Original Article

Prescription patterns of antipsychotics in the management of first episode psychosis at three psychiatric hospitals in Khartoum, 2018: A descriptive cross-sectional study

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Abstract

Background: First-Episode Psychosis (FEP) is defined as the first treatment contact with psychiatric service, regardless of the duration of symptoms. This study aims to determine the antipsychotics prescription patterns in FEP patients at three psychiatric hospitals in Khartoum. **Method:** A descriptive cross-sectional retrospective hospital-based study was conducted at Eltigani Elmahi, Taha Baasher, and Abd Elaal Aledrissi Psychiatric hospitals in Khartoum State, Sudan, during the period March to July 2018. Medical records of patients with FEP were identified and reviewed to look for demographic data, the onset of symptoms, investigations requested, and medications prescribed. Data were recorded and subjected to statistical analysis using the Statistical Package for Social Sciences. **Result:** Reviewing the medical records of the 98 FEP patients (66 males and 32 females) included in the study showed that the majority of patients (94.8%) were medicated with combinations of psychotropic medications. The most commonly used combination was Haloperidol, Olanzapine, Promethazine, and Benzodiazepines. And only 5.1% of the whole population was treated with an atypical antipsychotic (Olanzapine) as a monotherapy. **Conclusion:** Based on prescription patterns and requested investigations, there was a wide gap between the actual practice regarding antipsychotics prescriptions for FEP at the three psychiatric hospitals and the evidence-based guidelines in this respect.

Keywords: Antipsychotics, first-episode psychosis, prescription pattern

Introduction

A simple definition for First-Episode Psychosis (FEP) is the first treatment contact with psychiatric service regardless of the duration of symptoms. There is well-established evidence for the efficacy of antipsychotics in treating acute psychotic episodes. However, around 40% of psychotic patients have a poor response to typical antipsychotics and continue to develop moderate to severe, positive and negative psychotic symptoms.[1,2]

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Moreover, typical antipsychotics are linked to a wide range of side effects including extrapyramidal side effects such as tardive dyskinesia, which develops in around 20% of people medicated with typical antipsychotics.[3]

Although there is no specific medication has been proven as a first-line agent for the treatment of FEP, atypical antipsychotics are recommended by schizophrenia treatment guidelines as first-line medications,[4-7] as they have less extrapyramidal side effects compared with typical antipsychotics.[8] Nevertheless, they are notoriously known to cause obesity and metabolic syndrome (e.g. abnormal glucose and lipid metabolism).[8,9]

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This study was conducted due to the alarming increase in the incidence rate of psychosis in Sudan. Internationally, the trend toward more frequent use of second-generation antipsychotics (SGAs) over the first-generation antipsychotics has been reported in many countries between the 1990s and the early 2000s.[10,11] However, in Sudan, there are no enough studies about the changes in the prescription pattern of antipsychotics for the FEP after this shift toward increasing the use of SGAs. Therefore, this study aims to determine the trends of antipsychotics prescriptions for patients with FEP who attended three psychiatric hospitals in Khartoum State, Sudan.

Method

A descriptive cross-sectional retrospective, hospital-based study was conducted at Eltigani Elmahi, Taha Baasher, and Abd Elaal Aledrissi Psychiatric Hospitals, which are located at Khartoum state, Sudan, during the period of the study (March to July 2018).

All medical records of patients with FEP (aged 18–65 years) admitted to the inpatient and emergency units at the above-mentioned hospitals over the 5 months period of the study were included. An exclusion criterion was FEP patients treated in outpatient units during the same period.

The data were collected by the researcher using a structured checklist, which was piloted before the study. The checklist shows patient's demographic data and onset of symptoms, in addition to the prescribed medication(s). It also shows whether the baseline investigations were requested before prescribing the antipsychotic medication(s).

The collected data were entered into the Statistical Package for Social Sciences (SPSS) Version 22 program in order to be analyzed using descriptive statistical methods.

Results

Ninety-eight patients (67.3% males and 32.7% females) with FEP who met the inclusion criteria were admitted to Eltigani Elmahi, Taha Baasher, and Abd Elaal Aledrissi Psychiatric Hospitals during the period of the study. The majority of patients (51%) were admitted to Eltigani Elmahi Psychiatric Hospital and 26.5% of patients were admitted to Abd Elaal Aledrissi Psychiatric Hospital, whereas only 22.5% of patients were admitted to Taha Baasher Psychiatric Hospital. The highest percentage was for the first category 18–33 years (77.6%).

