Polypharmacy in psychiatric out-patient practice in northern Nigeria

AB Adeponle[1], AO Obembe[2], SO Adeyemi[1], GT Suleiman[1]
[1]Neuro-Psychiatric Hospital, Kaduna, Nigeria,
[2]Department of Psychiatry, Uthman Dan Fodio University, Sokoto, Nigeria

Abstract
Objective: To describe and analyze patterns of polypharmacy among psychiatric outpatients in northern Nigeria and identify predictors of psychotropic polypharmacy. **Method:** A cross-sectional study, using chart review of new patients at out-patient clinics of two regional psychiatric hospitals in northern Nigeria, measuring rates, patterns and predictors of psychotropic polypharmacy. **Results:** A total of 278 patients were seen, of whom 92% were given two or more psychotropic agents. The pattern of psychotropic polypharmacy revealed that total, multi-class and adjunctive polypharmacy rates were high, while augmentation and same class polypharmacy rates were low. Age of respondent and diagnosis were the factors associated with total polypharmacy. **Conclusion:** The complex interplay of factors influencing physician prescription practices requires that a more pragmatic approach be adopted in efforts to curtail polypharmacy practice, rather than a wholesale, absolute condemnation of the practice.

Keywords: Psychiatric; Polypharmacy; Patterns; Nigeria.

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Introduction

Polypharmacy in psychiatry refers to the concurrent use of two or more psychotropic medications in a patient. It is an old practice that is increasingly becoming the norm rather than the exception. In the 1960s and 70s, a limited understanding of therapeutics resulted in psychotropic polypharmacy that was completely irrational and naïve, although, advances in psycopharmacology and a better understanding of the principles of therapeutics seems not to have reduced its occurrence. Reported prevalence rates vary between 13%-90%, with continuing debate about the merits and demerits of the practice.[1,2,3,4] In more recent times, some investigators in the developed world have called for the recognition of 'rational polypharmacy' and the formulation of principles to regulate its practice.[5,6] These calls have arisen from the growing body of experience which indicates that polypharmacy may be beneficial for a subset of patients who respond poorly to antipsychotic monotherapy. The theoretical rationale for the use of combination of psychotropic drugs include boosting the effectiveness of monotherapy, optimizing the dopamine-2 receptor occupancy in refractory patients, targeting a diverse range of receptors and the treatment of patients with partial, inadequate or no response.[5,6,7] It is held that polypharmacy, in such instances, may lead to better symptom relief and functional outcomes with minimization of side-effects associated with higher doses of any single drug. However, it has been pointed out that much of the evidence supporting psychotropic polypharmacy appears to come from clinical experience, small clinical trials and case reports. There is therefore a need for more systematic research and the drawing up of guidelines for polypharmacy practice.[1,3] Many have thus cautioned against enthroning a culture of 'eminence-based' clinical practice as against that which is 'evidence-based'.[1,8,9] In this regard, some proponents of 'rational polypharmacy' have sought to draw up principles and clinical guidelines for use when considering whether or not to use polypharmacy. Preskorn (1995)[10], for example, presents the following as conditions under which clinicians may justifiably use polypharmacy;

i. To treat two pathophysiologically distinct but co-morbid illnesses in the same patient in contradistinction to treating the same condition or two 'co-morbid' syndromes in the same patient
ii. To treat an adverse effect produced by the primary drug
iii. To provide acute amelioration while awaiting the delayed effect of another medication
iv. To treat intervening phases of an illness
v. To boost or augment the efficacy of the primary treatment

In most developing countries, physicians are taught to embrace rational drug prescribing, defined as the use of the least number of drugs to obtain the best possible effect in the shortest period and at a reasonable cost.[11] Conversely, they are encouraged to eschew the use of polypharmacy, as it is associated with increased likelihood of adverse drug reactions and toxicity, increased risks of medication non-compliance and avoidable wastage of financial resources.[12,13] The issue of wastage of scarce resources, which is

