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Research Article

EVALUATION AND ANALYSIS OF ADVERSE DRUG REACTIONS OF SECOND GENERATION ANTIPSYCHOTICS IN A PSYCHIATRY OUT-PATIENT DEPARTMENT

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ABSTRACT

An antipsychotic drug is a tranquilizing psychiatric medication primarily used for the treatment of psychosis, schizophrenia , bipolar disorder, delusions, paranoid disorder, mental retardation, depression etc. These drugs also used in the management of non-psychotic disorders. First generation of antipsychotics, known as typical antipsychotics, were discovered in the 1950s and the drugs in the second generation came later, are known as atypical antipsychotics. In the present study 100 patients were screened, of whom 91 (91.00%) were suspected to suffer from adverse drug reactions (ADRs). Four atypical antipsychotic drugs were most frequently used such as olanzapine (5mg, 10mg), risperidone (2mg, 1mg), clozapine(0.5mg) and quetiapine (50 mg). Simultaneously informations regarding ADRs were obtained from the patients as well their guardians. Details study of prescribed medications, various adverse reactions, management of ADR as well as reports of laboratory investigations were entered in the format produced by Department of Clinical and Experimental pharmacology, Calcutta School of Tropical Medicine, Kolkata. Total171 adverse events were investigated and tabulated. Causality of adverse events was assessed by Naranjo's algorithm and World Health Organization-Uppsala Monitoring Centre (WHO-UMC) criteria.

Keywords: Antipsychotic, Schizophrenia, Adverse drug reactions, Olanzapine, Psychosis

INTRODUCTION

Adverse drug reaction (ADR) is an expression that describes harm related with the use of given medicines at a recommended dosage. ADRs may occur due to single dose, prolonged administration of a drug or result from the combination therapy of two or more drugs.[1,2] The study of ADRs is the concern of the field known as pharmacovigilance.[3] Generally pharmacovigilance is the science of collecting, monitoring, researching, assessing and evaluating information from healthcare personnel's and patients on the adverse effects of medications, biological products including herbal and traditional medicines. This pharmacovigilance process perform following roles such as identifying new information about hazards associated with medicines and preventing harm to the patients. Pharmacovigilance starts from the clinical stage and continues throughout the life cycle of the drug, mainly divided as pharmacovigilance during pre-marketing and post marketing stage. The process of collection of such information about a drug begins in the preclinical stage and continues through all phases of clinical trial and even in post marketing stage after receiving marketing approval. Various post-market safety studies are also conducted by drug regulatory agencies throughout the world. In 2006 a new concept of pharmacovigilance in environmental pharmacology, known as 'Pharmacoenvironmentology' as suggested by Syed Ziaur Rahman, surfaced as a separate section of pharmacovigilance. It is a form of pharmacovigilance which deals specifically with those pharmacological agents that have impact on the environment via elimination through living organisms subsequent to pharmacotherapy.[4-7]The atypical antipsychotics (AAP) also known as second generation antipsychotics(SGAs) are a group of antipsychotic tranquilizing drugs used to treat psychiatric manifestations. Some of them are FDA approved for use in the treatment of mental illness like schizophrenia. Some carry FDA approved indications for acute mania, bipolar disorder, psychotic agitation and other indications. Atypical antipsychotics differ from typical antipsychotics in that they cause less extrapyramidal motor control disabilities in patients, which include unsteady Parkinson's disease-type movements, body rigidity and involuntary tremors.[8] The currently available SGAs (clozapine, aripiprazole, olanzapine, quetiapine, zotepine, risperidone, ziprasidone) vary in their efficacy, formulation, biochemistry, receptor binding, and side effect profiles.[9-12] Therefore, the present work was planned to study to develop a protocol for ADR monitoring for second generation antipsychotics(SGAs) like olanzapine, clozapine,quetiapine and risperidone.

MATERIALS AND METHODS

Place of ADR monitoring Centre

The study was conducted in the psychiatry out-patient department (OPD) of Calcutta Medical College (CMC), Kolkata, for 5 months.

