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ANALYSIS OF ADVERSE DRUG REACTIONS AND DRUG UTILIZATION ASPECTS OF ANTIPSYCHOTIC MEDICATIONS AT PSYCHIATRY DEPARTMENT OF A TERTIARY CARE HOSPITAL IN GUJARAT

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Abstract
Analysing prescriptions for utilization and Adverse Drug Reactions is crucial for rational drug use. In the context of mental health, particularly in India, where limited healthcare funds demand optimal drug prescription, Understanding the prescription patterns becomes crucial. This study centres on antipsychotic medications, essential in treating various mental disorders, including schizophrenia and psychosis and adverse drug reactions associated with it. This aims to analyse the prescription patterns, adverse drug reactions (ADRs), and drug utilization aspects of antipsychotic medications and analysing prescriptions according to WHO/INRUD prescribing indicators in the Psychiatry department of a tertiary care hospital in Gujarat, India. To do so, a hospital-based observational study involving 400 patients from outpatient and inpatient departments was carried out. Collected data includes patient demographics, medical history, prescribed drugs and adverse reactions. The Institutional Ethics Committee provided approval and necessary permissions. Of all 400 patients analysed, 71% were male, with a predominant age group of 31-50 years. Atypical antipsychotics were more frequently prescribed (65%) compared to typical ones. Adverse drug reactions were reported in 31.25% of patients, with Chlorpromazine, Trifluoperazine, and Risperidone being associated with the highest number of ADRs. Schizophrenia accounted for 52% of prescriptions, and oral administration was the most common route (93.65%). In conclusion, the study reveals a notable utilization of atypical antipsychotics, shedding light on specific drugs associated with higher ADRs. These findings provide insights into prescription practices, aiding in the promotion of rational drug use in psychiatric settings, especially concerning the prevalent mental health disorders in India.

Keywords: Antipsychotics, Adverse drug reactions, Prescription pattern, WHO/INRUD prescribing indicators, Psychiatric disorders

Introduction

The National Mental Health Survey of India (2015-2016) reported a 13.7% lifetime prevalence of mental morbidity and 10.6% current prevalence. [1] Most conditions are managed with medications, yet irrational prescribing can lead to severe ADRs and increased treatment cost. Utilizing essential drug lists promotes Rational drug utilisation. [2]

Psychiatric medications are frequently associated with ADRs, and patients often require multiple drug trials due to varied responses. [3] Given the chronic and relapsing nature of many disorders, long-term

medication use is recommended by guidelines, [4] this increases ADR risks, including life-threatening (neuroleptic malignant syndrome) or disabling (tardive dyskinesia) ADRs. It becomes crucial for psychiatrists to be aware of the process involved in identifying and reporting ADRs, especially new and unrecognised ones.[5,6,7]

Psychosis is a key feature in various disorders, not just schizophrenia, making antipsychotics essential.[8] First-generation antipsychotics (FGAs) were the earliest treatments,[9] but second-generation antipsychotics (SGAs) are now preferred due to similar efficacy and lower extrapyramidal side effects.[10] SGAs primarily act via 5HT2A and D2 antagonism, reducing EPS and hyperprolactinaemia.[8]

This study aims to observe changing trends in antipsychotic use and document ADRs throughout treatment. Then such details were observed and recorded from 400 study participants cross-sectionally. Later data was entered in excel sheet to derive mean and percentage of observed trends.

Materials and Methods

This hospital-based observational study, conducted from November 2020 to December 2021 in a tertiary care hospital's Psychiatry Department, included 400 randomly selected patients (aged 18+). Relevant data was obtained cross sectionally after an approval from institutional ethics committee. Study conducted was in accordance with Declaration of Helsinki's principles. Included participants were prescribed at least one antipsychotic drug and consented to the study. Data, recorded in CRF, covered demographics, diagnosis, medical history, treatment details, and adverse drug reactions (ADRs). Prescriptions were assessed for rationality using WHO/INRUD prescribing indicators. Diagnosis, comorbidities, ADRs, medications, and treatment duration were documented. Data was analysed in Excel using statistical tests like MEAN ± SD and percentage

