

## Pattern of Psychotropic Drug Prescription in the Elderly with Chronic Schizophrenia

Mohammad Reza Khodaei; MD.; Arash Mirabzadeh; MD.; Hashem Shemshadi<sup>1</sup>; MD.; Zabihollah Ashtari; Maryam Ranjbar; MD.; Golnaz Faizzadeh; MD.; Mersedeh Samiei MD.;

University of Social Welfare and Rehabilitation Sciences, Tehran, Iran

Alireza Khodaei<sup>2</sup>

Islamic Azad University, Science and Research Branch, Tehran, Iran

**Objectives:** Psychotropic drug use in the elderly with chronic schizophrenia is an important issue in the field of psychiatry. The main goal of this study was to clarify the pattern of such drug use in these patients, in order to consider such therapy plan and focus on its cost attributing measures, for a more reasonable quality of care program.

**Methods:** In this descriptive study, participants included 52 elderly patients at Tehran's Razi Mental Hospital who had chronic schizophrenia in the residual phase. Selected patients were taking at least two psychotropic drugs equivalent to 500mg Chlorpromazine. We prepared the list of the drugs used by completing the pre-designed questionnaire charts. Data were analyzed with SPSS 17.

**Results:** In one case (1.92%) the entries were Risperidone, Chlorpromazine, Fluphenazine Decanoate, & Thiothixene). In 11 cases (21.2%) there were three entries and in 40 cases (76.8%) there were two. The Chlorpromazine equivalent dose in each group ranged from the lowest dose (750. mg) to the highest (5600. mg). The highest Chlorpromazine dose (5600. mg) equivalent per milligram belonged to the four entries of (Risperidone, Chlorpromazine, Fluphenazine Decanoate & Thiothixene). The lowest Chlorpromazine dose (750. mg) was seen in 3 entries of Risperidone, Chlorpromazine & Fluphenazine Decanoate .

**Conclusion:** There was a high prevalence of using more than two psychotropic medications from the first atypical antipsychotic category. Less frequently, the second and the third typical antipsychotics were used. We recommend further research into more feasible patterns of psychotropic prescriptions, lowering the amount of medication use and considering their cost-benefits in the elderly with chronic schizophrenia .

**Keywords:** psychotropic drugs, chronic schizophrenia, elderly, monotherapy, polypharmacy

Submitted: 15 Nov. 2012

Accepted: 27 March 2013

### Introduction

Psychotropic Polypharmacy in psychiatry is an exception rather than a rule. Furthermore, excessive use of drugs causes more confusion and is also an economic waste in the health system. Patients with a history of chronic mental health are at high-risk for polypharmacy (1). Polypharmacy causes major risk and adverse reactions, causing more serious medical complications, medical errors, increased hospitalization, increased health care costs and decreased quality of life. On the other hand, this can create an even greater financial burden on the patients as well. Polypharmacy should be applied only if psychotropic monotherapy has failed, thus justifying the rational use of multiple antipsychotics. In the scientific literature, there is no single definition

of polypharmacy. In general, two definitions are presented. Accordingly, prescription of two or more drugs is called 'polypharmacy'. Scientists consider using two to four drugs as minor and using more than five medications as minor and major polypharmacy, respectively. Another definition is based on the clinical indications and different effects of drug administration. Accordingly, the irrational use of drugs that are not prescribed for a defined clinical benefit is termed as polypharmacy (2).

Most health problems increase with age and are associated with increased per capita drug consumption. In the last decade, drug consumption per capita in the United States has increased from 27 to 35% (6). Although drugs are used at any age, but they are most commonly used in older adults.