Prescribed Drugs

Olanzapine, risperidone, clozapine were supplied from the hospital (CMC) and quetiapine was purchased from various private pharmacies by the patients.

Adverse event monitoring Study[13-20]

A longterm observational study was carried out in the outpatient department (OPD) of the concerned psychiatry department. Five consecutive psychiatric patients per week were observed over 5 months under supervision of one psychiatrist and one pharmacologist. A total of 100 patients were investigated for this clinical study, of whom 91 (91.00%) were suspected to suffer from ADR. Informations regarding various ADRs were obtained from the patients as well their guardians.These events were confirmed after consultation with the psychiatrist and simultaneously recorded for each patient. Details of prescribed medications, various adverse events, management of ADR as well as pathological investigations done were recorded in the format prepared by the department of Clinical and Experimental Pharmacology, Calcutta School of Tropical Medicine, Kolkata-700073. For causality assessment, all of these 91 patients were considered. Causality of adverse events was assessed by Naranjo's algorithm and WHO-UMC scale[18].

Table 1: Frequency of prescribing atypical antipsychotics and observed adverse events

Atypical antipsychotic	No. of times the drug have been prescribed n=91	No of adverse event n=171	Incidence of ADE per 100 prescriptions
Olanzapine	76(83.51%)	141(82.45%)	185.52
Risperidone	11(12.08%)	21(12.28%)	190.00
Quetiapine	01(1.09%)	03(1.75%)	300.00
Clozapine	3(3.29%)	06(3.50%)	200.00

Table 2: Spectrum of suspected ADR noted among 91 patients

Type of ADR	No (% of all ADR)
Weight gain	47(51.64)
Sedation	11(12.08)
Insomnia	09(9.89)
G.I. upset	08(8.79)
Aggressive behavior	06(6.59)
Dry mouth	05(5.49)
Alopecia	05(5.49)
Anxiety	04(4.39)
Sexual dysfunction	04(4.39)
Fatigue	04(4.39)
Dizziness	04(4.39)
Tremor	03(3.29)
Asthenia	03(3.29)
Anorexia	03(3.29)
Cough	03(3.29)
Headache	03(3.29)
Concentration difficulty	02(2.19)
Itching	02(2.19)
Nervousness	02(2.19)
Abdominal pain	02(2.19)
Hypersalivation	02(2.19)
Restlessness	02(2.19)

Table 2: Continued: Spectrum of suspected ADR noted among 91 patients

Type of ADR	No. % of all ADR
Increased tear production	02(2.19)
Neck pain	02(2.19)
EPS (Extrapyramidal Syndrome)	02(2.19)
Nausea	02(2.19)
Confusion	02(2.19)
Increased appetite	02(2.19)
Forgetfulness	02(2.19)
Oedema	02(2.19)
Blurred vision	02(2.19)
Myalgia	01(1.09)
Increased talk during sleep	01(1.09)
Reduce menstrual blood loss	01(1.09)
Anaemia	01(1.09)
Somnolence	01(1.09)
Burning sensation or finger	01(1.09)
Suspicious	01(1.09)
Talkative	01(1.09)
Irritable behavior	01(1.09)
Burning sensation all over the body	01(1.09)
Leucorrhea	01(1.09)
Polyuria	01(1.09)
Burning sensation of sole	01(1.09)
Premature Ejaculation	01(1.09)
Impaired memory	01(1.09)
Warm hand and leg	01(1.09)
Eye irritation	01(1.09)
Abnormal behavior	01(1.09)
Chest pain	01(1.09)

