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Adverse Drug Reaction Monitoring in Psychiatry Out-Patient Department of a Tertiary Care Hospital

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Abstract: Adverse drug reactions (ADRs) to psychotropic agents are common and can lead to non compliance or even discontinuation of therapy. There is paucity of such data in the Indian context. We deemed it worthwhile to assess the suspected ADR profile of psychotropic drugs in a tertiary care hospital in Chennai. A longitudinal observational study was conducted in the out-patient department (OPD) of the concerned psychiatry unit. Patients were screened for suspected ADRs irrespective of their psychiatric diagnosis for over a period of 12 months. Adverse event history, medication history and other relevant details were captured in a format adopted in the National Pharmacovigilance programme. Causality was assessed by criteria of Naranjo's algorithm. We screened 100 patients, of whom 45 were suspected of having at least one ADR, 55 had insufficient evidence about causality and were excluded from further analysis. Of 45 events recorded, 43 were "probable" and 2 were "possible". None was labeled "certain" as rechallenge was not performed. Eleven different kinds of ADRs were noted. Among the incriminated drugs, antipsychotics represented the majority. This study offers a representative profile of ADRs to be expected in psychiatry out-patients in an Indian public hospital.

Key words: Adverse Drug Reactions · Pharmcovigilance · Psychiatry · Psychotropic Drugs

INTRODUCTION

Psychotropic drugs are plentiful in number and their use is increasing day by day. These drugs are capable of causing a number of adverse drug reactions (ADRs), some of which may be fatal [1, 2]. ADRs associated with psychotropic drugs can lead to non-compliance and at times discontinuation of therapy [3]. Pharmacovigilance in psychiatry units can play a vital role in detecting ADRs and alerting physicians to the possibility and circumstances of such events, thereby protecting the user population from avoidable harm. In India, pharmacovigilance activities are still in nascent stage and there are few reports available on the ADR profile of medicines in psychotropic agents in particular [4]. This prompted us to evaluate the ADR profile of psychotropic drugs used by patients in a tertiary care hospital.

MATERIALS AND METHODS

A longitudinal observational study was undertaken in the psychiatry out-patient department (OPD) of Sree Balaji Medical Collage and Hospital, Chennai, between June 2012 and June 2013. It was part of ongoing pharmacovigilance activity at the institute which had the necessary administrative and Institutional ethics Committee clearance. The patients enrolled were residents of urban area, sub urban and rural areas of Chennai city, district of Kanchipuram, Villupuram and Cuddalore. Patients were selected after making the clinical diagnosis and confirmation of any psychiatric disorders. Informed consent was obtained from patients/relatives accordingly.

Patients were screened for suspected ADRs, irrespective of their psychiatric diagnosis for over a period of 12 months. The screening was carried out by psychiatry and pharmacology residents. Subjects and

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their accompanying family members were interviewed and past prescriptions and case notes were reviewed. A senior psychiatrist was available for consultation in the event of any difficulty. Patients who were known substance abusers and psychotic subjects not accompanied by a family member were not included in the study. Patient details (Age, Sex, Body weight), adverse event history, history of medication suspected of having caused the ADR and details of concomitant medication were recorded in the format followed by the Indian National Pharmacovigilance Programme [5].

Causality of the event was assessed by Naranjo's algorithm [6, 7]. This analysis was conducted by pharmacology residents in consultation with a senior pharmacologist.

RESULTS

A total of 100 patients were screened for the study, of whom 45 were suspected of having at least one ADR. On causality assessment, 55 were considered to have insufficient evidence about causality and they were excluded from further analysis. Of 45 patients 34(75.55%) were males and 11(24.44%) were females. The median age of the subjects was 34.4 years. A few subjects were taking concomitant medicines for other disorders such as dyspepsia and hypertension, started before their psychotropic medication, or OTC medicines casually from minor ailments such as cough and cold. The drug history was taken carefully in such cases before attributing suspected ADRs to the psychotropic medicines concerned.

Among the different psychotropic drugs used in the Department of Psychiatry, antipsychotics (Typical and atypical) were the most common group of agents causing ADRs, followed by selective serotonin reuptake inhibitors (SSRIs), benzodiazepines and central anticholinergics [8, 9].