Results

Out of 400 patients, 71% were male and 29% female, with a male-to-female ratio of 2.47:1. The majority (61.75%) were aged 31-50 years, followed by 51-70 years (22%) and 18-30 years (14.75%). Ages ranged from 18 to 82 years, with a mean ± SD of 42 ± 13 years. Schizophrenia was the most common reason for antipsychotic prescriptions (52%), followed by depression (16.75%) and alcohol use disorder (7.75%) [Figure 1]

A total of 1,409 drugs were prescribed, with an average of 3.7 ± 1.7 drugs per prescription. Among these, 590 (41.9%) were antipsychotics, averaging 1.47 ± 0.71 per prescription. Most (98%) were prescribed by generic names, with only 2% by brand names. Injectable antipsychotics accounted for 6.44%, primarily haloperidol (22 patients) and fluphenazine decanoate (16 patients), reflecting the predominance of outpatient-based treatment. [Figure 2]

Fixed-dose combinations (FDCs) constituted 7.45% of all drugs and 17.79% of antipsychotics. Adherence to NLEM 2015 was 34.74%, while 73.72% of antipsychotics were from the Gujarat State Drug Formulary. Polypharmacy, defined as prescribing more than five drugs per patient, was observed in 13.75% of cases, while 8% of patients received more than two antipsychotics. The findings indicate a high prevalence of generic prescribing, limited use of injectables, and moderate adherence to essential medicine lists, suggesting opportunities for optimizing prescription patterns [Table 1]

Table 1: Prescription pattern analysis based on WHO/INRUD:

Drug use Indicators	Result of analysis
Total no. of prescriptions	400
Total no. of drugs	1409
Total no. of Antipsychotics	590
Average no. of drugs per prescription	3.7±1.7
Average no. of the Antipsychotic drugs per prescription	1.47±0.71
Percentage of the Antipsychotics prescribed by generic name	98%
Percentage of Injectable antipsychotics prescribed	6.44%

Percentage of Prescriptions containing FDCs: out of total 1409 drugs, out of 590 antipsychotics	7.45% 17.79%
Percentage of the Antipsychotics prescribed from Gujarat essential drug list (2020-'21)	73.72%
Percentage of the Antipsychotics prescribed from NLEM (2015)	34.74%

Many antipsychotics share overlapping side effects, making it challenging to identify the causative agent in combination therapy without de-challenge and rechallenge. Among 14 patients on Risperidone + Trifluoperazine, 4 developed tremors. In 9 patients on Risperidone + Haloperidol, one experienced tremor. Chlorpromazine + Trifluoperazine was given to 16 patients, with 4 reporting tremors. Both patients on Clozapine + Risperidone developed tremors. Of 3 cases on triple therapy (Risperidone, Haloperidol, Trifluoperazine), 1 had tremors. Given that all these drugs can cause extrapyramidal side effects, identifying the exact cause remains difficult. [Table 2]
Duration at which ADR appeared also varied based on type of ADR and duration of treatment. [Table 3]

Table 2: Adverse Drug Reactions:

ADR	Drug Suspected	No. of prescriptions	No. of ADR	Percentage of ADR developed
Tremors	Risperidone	111(monotherapy)	21	18.91%
	Trifluoperazine	30	8	26.66%
	Haloperidol	29	3	10.34%
	Flupentixol	28	1	3.57%
	Thioridazine	28	3	10.71%
	Risperidone+ Trifluoperazine	14	4	28.57%
	Risperidone + Haloperidol	9	1	11.11%
	Chlorpromazine+Trifluoperazine	16	4	25%
	Risperidone+ Haloperidol+ Trifluoperazine	3	1	33.33%
Sialorrhea	Haloperidol	43	2	4.65%
	Trifluoperazine	63	1	1.58%
Sedation	Clonazepam	46	7	15.21%
	Chlorpromazine	24	14	58.33%
	Thioridazine	28	1	3.57%
Weight gain	Olanzapine	120	11	9.16%
	Clozapine	9	1	11.11%
Diarrhea	Escitalopram	40	2	5%
Constipation	Benzhexol	158	6	3.16%
	Risperidone	137	5	3.64%
Dry mouth	Benzhexol	158	20	12.65%
Urinary Retention	Benzhexol	158	4	2.53%
Orthostatic Hypotension	Trifluoperazine	63	2	7.93%
	Chlorpromazine	24	2	8.33%
	Risperidone	137	1	0.72%