Correspondence:
Dr AB Adeponle
Federal Neuro-Psychiatric Hospital, PMB 2187, Kaduna, Nigeria
email: dradeponleab@yahoo.com

inherent in polypharmacy practice, has necessarily been a major point in discussions of the merits and demerits of the practice, given the fact that in most developing, and African countries, competing needs are many and public health resources are often inadequate.[9] However, studies of psychotropic drugs prescription indicate that polypharmacy is common in psychiatric practice in most developing countries , in spite of admonitions to the contrary.[12,13,14] In Nigeria, earlier studies of psychotropic drugs prescription in psychiatric practice found that polypharmacy is high, with the authors emphasizing the need for clinicians to comply with acceptable pharmacotherapeutic principles so as to avoid unnecessary waste of scarce resources and to improve prescription practice.[13,16,17] More than a decade after the last of these studies was carried out, there has undoubtedly been an increase in number, as well as a better spread of psychiatric services and personnel in the country. Yet, anecdotal observations indicate that prescription practices are far from ideal, polypharmacy appears to be on the increase, local prescription practice guidelines are lacking and there is little or no continuing medical education for physicians. Given the latter prevailing circumstances, it seems hardly surprising that polypharmacy practice prevails among Nigerian physicians. Perhaps it is time to review the practice if clinicians feel so strongly drawn to, and persist, in using it. We need to make efforts to elicit the factors that may contribute to the practice of polypharmacy by practitioners, sensitize them to these and also attempt to draw up guidelines if practitioners feel so compelled to use polypharmacy. In this regard, the present study set out with the following aims:

i) To describe and analyze patterns of psychotropic polypharmacy for new patients seen at the out-patient clinics of two Federal Neuro-Psychiatric Hospitals in northern Nigeria (Kaduna and Sokoto, respectively)
ii) To Identify possible predictors of psychotropic polypharmacy

Method

The study employed a cross-sectional survey, involving new patients, first time attendees, with no history of previous contact with orthodox psychiatric services, seen consecutively over a month period at the general outpatient clinics of the two hospitals in the month of July 2004. The two hospitals are the major treatment and referral centres for mental illness in the northwest and north central parts of the country and service provision at the two hospitals is of a similar nature i.e. emergency, inpatient admission and general outpatient clinics, provided within the premises off the hospitals. The two hospitals are staffed by an equivalent complement of consultant psychiatrist staff (3 each), resident doctors, nursing staff and social workers. The outpatient clinics are run mainly as walk-in clinics and the majority of patients seen do not arrive with referrals, or prior contact with orthodox general medical services, with the visit to the outpatient clinic being their first contact with orthodox psychiatric care.

Data collection involved an evaluation of the case file of each patient at the end of clinic for information on socio-demographics, medications, co-existing illnesses, diagnosis, cadre of doctor. Since the study was cross-sectional in nature, data collection for each individual patient was done once, on the day the patient was first seen in the outpatient clinic. The attending doctors were unaware of the study for the duration of data collection. The diagnoses were reviewed by the authors to ensure that enough information was elicited to make International Classification of Diseases (ICD-10) diagnoses.

Data analysis was done with aid of a statistical package, SPSS for Windows.[18]

Results

A total of 278 new patients were seen during the study period, comprising of 161(57.9%) males and 117(42.1%) females. A summary of socio-demographic and clinical attributes, of respondents, appear in Table 1 and Table 2 respectively.

Table 1: Socio-demographic characteristics of respondents by total polypharmacy

	Polypharmacy n (%)	*No Polypharmacy* n (%)
Characteristic		
Age (years)		
<10	3 (1.5)	10(13.5)
11-20	37(18.1)	20(27)
21-30	99(48.5)	25(33.8)
31-40	35(17.2)	5(6.8)
41-50	15(7.4)	6(8.1)
>51	15(7.4)	8(10.8)
Gender		
Male	124 (60.8)	37 (50)
Female	80 (39.2)	37 (50)
Marital status		
Single	97(47.5)	44 (59.5)
Married	97 (47.5)	27(36.5)
Divorced	9 (4.4)	1 (1.4)
Widow	1 (0.5)	2 (2.7)
Employment status		
Unemployed	124 (60.8)	50(67.6)
Employed	80 (39.2)	24 (32.4)

Table 2: Clinical characteristics by total polypharmacy

	Polypharmacy n (%)	*No Polypharmacy* n (%)
Diagnosis		
Organic disorders	25(12.3)	7(9.5)
Substance use	33(16.2)	0(0)
Schizophrenia	94(46.1)	3(4.1)
Affective disorders	43(21.1)	18(24.3)
Anxiety disorders	0(0)	5(6.8)
Puerperal psychoses	3(1.5)	0(0)
Childhood psychoses	1(0.5)	1(1.4)
Seizure disorder	5(2.5)	38(57.4)
Headaches	0(0)	2(2.7)
**Coexisting medical illness*		
Present	16 (61.5)	5(55)
Absent	10 (38.5)	4(44.4)
Cadre of prescribing doctor		
Consultant/Snr. Registrar	35 (17.2)	9(12.2)
Registrar	169 (82.8)	65(87.8)