1- All correspondences to Dr. Hashem Shemshadi, email: <shemshadii@gmail.com>

2- Doctoral student

Treatment of elderly patients with multiple chronic diseases often requires prescribing multiple medications, which may be accompanied by dangerous complications (7). The side effects of Polypharmacy increase with other risk factors such as chronic geriatric diseases, age, lifestyle, gender and factors related to service providers (7). Each year 30000 people in the United States expire due to adverse effects of medications (8). Appropriate reduction of drug use is one of the best ways to enhance the quality of care in elderly with chronic schizophrenia. Today, new drugs can be used to treat a variety of such problems. Despite the multi-manufacturing of many psychotropic drugs, there is limited information about their efficacy, safety and concomitant use. Polypharmacy requires a medication guide entitled Guideline for Polypharmacy (14). Traditionally, polypharmacy is known as multi or irrational drug misuse, but sometimes the use of combined drugs is clinically effective. Some acceptable categorized definitions for such drug combinations are as follows;

1. Same-Class Polypharmacy: the use of two or more drugs of the same class such as specific Serotonin inhibitors.
2. Multi-Class Polypharmacy: the use of full therapeutic doses of drugs in different therapeutic groups, such as using Fluoxetine and Olanzapine in the treatment of mania.
3. Adjunctive Polypharmacy: the use of a drug that helps another drug's clinical effects.
4. Augmentation Polypharmacy: the use of a drug that potentiates another drug's effects.
5. Total Polypharmacy: a rough count of the patient's medications, or drugs in general.

Certainly, in some set of clinical situations the appropriate combination of drugs may even be necessary. For example, the use of a mood stabilizer in patients with bipolar disorder is accepted experimentally. (14). the use of antipsychotic drugs is a very common practice, but their inappropriate prescription is another issue. A study in Missouri showed that 25% of patients admitted to the emergency department and 33% of patients who were subsequently hospitalized, had misused some sort of antipsychotic medication. However, the use of antipsychotic drugs has consistently risen. The monitoring and control of antipsychotics abuse has been associated with success in some U.S. states. In Illinois, for example, the use of two or more antipsychotic drugs in the treatment of psychosis - for more than 10 days- must be confirmed (14).

The clinical symptoms of the patient as a whole deserve special attention when reducing the number of medications. The first source of information in such cases is the patient or the caretaker. Improved communications with the patient and his/her family is probably the most important step in resolving inappropriate polypharmacy. Involving patients and relatives in clinical assessments and treatment can be very helpful in assessing the rate of patient compliance. The physician and patient should discuss the results and outcomes of such therapy with each other. Every doctor has a different view of the patient and the treatment itself which provides a reasonable clinical benefit. Creating a bridge of trust between the physician and patient will make the drug administration process much easier. Adequate time spent with the patient's caretakers, which is much more difficult, will guarantee proper polypharmacy (18, 15, 14). For example, when combining the medication, the physician should be aware that if drug therapy is to be strengthened, antipsychotic drugs should not be combined with other categorical medications such as thyroid pills (18, 16). However, antidepressants & dopamine antagonists or serotonin antagonists are commonly prescribed in the treatment of psychotic depression (14). Almost all bipolar patients use more than one drug. Adding a serotonin antagonist (a specific inhibitor of serotonin) or dopamine drugs can be effective in such cases. Thus, polypharmacy in some circumstances may be unavoidable or even necessary for the elderly patients who suffer from chronic and severe psychotic disorders such as chronic schizophrenia (15). Little research has been conducted on the combined use of anti-psychotics. Most of the clinical trials and case studies have mainly reported addition of an atypical anti-psychotic drug such as clozapine to a typical psychotic patient's drug regimen. although many studies have investigated the short-term side effects of polypharmacy in different ages, genders and ethnicities, the long-term effects of such treatments is still unknown (14).

### Methods

In this descriptive research, the study population consisted of elderly patients (over 60 years) with chronic (more than 2 years) schizophrenia who were admitted in Tehran's Razi Psychiatric Hospital. After considering the inclusion and exclusion criteria, selected patients responded to a questionnaire form pre-designed by the researchers. The variables covered

by the data collection form such as gender, age, education, employment, duration of illness, duration of hospitalization, psychotropic drug use and their dosages were assessed via descriptive statistics such as mean, standard deviation, and relative frequency distribution. We assured the individuals that their information would be kept confidential. The collected

data were statistically analyzed by SPSS software version 17.

### Results

We obtained the outcome of variables with regards to age, gender, education and occupation (Chart 1).

