

Polypharmacy, An Option Prior To Clozapine?: A Case Report

Amer Siddiq AN

Department of Psychological Medicine, Faculty of Medicine, University of Malaya, Kuala Lumpur

ABSTRAK

Ini merupakan satu laporan kes klinikal seorang pesakit yang menghadapi penyakit skizofrenia. Biasanya, menggunakan berbagai kombinasi ubat untuk rawatan penyakit ini tidak digalakkan, akan tetapi dengan wujudnya ubat-ubatan baru seperti "atypical antipsychotic", cara rawatan sebegini harus dilihat semula. Kes klinikal ini membincangkan penggunaan kombinasi ubat-ubatan untuk rawatan pesakit skizofrenia sebelum mereka dimulakan dengan ubat clozapine yang merupakan "benteng terakhir rawatan".

Kata kunci: laporan kes klinikal, skizofrenia, Malaysia

ABSTRACT

This is a report of a patient on multiple antipsychotic medications for the treatment of schizophrenia. Often, polypharmacy is not encouraged, however, with the advent of newer atypical antipsychotic agents, this practice may need review. This case will be used to highlight the rare instances when polypharmacy may be useful prior to the commencement of clozapine for the treatment of schizophrenia.

Key words: case report, schizophrenia, polypharmacy, Malaysia

INTRODUCTION

Schizophrenia is the most difficult mental illness to define and describe (Gelder et al. 2000). The course of illness can be poor and life long treatment is needed. An early observation by Kraplin (Henry & Smeltzer 2003) noted that 2.5% of patients with schizophrenia recover fully but more recent studies (Kane et al. 1988)

have been more optimistic quoting 25% full recovery. The same study also found that 10 -15% of patients with schizophrenia do not recover fully. For this group of patients, a number of them do not respond to standard treatment using single anti-psychotic regime and have been coined treatment resistant. Patients who are resistant to treatment have only been shown to respond to clozapine. Cloza-

Address for correspondence and reprint requests: Dr. Amer Siddiq Amer Nordin, Department of Psychological Medicine, Faculty of Medicine, University Malaya, 50603 Kuala Lumpur. Tel: 03-79492068. Fax: 03-79556477. Email: amersiddiq@um.edu.my

pine however is not without problems, among them agranulocytosis can occur, which is a fatal complication that may lead to death if not detected and treated early. Keeping this fact in mind, is there a role for polypharmacy?

This case will be used to highlight the rare instances when polypharmacy may be useful prior to the commencement of clozapine for the treatment of schizophrenia.

CASE REPORT

A 19 years old college student of Chinese descent presented to our center with a week history of aggression and irritability. She was also noted to be talkative and there was a history suggestive of depressive illness whereby she was keeping to herself, crying at times and had poor concentration a year before. She however had strong persecutory delusions of being victimized by the public and kept saying that she was publicly discriminated against. She also claimed to be a special being and able to communicate with her boy friend telepathically whom she blamed to be the reason for this. Mentally, she was hostile, but her mood was happy. However her affect was inappropriate, she had flighty ideas and pressure of speech. Her insight was poor. She was initially treated for bipolar affective disorder with quetiapine 400mg twice daily and a mood stabilizer, and was discharged 15 days later. She presented the next day with relapse of symptoms when she had suddenly hit her father in the car and almost caused a motor vehicle accident. During this admission her medication was increased and she was discharged 9 days later. She came for one follow up visit but was again admitted two weeks later with relapsing symptoms. Her case was dis-

cussed in the postgraduate conference and a revised diagnosis of schizophrenia was made. On this admission, her psychotic symptoms were more prominent with persecutory delusions of discrimination, thought broadcasting, neologism, inappropriate affect and intermittent hostility. Her mood symptoms had all but disappeared. She received electroconvulsive therapy during this admission and aripiprazole at 10mg daily was started. Quetiapine was planned to be tapered off slowly. She was discharged 14 days later with this combination. During her admissions her biochemical investigations were normal, these included full blood test, renal and liver function test and fasting glucose levels.

She was followed up in the clinic and was compliant to both medication and follow up. The quetiapine was reduced gradually and her aripiprazole was increased to 15mg once daily. She responded well to this new regimen until she was on aripiprazole 15mg once daily and quetiapine 200mg at night. A reduction of quetiapine would bring back the delusions and any increase would make her to become too sedated.