**- Coexisting physical illness was enquired after by attending doctors in 35 respondents only.*

Conventional antipsychotic agents were prescribed for 189 (67.9%) respondents making them the most prescribed psychotropic. No patient was prescribed an atypical antipsychotic. Triphenylhexidyl, an anticholinergic agent, was given to 174 (62.5%) respondents. Tricyclic antidepressants were given to 98 patients (35.2%), while 7(2.5%) respondents were given a Serotonin Selective Reuptake Inhibitor (SSRI) . 16 (5.8%) respondents were placed on a benzodiazepine, while 71(25.5%) respondents were placed on an anticonvulsant agent.

In this study, poly-pharmacy was broadly defined as the concurrent use of two or more psychotropic medications in the same patient. The pattern of polypharmacy was described using the National Association of State Mental Health Programme Directors categorization.[9] The categories are;

I. Same-Class Polypharmacy

This refers to the use of more than one medication from the same medication class, e.g, the use of chlorpromazine and trifluperazine. Thirteen respondents were given two or more conventional anti-psychotic, while one patient was prescribed Sertraline and Fluoxetine together. One patient had two anti-convulsants prescribed for his seizure disorder, while another had a TCA given along with a Serotonin Selective Reuptake Inhibitors (SSRIs). Thus, 16 (5.8%) respondents had same class polypharmacy.

II. Multi-Class Polypharmacy

This is the use of full doses of more than one medication from different medication classes for the same symptom cluster, e.g, use of haloperidol plus a benzodiazepine and mood stabilizer for treatment of bipolar mania. Multi-class polypharmacy was seen in ninety patients (32.3%), and included cases of combined use of a conventional anti-psychotic and tricyclic antidepressants for patients with F01-F39 diagnoses (ICD-10); the combination use of conventional anti-psychotics, mood stabilizing agent (carbamazepine) and benzodiazepines for bipolar affective disorder; and the combination use of TCAs/SSRIs and benzodiazepines in patients with depressive illness.

III.Adjunctive Polypharmacy

The is the use of one medication to treat the side effects or secondary symptoms of another medication from a different medication class, e.g, the use of anti-cholinergic to treat the parkinsonian side effects of anti-psychotic agents. In this study, trihexyphenidyl was prescribed to 174 (62.6%) study respondents to counter the adverse effects of prescribed conventional anti-psychotic agents.

IV. Augmentation Polypharmacy

This is the use of a medication at a lower than normal dose, along with another medication from a different class at its full therapeutic dose, for treating the same symptom cluster (none was observed in this study). Augmentation also refers to the addition of a medication that would not be used alone for the same symptom cluster, e.g, the addition of a Benzodiazepine/Beta-blocker to TCAs/SSRIs. This was seen in 22(7.9%) respondents

V. Total Polypharmacy

This is the total count of medications used by a patient, or total drug load. Seven (2.5%) patients had one medication prescribed for them, i.e, monotherapy. Thus 271(97.5%) respondents were on polypharmacy. Of these, ninety one (32.7%) patients had 2 medications prescribed for them, of which 15(5.4%) had B complex tablets as the second medication. Thus, if the patients on B complex tablets as 2nd medication are excluded, total polypharmacy rate falls to 92%. Eighty four (30.2%) patients had 3 medications prescribed, 78 (28.1%) had 4 medications prescribed, 17 (6.1%) had 5 medications prescribed and one (0.3%) patient had 6 medications prescribed. Psychotropic monotherapy was seen most with the use of antidepressant for depressive illness and use of anticonvulsant for seizure disorder, although B complex was often given as well to these patients.

Factors associated with polypharmacy

The factors associated with psychotropic polypharmacy (total), using cross tabulations (Tables 1,2), were age of respondents (χ^2 =26.5, df=5, p<0.001) and diagnosis (χ^2 =149.9, df=8, p<0.001). Stepwise multiple linear regression analysis, using total polypharmacy as the dependent variable and diagnosis, cadre of doctor, age of respondent, sex of respondent and marital status, as independent variables was carried out. Diagnosis was the only predictor of psychotropic polypharmacy (Sum of squares=21.88, F=186.26, df=1, p<0.001).

Discussion

The study established that 92% of respondents were given two or more psychotropic agents. The pattern of psychotropic polypharmacy revealed that total, multi-class and adjunctive polypharmacy rates were high, while augmentation and same class polypharmacy rates were low. Age of respondent and diagnosis were the factors associated with total polypharmacy.