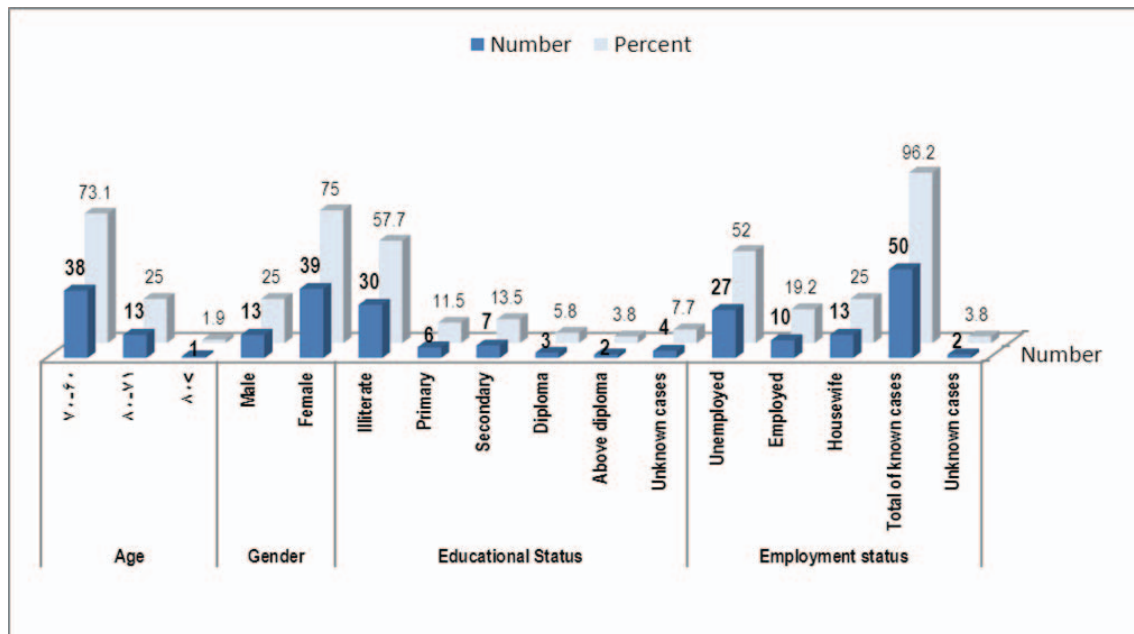


Chart 1. Distribution of demographic variables

The most common age group was between 60-70 years of age (71.2%); the majority were females (71%). Mostly, they were illiterate (57.7%) and the

majority were unemployed (52%). The duration of disease in the majority of the patients (71.2%) was more than 20 years (Table.1).

Table 1. Distribution of disease duration

Disease duration	Number	Percent
Under 20 Years	2	3.8
20 years and over	37	71.2
Total of known cases	39	75
Unknown cases	13	25
Total	52	100

Hospital stay for 31-40 years was observed in 30.8% and over 40 years of stay was observed in 7.7%, as

illustrated in Table (2).

Table 2. Distribution of hospital stay

Hospital stay	Number	Percent
Under 10 years	5	9.6
11-20 years	8	15.4
21-30 years	15	28.8
31-40 years	16	30.8
Over 40 years	4	7.7
Total of known cases	48	92.3
Unknown cases	4	7.7
Total	52	100

The pattern of psychotropic use is shown in Table (3). Two different antipsychotic medications were used in 11 cases, and three were used in the remaining 40 patients. Most of them were associated with the concomitant use of Risperidone & Fluphenazine Decanoate, Risperidone & Haloperidol, and

Risperidone & Chlorpromazine (19-23). In one patient, four drugs namely Risperidone, Fluphenazine Decanoate, Chlorpromazine & Thioridazine were used. Triple polypharmacy was observed in the concurrent use of Risperidone, Fluphenazine Decanoate & Chlorpromazine.

