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Drug Prescribing Pattern and Cost Analysis of Antipsychotics at a Tertiary Care Hospital in South India

S. Vedha Pal Jeyamani[1*], Asha K Rajan[1], R Gowri[1], R Monica[1], M Prema[1], M Mohamed Javith[1], M Murugan[2]

[1]Jaya College of Paramedical Sciences, Chennai, India
[2]EGS Pillay College of Pharmacy, Nagore Road, Nagapattinam, India

***Corresponding author e-mail:** swetha21112000@gmail.com

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ABSTRACT

Aim: The aim of the present study was to analyze the cost of Psychiatric drugs in the elderly and to evaluate potentially inappropriate medications (PIMs) in them at the Neurology Outpatient department of a tertiary care hospital using Beers criteria and factors associated with it. **Study design:** An observational cross-sectional study was carried out in the elderly patients aging ≥ 60 years from the Neurology OPD department for a period of 6 months. PIMS and other risk factors were identified with the help of Beers 2015 criteria. Direct cost of prescribed drugs was calculated making use of guidelines like CIMS, MIMS etc., **Results and discussion:** Among the psychological conditions evaluated Epilepsy (23.6%) and Schizophrenia (15.6%) were found to be more common among others. Sedative-Hypnotics (39.2%) and anti-epileptics (23.6%) were the commonly prescribed category of drugs. Cost-ratio analysis of Anti-psychotics was found to vary greater when compared to others. Olanzapine (1:12), Chlorpromazime (1:5.1) and Risperidone (1:15) were the prescribed anti-psychotics. All other categories of drugs were found to comply to certain extent with economic status of patients. Antidepressants prescribed posed about 30% patients with PIMs. Typical and atypical anti-psychotics also were PIM with a percentage of 25.7%. Other PIMs due to disease, drug interactions were also studied. **Conclusion:** A cost-effective management with availing of more economic therapy to the patients could be carried by a clinical pharmacist. Programs encouraging the prescribing of generic drug practice and their benefits compared to brand drugs could be clearly worked out bring more awareness to public.

Keywords: Anti-psychotics, Psychosis, Neurology, Olanzapine.

INTRODUTION

Mental and behavioral problems are increasing part of the health conditions all over the world. The burden of illness resulting from psychiatric and behavioral disorder is enormous [1-3]. It remains grossly under represented by conventional public health statistics which focus on mortality rather than morbidity or dysfunction [4-7]. The psychiatric disorders account for 5 of 10 leading causes of disability as measured by years lived with a disability. The burden for neuropsychiatric disorders is projected to increase to 15% by the year 2020 [8-10]. At the international level mental health is receiving increasing importance as reflected by the WHO focus on mental health as the theme for various occasions.

Resources and services for mental and behavioral disorders are disproportionately low compared to burden caused by these disorders the world over. In most developing countries care programs for the individuals with mental and behavioral problems have a low priority [11-14]. Provision of care is limited to a small number of institutions usually over-crowded

and under-staffed. Due to widely reported inappropriate drug prescriptions common in clinical practice with implication for significant economic and clinical consequences, drug utilization research became essential for regularly assessing drug use patterns in health facilities, in order to identify opportunities for remedial measures to enhance achievement of therapeutic goals and patient's quality of life [15-19].

Rational drug prescription entails the use of minimum number of drugs to obtain the best possible effects at reasonable cost. Antipsychotic prescription pattern are fundamentally different across countries and regions due to variations in factors including health care policies availability and cost of drugs [20-24]. For developing countries where resources are more limited, the cost of inappropriate drug prescription can be enormous in addition to the risk of clinical consequences. It becomes necessary that regular auditing of prescription be carried out to ensure rational and cost effective use of drugs to increase efficacy, reduce side effects and provide feedback for prescribers [25-28].

Antipsychotic is a class of agents which are able to reduce psychiatric symptoms in a wide range of conditions like Schizophrenia, Bipolar disorders, Psychotic Depression, Organic Psychosis, Drug induced psychosis [29-33]. Among the psychiatric illness detected, affective disorders, especially depression out-numbered the others. Acute organic brain syndrome and dementia formed one-third of the diagnosis. Depression involved both sexes but Mania was five times common in males.