The high rate of psychotropic polypharmacy found in this study is consistent with those reported by studies from the southern parts of Nigeria[13,16] and other parts of the world.[2,12,14,19] That the figure is similar to those reported by studies carried out in the country over a decade ago suggests a persistent trend in the use of psychotropic polypharmacy in psychiatric practice. That such a trend persists, in spite of the recommendations of earlier studies that physicians should eschew the use of polypharmacy[13,16,17], is instructive. It has been pointed out that the concept of adequate, rational prescription is almost as abstract as that of health.[20] To define what constitutes an adequate psychotropic drug prescription is a complex task, as pharmacological, clinical, social and economic factors influence both the adequacy and rationality or otherwise, of prescriptions.[14] In addition, prescribing medication provides the doctor with an opportunity to "do something" and to prescribe a "rational treatment" for problems with a predominantly psychosocial basis in a manner which complies with the expectations associated with the role of a doctor. This is a scenario that is no doubt played out daily in consulting rooms not only in Nigeria, but in many other developing countries. Experience also reveals that from an economic point of view, for the average patient and caregiver, it appears that a linear relationship may exist between number of drugs prescribed and the perceived adequacy or otherwise of treatment. Apparently then, if a patient centered perspective is taken, polypharmacy is seen as not only rational, but expected. When these socio-cultural factors are considered, along with the clinical and pharmacological arguments for use of polypharmacy mentioned earlier, polypharmacy appears to

have its merits which are apparently recognized by clinicians and may partly explain its increasing use. It would appear that if and where warranted, such prescribing should be rational and preferably evidence driven. In this regard, the patterns of psychotropic polypharmacy observed in this study are revealing. There is growing evidence of a wide range of situations where multi-class polypharmacy, adjunctive polypharmacy and augmentation polypharmacy are safe and effective treatments. The only case of adjunctive polypharmacy in the current strudy, found in 63% of the respondents, was in the use of an anti-cholinergic agent (triphenylhexidyl) as an adjunctive treatment in patients prescribed anti-psychotics. This is a worldwide practice and the rationality behind its high use in outpatient settings in Nigeria has been explained.[13] The use of benzodiazepines as augmentation therapy to anti-depressants, in 7.9% of respondents, was the only case of augmentation polypharmacy. Benzodiazepines are often used in this way, usually for their hypnotic or anxiolytic effect, for a short period pending the onset of action of anti-depressant medication.

The medication combinations in the current study which fall into the category of multi-class polypharmacy are routinely encountered and accepted in clinical practice, an example being the use of a combination of an anti-psychotic, a mood stabilizing agent and a benzodiazepine in bipolar disorder patients. Currently, there is no evidence to justify same-class polypharmacy and it is the polpharmacy practice, in particular, same-class anti-psychotic polypharmacy, that physicians are most enjoined to avoid. In the current study, only 16 respondents (5.6%) were on same-class polypharmacy, a relatively low figure, and indicative perhaps, of some reasonableness in the way the doctors use polypharmacy. This aforementioned figure of same-class polypharmacy may be an indication that physicians are indeed mindful of the advice that there is little or no benefit in the practice of same-class anti-psychotic polypharmacy. It is therefore important that this message continue to be spread, if the practice of same-class polypharmacy is to be curtailed.

The age of respondents and diagnosis were the factors that demonstrated an association with psychotropic polypharmacy. Specifically, 21-50yrs age and a diagnosis of schizophrenia and psychoactive substance use disorder were more likely to be associated with use of polypharmacy. Both age and diagnosis have previously been reported to be associated with psychotropic polypharmacy[2,14], though no conclusive explanations have been proffered to explain these associations

Conclusion

Polypharmacy is common in psychiatric practice in northern Nigeria, with the relatively safer multi-class, adjunctive and augmentation polypharmacy being commonest, while the more problematic same class polypharmacy is less common. Diagnosis and age are factors associated with use of polypharmacy. The complex interplay of factors influencing this prescription trend suggests that efforts at curtailing psychiatric polypharmacy may require a more pragmatic approach, including the development of local prescription practice guidelines based on available evidence rather than to simply condemn the practice. It seems that efforts targeted at discouraging the use of same-class polypharmacy by practitioners appear to be yielding positive results, in the setting studied. These efforts need to be intensified to ensure appropriate and optimal pharmacological interventions.

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