**Table 3.** Distribution of psychotropic polypharmacy

Type of Polypharmacy	First Atypical Antipsychotic	Second Atypical Antipsychotic	First Typical Antipsychotic	Second Typical Antipsychotic	Third Typical Antipsychotic	Number	Percent
4 entries	Risperidone		Chlorpromazine	Fluphenazine Decanoate	Thiothixene	1	1.92
	Risperidone		Chlorpromazine	Fluphenazine Decanoate		3	5.77
	Risperidone		Chlorpromazine	Thiothixene		2	3.85
	Risperidone		Thioridazine	Fluphenazine Decanoate		1	1.92
3 entries	Olanzapine		Fluphenazine Decanoate	Thioridazine		1	1.92
	Olanzapine		Fluphenazine Decanoate	Haloperidol		1	1.92
	Olanzapine		Fluphenazine Decanoate	Perphenazine		1	1.92
	Risperidone	Olanzapine	Chlorpromazine			1	1.92
	Risperidone		Chlorpromazine	Perphenazine	Haloperidol	1	1.92
	Risperidone		Fluphenazine Decanoate			9	17.31
	Risperidone		Chlorpromazine			7	13.46
	Risperidone		Haloperidol			5	9.61
	Risperidone		Haloperidol	Fluphenazine Decanoate		4	7.69
	Risperidone		Thiothixene			2	3.85
2 entries	Risperidone		Perphenazine			2	3.85
	Risperidone		Chlorpromazine	Haloperidol		2	3.85
	Olanzapine		Haloperidol			2	3.85
	Risperidone	Olanzapine				1	1.92
	Risperidone		Thioridazine			1	1.92
	Olanzapine		Chlorpromazine			1	1.92
	Olanzapine		Thioridazine			1	1.92
			Chlorpromazine	Fluphenazine Decanoate		1	1.92
			Chlorpromazine	Thiothixene		1	1.92
			Chlorpromazine	Perphenazine		1	1.92
						52	100

None of the patients used the atypical antipsychotics Risperidone and Olanzapine together, except in prolonged therapeutic cases. In all but 6 patients at least one atypical antipsychotic medication had been used. Illustrations of the polypharmacy are in order

of antipsychotic dose equivalents per mg of Chlorpromazine, showing the polypharmacy dose for some antipsychotic drugs equivalent to 5600 mg Chlorpromazine (Table 4).

**Table 4.** Psychotropic polypharmacy distribution in order of Chlorpromazine dose equivalent per milligram

Type of Polypharmacy	First Atypical Antipsychotic	Second Atypical Antipsychotic	First Typical Antipsychotic	Second Typical Antipsychotic	Third Typical Antipsychotic	Chlorpromazine dose equivalent per milligram
4 entries	Risperidone		Chlorpromazine	Fluphenazine Decanoate	Thiothixene	5600
	nzapineOla		Fluphenazine Decanoate	Thioridazine		2600
	Olanzapine		Fluphenazine Decanoate	Haloperidol		2300
	Olanzapine		Fluphenazine Decanoate	Perphenazine		1500
3 entries	Risperidone		Chlorpromazine	Fluphenazine Decanoate		1425
	Risperidone		Chlorpromazine	Thiothixene		1400
	Risperidone		Thioridazine	Fluphenazine Decanoate		1365
			Chlorpromazine	Perphenazine	Haloperidol	1150
	Risperidone		Chlorpromazine	Fluphenazine Decanoate		1000
	Risperidone		Chlorpromazine	Thiothixene		950
	Risperidone	Olanzapine	Chlorpromazine			800
2 entries	Risperidone		Chlorpromazine	Fluphenazine Decanoate		750
			Fluphenazine Decanoate	Haloperidol		3500
			Fluphenazine Decanoate	Haloperidol		2500
			Fluphenazine Decanoate	Haloperidol		2500
			Fluphenazine Decanoate	Haloperidol		1915
	Risperidone		Fluphenazine Decanoate			1800
	Risperidone		Haloperidol			1600
	Risperidone		Chlorpromazine			1400
	Risperidone		Fluphenazine Decanoate			1400
	Risperidone		Fluphenazine Decanoate			1400
	Risperidone		Haloperidol			1400
	Olanzapine		Haloperidol			1350
	Olanzapine		Haloperidol			1200
	Risperidone		Fluphenazine Decanoate			1200
	Risperidone		Fluphenazine Decanoate			1100
	Risperidone		Fluphenazine Decanoate			1100
	Risperidone		Fluphenazine Decanoate			1100
	Risperidone		Chlorpromazine			1000
	Risperidone	ineOlanzap				1000
	Risperidone		Haloperidol			950
Risperidone		Chlorpromazine	Thiothixene		950	
Risperidone		Chlorpromazine			950	