Handicaps and physical illness were significantly more in the study subjects. In India dementia is more prevalent, multi-infract type is commoner than senile dementia Alzheimer's type (SDAT). Among the rural people, family and social integration of the elderly was not a much problem. Their involvement in it was found to be varied from person to person [34-37]. Urbanization brings deleterious consequences for mental health through the influence of increased stressors and factors such as overcrowded or polluted environment, dependence on a cash economy, high level of violence and reduced social support. Thus there is a considerable stigma attached with mental disorders and ignorance regarding information about mental illness and available help and treatment [38-40].

The present study focuses on reporting the potentially inappropriate medications among the Geriatrics making use of Beer's criteria and reporting even on the co-morbid conditions faced by them with an Analyzation made on the cost of various categories of psychiatric drugs with their cost variations [41,42].

MATERIALS AND METHODS

An observational cross-sectional study was carried out with a number of 250 patients of both sexes from age of ≥ 60 years. Complete demographic details were collected including their history and family conditions, therapy being processed with combinational treatment also considered. Analysis of the prescriptions was done by following CIMS, MIMS, other documents like IDR (Indian drug review) for calculating cost among various brands, average cost, ratio etc. PIMs found out among the patients were reported with conformation from Beer's criteria.

Study duration: It was carried out for a period of 6 months from June 2017 to December 2017.

Study setting: Study was conducted at the out-patient department of neurology at the Tiruvallur government hospital with frequent monitoring on patients.

Design of the study: It was an observational study on cost analysis carried out with the reporting of PIMs in the geriatric.

Inclusion criteria of the patients:

- Willingness of the patients in the study was ensured with consent.
- Age of the patients was selected from 60-80 years.
- Patients who were being on therapy and their symptoms still persisting were only selected for study.
- Patients who made a regular visit and had been for past 1 month before the study to clinic were only selected.
- Patients showing symptoms of psychotic conditions like hallucinations, delusions etc, were selected.

Exclusion criteria were those who are unconscious, drug-addicts, not able to respond well due to mental retardation etc.

RESULTS AND DISCUSSION

Table 1: Predominant morbidities of the patients

Conditions	Number of patients	% of patients
Neurological	46	18.7
Cardiovascular	42	17.4
Dermatological	32	13.3
Respiratory	14	6.1
Genitourinary	8	3.5
Psychiatry	20	8.1
Oncological	15	6
Gastrointestinal	23	9.9
Hearing	20	8.2
Visual	21	8.8
Locomotor	9	4

Among the 250 patients analyzed the following predominant factors given under Table 1 were found to persist in them. Out of this neurological (18.7%) and cardiovascular (17.4%) were found to be in a greater number. The least was locomotor morbidities (4%) (Tables 2 and 3).

Table 2: Indicators used in the study

Indicator parameters	Result
Total number of prescriptions analyzed	250
Average number of prescriptions per day	2.7 (± 0.75)
Percentage of psychotic drugs prescribed by generic name	85%
Percentage of psychotic drugs prescribed by brand name	15%

Table 3: Distribution regarding number of drugs per prescription

Number of drugs per prescription	Number of prescription	% of prescription
1	48	19.2
2	96	38.4
3	87	34.8
4	16	6.4
Above 4	3	1.2
Total	250	100

Most of the prescriptions had a minimum number of 2-3 psychotic drugs in them. 38.4% had 2 drugs and 34.8% had 3 drugs. 3 to 4 drugs were found only under certain conditions (Table 4).

Table 4: Prevalence of severe mental morbidity

Psychotic condition	Number of patients	% of patients
Epilepsy	59	23.6
Schizophrenia	39	15.6
Mania, Panic disorder	35	14
Depressive Psychosis	30	12
Parkinson disorder	16	6.4
Alzheimers disorder	20	8
Anxiety	28	11.2

Insomnia	23	9.2

Most common condition persisting among the geriatrics was Epilepsy (23.6%), Schizophrenia (15.6%), Depressive psychosis (12%), Mania (14%). All other prevailing conditions were in normal numbers (Table 5).

Table 5: Gender distribution

Sex	Number of patients	% of patients
Male	132	52.8
Female	118	47.2

Male patients consisted of about 52.8% whereas female patients were about 47.2% due to more number of males in mania and schizophrenic condition (Table 6).