It is important to note that in 61.2% of patients, the symptoms started within 3 months prior to admission. In 10.2%, the symptoms began within 3–6 months prior to admission, while in 23.5%, the illness started more than 6 months prior to admission. However, time of onset was not mentioned in the medical records of 5 patients (5.1%). Therefore, they were treated as missed values during the process of the statistical analysis [Table 1].

According to the international guidelines of antipsychotics prescription, a number of investigations must be requested before prescribing an antipsychotic.[4-6] In this study, the blood glucose test was requested for 64.2% of patients. Regarding the cardiovascular system, pulse and blood pressure were examined in 49% and 38.8%, respectively, whereas only 4.1% underwent ECG analysis. Moreover, 83.7% of patients were asked about their Diabetes and cardiovascular history, and the nutritional status was assessed in only 38.8% of patients. However, no patient was subjected to measurement of weight, waist circumference, HbA1c, lipid profile, prolactin level, movement disorder assessment, and physical activity assessment.

Medications were categorized into four groups: Typical antipsychotic medications, atypical antipsychotic medications, adjunctive medications, and combined therapy [Table 2]. Typical antipsychotics were prescribed to 93.9% of patients: 90.2%

Table 1: Descriptive data of the studied participants (*n*=98)

Descriptive data	Percentage
Gender	
Males	67.3
Females	32.7
Age	
18-33 years	77.6
34-49 years	12.2
50-65 years	10.2
Distribution of patients among the three psychiatric hospitals	
Eltigani Elmahi	51
Abd Elaal Aledrissi	26.5
Taha Baasher	22.4
Time of onset of symptoms	
1 days to 3 months	64.5
More than 3 months to 6 months	10.8
More than 6 months	24.7

Table 2: Medications that prescribed to the patients included in the study

Medication	Percentage
Typical antipsychotic	93.9
Haloperidol	90.2
Fluphenazine	2.17
Haloperidol + Fluphenazine	6.5
Haloperidol + Zuclopenthixol	1.09
Atypical antipsychotic	83.7
Olanzapine	82.9
Risperidone	15.85
Quietiapine	1.22
Adjunctive medication	93.9
Promethazine	97.8
Diazepam	36.95
Lorazepam	27.17
Trihexyphenidyl	2.17
Combined therapy	94.8
Typical + atypical + adjunctive medication	80.6
Typical + adjunctive	17.2
Typical + atypical	1.08
Atypical + adjunctive	1.08

with Haloperidol alone, 2.17% with Fluphenazine alone, 6.5% with both Haloperidol and Fluphenazine, and only 1.09% was medicated with both Haloperidol and Zuclopenthixol, whereas atypical antipsychotics were prescribed to 83.7% of cases: 82.9% were medicated with Olanzapine, 15.85% with Risperidone, while only 1.22% was treated with Quetiapine. Furthermore, adjunctive medications were prescribed to 93.9% of cases in addition to antipsychotics: 97.8% were medicated with Promethazine, 36.95% with Diazepam, and 27.17% with Lorazepam, while only 2.17% of patients were prescribed Trihexyphenidyl. Last, ninety-three patients (94.8%) were medicated with combinations: 80.6% were prescribed typical + atypical + adjunctive medication, 17.2% typical + adjunctive, 1.08% typical + atypical, and 1.08% was prescribed atypical + adjunctive. The most commonly used combination was Haloperidol + Olanzapine + Promethazine + Benzodiazepine.

Assessment of adherence to the guidelines of antipsychotics prescriptions was based on two criteria: The requested examinations and prescribed medications. Seven out of the fourteen investigations listed on the guidelines were not requested for any patient in the study. In addition, random blood sugar test was more likely to be requested than fasting blood sugar test. Regarding to the prescribed medications, only 5.1% of the whole population were prescribed an atypical antipsychotic (Olanzapine) as a monotherapy, whereas the majority of patients were treated with typical antipsychotics combined with other medication (atypical antipsychotic and/or anticholinergic and/or benzodiazepine). Therefore, based on the prescription patterns and requested investigations, there was a wide gap between the actual practice regarding antipsychotics prescriptions for FEP at the three psychiatric hospitals where the study was conducted and the evidence-based guidelines in this respect.

