Asian Journal of Psychiatry 17 (2015) 42–49

Contents lists available at ScienceDirect

Asian Journal of Psychiatry

journal homepage: www.elsevier.com/locate/ajp

Adverse drug reactions in a psychiatric department of tertiary care teaching hospital in India: Analysis of spontaneously reported cases

Tejas K. Patel [a,*], Prakash H. Bhabhor [a], Nimisha Desai [b], Saurabh Shah [b], Parvati B. Patel [a], Ela Vatsala [b], Sanjibani Panigrahi [b]

[a] Department of Pharmacology, GMERS Medical College, Gotri, Vadodara, Gujarat, India
[b] Department of Psychiatry, GMERS Medical College, Gotri, Vadodara, Gujarat, India

ARTICLE INFO

Article history:
Received 24 March 2015
Received in revised form 7 July 2015
Accepted 9 July 2015

Keywords:
Adverse drug reaction
Causative drugs
Serious reactions
Preventable reactions
Drug interactions

ABSTRACT

The epidemiological data are limited for the spontaneous adverse drug reaction (ADR) reporting system in psychiatry and its comparison with intensive monitoring studies in terms of causative drugs, seriousness, preventability and drug interactions. This spontaneous ADR reporting study was carried out over a period of three years in the psychiatry department. We adopted WHO definition for an ADR, Naranjo's algorithm for causality, WHO-ADR terminology for the labeling of involved organ-system, International conference on harmonisation (ICH) E2A guidelines for seriousness, modified Schumock and Thornton's criteria for preventability and Medscape drug interaction checker for drug interactions. Two subgroup analyses were performed to find out the risk factors for the serious and preventable reactions. A total of 97 ADRs from 67 patients were included for analysis. The incidence of 'overall' and 'serious ADRs were 0.69% (95% CI: 0.54%, 0.88%) and 0.18% (95% CI: 0.12–0.29%), respectively. The females experienced more ADRs than males. The most commonly reported ADR, incriminated pharmacology group and drug, were extrapyramidal movement disorders (22.68%), atypical antipsychotics (35.62%) and escitalopram (13.91%), respectively. One out of five and one out three reactions were considered as 'serious' and 'preventable', respectively. The drug interactions contributed in 34.02% reactions. The factors significantly associated with 'serious' reactions were typical antipsychotics [OR: 5.47 (1.68, 17.87)], central and peripheral nervous system disorders [OR: 24.00 (5.12, 112.5)] and extrapyramidal reactions [OR: 14.03 (4.43, 44.43)]. The polypharmacy [OR: 5.85 (1.90, 18.03)] was significantly associated with 'preventable' reactions. The spontaneous reporting system is efficient to detect serious reactions and preventable reactions.

1. Introduction

The prevalence of psychiatric disorders is 9.5–370 per 1000 populations in India. Approximately, 20% of the adult population is affected with one or the other psychiatric disorder. They range from sub-clinical states to very severe forms of disorders (Math and Srinivasaraju, 2010). Neurotic disorders, psychoses, alcohol/drug addiction, mental retardation and epilepsy are common mental and behavioral disorders in India (Reddy and Chandrashekar, 1998). Most mental illnesses require medications for longer duration ranging from several months to years (Math and Srinivasaraju, 2010). Because of longer duration of therapy, wide range of adverse drug reactions (ADRs) is associated with it. ADR monitoring holds special importance as they account for non-adherence and relapse.

The spontaneous reporting system for ADR monitoring operates for all drugs throughout their life span. It can identify serious as well as rare ADRs (Mann and Andrews, 2007). This system has generated many early safety signals for antidepressants and antipsychotics that lead to changes in their labels for warnings, precautions and contraindications (Medicines and Healthcare Products Regulatory Agency, 2015). Intensive monitoring studies are considered superior in terms of identifying accurate incidence and risk factors for ADRs. However, they are cumbersome and not suitable for routine monitoring purpose. Spontaneous reporting system is affordable and convenient for day-to-day monitoring. The studies conducted in this field from India are scarce. Hence,

* Corresponding author at: Department of Pharmacology, GMERS Medical College, Gotri-390021, Vadodara, Gujarat, India. Tel.: +91 9909105876.
E-mail address: dr.tkp2006@yahoo.co.in (T.K. Patel).

http://dx.doi.org/10.1016/j.ajp.2015.07.003
1876-2018/

this study is undertaken to analyze data generated by spontaneous reporting system and its comparison to intensive monitoring Indian as well as abroad studies.

2. Methodology

This observational, spontaneous ADR reporting, case-series study of out-patients and in-patients was started after approval from the Institutional Human Ethics Committee (IHEC). The consent waiver was approved by IHEC. The case record forms were coded, access was restricted and patients were identified through initials to maintain the confidentiality of the collected information.