Type of Polypharmacy	First Atypical Antipsychotic	Second Atypical Antipsychotic	First Typical Antipsychotic	Second Typical Antipsychotic	Third Typical Antipsychotic	Chlorpromazine dose equivalent per milligram
	Risperidone		Haloperidol			900
	Risperidone		Thiothixene			900
	Olanzapine		Chlorpromazine			850
			Chlorpromazine	Fluphenazine Decanoate		800
	Risperidone		Chlorpromazine			800
	Risperidone		Thiothixene			800
	Risperidone		Chlorpromazine			700
			Chlorpromazine	Haloperidol		700
	Risperidone		Fluphenazine Decanoate			700
	Risperidone		Fluphenazine Decanoate			700
	Risperidone		Thioridazine			700
	Risperidone		Perphenazine			700
	Olanzapine		Thioridazine			700
	Risperidone		Chlorpromazine			700
	Risperidone		Chlorpromazine			675
	Risperidone		Haloperidol			600
			Chlorpromazine	Haloperidol		600
			Chlorpromazine	Perphenazine		600
	Risperidone		Perphenazine			600

Maximum Chlorpromazine equivalent dosages of polypharmacy in triple antipsychotic drugs used were 2600 and 3500 mg, respectively. The majority of patients had used more Trihexyphenidyl. The use of Biperiden as an anticholinergic was less common (chart 2).

Table (5) shows the distribution of mood stabilizer drugs, Chart (2) Selective Serotonin Reuptake Inhibitors and Tricyclic Anti-depressants used respectively (12). As evident, the majority of

patients did not use antidepressants. Most antidepressants prescribed were Selective Serotonin Reuptake inhibitors and Tricyclic antidepressants (Fluoxetine and Nortriptyline) respectively. The most common Benzodiazepine used was Clonazepam (Chart 2). It is worth mentioning that the average Clonazepam dosage use was 65.1mg. We also found no concurrent use of Benzodiazepine drugs. Most of the patients were not using adjuvant medications (Table 6).

**Table 5.** Mood stabilizer drugs use distribution

Type of drug combination	First Mood stabilizer	Second Mood stabilizer	Number	Percent
Monotherapy	Carbamazepine	Lithium Carbonate	1	1.92
	Carbamazepine	Valproate Sodium	1	1.92
	Carbamazepine	-	8	15.38
Polypharmacy	Valproate Sodium	-	6	11.54
	Lithium Carbonate	-	2	3.85
	No drug		34	65.38
	Total		52	100