Discussion

Ninety-eight medical records of patients with FEP were included in the study. The majority of cases were adult men, this might be due to the imbalance in the number of available beds (proportion of males' beds is larger than females' beds in Eltigani Elmahi and Abd Elaal Aledrissi psychiatric hospitals, while Taha Baasher contains equal proportions for both sexes). Moreover, according to a meta-analysis showing the sex differences in the risk of schizophrenia,[12] it has been noticed that the incidence of schizophrenia in males is higher than in females; the ratio of men to women is 1.4 to 1.[12]

A considerable proportion of patients presented late to psychiatric services, this might be socially related due to fear of stigma. It might also be culturally related; as many people interpret the symptoms of psychosis as sorcery, they tend to bring the patient to a traditional or religious healer first rather than to a psychiatrist. Therefore, they do not bring the patient to the psychiatric hospital unless the situation gets worse. According to a systematic review and meta-analysis study,[13] nearly 50% of patients with mental disorders in Africa choose traditional and religious healers as their initial care providers. The majority of cases in this study have been treated with typical antipsychotics (mainly Haloperidol) to tranquilize the patient while being in the acute/disturbed/excitement state.

According to a meta-analysis, a prolonged period of untreated psychosis is associated with lower chance of functional recovery and symptomatic treatment of the first psychotic episode,[14] as well as higher risk of treatment resistance.[15] Also, another study that conducted in order to evaluate the duration of untreated psychosis found a significant relationship between prolonged duration of untreated psychosis and risk of relapse at 6-year follow-up. Hence, it is advisable to seek medical assistance once the symptoms appear.[16]

Guidelines recommend initiating the treatment with only one antipsychotic agent at a time.[17,18] If no adequate response is achieved or the patient's symptoms are resistant to monotherapy, another antipsychotic could be added at a separate interval.[18] Atypical antipsychotics (other than Olanzapine) are recommended as first-line and second-line treatment for FEP patients due to their better tolerability than typical antipsychotics,[19] as they have lower risk of extrapyramidal side effects.[18]

According to some studies comparing atypical with typical antipsychotics, atypical antipsychotics showed greater long-term benefits. Higher treatment retention, remission rates, and patients adherence were observed with Olanzapine compared to Haloperidol in a 2-year study comparing both agents.[20] In another long-term study comparing Risperidone and Haloperidol, the median time to relapse was significantly longer in the Risperidone group (466 vs 205 days).[21]

In contrast to the guidelines, the majority of patients included in this study (94.8%) were treated with more than one psychotropic medication (typical and/or atypical and/or anticholinergic and/or benzodiazepine). The most commonly used combination was (Haloperidol + Olanzapine + Promethazine + Benzodiazepine). Promethazine was used concomitantly with Haloperidol to overcome the expected extrapyramidal side effects of Haloperidol (91.8% of cases). Trihexyphenidyl was added in cases at which extrapyramidal side effects appeared in spite of the concomitant use of Promethazine (2% of cases). Benzodiazepines were used as anxiolytics for patients presenting with excitement state in addition to psychotropic medications (60.1% of cases). Studies have shown that use of benzodiazepines as adjunctive agents to typical antipsychotics can improve insomnia, agitation, anxiety, and psychotic symptoms.[22,23] Although a recent study comparing one group of psychotic patients taking antipsychotics alone with another group treated with benzodiazepines in addition to antipsychotic therapy showed no difference between the two groups in term of violence and aggression[24], there is small scientific evidence that supports the clinical use of concomitant medications and their use can be linked to side effects, including a worsening of

psychotic symptoms.[25] Moreover, combined therapy increases the risk of adverse drug reactions and results in poorer patient compliance with therapy.[26-28]

Regarding the side effects of antipsychotics, according to a retrospective chart review study that compared long-term incidence rates of the metabolic syndrome in FEP who were medicated with typical and atypical antipsychotics, it has been noticed that patients treated with atypical antipsychotics were associated with three times higher incidence rate of metabolic syndrome, and two times average increase in weight and body mass index.[29]

In addition, a prospective study that examined the cumulative incidence of definitive tardive dyskinesia at 1, 3, and 6 months of antipsychotic treatment among psychiatric patients found that patients medicated with typical antipsychotics were approximately two times more likely to develop definitive tardive dyskinesia during the period of the study than those medicated with atypical antipsychotics (P <.001). This difference was found although patients in the atypical antipsychotic group were significantly older and had more severe extrapyramidal symptoms at baseline than those in typical antipsychotics group.[30]

Therefore, guidelines recommend requesting baseline investigations before starting antipsychotic treatment in order to avoid exposing patients to a wide range of adverse effects of antipsychotics.[17] Regarding our study, it has been noticed that there is a variation in the investigations being requested. For example, blood glucose level, pulse, blood pressure, and ECG were ordered for 64.2%, 49%, 38.8%, and 4.1% of patients, respectively. On the other hand, measurements of weight, waist circumference, HbA1c, lipid profile, and prolactin level were never requested. An explanation for that maybe there are no clear written protocols in the three hospitals where the study was conducted or otherwise adherence depends on the degree of awareness of the prescribing doctor about these guidelines. Hence, adherence to the international guidelines becomes quite challenging.