2.1. Study procedure

All ADRs reported by psychiatry department to the pharmacovigilance cell of the institute from January 2012 to December 2014 were evaluated. All psychiatrists were informed about the study. They were sensitized through monthly reminder letters, analysis of reported ADRs and one-to-one meeting. They were asked to notify all suspected ADRs. Psychiatrists identified ADRs based on patient interview, case records review and clinical examination. Movement disorders were labeled as per diagnostic and statistical manual of mental disorders IV (DSM-IV TR) criteria (American Psychiatric Association, 2000). Pharmacologist analyzed the causal association between drug and ADR pair through Naranjo's algorithm (Naranjo et al., 1981). We used ADR form designed by Central Drug Standard Control Organization, India as a case record form for the study (Central Drugs Standard Control Organization, 2012). Two pharmacologists independently applied the inclusion and exclusion criteria for the selection of ADRs. Any discrepancies were resolved by discussion, consensus and by the third investigators.

2.2. Inclusion criteria

- The reported reactions following WHO's definition of ADR – "any noxious, unintended and undesired effect of a drug, which occurs at doses used in humans for prophylaxis, diagnosis or therapy (Edwards and Aronson, 2000)".
- ADRs with definite or probable or possible causality with Naranjo's algorithm (Naranjo et al., 1981).

2.3. Exclusion criteria

- ADRs with doubtful causality with Naranjo's algorithm (Naranjo et al., 1981).
- ADR forms with insufficient information.
- Medication errors.

2.4. Collection of data

Data for demographics, diagnosis, suspected ADRs, causative drugs, concomitant medications, incubation period for the development of ADRs, dechallenge, rechallenge, outcome, seriousness of reactions and relevant investigations were extracted to Microsoft Excel data sheet. Two investigators cross checked the data for the accuracy.

The incriminated drugs were labeled as per 'World health organization-anatomical therapeutic chemical (WHO-ATC) classification' (ATC/DDD Index, 2014). Involved organ systems were labeled as per 'WHO-adverse reaction terminology' (WHO Adverse Reaction Terminology, 2007). The seriousness of reactions was assessed as per International conference on harmonisation (ICH) E2A guidelines by psychiatrists. It classifies 'serious' reactions as those results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, or is a congenital anomaly/birth defect (ICH Harmonised Tripartite Guideline, 1994). Preventability of reactions was analyzed as per modified Schumock and Thornton's criteria into 'definitely preventable', 'probably preventable' and 'not preventable' reactions (Lau et al., 2003). We also evaluated ADRs due to drug interactions where more than one drugs were suspected or at least one concomitant medication/alcohol intake in case of single drug suspect. Drug interactions were assessed online through 'Medscape drug interaction checker' (Medscape, 2015). We only considered drug interactions when descriptions of potential interaction on 'Medscape drug interaction checker' match with description of suspected reactions. It was assessed by two pharmacologists and if required psychiatrists were also contacted for further information.

2.5. Subgroup analysis

Two subgroup analyses were done based on seriousness and preventability of the reactions. In first subgroup analysis, ADRs were divided into 'serious' and 'non-serious' according to ICH E2A guidelines. In second analysis, ADRs were divided into 'preventable' and 'not-preventable' according to modified Schumock and Thornton's criteria. In this analysis, 'definitely preventable' and 'probably preventable' ADRs were considered as one category of 'preventable' reactions. The groups were compared for demographics, causative drugs, organ system involvement, common reactions and polypharmacy to find out the risk factors for the serious and preventable reactions.

3. Statistical analysis

The qualitative and quantitative data were presented in proportions and mean (95% confidence interval: CI), respectively. The categorical data were compared by *Chi*-square test/Fisher's exact test and their odds ratio (OR) were expressed. All the statistical analysis was performed through Graph Pad Prism 6.0 demo version software. A *P*-value <0.05 was considered statistically significant.

4. Result

A total of 9701 patients (5757 males and 3944 females) attended psychiatry department of GMERS General Hospital, Gotri, Vadodara, India during the study period. A total of 97 ADRs from 67 patients (30 males and 37 females) were included for the analysis. The incidence of psychiatric ADRs was 0.69% (95% CI: 0.54%, 0.88%). The male to female ratio was 1:1.23. The incidences for males and females were 0.52% (95% CI: 0.37–0.74%) and 0.94% (95% CI: 0.68–1.29%), respectively ($P = 0.02$, *Chi*-square test). The average age of the patients was 39.31 (95% CI: 35.54, 43.09). The distribution for the age groups infancy and childhood (0–9), adolescent (10–19), adult (20–59), and elderly (>60) years was (2.98%), 3 (4.48%), 54 (80.60%), and 8 (11.94%), respectively (WHO Women's Health, 2013).

4.1. Psychiatric ADRs

We observed 42 different types of psychiatric ADRs belonged to nine different organ systems (Table 1). The commonly involved organ systems were central and peripheral nervous system 39 (40.21%), gastro-intestinal system 33 (34.02%) and metabolic and nutritional 7 (7.22%). The commonly reported reactions were extrapyramidal movement disorders (parkinsonism-18, tardive