Discussion

Mental health disorders in India are prevalent, yet stigma, discrimination, and limited access create a substantial treatment gap. A 2017 survey reported a 9.3% lifetime mental morbidity in Gujarat, with the 40-49 age group most affected. Alcohol use disorder was higher in males (9.1% vs. 0.5%), while depressive and stress-related disorders were more common in females. [1]
A 2014 Karnataka study found 71% of antipsychotic prescriptions were for males. Smitha R. et al (2014) observed similar result showing 69% males and 31% females. [11,12]

Table 3. ADR lag period

ADR	No. of ADR	Duration between start of treatment and Onset of ADR (mean duration)
Tremors	46	2.75 years
Sialorrhea	3	2 years
Sedation	22	12.45 months
Weight gain	12	2.41 years
Diarrhoea	2	1.5 years
Constipation	6 (Benzhexol)	5.8 months
	5 (Risperidone)	3.4 years
Dry mouth	20	8.5 months
Urinary Retention	4	4.75 months
Orthostatic Hypotension	5	3.1 years

In our study of 400 patients, schizophrenia was the most common indication (52%), followed by mood disorders (25.25%). Oral administration was dominant (93.65%), with risperidone (23.22%) and olanzapine (20.33%) as the most prescribed atypical antipsychotics. Injectable antipsychotics were 6.44%, included haloperidol and fluphenazine decanoate injections. Shweta. O et al (2019) reported similar findings. [13] More of Atypical antipsychotics were used [65%]. Similarly, in a study done by Banerjee et al (2013), most patients received atypical antipsychotics (59%) while only 28.9% received typical antipsychotics.[14] In some studies, use of Typical antipsychotics was only 4-6%[15,16,17].Contrary to this, Thakkar K.B et al (2013) reported typical antipsychotics predominance. Cost effective availability from government hospital supply, from previous NLEM list can be one of reasons. [18] FDCs accounted for 7.45% of prescriptions. Mukherjee et al. (2014) found 18.36% of psychotropic prescriptions contained FDCs. [19]

Of all prescribed drugs, 73.72% were from the Gujarat Essential Drug List (2020-2021) and 34.74% from NLEM (2015). The average drugs per prescription (3.7) exceeded the WHO standard (<2), indicating a need for multidrug therapy in psychiatric cases. In a study done by Tejus et al (2020), an average of 2.35 drugs were prescribed. Gosh et al. (2013) reported similar trends, attributing them to government drug supply. [20,21] ADRs were reported in 31.25% of patients (125 ADRs in 95 patients). Chlorpromazine caused the most ADRs, followed by trifluoperazine and risperidone. EPS (11.5%), primarily tremors and sialorrhea, was the most common ADR. Chawla et al. (2017) found risperidone had the highest ADRs, followed by olanzapine and aripiprazole. [22] ADR patterns varied across studies. Risperidone was linked to tremors, constipation, and hypotension, while Balaji et al. (2017) and Ranjan et al. (2020) reported weight gain, anorexia and rashes. [23,24]

Kiran et al. (2011) observed gastrointestinal and sleep disturbances as short-term ADRs, with EPS, fatigue, and seizures as long-term effects. [25] Short-term ADRs appeared within days to months, with some developing tolerance, while long-term ADRs emerged over months to years with lower tolerance. Anticholinergic effects appeared within month(s), EPS and weight gain after two years, and sedation within one year. This study has limitations. More data is needed with a balanced case selection. Active ADR follow-up was not feasible for many patients. Factors like special populations, switching strategies, and side effect monitoring should be considered. Findings from a single tertiary care hospital in western India may not be generalizable nationwide.