Table 3: Suspected ADRs categorized as probable (n=99) and offending agents

Category of ADR	Total no of adverse events (n=171)	Adverse drug Event	Offending Drug(s)
Probable	47(27.48)	Weight gain	O(40),R(5),Q(1),C(1)
Probable	11(6.43)	Sedation	O(8),R(3)
Probable	6(3.50)	Aggressive behaviour	O(6)
Probable	4(2.33)	Fatigue	O(3),R(1)
Probable	4(2/33)	Dizziness	O(4)
Probable	3(1.75)	Headache	O(1),R(1),Q(1)
Probable	3(1.75)	Cough	O(3)
Probable	3(1.75)	Asthenia	O(3)
Probable	2(1.16)	Concentration difficulties	O(1),R(1)
Probable	2(1.16)	EPS	R(2)
Probable	2(1.16)	Abdominal pain	O(2)
Probable	2(1.16)	Nervousness	O(2)
Probable	2(1.16)	Hypersalivation	O(2)
Probable	1(0.58)	Insomnia	R(1)
Probable	1(0.58)	Blurred vision	R(1)
Probable	1(0.58)	Anxiety	R(1)
Probable	1(0.58)	G.I. upset	R(1)
Probable	1(0.58)	Sexual dysfunction	R(1)
Probable	1(0.58)	Myalgia	O(1)
Probable	1(0.58)	Somnolence	O(1)
Probable	1(0.58)	Oedema	O(1)

Causality assessment as per Naranjo's algorithm and WHO-UMC scale.

O-olanzapine, R-risperidone, Q-quetiapine, C- clozapine

Table 4: Suspected ADRs categorized as possible (n=72) and offending agents

Category of ADR	Total no of adverse events (n=171)	Adverse drug Event	Offending Drug (s)
Possible	8(4.67)	Insomnia	O(7),Q(1)
Possible	7(4.09)	G.I. upset	O(7)
Possible	5(2.92)	Dry mouth	O(5)
Possible	5(2.92)	Alopecia	O(5)
Possible	3(1.75)	Sexual dysfunction	O(2),Q(1)
Possible	3(1.75)	Anxiety	O(3)
Possible	3(1.75)	Anorexia	O(3)
Possible	3(1.75)	Tremor	O(3)
Possible	2(1.16)	Forgetfulness	O(2)
Possible	2(1.16)	Nausea	O(2)
Possible	2(1.16)	Restlessness	R(1),Q(1)
Possible	2(1.16)	Itching	O(1),R(1)
Possible	2(1.16)	Neck pain	O(1),Q(1)
Possible	2(1.16)	Confusion	O(2)
Possible	2(1.16)	Increase appetite	O(2)
Possible	2(1.16)	Increase tear frequently	O(2)
Possible	1(0.58)	Burning sensation in sole	O(1)
Possible	1(0.58)	Premature ejaculation	O(1)
Possible	1(0.58)	Polyuria	O(1)
Possible	1(0.58)	Leucorrhea	O(1)
Possible	1(0.58)	Irritable behavior	O(1)
Possible	1(0.58)	Suspicious	O(1)
Possible	1(0.58)	Burning sensation in finger	Q(1)
Possible	1(0.58)	Oedema	R(1)
Possible	1(0.58)	Talkative	R(1)
Possible	1(0.58)	Chest pain	O(1)
Possible	1(0.58)	Talkative during sleep	O(1)
Possible	1(0.58)	Reduced menstrual blood loss	O(1)
Possible	1(0.58)	Anaemia	O(1)
Possible	1(0.58)	Burning sensation in whole body	O(1)
Possible	1(0.58)	Warm hand & leg	O(1)
Possible	1(0.58)	Impaired memory	O(1)
Possible	1(0.58)	Eye irritation	O(1)
Possible	1(0.58)	Abnormal behaviour	O(1)
Possible	1(0.58)	Blurred vision	Q(1)

Causality assessment as per Naranjo's algorithm and WHO-UMC scale.

