Original Article

Prevalence and Correlates of "High Dose" Antipsychotic Prescribing: Findings from a Hospital Audit

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Abstract

Background: High dose antipsychotic prescribing is common in psychiatric care, despite a lack of its benefit from research evidence. While several studies have explored the prevalence and factors associated with high dose antipsychotic prescribing, no such report has emanated from a developing country like Nigeria. **Aim:** The aims of this study were to determine the prevalence of high dose prescribing among in-patients at a tertiary psychiatric hospital and to determine the pattern of antipsychotic drugs prescribed. **Materials and Methods:** An audit of in-patients at a regional tertiary psychiatric facility was carried out. We examined case notes and conducted oral interviews where necessary, on all patients receiving antipsychotics using a proforma designed for the study. **Results:** The prevalence of high dose prescribing was 38% (65/171) using a prescribed daily dose/defined daily dose ratio of 1.5. The rate of antipsychotic polypharmacy was 7% (12/171). The atypical antipsychotic, olanzapine was the most commonly prescribed antipsychotic in monotherapy. Predictors of high dose prescribing were diagnoses ($P = 0.04$), polypharmacy ($P = 0.04$), a history of previous in-patient care ($P = 0.02$), and use of anticholinergic drugs ($P = 0.01$). **Conclusions:** High dose prescribing was common among in-patients audited. Further studies are needed to examine factors that promote "high dose" prescribing.

Keywords: Antipsychotics, Defined daily dose, In-patients, Polypharmacy

Introduction

High dose antipsychotic prescribing is a common practice among psychiatrists, although evidence for its efficacy is limited but not supported by controlled studies.[1] A recent in-patient survey in the UK revealed a rate of about 20%.[2] This practice has persisted despite the lack of convincing evidence to support its effectiveness.[3] On the contrary, increasing evidence supported by functional neuro-imaging studies suggests that low to moderate doses of antipsychotics may be equally as effective in preventing and ameliorating adverse effects.[4]

There is as yet no consensus on what constitutes high dose prescribing. However, a chlorpromazine equivalent in excess of 1000 mg/day is considered as high dose prescribing. Furthermore, doses exceeding the maximum daily dose as stated in the British National Formulary (BNF) or a combination of percentages of maximum daily dose exceeding 100% if a patient is prescribed more than one antipsychotic are considered as high dose.[5] More recently, multiples of the defined daily dose (DDD) are used in the determination of high dose antipsychotic prescribing.[6-8] The DDD has been found to correlate well with chlorpromazine equivalents and percentages of the BNF maximum daily dose.[9]

Studies have shown that high dose prescriptions are commoner among in-patients compared to out-patients, though the specific in-patient setting was not specified.[5] Also, treatment resistance, longer duration of illness, history of illness, and antipsychotic polypharmacy are other factors.[10-12]

Polypharmacy has been identified as a predictor of high dose prescribing.[13] Earlier reports from Nigeria suggest that polypharmacy and high dose prescribing are common.[14,15] A recent review has suggested the possibility of racial differences in prescription patterns influenced by symptom severity and genetic variations.[16]

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The aims of this study were to determine the prevalence of high dose prescribing among in-patients at a tertiary psychiatric hospital, to determine the pattern of antipsychotic drugs prescribed and compare same with findings from an earlier study in this environment. We also aimed to determine the correlates (socio-demographic and clinical) of high dose prescribing. Our findings we believe would help alert clinicians to the detrimental effects of this pattern of prescribing with the resultant effect of improving patient outcomes and reduce iatrogenic factors that increase patient morbidity and mortality.

Materials and Methods

Study design

A cross-sectional analytic study was carried out in a psychiatric in-patient facility located in the south–south geopolitical zone of Nigeria in March 2012.

Study setting

We audited the prescribing patterns and dosing of antipsychotics at the Federal Neuropsychiatric Hospital, Uselu, Benin City, Nigeria (FNPHU). The FNPHU is a facility with 12 wards including male, female, addiction, and child and adolescent (C and A) wards. For this study, the C and A ward was excluded.