Figure 1. Common Psychiatric Conditions observed

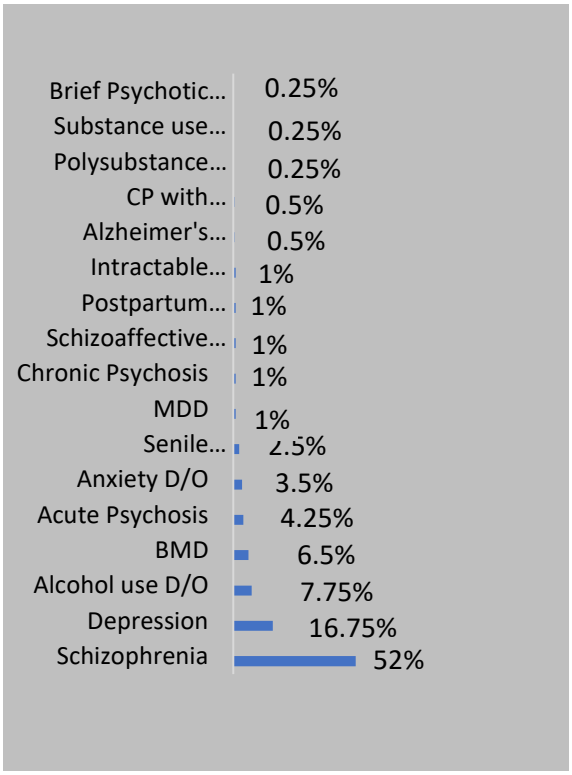
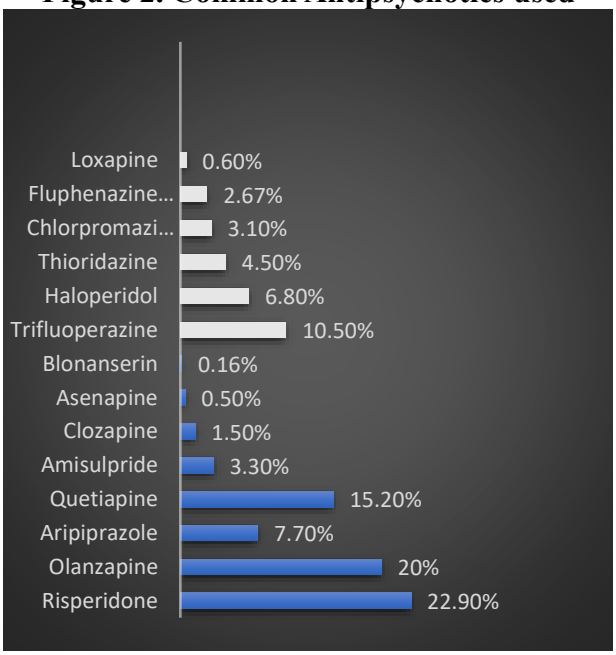


Figure 2. Common Antipsychotics used



Conclusion

This study examines changing trends in medication use from the Essential Drug List (EDL), with 73.72% of antipsychotic utilization sourced from the state's supply. This reflects improved availability of safer, diverse medications. Increased EDL usage and generic prescribing indicate progress toward rational drug use. Early detection strategies, as recommended by guidelines, are crucial to preventing ADRs, especially with psychotropic drugs for chronic conditions. Active ADR reporting is essential, yet underreporting by healthcare professionals and patients remains a limitation. Overall, this study provides valuable insights into drug utilization and common ADR patterns of antipsychotics in a district-level tertiary care hospital in western India.

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Declaration of Conflicting Interests
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Respective authors' contributions:
1. Dr. Shreya Shah [Professor & Head of department, department of Pharmacology, Medical College Baroda]
-Coming up with research question and objectives
-Providing guidance in preparing protocol, case report form as well as research article
-Proof reading
-Reviewing initial draft and finalizing research article
2. Dr. Krishna Patel [Assistant Professor, department of pharmacology, GCS Medical College]
-Collecting data in case record form, data compilation & entry as well as analysis
-Preparing research article.

Footnotes
Abbreviations
FGA: First Generation Antipsychotics
SGA: Second Generation Antipsychotics
FDC: Fixed dose combinations
ADR: Adverse Drug Reaction
WHO/INRUD: World Health Organization/ International Network for Rational Use of Drugs

Data availability
Can be received on proper request

Artificial Intelligence use
AI was not used in this study

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