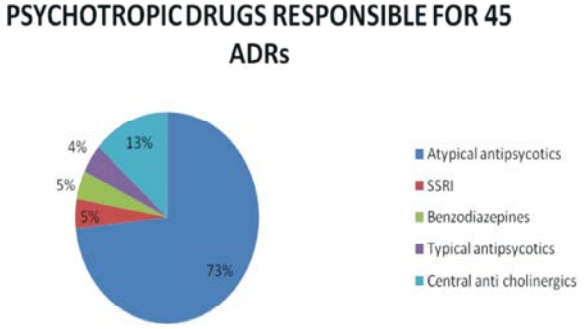
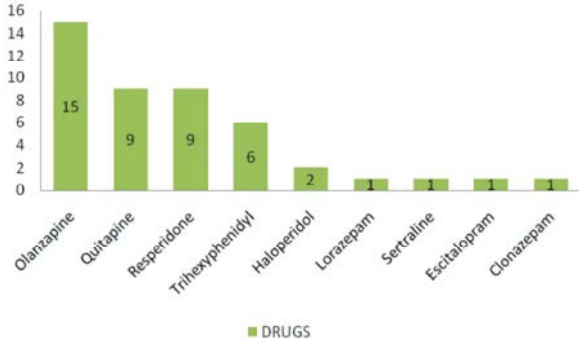


Table 1: Spectrum of suspected adverse drug reactions noted among 45 patients

TYPE OF ADR	No (percentage of all ADRs n=45)
Weight gain	15(33.33)
Constipation	12(26.66)
Tremor	7(15.55)
Sedation	3(6.66)
Increased appetite	1(2.22)
Headache	2(4.44)
Drymouth	1(2.22)
Increased appetite	1(2.22)
Fatigue	1(2.22)
Swelling of lips	1(2.22)
Mouth ulcer	1(2.22)
Palpitation	1(2.22)

Eleven different kinds of treatment emergent ADRs were encountered in the patients as listed in Table 1. Weight gain was the most common ADR noted followed by constipation and tremor.

Causality assessment by Naranjo's scale revealed that 43 ADRs belonged to "Probable" category, whereas 2 were of "Possible" category. No case could be labeled "Certain", as the rechallenge was not attempted by the attending psychiatrist, once the drug was withdrawn.



DRUGS RESPONSIBLE FOR 45 ADRs

No ADR encountered turned out to be fatal, life-threatening or required hospitalization for management. Mild to moderate ADRs such as oral ulcer, dry mouth, palpitation and headache were treated by dose adjustment and/or relevant medications to treat the symptoms.

DISCUSSION

The present study has reported the incidence and attempted to profile suspected ADRs to psychotropic drugs in the Psychiatry department setting in the Indian context. In contrast to reports of ADR profiles of individual drugs, there is a dearth of pharmacovigilance

Table 2: Causality of ADR by naranjo's scale

Category of ADR*	Instances of event n=45(%)	Adverse drug events	Offending drug(s)
Probable (43)	15(33.33)	Weight gain	Olanzepine(6),quitiapine(5),risperidone(4)
	12(26.66)	Constipation	Olanzapine(4),quitiapine(2),
Trihexyphenidyl(8)	7(15.55)	Tremor	Olanzapine(3),risperidone(2),
Haloperidol(2)	3(6.66)	Sedation	Lorazepam(1),sertraline(1),escitalopram(1)
	1(2.22)	Increased appetite	Olanzapine(1)
	2(4.44)	Headache	Clonazepam(1),quitiapine(1)
	1(2.22)	Dry mouth	Risperidone plus(1)
	1(2.22)	Fatigue	Risperidone(1)
	1(2.22)	Swelling of lips	Quitiapine(1)
Possible(2)	1(2.22)	Mouth ulcer	Risperidone(1)
	1(2.22)	Palpitation	Olanzapine(1)
Total	45		

*Causality assessment as per naranjo's scale, ADR-adverse drug reaction

profiling of psychotropic agents in general, not only in India but also worldwide. A Brazilian study, conducted in 2001, analyzed 219 notifications of suspected ADRs of psychoactive medicaments and incriminated antidepressants as the commonest group responsible for ADRs, followed by antipsychotics [10]. A Bulgarian study reported that the ADR frequency of individual psychotropic drugs studied is less than 1% [11]. A knowledge, attitude and practice based study conducted in Norway found that ADRs can be prevented by collecting reliable information about their frequencies and possible risk factors [12]. In our study, which is based on active surveillance rather than spontaneous reporting, we found antipsychotics to be most commonly responsible; this could be partly related to the frequency and duration of their use in the hospital setting.