In Nigeria, psychiatric services are poorly developed. A large proportion of patients receive care in large psychiatric hospitals or psychiatry departments in teaching and general hospitals. These facilities are located almost exclusively in urban areas. Community care is scant, with a few hospitals now trying to pioneer community and rehabilitative services in their catchment areas. Subsequently, out-patient and in-patient care is closely linked with tertiary psychiatric services.

Participants

Participants were patients aged 18 yr and above on admission at the wards of the facility in March 2012. To be included, they were to be on at least one antipsychotic medication regardless of the clinical diagnoses.

Instruments

We developed a proforma containing three sections: (i) socio-demographic, (ii) illness, and (iii) pharmacotherapy characteristics. Using the proforma, we obtained information regarding the above-listed characteristics including patterns of antipsychotics prescription and dosage regimes.

For this study, a "high dose" meant a ratio of prescribed daily dose (PDD) to defined daily dose (DDD) >1.5.[8,17] We also determined a "high dose" antipsychotic prescription using doses in excess of 1 g/day in chlorpromazine equivalent (CPZeq) and dosage exceeding recommended BNF limits or in the case of multiple antipsychotics prescribed, a combination of percentages of individual antipsychotics of maximum BNF limits exceeding 100%. We based our choice of the PDD/DDD ratio on the fact of the unreliability of the CPZeq criteria in the view of an increasing use of atypical antipsychotics and the nonuniversal application of a single country's (BNF) drug formulary. These limitations are factored in the DDD classification.

Ethical considerations

We obtained ethical clearance from the Ethics and Research Committee of the Federal Neuropsychiatric Hospital, Uselu. For each patient, that required corroboration of their details if incomplete data were found; we explained the nature and purpose of the study to them and obtained a signed written consent.

Procedure

After obtaining written consent, we filled the proforma with necessary information from the case notes. We also interviewed some patients especially in situations where some other information relevant for the study was not provided in the case notes.

Data analysis

The data were analyzed using SPSS (Chicago, Illinois, USA) version 16 and summarized into means and standard deviations. Categorical and continuous data were compared using Chi-squared and student *t*-test, respectively. Significant associations between high dose antipsychotic prescription and socio-demographic and clinical variable were entered into a binary logistic regression model to identify predictors. Level of significance was set at $P < 0.05$.

Results

Socio-demographic characteristics

A total of 171 in-patients met the study inclusion criteria. Two-fifths (40.9%; 70/171) of the respondents were aged between 18 and 29 yr. A majority were males (70.2%; 120/171) and unemployed (74.3%; 127/171). About half of the in-patients resided in an urban area (49.1%; 84/171). The commonest ethnic groups were Benin (25.1%) and Ibo (17%). Nearly all were Christians (96.5%; 165/171), single (81.3%; 139/171), with over half with at least a secondary level of education (63.7%; 109/171).

Illness characteristics

Over half (56.7%; 97/171) and one third (36.3%; 62/171) of the respondents satisfied the criteria for the diagnostic grouping of F20-29 (schizophrenia, schizoptypal, and delusional disorders) and F31 (bipolar affective disorders), respectively. Over half (53.2%; 92/171) had no previous admission at this facility, half (50.9%; 87/171) had a history of violence and just over a third (39.8%; 68/171) had a history of co-morbid substance use.

Prescribing patterns

Nearly (93.0%; 159/171) all the respondents were on one

antipsychotic, with olanzapine being the most commonly prescribed. A minority (7%; 12/171) were on two antipsychotics with the haloperidol and chlorpromazine combination being the most commonly prescribed. Just over two-thirds (45.6%; 78/171) were on the anticholinergic; benzhexol.

Employing a PDD/DDD ratio >1.5, we found that 65 of the participants (38%) were on high doses of antipsychotics prescribed. The proportion of participants on high dose reduced to 9.9% (17/171) when we used the chlorpromazine equivalent in excess of 1000 mg/day criteria. We observed a further reduction to 5.3% (9/171) when we classified according to excess of BNF maximum recommended daily dose criteria.