Continuous studies on antipsychotics prescription patterns for FEP patients are beneficial to monitor the use of these medications in the practice setting. The above-mentioned results are important for primary care physicians to aid in prescribing the appropriate medications for patients with FEP, considering the efficacy and safety profile of the chosen medication as well as the clinical characteristics and baseline investigations of the patient. Therefore, following the international guidelines of antipsychotic prescription and requesting baseline investigation prior to initiating the treatment will definitely improve the health outcomes of patients with FEP.

Conclusion

Typical antipsychotics were routinely used to stabilize disturbed and/or excited patients at the three hospitals. Atypical antipsychotics are also used for treatment and as maintenance therapy. Combined therapy is the most commonly used trend in treating FEP patients. Based on prescription patterns and requested investigations, there was a wide gap between the actual practice regarding antipsychotic prescriptions for FEP at the three psychiatric hospitals where the study was conducted and the evidence-based guidelines in this respect.

Ethical approval

The ethical clearance (FPEC-09-2018) was obtained from the Ethical Committee of the Faculty of Pharmacy, University of Khartoum on March, 2018. Additional approval for checking the medical records was obtained from Eltigani Elmahi, Taha Baasher, and Abd Elaal Aledrissi Psychiatric Hospitals. All checklists were coded with ensuring confidentiality throughout the study.

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Conflict of interest

There is no conflict of interest.

References

1. Kelly DL, McMahon RP, Weiner E, Boggs DL, Dickinson D, Conley RR, *et al.* Lack of beneficial galantamine effect for smoking behavior: A double-blind randomized trial in people with schizophrenia. Schizophr Res 2008;103:161-8.
2. Sacco KA, Creeden C, Reutenauer EL, Vessicchio JC, Weinberger AH, George TP. Effects of atomoxetine on cognitive function and cigarette smoking in schizophrenia. Schizophr Res 2009;107:332-3.
3. Con- CD, Drugs AA, Inven- BD, Edition S, Mania Y, Scale R, *et al.* Letters to the editors high-dose ziprasidone monotherapy in bipolar i disorder patients with depressed or mixed episodes clinical experience with carbamazepine overdose relationship between serum concentration and neurological severity. J Clin Psychopharmacol 2008;28:240-60.
4. Moore TA, Buchanan RW, Buckley PF, Chiles JA, Conley RR, Crismon ML, *et al.* The texas medication algorithm project antipsychotic algorithm for schizophrenia: 2006 Update. J Clin Psychiatry 2007;68:1751-62.
5. Falkai P, Wobrock T, Lieberman J, Glenthoj B, Gattaz WF, Moller HJ, *et al.* World federation of societies of biological psychiatry (WFSBP)-Guidelines for biological treatment of schizophrenia, part 1: Acute treatment of schizophrenia. World J Biol Psychiatry 2005;6:132-91.
6. Lehman AF, Lieberman JA, Dixon LB, McGlashan TH, Miller AL, Perkins DO, *et al.* Practice guideline for the treatment of patients with schizophrenia, second edition. Am J Psychiatry 2004;161:1-56.
7. Grover S, Avasthi A. Clinical practice guidelines for the management of schizophrenia in children and adolescents. Indian J Psychiatry 2019;61:277-93.
8. Singh R, Bansal Y, Medhi B, Kuhad A. Antipsychotics-induced metabolic alterations: Recounting the mechanistic insights, therapeutic targets and pharmacological alternatives. Eur J

Pharmacol 2019;844:231-40.