RESULTS

During pharmacovigilance study a total 100 patients were investigated, of whom 91(91.00%) patients were suspected of having at least one ADR. Of these 91 patients, 53 (58.24%) were males and 36 (39.56%) were females and 2(2.20%) were children. During the 5 months observation period, it was seen that a total of 91 patients were treated mostly with four different second

generation antipsychotics (SGAs) such as clozapine, olanzapine, quetiapine, and risperidone (Table1). It was also noted that atypical antipsychotic drugs were used in the following dosages i.e. olanzapine (5mg, 10mg), risperidone(2mg, 1mg), clozapine(0.5mg) and quetiapine (100mg, 50 mg & 25 mg). Among 91 patients in total 171 adverse event were noted. Most common ADRs were weight gain 47(51.64%), sedation 11(12.08%), insomnia 09(9.89%), G.I.upset 08(8.79%), aggressive behavior 06(6.59%), dry mouth 05(5.49%), alopecia05(5.49%), anxiety 04(4.39%), sexual dysfunction 04(4.39%), fatigue 04(4.39%), dizziness 04(4.39%), tremor 03(3.29%), asthenia 03(3.29%), anorexia 03(3.29%), cough 03(3.29%), headache 03(3.29%), concentration difficulty 02(2.19%), itching 02(2.19%), nervousness02(2.19%), The spectrum of suspected ADRs as noted among 91 patients are presented in Table 2. Causality assessment had done according to the both Naranjo's algorithm and WHO-UMC assessment scale which revealed that 99 ADRs (57.89%) belonged to "probable" category, whereas 72 (42.11%) were of "possible" type.

DISCUSSION

A mental disorder or mental illness is a psychological pattern, actively reflected in behavior, that is generally associated with distress or disability. This symptom is not considered a part of normal development of a person's culture. Mental disorders are generally defined as (in one extreme argues), that it is entirely a matter of value judgements while another proposes that it is or could be entirely objective and scientific. This may be associated with particular regions or functions of the brain as well as rest of the nervous system. The recognition and understanding of mental health conditions have changed over time and across cultures, and there are still variations in definition, assessment as well as classification.[21-23] During this observational study 91 patients were treated with atypical antipsychotic drugs such as olanzapine (5mg,10mg), risperidone(2mg, 1mg), clozapine(0.5mg) and quetiapine (50.00mg). Patients were diagnosed as chizophrenia(33 patients), it is a mental disorder characterized by a breakdown of thought processes and by poor emotional responsiveness. It is related with various clinical symptoms like as auditory hallucinations, paranoid ,bizarre delusions & disorganized speech and thinking.[24-25]

(ii)bipolar affective disorders(24 patients),historically known as manic-depressive disorder, is a psychiatric diagnosis that describes a category of mood disorders defined by the presence of one or more episodes of abnormally elevated energy levels, cognition, and mood with or without one or more depressive episodes.[26-27] (iii)depression(12 patients) is a state of low mood and aversion to activity that can affect a person's thoughts, behavior, feelings etc. symptoms of depressed people associated sad, anxious, empty, hopeless, helpless, worthless, guilty, irritable, or restless.[28-29](iv)mental retardation(10 patients),it is a generalized disorder appearing before adulthood, characterized by significantly impaired cognitive functioning and deficits in two or more adaptive behaviors.[30] (v)delusions (7 patients), it is associated with dogma, poor memory, illusion, or other effects of perception. [31-32] (vi)paranoid (5 patients), is a thought process believed to be heavily influenced by anxiety or fear, often to the point of irrationality and delusion[33]. In this experimental study it has been observed that continuous use of second generation antipsychotics like as olanzapine, risperidone, quetiapine, clozapine minimizes the mental disorders simultaneously those are causes diverse adverse drug reaction. During study total 171 number of adverse events were observed such as weight gain, sedation, insomnia, G.I. upset, aggressive behavior, dry mouth, alopecia, anxiety, sexual dysfunction, fatigue, blurred vision, burning sensation of finger etc. All adverse events were investigated in each patient and reported time to time. After then causality assessment of suspected ADRs were also done for 91 patients.

CONCLUSION

Existing data suggested that continuous administration of second generation antipsychotics such as olanzapine, risperidone, quetiapine, clozapine provide symptomatic relief in mental disorders and simultaneously cause various adverse drug reactions. These documented ADR reports and the result of the present study may be helpful for the future researchers to carry out further study in this area as well as may aware the clinicians regarding the ADR profile of the otherwise very frequently prescribed class of antipsychotic agents.

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