Table 1: Contigency table showing association between patient characteristics and high dose prescribing

Variables	High dose		Statistic
	Yes	No	
Gender			
Male	46	74	χ^2=0.08, *P*=1.00
Female	19	32	
Occupation			
Employed	16	28	χ^2=0.068, *P*=0.79
Unemployed	49	78	
Residence			
Urban	32	52	χ^2=1.976, *P*=0.37
Rural	8	21	
Semiurban	25	33	
Religion			
Christian	63	102	χ^2=0.058, *P*=0.81
Muslim+others	2	4	
Marital status			
Single+widowed+separated	55	132	χ^2=0.158, *P*=0.69
Married	10	22	
Educational status			
<12 yr of formal education	52	85	χ^2=0.001, *P*=0.69
>12 yr of formal education	13	21	
Diagnosis			
Bipolar disorder	31	31	χ^2=8.994, *P*=0.03
Depression	1	9	
Schizophrenia	33	64	
Mental disorders associated with substance use	0	2	
On anticholinergics?			
Yes	40	38	χ^2=10.719, *P*=0.001
No	25	68	
Co-morbid substance use			
Yes	25	43	χ^2=0.075, *P*=0.79
No	40	63	
History of violence			
Yes	35	52	χ^2=0.370, *P*=0.54
No	30	54	
Number of antipsychotics			
≥2	10	2	χ^2=11.12, *P*<0.001
1	55	104	

Correlates of high dose prescribing

We found no significant associations between high dose prescribing (calculated using a PDD/DDD ratio >1.5) and the socio-demographic variables of gender ($P = 1.00$), being employed ($P = 0.794$), living in an urban area ($P = 0.37$), religion ($P = 0.81$), marital status ($P = 0.69$), educational status ($P = 0.983$), number of previous admissions ($P = 0.061$), history of violence ($P = 0.54$), and co-morbid substance use (0.791). Patients with a diagnoses of bipolar disorder ($P = 0.030$), polypharmacy ($P < 0.001$), and prescribed an anticholinergic ($P < 0.001$) were significantly more likely to be on high dose antipsychotics. Half (50%) of the patients with bipolar disorder, compared to 34% of those with schizophrenia spectrum disorders, then 10% of those with depression were prescribed high doses of antipsychotics [Table 1].

Patients on high dose antipsychotics were prescribed on average more antipsychotics, 1.15 vs 1.02 ($t = 3.450$, df = 169, $P < 0.001$), and had a higher number of previous admissions, 1.22 vs 0.63 ($t = 2.771$, df = 169, $P = 0.006$). There were no significant differences in terms of age ($P = 0.913$) and duration of untreated symptoms (0.474).

We entered variables (categorical and continuous) that were significantly associated with high antipsychotic dose into a binary logistic regression model and found number of antipsychotics ($P = 0.040$), number of previous admissions ($P = 0.023$), use of anticholinergics ($P = 0.011$), and diagnoses ($P = 0.044$), to be independent predictors of high dose antipsychotic prescription. [Table 2].

Discussion

High dose prescribing was a common practice by psychiatrists at the center audited. On the contrary, the prevalence of polypharmacy was very low. We also observed a change in the types of antipsychotics prescribed with a change toward more atypical antipsychotic use. Diagnoses of the schizophrenias, higher number of previous admissions, and use of anticholinergics were predictors of high dose antipsychotic prescriptions.

Table 2: Binary logistic regression showing predictors of high dose prescribing

Variables	B	SE	ExpB	Wald	*P* value	95% CI
Diagnoses	0.360	0.178	1.434	4.086	0.04	0.002 – 2.110
Number of antipsychotics	-1.696	0.838	0.183	4.100	0.04	0.031 – 2.033
Number of previous admissions	-0.319	0.138	0.727	5.335	0.02	0.493 – 1.358
Use of anticholinergics	0.973	0.347	2.645	7.846	0.01	0.055 – 2.967

We discuss our findings with the following limitations in mind. Our audit was from a single center and may not reflect prescribing practices across the country. We cannot, therefore, generalize our current findings to other psychiatric hospital settings. Second, we did not use standardized measures to assess the severity of illness among patients whose prescriptions we studied. Illness severity especially among in-patients in general adult settings may influence prescribing patterns. We also did not factor anthropometric factors like the body mass index. The sample comprised all patients on antipsychotics and unlike previous reports that examined distinct diagnostic groups and may have influenced the overall prevalence rate.