Quitiapine is the most commonly used among atypical antipsychotics in our hospital set up and followed by Olanzapine and other atypical antipsychotics. Although several new psychotropic drugs have been introduced in the Indian pharmaceutical market over the last few years (E.g., aripiprazole, reboxetine, venlafaxine, ziprasidone), were not prescribed as frequent as that of the others because they are relatively expensive [13]. Hence, they were seldom prescribed in our setting a public hospital catering mostly to economically weaker sections of society.

Present study for assessment of ADR of psychotropic drugs was based on active surveillance through questionnaire in addition to the ADR spontaneously reported by patients or consultants [14]. We found that spontaneous reporting by the patients was poor during initial visits and was restricted to those ADRs that were troublesome. It was observed that spontaneous reporting rate increased after exposure to the questionnaire. Ordinarily, in spontaneous reporting, adverse effects, status of the patient, disease and the drug(s) are recorded at that particular time only [15]. In this study, we have tried to relate the ADR with the duration of treatment with that particular drug. Certain ADRs require comparison with previous status in the same patient (E.g., weight gain is a common adverse effect associated with atypical antipsychotics).

Weight gain is considered clinically significant if it exceeds 7% of the initial weight after 10 weeks. We observed weight gain with quitiapine, Olanzapine and risperidone, which accounted for 33.33% of total ADRs. Magnitude of weight gain and its time course varies among atypical antipsychotics. Weight gain can be a disincentive to comply with treatment and complicates co-morbid medical conditions such as obesity and heart diseases.

Regarding the drugs responsible for the 45 ADRs, olanzapine (33.33%) showed maximum followed by quitiapine and risperidone [16]. Regarding causality assessment, our study had no "certain" cases since the suspected ADRs were mostly of mild to moderate severity and hence did not require withdrawal of therapy. In cases where dechallenge was done, rechallenge was not attempted with the offending drug. This is in contrast to the Brazilian study where 24 cases were found to be "Definite" after rechallenge was attempted.

Our study had limitations. For logistical reasons, we screened patients on fixed days for a period of 52 weeks, rather than rotating days and this could introduce potential bias in the sample. Being an observational study, it is likely that we have missed ADRs that were transient or too mild to have inconvenienced the patient to an extent sufficient to report to the doctor on the next hospital visit. Although routine hematological and clinical chemistry (E.g., blood sugar, lipids) reports were available, we could not generally order tests like ECG, screening of patients for QT interval prolongation or blood sampling to determine serum prolactin concentration.

CONCLUSION

Data on adverse effects are available from a range of sources, including randomized controlled trials, post-marketing surveillance and naturalistic studies. The best overview of adverse effects comes from considering all sources together. Future research would benefit greatly if standardization for the reporting of adverse effects could be reached. It is important that the patient's subjective experiences, in which adverse effects have a role, are considered in the assessment of a drug. In clinical practice, patients should be informed of common side-effects prior to treatment and monitored for their occurrence during treatment.

Although post-marketing surveillance study cannot provide true incidence or prevalence figures, it offers a representative idea of the ADR profile of psychotropic drugs likely to be encountered in ambulatory patients in an Indian public hospital [17, 18]. Compliance with therapy is a major issue in psychiatric patients. Constant vigil in detecting ADRs and subsequent dose adjustments can make therapy with psychotropic drugs safer and more effective [19]. ADRs can perhaps also be reduced by using less medication and with adequate knowledge of drug interactions. A psychotropic drug ADR database built up on the basis of such studies conducted across multiple centers, through active collaboration of psychiatrists and pharmacologists can be a worthy long-term goal in the Indian context. Such a database can provide early warning signals of drug-reaction links if kept under active scrutiny.