Table 6: Age distribution

Age of the patients	Number of patients	% of patients
60-65	92	36.8
65-70	85	34
70-75	50	20
75-80	23	9.2

About 36.8% patients were chosen from age category of 60-65 years, and 34% from 65-70 years. Low numbers were found in the range of 75-80 years (Table 7).

Table 7: Distribution of drugs

Category of drugs	Number of prescriptions with this drugs	% of prescriptions
Typical antipsychotics	37	14.8
Sedative-hypnotics	98	39.2
Anti-epileptics	59	23.6
Anti-depressants	35	14
Atypical antipsychotics	28	11.2
Anti-Parkinson's	16	6.4
Anti-cholinergic	27	10.8

Sedative-hypnotics (39.2%) were found to have greater number among the commonly used drugs. Typical and atypical antipsychotics (26%) were also used to a large extent next to sedative-hypnotics. Anti-epileptics (23.6%) were the next most commonly used drug under psychotic conditions. All others were used in nominal rates. The least commonly used was Anti-Parkinson this was only about 6.4% (Table 8).

Table 8: Cost analysis of various brands of anti-psychotic drugs in the prescriptions

Generic name of the drug	Category	Strength of tablet form of doses	Minimum cost	Maximum cost	Average cost	Cost difference	Cost ratio
Alprazolam	Sedative-hypnotics (Benzodiazepine)	0.25 mg	7.50	15.20	11.35 ± 3.5	7.70	1:2
		0.5 mg	13.50	44.50	29 ± 15.5	31.00	1:3.3
		1 mg	18.00	50.60	34.3 ± 16.3	32.60	1:2.8
Chlordiazepoxide		10 mg	17.00	35.00	25.87 ± 9	18.00	1:2
		25 mg	25.30	52.50	38.9 ± 13.6	27.20	1:2
Diazepam	(Barbiturates)	2 mg	5.00	20.20	12.6 ± 7.6	15.20	1:4
		5 mg	7.00	33.21	20.1 ± 13	26.21	1:4.7
		10 mg	10.00	40.85	25.4 ± 15.4	30.85	1:4

Phenobarbital	(Benzodiazepine)	15 mg	35.17	57.25	46.21 ± 11.04	22.08	1:1.6
		30 mg	41.08	89.70	65.39 ± 24.31	48.62	1:2.1
		100 mg	82.72	156.52	119.62 ± 36.9	73.80	1:1.9
Flurazepam		15 mg	38.00	96.71	67.3 ± 29.3	58.71	1:2.5
Amitriptylline	Anti-depressant	10 mg	9.60	22.00	15.8 ± 6.2	12.4	1:2.3
	(NRIs)	50 mg	39.70	104.00	71.85 ± 32.15	64,3	1:2.6
		75 mg	20.00	58.40	39.2 ± 19.2	38.4	1:2.9
Fluoxetine	(SSRIs)	10 mg	21.00	30.00	25.5 ± 4.5	9.00	1:1.4
		20 mg	26.85	52.80	39.8 ± 12.9	25.95	1:1.9
	(MOI)	40 mg	48.00	58.50	53.2 ± 5.25	10.50	1:1.2
Selegiline		5 mg	49.10	121.80	85.45 ± 36.35	72.70	1:2.5
Chlorpromazine	Anti-psychotics	25 mg	7.14	36.90	22 ± 14.8	29.76	1:5.1
	(phenothiazine)	50 mg	10.25	47.80	29 ± 18.7	37.55	1:3.8
		100 mg	13.96	52.70	33.3 ± 19.3	38.74	1:4.6
	(Hetero-cyclic anti-						
Clozapine	Psychotic)	25 mg	18.00	25.00	21.5 ± 3.5	7.00	1:1.4
		50 mg	25.00	53.00	39 ± 14	28.00	1:2.1
		100 mg	60.50	82.00	71.25 ± 10.75	21.50	1:1.3
Olanzapine		2.5 mg	14.00	25.00	19.5 ± 5.5	11.00	1:1.8
		5 mg	19.50	240.00	129.75 ± 110.2	220.50	1:12.3
		10 mg	38.00	470.00	254 ± 216	432.00	1:12.3
Risperidone		1 mg	9.08	135.00	72 ± 62.9	125.92	1:15
		2 mg	17.70	270.00	143.8 ± 126	252.30	1:15
		4 mg	29.90	540.00	284 ± 255	510.10	1:18
Carbamazepine		100 mg	6.69	9.64	8.1 ± 1.5	2.95	1:1.4
		200 mg	12.10	23.50	17.8 ± 5.7	11.40	1:1.9
		400 mg	26.50	41.25	33.8 ± 7.3	14.75	1:1.5
Levetiracetam		250 mg	49.00	99.00	74 ± 25	50	1:2
	Anti-epileptics	500 mg	98.00	153.00	125.5 ± 27.5	55	1:1.5
		750 mg	115.00	238.00	176.5 ± 61.5	123	1:2
Valporate		250 mg	32.00	64.00	48 ± 16	32	1:2
		500 mg	72.00	152.00	112 ± 40	80	1:2
Carbidopa /		25 + 100 mg	23.06	47.10	35.08 ± 12	24.04	1:2
levodopa		25 + 250 mg	26.54	59.85	43 ± 16.6	33.31	1:2.2
	Anti-parkinsons	10 + 100 mg	11.35	41.25	26.3 ± 14.9	29.90	1:3.6
Amantadine		100 mg	69.30	108.75	89 ± 19.7	39.45	1:1.5
Trihexyphenydyl		2 mg	7.47	22.00	14.7 ± 7.2	14.53	1:3
Donepezil	Anti-cholinergic	5 mg	153.00	270.53	211.7 ± 58.71	117.53	1:1.7
		10 mg	216.00	489.97	352.9 ± 136.9	273.97	1:2.2