The prevalence of high dose prescribing in this study was 38% using the criteria of a ratio >1.5 of the PDD to that of the DDD for the drug prescribed. The PDD/DDD ratio of >1.5 employed here is similar to that used in the study by Barbui, *et al.*,[8] in their prospective study in Italy. Though a PDD/DDD ratio >1 may be argued as indicative of a high dose, it has been further argued that a larger ratio may be more appropriate to in-patient care where acute psychotic states often require higher antipsychotic doses and the use of p.r.n parenteral antipsychotics. That said, we observe that the prevalence observed in this audit was much higher than that from the Italian study.[8] A possible reason for the difference in prevalence might be the type of in-patient care offered. At our setting, care is offered to a large proportion of patients who are involuntarily admitted unlike the case in Italy.

This prevalence fell to 9.9% and 5.3% using the CPZeq and BNF maximum dose criteria, respectively. Though the DDD has been reported to correlate well with the BNF and CPZeq criteria, respectively,[9] further research is needed to determine what should be considered an appropriate cutoff for high dose antipsychotic prescription. Comparing our findings with similar studies that employed either the CPZeq or BNF criteria, we note that the prevalence was lower than rates obtained in the UK[18] and Hong Kong.[5,19,20] The prevalence ratio was highest among patients with bipolar disorders and least among patients with severe depression with psychotic symptoms. It is possible that prescription patterns may be reflective of in-patient agitation or aggression which we did not control for in this audit.

Of note was the low prevalence of polypharmacy in this audit. Polypharmacy has been reported in previous local studies to be commonplace[14,15] and has been identified as a strong predictor of high dose prescribing.[7,8] The low prevalence seen in this study may reflect clinicians adherence to established guidelines on monotherapy as a majority of in-patients (93%) were on a single antipsychotic.

Unlike in previous reports, we found no significant associations between socio-demographic variables and high dose prescribing. As in the study in Hong Kong,[20] a prior history of violence was not associated with high dose prescribing in our study. Unlike in the study in the UK,[9] where reasons for polypharmacy included treatment resistance, switching antipsychotics, and control of acute positive symptom exacerbation, we observed that chlorpromazine was the commonest antipsychotic included in combination treatment or polypharmacy. One possible reason for this common combination by clinicians at this center was to utilize the sedative properties of chlorpromazine in the treatment of individuals with psychotic disorders. No doubt, this practice is not evidence based and the use of benzodiazepenes or atypical antipsychotics with better sedative profiles are desirable. Use of routine anticholinergics was common and was predictive of high dose prescriptions.

We also noted a change in the patterns of antipsyhotics prescribed at this center. In a previous study on psychotropic drug prescribing at this hospital in 2007,[21] it was found that haloperidol was the most commonly prescribed antipsychotic drug, followed by chlorpromazine and trifluoperazine. This pattern contrasts with our findings in which olanzapine; risperidone and trifluoperazine were the most commonly prescribed. This change in prescribing patterns may be due to an increased availability of atypicals in generic forms, which are more affordable. Furthermore, clinicians may favor the better side effect profile as it pertains to extrapyramidal side effects.

None of the patients included in this audit had undergone an electrocardiogram (ECG) prior to the clinicians increasing to dose ranges considered to be high. Higher doses carry an increased risk of untoward cardiac events as antipsychotic drugs are known to prolong Q-T intervals. Clinicians would require sensitization and education on this practice which may result in adverse physical health outcomes for their patients. The Royal of College of Psychiatrists recommends routine ECG for patients scheduled to receive high dose antipsychotics.[22] A similar survey in Hong Kong also observed that a very small minority of patients on high dose antipsychotics had a prior ECG.[20]

This study provides useful findings in a setting where similar research has not been conducted and should serve as a template for future research. A nationwide survey of the prevalence and determinants of high dose prescribing is desirable and may inform evidence-based guidelines and promote a change in practice by clinicians.

Conclusion

High dose prescribing is common among in-patients. Use of anticholinergics, polypharmacy, a history of previous admissions and diagnoses were predictors of high dose prescribing. Efforts to reduce this practice are highly desirable.

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