathy and sedation.(9) Although clozapine has a high side effect burden; for patients suffering from treatment-resistant schizophrenia cloza-

pine is their last hope to manage their illness and live a 'normal' life.

It is apparent that even with the adverse side effects clozapine treatment can cause, clozapine therapy can have a significantly beneficial impact on the lives of people with refractory schizophrenia. However there is disparity in the reported prescription rates between studies; as numerous studies have reported that clozapine treatment is underutilised.(10) Whereas others have reported that clozapine is well utilised and the rates of prescription lie within the realm of the estimated prevalence rates of refractory schizophrenia.(11)

Therefore this paper investigates the prescription of clozapine in a region of New South Wales (NSW), Australia between 2005 and 2010. In order to ascertain whether clozapine therapy is being prescribed at a rate that reflects the predicted prevalence of refractory schizophrenia in the region. As it is only through reports detailing the 'real world' usage of anti-psychotics in clinical practice that future research can be shaped (12), as well as highlighting issues of importance to clinicians.

Methodology:

This study is a retrospective review of the prescribing practices of clozapine for the treatment of schizophrenia in a region of NSW, Australia for the time period between 2005 and 2010. The archival data on the rates of the prescription of clozapine are compared to the estimated prevalence rates of refractory schizophrenia in the area.

This study is based on data from region of NSW, Australia that covers approximately 6631 square kilometres and 13 different local Government areas. The most recent census in 2006 reported the population in the region to be 1.1 million. This is a total of 20% of the population of the state of NSW. The socio-economic status of the area is comparatively less disadvantaged than the rest of NSW. However there is significant variation between the 13 local Government areas on this indicator.

Results:

Estimated Prevalence Rates of Schizophrenia & Refractory Schizophrenia

It is well known that schizophrenia has a global prevalence rate of 1% (1), therefore based upon the region's population of 1.1 million it would be expected that 11'000 individuals in the region are suffering from schizophrenia. Furthermore it is also apparent from previous work that of those individuals afflicted with schizophrenia approximately 30% will have refractory or treatment resistant schizophrenia (2; 3). Therefore from the

above prevalence rate, a total 3'300 individual's with treatment-resistant schizophrenia are estimated to reside in the area.

Clozapine Prescription in the Region

Between the period of 2005 and 2010 a total of 277 individuals within the region were prescribed clozapine. This is a mere 8.4% of the individuals estimated to be suffering from treatment-resistant schizophrenia in the region. Furthermore 141 of these individuals ceased clozapine treatment during this time with only 136 patients continuing treatment to the present time. Therefore only a total of 4.1% of those estimated to be suffering from refractory schizophrenia are currently receiving clozapine treatment in the area. This implies that the vast majority 95.9% or 3'164 individuals estimated to be suffering from treatment-resistant schizophrenia in the region are not receiving appropriate or the superior evidenced based treatment for their condition.

Discussion:

It is evident from the above study that the prescription of clozapine in this region of NSW, Australia for the treatment of refractory schizophrenia is immensely under-prescribed based upon the estimated prevalence rates of treatment-resistant schizophrenia in the area. As out of the 3'300 individuals estimated to be suffering from treatment-resistant schizophrenia in the area only 8.4% or 277 patients had been prescribed clozapine. Furthermore only 4.1% or 136 patients had continued clozapine treatment in the reported time period.

These findings are in accordance with findings in the United States (U.S.) where clozapine prescriptions only accounted for 5% of all anti-psychotics prescribed.(6,13) Whereas Conley et al (13) study reported that clozapine was used significantly more often in Australia in comparison to Maryland in the U.S. However the study assessed clozapine use in a different state of Australia; thus displaying the disparity in prescribing patterns even in the same country. Similarly Fayek (14) reported that the rates of prescribing clozapine were significantly different throughout the United Kingdom. However other studies have reported that clozapine is well utilised.(11,15,16) Therefore it is evident that there are inconsistencies both in the practice of prescribing clozapine as well as the reports of prescribing patterns in the literature.

The under utilisation and disparity in the prescribing practices pertaining to clozapine; an evidenced based treatment for refractory schizophrenia not only results in significant costs to patients, their families, and society, it leads to significant costs for the health system. Wheeler et al (5) reports that the medical costs that result from patients with refractory schizophrenia are high and account for the majority of the overall cost of treating schizophrenia due to hospitalisations. Furthermore Drew et al (17) found that long term use of clozapine (3-5 years) accounted for a \$12 000 reduction in costs per patient per annum in Australia.

It is thought that the low prescription rates of clozapine in comparison to the estimated prevalence rates may be related to the knowledge and attitudes of prescribing clinicians. Nielsen et al (10) conducted a study in Denmark and found that many psychiatrists were reluctant to prescribe clozapine and had limited knowledge on the use of clozapine. Furthermore the low prescription rates could pertain to the actual or perceived logistical support for the necessary monitoring of patients on clozapine.

Future research needs to systematically address this issue by assessing the beliefs, knowledge and attitudes of prescribing clinicians towards clozapine. Such an endeavour would allow for the delineation of the reasons behind the low prescription rates of clozapine. This would facilitate the development of solutions to deal with the prevailing issues. Therefore bettering the prognosis for those patients suffering from refractory schizophrenia, helping their families and society; as well as lowering the health related costs of caring for these individuals.

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