She has since been maintained on this dose and has responded very well. She plans to continue her studies for which she had stopped for eight months. Her family is also very happy with her progress.

DISCUSSION

For the pharmacological treatment of schizophrenia, monotherapy has always been encouraged and advocated in most guidelines (Weiden & Casey 1999, APA 2004). However, polypharmacy has been recognized by some and usually suggested as the last resort (Faries et al. 2005). Among reasons why monotherapy

is preferred are to allow psychiatrist to accurately evaluate patient's response to the new treatment (Weiden & Casey 1999) to allow adequate trial of each medication, to reduce the complexity of the medication regimen, to reduce side effects and also to assess and manage future symptom exacerbations (Miller & Craig 2002).

The literature has very little evidence supporting the use of polypharmacy with atypical antipsychotics and is divided on its long-term use this way (Stahl & Grady 2004, Picker et al 2008). Although polypharmacy has been used for a variety of reasons with the favorite being to bolster medication effectiveness in treating patients with refractory psychotic symptoms, mood symptoms or behavioral problems, the risk of combining two atypical antipsychotic appears to outweigh the benefits (Stahl & Grady 2004). Among these risk is a potentially higher mortality and an increase in metabolic problems (Faries et al. 2005, Stahl 2004).

For our patient, polypharmacy appears to work well for her. It has given her an option to recover fully. It has also saved her the option of treatment with clozapine which was impending in view of her poor response to quetiapine and aripiprazole at high doses individually. Although clozapine has been proven for difficult cases like our patient, the side effects and regular blood monitoring may be cumbersome given other options in treatment. The use of aripiprazole which is claimed to be weight neutral and less sedating (Lieberman 2004) is better suited for a young and active individual and will hopefully encourage compliance. Although the combination of aripiprazole and quetiapine has not been studied in detail, her low dose of quetiapine at night may be useful for sleep as it is more se-

dating but may not be sufficient to cause weight gain as a side effect.

Another explanation which may explain her response to this combination could well be that she had improved on the dose of aripiprazole 15mg which she has been taking for more than 3 months. The relapse of symptoms when quetiapine was titrated down and when aripiprazole was increased could well be due to akathisia, or inner restlessness, which is a known side effect in the initial stages. It can be very discomforting to the patient and may lead her to have a persecutory type of delusion.

Whichever the explanation, in the end it is all about the patient and her recovery that matters most.

REFERENCES

- American Psychiatric Association. 2004. Practice Guidelines for the Treatment of Patients with Schizophrenia. *Am J Psychiatry* 161:1-56.
- Faries, D., Ascher-Svanum, H., Zhu, B., Correll, C., Kane, J. 2005. Antipsychotic monotherapy and polypharmacy in the naturalistic treatment of schizophrenia with atypical antipsychotics. *BMC Psychiatry* 5:26.
- Gelder, M., Gath, D., Mayou, R., Cowen, P. 2000. Oxford Textbook of Psychiatry. Oxford University Press.
- Nasrallah, H.A., Smeltzer, D.J. 2003. The patient with Schizophrenia. USA. Handbooks in Healthcare Co.
- Kane, J., Honigfeld, G., Singer, J., Meltzer, H., and the Clozaril study Group. 1988. Clozapine for the Treatment Resistant Schizophrenic. *Arch Gen Psychiatry* 45:789-796.
- Lieberman, J. 2004. Dopamine Partial Agonists: A new Class of Antipsychotic. *CNS Drug* 18(4):251-267.
- Miller, A.L., Craig, C.S. 2002. Combination antipsychotics: pros, cons, and questions. *Schizophrenia Bull* 28:105-109.
- Picker, D., Vinik, J., Bartko, J.J. 2008. Pharmacotherapy of Schizophrenic Patients: Preponderance of Off-Label Drug Use. *PLoS ONE* 3(9):e3150.
- Stahl, S.M., Grady, M.M. 2004. A critical review of

atypical antipsychotic utilization: comparing monotherapy with polypharmacy and augmentation. *Current Medical Chemistry* 11(3):313–327

Stahl, S.M. 2004. Focus on antipsychotic polypharmacy: evidence-based prescribing or prescribing-based evidence? *Int J Neuropsychopharmacology* 7(2):113–116.

Weiden, P.J., Casey, D.E. 1999. "Polypharmacy": Combining Antipsychotic Medication in The Treatment of Schizophrenia. *J Prac Psych and Behav Hlth* 7:229-233.