9. Xu H, Zhuang X. Atypical antipsychotics-induced metabolic syndrome and nonalcoholic fatty liver disease: A critical review. Neuropsychiatr Dis Treat 2019;15:2087-99.
10. Yang M, Barner JC, Lawson KA, Rascati KL, Wilson JP, Crismon ML, *et al.* Antipsychotic medication utilization trends among Texas veterans: 1997-2002. Ann Pharmacother 2008;42:1229-38.
11. Gallego JA, Bonetti J, Zhang J, Kane JM. Prevalence and correlates of antipsychotic polypharmacy: A systematic review and meta-regression of global and regional trends from the 1970s to 2009. Schizophr Res 2012;138:18-28.
12. Aleman A, Kahn RS, Selten J-P. Sex differences in the risk of schizophrenia: Evidence from meta-analysis. Arch Gen Psychiatry 2003;60:565-71.
13. Burns JK, Tomita A. Traditional and religious healers in the pathway to care for people with mental disorders in Africa : A systematic review and meta- analysis. Soc Psychiatry Psychiatr Epidemiol 2015;50:867-77.
14. Perkins DO, Gu H, Boteva K, Lieberman JA. Relationship between duration of untreated psychosis and outcome in first-episode schizophrenia: A critical review and meta-analysis. Am J Psychiatry 2005;162:1785-804.
15. Bozzatello P, Bellino S, Rocca P. Predictive factors of treatment resistance in first episode of psychosis : A systematic review. Front Psychiatry 2019;10:67.
16. De Haan L, Linszen DH, Lenior ME, De Win ED, Gorsira R. Duration of untreated psychosis and outcome of schizophrenia: Delay in intensive psychosocial treatment versus delay in treatment with antipsychotic medication. Schizophr Bull 2003;29:341-8.
17. Kuipers E, Yesufu-Udechuku A, Taylor C, Kendall T. Management of psychosis and schizophrenia in adults: Summary of updated NICE guidance. BMJ 2014;348:g1173.
18. Galletly C, Castle D, Dark F, Humberstone V, Jablensky A, Killackey E, *et al.* Royal Australian and New Zealand college of psychiatrists clinical practice guidelines for the management of schizophrenia and related disorders. Aust N Z J Psychiatry 2016;50:410-72.
19. Buchanan RW, Kreyenbuhl J, Kelly DL, Noel JM, Boggs DL, Fischer BA, *et al.* The 2009 schizophrenia PORT psychopharmacological treatment recommendations and summary statements. Schizophr Bull 2010;36:71-93.
20. Green AI, Lieberman JA, Hamer RM, Glick ID, Gur RE, Kahn RS, *et al.* Olanzapine and haloperidol in first episode psychosis: Two-year data. Schizophr Res 2006;86:234-43.
21. Schooler N, Rabinowitz J, Davidson M, Emsley R, Harvey PD, Kopala L, *et al.* Risperidone and haloperidol in first-episode psychosis: A long-term randomized trial early psychosis global working group. Am J Psychiatry 2005;162:947-53.
22. Wolkowitz OM, Pickar D. Benzodiazepines in the treatment of schizophrenia. A Review and re-appraisal Am J Psychiatry 1991;148:714-26.
23. Stimmel GL. Benzodiazepines in schizophrenia. Pharmacotherapy 1996;16:166S-8S.
24. Baranchik S, Stryjer R, Weizman A, Shelef A. Add-on benzodiazepines for psychosis-induced aggression. Int Clin Psychopharmacol 2019;34:119-23.
25. Singh MM, Kay SR. Therapeutic antagonism between anticholinergics and neuroleptics: Possible involvement of cholinergic mechanisms in schizophrenia. Schizophr Bull 1978;4:3-6.
26. Beyth RJ, Shorr RI. Epidemiology of adverse drug reactions in the elderly by drug class. Drugs Aging 1999;14:231-9.
27. Fattinger K, Roos M, Vergères P, Holenstein C, Kind B, Masche U, *et al.* Epidemiology of drug exposure and adverse drug reactions in two Swiss departments of internal medicine. Br J Clin Pharmacol 2000;49:158-67.
28. Marder SR. Overview of partial compliance. J Clin Psychiatry 2003;16:3-9.
29. De Hert M, Schreurs V, Sweers K, Van Eyck D, Hanssens L, Šinko S, *et al.* Typical and atypical antipsychotics differentially affect long-term incidence rates of the metabolic syndrome in first-episode patients with schizophrenia: A retrospective chart review. Schizophr Res 2008;101:295-303.
30. Dolder CR, Jeste DV. Incidence of tardive dyskinesia with typical versus atypical antipsychotics in very high risk patients. Biol Psychiatry 2003;53:1142-5.