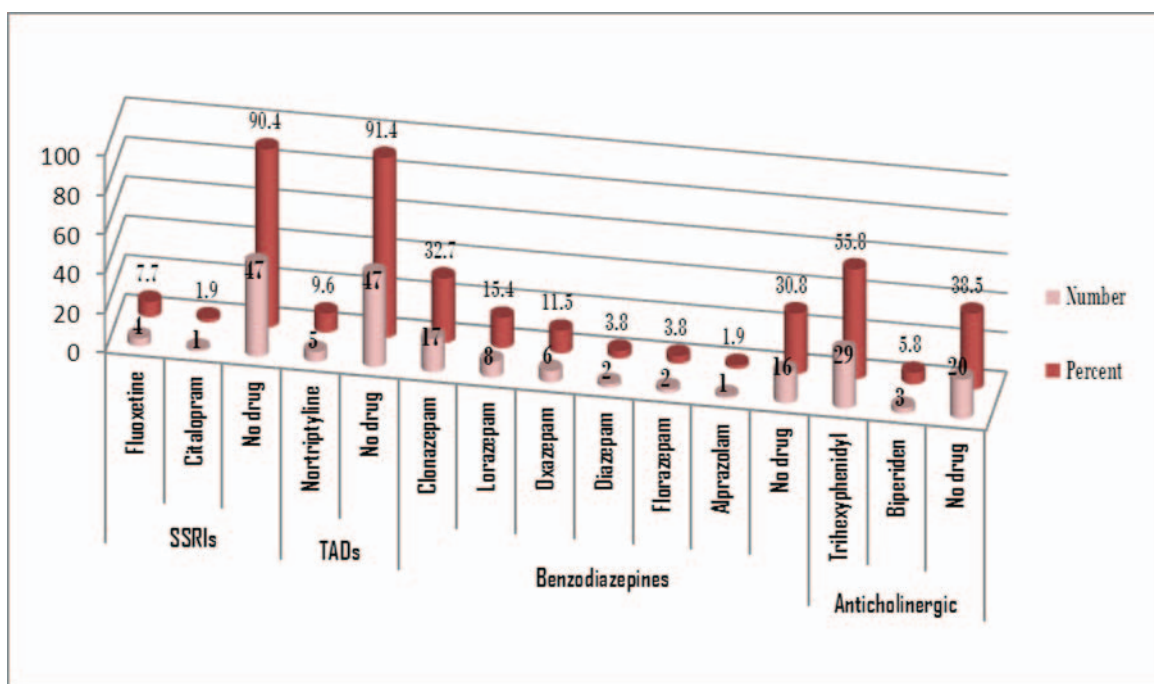


Chart 2: Distribution of drug use

Table 6. Distribution of adjuvant drug use

Type of drug combination	First Adjuvant drug	Second Adjuvant drug	Number	Percent
Monotherapy	Folic Acid	Hydroxyzine	1	1.92
Polypharmacy	Folic Acid	-	7	13.46
	Propranolol	-	6	11.54
No drug			38	73.08
Total			52	100

### Discussion

Seventy-five percent (75%) of patients were female. This may be attributed to the following factors: firstly, the female ward had been established long before the male ward, and secondly, life expectancy in females is longer than in males. Moreover, chronic hospitalization was better tolerated by females than males, and there were fewer confrontations in the female unit. Male patients had more multiple drug use frequency and more physical drug tolerances as opposed to females. Approximately 27% of our patients were over 70 years old. Despite uncertainties about the patients' educational status, over 57% of them were illiterate. The patients' children's social and cultural status were appropriate to the patients' educational status (23, 24). Higher incidences of unemployment in patients with schizophrenia and a long-term downfall (25) of the disease are expected as the natural course of the disease.

Despite uncertainties about the duration (26, 27) of illness in patients, at least 70% of the patients had suffered from the disease for more than twenty years (28). More than 37% of patients were hospitalized for more than 30 years. In all patients except 6 cases at least one atypical antipsychotic was used. There were more cases of mood stabilizer use -as polypharmacy- rather than single drug use. The most common type of tricyclic antidepressant used was Nortriptyline and the most common Selective Serotonin Reuptake Inhibitor used was Fluoxetine.

### Conclusion

As one can see, there is room for further research in antipsychotic polypharmacy in elderly patients suffering from chronic schizophrenia. The pattern of such prescriptions should be tabulated individually and the judgements of such medication use should rely on the patients' different clinical responses after prescribing multiple antipsychotic medications (29, 30).