REFERENCES

1. Brown, S., J.S. Markowitz, T.R. Moore and N.G. Parker, 1999. Atypical antipsychotics: Adverse effects, drug interactions and costs. The Annals of Pharmacotherapy, 33(2): 210-217.
2. Corell, C.U., S. Leucht and J.M. Kane, 2004. Lower risk of tardive dyskinesia associated with second generation antipsychotics: A systemic review of 1 year studies. Am. J. Psychiatry, 161: 414-25.
3. Sinikka Sihvo, Erkki Isometsä, Olli Kiviruusu, Juha Hämäläinen, Jaana Suvisaari, Jonna Perälä, Sami Pirkola, Samuli Saarni and Jouko Lönnqvist, 2008. Antidepressant utilisation patterns and determinants of short-term and non-psychiatric use in the Finnish general adult population. Journal of Affective Disorders, 110: 94-105.
4. Gairik Sengupta, Subhrojyoti Bhowmick, Avijit Hazra, Ananya Datta and Musfikur Rahaman, 2011. Adverse drug reaction monitoring in psychiatry out-patient department of an Indian teaching hospital. Indian J. Pharmacol., 43(1): 36-39.
5. Sarfaraz Alam Khan, Chhaya Goyal, Nitibhushansingh Chandel and Mohammed Rafi. Knowledge, 2013. Attitudes and practice of doctors to adverse drug reaction reporting in a teaching hospital in India: An observational study. J. Nat. Sci. Biol. Med., 4(1): 191-196.
6. Syed Ahmed Zaki, 2011. Adverse drug reaction and causality assessment scales. Lung India, 28(2): 152-153.
7. The use of the WHO-UMC system for standardized case causality assessment[monograph on the Internet]. Uppsala: The Uppsala Monitoring Centre, 2005.
8. Glassman, A.H. and J.J. Bigger, 2001. Antipsychotic drugs, prolonged QTc interval, torsades de pointes and sudden death. Am. J. Psychiatry., 158: 1774-82.
9. Newcomer, J.W., 2005. Second-generation (atypical) antipsychotics and metabolic effects: A comprehensive literature review. CNS Drugs., 19: 1-93.
10. Carlini, A.E. and A.S. Nappo, 2003. The pharmacovigilance of psychoactive agents in Brazil. Rev Bras Psiquiatr, 25: 200-5.
11. Dimitrova, Z., A. Doma, V. Petkova, I. Getov and E. Verkkunen, 2002. Psychotropic drugs in Bulgaria-frequency and risk of adverse drug reactions. Boll Chim Farm., 141: 75-9.
12. Castberg, I., A. Reimers, P. Sandvik, T.O. Aamo and O. Spiqset, 2006. Adverse drug reactions of antidepressants and antipsychotics: Experience, knowledge and attitudes among Norwegian psychiatrists. Nord J. Psychiatry, 60: 227-33.
13. Gardner, D.M., R.J. Baldessarini and P. Waraich, 2005. Modern antipsychotic drugs: A critical overview. CMAJ, 172: 1703-11.
14. Faich, G.A., 1996. US adverse drug reaction surveillance 1984-1994. Pharmacoepidemiol Drug Saf, 5: 393-8.
15. Mann, R.D., 1998. Prescription-event monitoring recent progress and future horizons. British Journal of Clinical Pharmacology, 46: 195-201.
16. Ibrahim, E., R. Ozcankaya and V. Altinayazar, 2004. Risperidone-induced rabbit syndrome in mood disorder. Eur Psychiatry, 19: 452-3.

17. Fontanarosa, P.B., D. Rennie and C.D. De Angelis, 2004. Postmarketing surveillance lack of vigilance, lack of trust. JAMA, 292: 2647-2650.
18. Gough, S., 2005. Post-marketing surveillance: a UK/European perspective. Current Medical Research and Opinion, 21: 565-570.
19. Awad, A.G. and T.P. Hogan, 1994. Subjective response to neuroleptics and the quality of life: implications for treatment outcome. Acta Psychiatrica Scandinavica Supplementum, 380: 27-32.