Table 9: Combinations of antipsychotic drugs made use of and their cost analysis

Generic name of the drugs	Minimum cost	Maximum cost	Average cost	Cost difference	Cost ratio
Trihexyphenidyl Hcl 2 mg+ Trifluperazine 5 mg + Chlorpramazine Hcl 50 mg	13.45	52.51	32.9 ± 19.5	39.06	1:4
Alprazolam 0.25 mg + Sertraline 25 mg	33.00	56.00	44.5 ± 11.5	23	1:1.7
Amitryptyline 25 mg+ chlordiazepoxide 10 mg	15.00	43.85	29.4 ± 14.4	28.85	1:3

Phenobarbitone 30 mg+ Phenytoin 100 mg	9.20	13.30	11.25 ± 2	4.1	1:1.4
Olanzapine 5 mg+ Fluoxetine 20 mg	60.00	86.00	73 ± 13	26	1:1.4

In the cost analysis carried out among the psychotic drugs prescribed to the patients with their cost in India, it was clearly evident that anti-depressants like Olanzapine (1:12), Risperidone (1:15), chlorpromazine (1:5.1) showed a varied difference among the various brands of the same drug. This showed a clear benefit of prescribing of medicines in their generic name when compared to brand name which cuts down the extra expenses and increases the socioeconomics of common people [25,32,34]. The commonly used drugs were found to be in accordance with the economy of common people. Among the combination drugs prescribed combination of Trihexyphenidyl + trifluperazine + chlorpromazine was found to be with high cost ratio among others (1:4) (Table 9).

Table 10: Common PIM's monitored in older adults

Drugs	Rationale	No. of patients
Anti Parkinson agents	Not recommended for prevention of extra pyramidal symptoms with anti psychotics.	2
Anti depressants (alone or in combination) • Amitriptyline • Imipramine • Nortriptyline • Paroxetine	Highly anticholinergic, sedating &cause orthostatic hypotension.	4
Typical and atypical antipsychotics	Increased risk of cerebro vascular accident (stroke) and greater rate of cognitive decline & mortality in persons with dementia. Avoid anti psychotics for behavioral problems of dementia or delirium unless the older adults is threatening substantial harm to suffer others.	3
Barbiturates • Phenobarbital	High rate of physical dependence tolerance to sleep benefits greater risk of overdose at low dosages.	1
Benzodiazepines • Alprazolam • Lorazepam • Triazolam	Older adults have increased sensitivity to benzodiazepines & decreased metabolism of long acting agent in general, all benzodiazepine increase risk of cognitive impairment, delirium, falls, fractures, & motor vehicle crashes in older adults.	5

Among the commonly monitored PIMs, an increased rate was found in the use of Anti-depressants and Benzodiazepines, which were the commonly used drugs too. Anti-psychotics were also found in greater number next to Anti-depressants [43] (Table 10).