## References

1. Brend R, Herman E, Marc Z. Patterns of Drug Prescription in a Psychiatric Outpatient Care Unit, The Issue Of Polypharmacy. *German J Psychiatry* 2008;11: 1-6.
2. Reka V, Katalin C, Peter D, et al. Reasons for polypharmacy among psychiatric patients. *Pharma World Sci* 2004; 26: 143-147 .
3. Rittmannsberg H. The use of drug monotherapy in psychiatric inpatient treatment. *Prog Neuro-Psychopharmacol Biol Psychiatry* 2002; 26: 547-51.
4. Linden M, Scheel T, Xaver EF. Dosage finding and outcome in the treatment of schizophrenic inpatients with amisulpride. Results of a drug utilization observation study. *Hum Psychopharmacol* 2004; 19: 119.
5. Statistical Center of Iran. Management & Planning Organization, Status of the Aged nationwide, Islamic Republic of Iran: 2002.
6. Mehl B, Santell J. Projecting future drug expenditures. *Am J Health System Pharm* 1999; 56: 31-9.
7. Wyles H, Rehman HU. Inappropriate polypharmacy in the elderly. *European Journal of Internal Medicine* 2005; 16: 311-13.
8. Woodard K, Franklin R. Treating elderly Patients. *Pharmacist* 1999; 24: HS-7-HS-16.
9. Dawling S, Crome P. Clinical pharmacokinetic considerations in the elderly. *Clin Pharmacokinetic* 1989; 17: 236-63.
10. Hallas J, Worm J, Beck-Nielsen J, Gram LF, Grodum E, Damsbo N, et al. Drug related events and drug utilization in patients admitted to a geriatric hospital department. *Dan Med Bull* 1991; 38: 417-20.
11. Lamy PR. Prescribing for the Elderly. Littllon, Mess PSG Publ Company 1980.
12. Ryan A, Jacques I. Medication compliance in older people. *Elderly Care* 1997; 5: 16-20.
13. Ghaemi N. Polypharmacy in Psychiatry. New York: Marcel Dekker, 1st, 2002.
14. Flaum M, Karp S, Parks J. Technical Report of Psychiatric Polypharmacy. A series of technical reports prepared by the: National Association of State Mental Health Program Directors (NASMHPD) 2001; 1-24.
15. Rational and Irrational Polypharmacy. *Psychopharmacology, psychiatric services*, August 2001.
16. Sadock BJ, Sadock VA. Kaplan and Sadock's Synopsis of Psychiatry. 10th ed. Philadelphia: Lippincott Williams and Wilkins, 2007.
17. Steven J, Megan L. Psychiatric Polypharmacy: The Good, the Bad, and the Ugly. *Psychiatric Times* 2007; 4: 32.
18. Sadock BJ, Sadock VA. Kaplan and Sadock's Comprehensive textbook of psychiatry. 9th ed. Lippincott Williams and Wilkins, 2009.
19. Rittmannsberger H, Meise U, Schauflinger K, et al. Polypharmacy in psychiatric treatment. Patterns of psychotropic drug use in Austrian psychiatric clinics. *Eur Psychiatry* 1999; 17: 1-8 .
20. Davids E, Bunk C, Specka M, et al. Psychotropic drug prescription in a psychiatric university hospital in Germany. *Neuro-Psychopharmacology & Biological Psychiatry* 30 (2006) 1109-1116.
21. Ananth J, Parameswaran S, Gunatilake S. Antipsychotic polypharmacy. *Curr Pharm Res* 2004; 10: 2231-8.
22. Centorrino F, Eakin M, Bahk WM, Kelleher JP, Goren J, Salvatore P, et al. Inpatient antipsychotic drug use in 1998, 1993, and 1989. *Am J Psychiatry* 2002; 159:1932-5.
23. Weinmann S, Janssen B, Gaebel W. Switching antipsychotics in inpatient schizophrenia care: predictors and outcomes. *J Clin Psychiatry* 2004; 65:1099-105.
24. Tapp A, Wood A, Secret L, et al. Combination Antipsychotic Therapy in Clinical Practice. *Psychiatric Services* 2003; 54: 55-59 .
25. Ito C, Kubota Y, Sato M: A prospective survey on drug choice for prescriptions for admitted patients with schizophrenia. *Psychiatry and Clinical Neurosciences* 1999; 53: 35-S40 .
26. Miller AL, Chiles JA, Chiles JK, Crismon ML, Rush AJ, Shon SP. The Texas medication algorithm project (TMAP) schizophrenia algorithms. *Journal of Clinical Psychiatry* 1999; 60, 649-657.
27. Clark RE, Bartels SJ, Mellman TA, Peacock WJ. Recent trends in antipsychotic combination therapy of schizophrenia and schizo affective disorder: implications for state mental health policy. *Schizophrenia Bulletin* 2002; 28, 75-84.
28. Procyshyn RM, Kennedy NB, Tse G, Thompson B. Antipsychotic polypharmacy: a survey of discharge prescriptions from a tertiary care psychiatric institution 2001; *Canadian Journal of Psychiatry* 46, 334-339.
29. Williams CL, Johnstone BM, Kesterson JG, Javor KA, Schmetzer AD. Evaluation of antipsychotic and concomitant medication use patterns in patients with schizophrenia 1999; *Medical Care* 37, AS81-AS86.
30. Patterson TL, Larco J, McKibbin CL, Davidson K, Jeste DV: Direct observation of medications management (MMAA): results from a new performance-based test in older outpatients with schizophrenia. *J Clin Psychopharmacol* (in press)