

**Adverse drug reaction profile at psychiatry out-patient department of a tertiary referral centre in Central India**

Sir,

Modern lifestyle and unfulfilled desires leads to very common diseases of today like anxiety, depression and schizophrenia. Therefore, last one and half decade there has been an exponential rise in the use of psychotropic medication. Antipsychotic polypharmacy is being practiced with increasing frequency.<sup>1</sup> Polypharmacy is one of the leading cause of adverse drug reactions (ADRs) in psychiatric patients.<sup>2</sup> In India, pharmacovigilance activity is still in initial stages and there are only few reports available on incidence of ADRs due to psychopharmacological agents (PPAs). Also, India rates below 1% in terms of ADR reporting against the world's rate of 5%.<sup>3</sup> Very few studies have described patient characteristics and treatment patterns associated with long-term use of the drugs. This prompted us to do evaluation of adverse drug reactions of PPAs in tertiary referral centre for a longer duration. This study was designed to prospectively monitor and analyze the pattern of occurrence of ADRs to PPAs in OPD of our tertiary care hospital. Our further aim was to make causality and severity analysis of psychopharmacological drug reactions.

An observational, prospective, active surveillance was conducted in the psychiatry OPD of the tertiary referral centre after approval from Institutional Ethics Committee over the period of 2 years. The data was recorded on ADR form obtained from CDSCO website. Case reports were assessed by first evaluating cases individually and secondly interpreting the aggregated data. The data was analyzed and causality was done by using WHO-UMC causality scale. Subsequently, the ADRs were classified as certain, probable/ likely, possible, unlikely, conditional/ unclassified and unassessable/unclassifiable.<sup>4</sup> ADRs were studied to assess their severity as per Modified Hartwig and Siegel ADR severity assessment scale. Accordingly, the ADRs were classified as mild, moderate and severe.<sup>5</sup> Moreover the patients were assessed based on age, polypharmacy of PPAs. All the statistical analysis was done by using simple proportions.

A total of 3831 patients were screened, out of which 192 patients were diagnosed of having ADRs due to PPAs. The overall incidence rate was found to be 5.01%. Maximum percentage of ADRs was observed with olanzapine (18.75%), followed by amitriptyline (13.02%) and clozapine (12.5%). Distribution of group of PPAs and the nature of ADRs was depicted in table 1.

**Table 1: Spectrum of suspected adverse drug reactions seen during the study period.**

PPAs		No. of ADR (%)	Individual drugs	Adverse reactions
Antipsychotics	Typical	22 (11.45)	Haloperidol(17), Fluphenazine(03), Trifluoperazine(01), Chlorpromazine(01)	EPR(16), Mental confusion(2), Excessive sedation(01), Galactorrhoea(01), Malignant neuroleptic syndrome(01), Tardive dyskinesia(01)
	Atypical	77 (40.10)	Olanzapine(36), Clozapine(24), Risperidone(13), Quetiapine(2), Paliperidone(2)	Weight gain(32), Excessive sedation(23), EPR(09), Hypersalivation(04), Convulsion (01), Palpitation(02), Urinary hesitancy(01), nausea& vomiting(01), Oral ulcer(01), rash(01), Constipation(01), Galactorrhoea(01)
Antidepressants	TCA	49	Amitriptyline(25), Clomipramine(08),	Constipation(12), Excessive sedation(10), Mental confusion(08),

	(25.52)	Nortriptyline(06), Riboxetine(05), Dothiepin(03), Imipramine(02)	Dryness of mouth(06), Nausea& vomiting(03), Weight gain(03), Urinary hesitancy(02), Excessive sweating(02), Palpitation(01), rash(01), Blaring of vision(01)
SSRI	20 (10.41)	Sertraline(09), Escitalopram(06), Fluoxetine(05)	Nausea& vomiting(03), Sexual dysfunction(03), Excessive sedation(03), Mental confusion(02), Palpitation(02), restlessness(02), Muscle pain(01), Headache(01), insomnia(03)
Atypical	4 (2.08)	Mirtazepine(04)	Excessive sedation(02), Urinary hesitancy(01), Tremor(01)
Antimanic agents	4 (2.08)	Lithium(04)	Polyuria(02), Tremor(01), nausea& vomiting(01)
Antiepileptic agents	11 (5.72)	Sodium valproate(05), Topiramate(01), Carbamazepine(04), Clobazam(01)	Excessive sedation(02), Alopecia(02), rash(04), Vomiting(02),tremor(01)
Antianxiety agents	3 (1.56)	Clonazepam(01), Zolpidem(01), Lorazepam(01)	Excessive sedation(01), nausea& vomiting(01), Muscle pain(01)
Cognition enhancers	2 (1.04)	Memantine(02)	Headache(01), Constipation(01)
Total No. of ADR (%)	192 (100)	192 (100)	192 (100)

N= 192, PPAs- Psychopharmacological agents, ADRs- Adverse drug reactions, TCA- Tricyclic antidepressants, SSRI- Selective Serotonin reuptake inhibitors, EPR- Extrapyramidal reaction, Figure in ( ) indicate number of ADRs.

Atypical antipsychotics caused the most frequent ADRs in 40.10% patients followed by tricyclic antidepressants in 25.52% patients. On causality assessment 78% and 22% ADRs were categorized as probable and possible cases respectively. Analysis of the outcome of such reactions revealed clinical improvement and abatement of reactions within 7 days of dechallenge. There was no certain causality as re-challenge was not done due to ethical concerns.

Severity assessment of ADRs revealed that maximum patients were in mild group (84.89%) and moderate group included 12.5% patients. Severe ADRs were reported in 2.60% patients. Most of the mild ADRs subsided on reduction of the suspected drug while the moderate ones required discontinuation of the drug and other treatment such as administration of anticholinergic drugs. Severe reactions such as malignant neuroleptic syndrome, convulsions required intensive medical care while tardive dyskinesia caused permanent disability.

Maximum ADRs (54.68%) were observed in the age group of 21-40 years followed by 22.39% ADRs in 41-60 years. 44.27% patients with ADRs were males and

55.72% patients were females. Single PPA was received by 10.41% patients, two PPAs by 72.91% patients, more than two PPAs by 16.66% patients. Central nervous system was involved in 31.25% patients followed by weight gain in 17.18% patients.

Since most of the patients attending the psychiatry OPD of this hospital belong to relatively poor socio-economic status, the pattern of drug usage amongst them is mostly restricted to the drugs that are supplied free of cost from the hospital. As a consequence, this study might not be a true mirror of the ADRs of all PPAs. Atypical antipsychotic drugs are more frequently prescribed than typical antipsychotics, so maximum ADRs could have occurred due to atypical antipsychotics. In the present study, maximum ADRs were mild. This may be due to different prescribing preferences in our hospital as compared to the other hospitals. In the present study, maximum number of patients received two or more than two PPAs. The trend of prescribing multiple antipsychotics is increasing day by day. The difference in the systems affected due to ADRs might be because of difference in prescribing preferences at the different hospitals. Present study revealed the nature and

presentation of different ADR to PPAs with a positive attempt to estimate incidence and establish a causal link between the suspected drug and ADR.

This study is an attempt to generate more systematic knowledge about ADRs to PPAs with ultimate aim of improving quality of patient care and also the community. A psychotropic drug ADR database built up on the basis of such studies conducted across multiple centers, through combined efforts of psychiatrists and pharmacologists can be worthy long term goal. Also this data can be an important source for psychiatrists in avoiding ADR, creating awareness and reporting the ADRs due to PPAs.

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