Table 11: PIM's due to drug-disease or drug-syndrome interactions in accordance with Beer's criteria

Diseases	Drugs	Rationale	Recommendation	No of patients
Chronic seizures /epilepsy	Chlorpromazine Clozapine Olanzapine	May be used in individuals with well controlled seizures in whom alternati ve agents have not been affective.	Avoid	2

Delirium	Anticholinergics Antipsychotics Benzodiazepines Chlorpromazine Sedative Hypnotics	Avoid in old adults with or high risk of delirium due to the potential of producing or worsening delirium. Avoid antipsychotics for behavioral problems of dementia or delirium. Antipsychotics are associated with greater risk of cerebro vascular accident & mortality in persons with dementia.	Avoid	4
Dementia or cognitive impairment	Anticholinergics Benzodiazepines Antipsychotics	Avoid because of adverse CNS effect. Avoid antipsychotics for behavioral problems of dementia or delirium. Antipsychotics are associated with greater risk of cerebro vascular accident & mortality in persons with dementia.	Avoid	2
History of falls or fractures	Antipsychotics Anticonvulsants Benzodiazepines SSRI'S	May cause ataxia, impaired psychomotor function, syncope shorter acting benzodiazepines are not safer than long acting ones. If one of the drugs must be used consider reducing use other CNS active medication that increase risk of falls & fractures & implement other strategies to reduce fall risk.	Avoid unless safer alternatives are not available avoid anti convulsants except for seizures and mooddism.	3
Parkinson diseases	All antipsychotics (except aripiprazole, quetiapine, clozapine)	Dopamine receptor antagonists with potential to worsen Parkinson symptoms.	Avoid	2

Among the drug-disease interactions of PIMs a greater percentage was found in Delirium and history of falls and fractures to be more common interacting with most of the psychotic drugs. Others like dementia, Parkinson, epilepsy were found in small number among patients but still persisted [43] (Table 11).

Table 12: Medications to be used with caution according to Beers posing PIMs

Drugs	Rationale	Recommendation	No of patients
Antipsychotics- Carbamazepine SSRI'S TCA'S	May exacerbate or cause syndrome of inappropriate Antidiuretics hormone secretion or Hyponatremia.	Monitor Na level closely when starting or changing dosages in older adult.	5

Anti-psychotics, anti-depressants were found to be used with caution among the patients due to their increasing levels of ADH. 5 patients among the wholesome were found and advised on monitoring of their sodium levels [43,40] (Tables 12 and 13).

Table 13: Drug-drug interactions to be avoided which are PIMs

Object Drug & Class	Interacting Drug & Class	Risk Rationale	Recommendation	No of patients
Anticholinergic	Anticholinergic	Increased risk of cognitive decline	Minimize no of anticholinergic drugs.	3
Antidepressants (TCA'S,	≥ 2 others CNS active drugs.	Increased risk of falls.	Avoid total of ≥ 3 CNS –	5

SSRI'S)			active drugs minimize number of CNS active drugs.	
Benzodiazepines	≥ 2 other CNS active drugs	Increased risk of falls & fractures.	Avoid total of ≥ 3 CNS active drugs minimize drugs minimize no of CNS active drugs.	4

Generally drug-drug interactions were common in a prescription containing more than 2 centrally active psychotic drugs. Hence maximum avoidance of this condition could be avoided. It in addition also increases the co-morbid conditions associated with them.

CONCLUSION

The cost analysis study carried out in the work inferred that Anti-psychotic drugs were prescribed to most of the patients under many conditions of Psychosis. But its cost was found to be varying in a wide condition which was not economical to the patients. Making use of poly-psycho-pharmacy was very common in the therapy which terribly created an increase in the number of PIMs. As a clinical pharmacist, more participation in such emergencies could be carried out which would be well benefitted. Optimization and rationalization of the therapy could be enrolled in the society by the clinical pharmacist.

COMPLIANCE WITH ETHICAL STANDARDS

Written informed consent was obtained from the patient for publication of the case study, inclusion of the accompanying images. Copies of written consent may be requested for review from the corresponding author.

CONFLICT OF INTREST

The authors declare no conflicts of interest concerning the content of this case report.

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