Antipsychotic Use Pattern in People with Psychotic Disorder Living in Board and Care Facilities

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ABSTRACT

Introduction: The aim of this survey is to determine the pattern of antipsychotic drug use in patients with psychotic disorders, living in board and care facilities and to investigate the related factors.

Methods: We evaluated the antipsychotic drug use pattern in outpatients with psychotic disorders according to DSM-IV, living in board and care facilities. Patients using polypharmacy at least one month were compared with patients using monotherapy in terms of clinical and demographic characteristics.

Results: Antipsychotic polypharmacy (with two: 34%, with more than two: 28%) was identified in 62% of the patients. The most frequently prescribed combination was olanzapine+quetiapine (13%), the rate of first and second generation combination was 50%, the rate of second generation antipsychotic combination was 44%, and the rate of first

generation antipsychotic combination was 4% in the two antipsychotic drug combination group. The rate of clozapine use was 3%. Use of polypharmacy was associated with the diagnosis of schizophrenia and schizoaffective disorder; young age, suicidal behavior; multiple hospitalizations, clinical severity, and the need of anticholinergic drug.

Conclusion: The ratio of using more than two antipsychotic drug combination is high (28%) in psychotic patients living in board and care, and rate of clozapine use is low, which shows that clinical practice is inconsistent with the treatment guidelines recommendations. It appears that further education to rationale antipsychotic drug use in psychiatric practices is required.

Keywords: Psychotic disorder; schizophrenia, antipsychotics, polypharmacy, monotherapy, outpatient, board and care facility

INTRODUCTION

Guidelines for treating patients with psychotic disorder (1) have consistently recommended antipsychotic monotherapy (APMT) as the treatment of choice; however, polypharmacy (APPP) is widespread in daily clinical routine (1). Although studies are not sufficient, polypharmacy has been used for a long time in clinical practices (2). Schizophrenia is a chronic and mainly treatment-resistant disease, in which treatment response is limited, drugs have side-effects, drug potentiation is generally needed on the basis of clinical experience, APMP is not attempted in sufficient doses, doctors want to observe rapid clinical improvements, psychotic anxiety causes difficulties, and patients want to be discharged from hospital in a short-time. Because of these factors, antipsychotic drugs (APDs) are mainly used in combination (2,3,4,5). New generation APDs again lead to polypharmacy for schizophrenia patients (4).

According to the guidelines for treating patients with schizophrenia, when patients fail to respond to an adequate dose of an antipsychotic trial during an adequate period, combinations may be used. According to these guidelines, polypharmacy is optimal only for resistant patients and during antipsychotic switching periods (6,7,8). The Texas Medication Algorithm recommends polypharmacy after three monotherapy regimes including clozapine (8). The Schizophrenia Treatment Guideline of Psychiatric Association of Turkey suggests that APMT is important, but their view is line with the Texas Medication Algorithm in terms of polypharmacy (9). The controlled studies on APPP are not sufficient. Therefore, we should avoid from routine polypharmacy.

In previous studies, a few patients have benefited from APPP; however, the prevalence of APD combination is 10–75% in schizophrenia patients (10,11,12,13,14,15). In the studies performed in Turkey, the prevalence of APD combinations is similar (16,17,18,19,20). APD combinations are frequently used, but evidence-based data are lacking, and antipsychotic polypharmacy is not found to be superior than monotherapy (21).

Several studies have shown that the drug–drug interactions of APPP cannot be considered as safe; it is also expensive and increases mortality rate in schizophrenia patients (22,23,24). We should cautiously consider mortality risk, risk-benefit, and cost-expense profile of APD use before polypharmacy trial (25).

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Table 1. The demographic and clinical characteristics of the patients and associations with mono or polytherapy use

Characteristics	Number	Percent	Mean±SD (range)	Statistics
Sex (male)	129	64.5		
Age			43.8±12.1 (16–81)	p<0.001**
Education			6.2±3.2 (0–15)	
Marriage status (married)	20	10.0		
Occupation (not working)	173	86.5		
Family support (none)	123	61.5		
Physical disease (none)	165	82.5		
Physical violence	75	37.5		
Suicide attempt	40	20.0		p<0.05**
Number of hospitalization (n=150)			4.2±4.18 (0–15)	p<0.005**
CGI-S*			4.8±1.3 (2–7)	p<0.05**
Mental disease				
Schizophrenia+SAD	161	80.5		p<0.001**
NOS psychotic disorder	39	19.5		

*CGI-S: Clinical Global Impression-Severity, **APPP use was common in young patients, suicide attempt cases, frequently hospitalized patients, patients with higher Clinical Global Impression scores, patients with schizophrenia, and schizoaffective disorders. SAD: schizoaffective disorder; NOS: not otherwise specified; SD: standard deviation

In Turkey, APPP studies are generally performed in wards or outpatient clinics during maintenance treatment periods. Institutional studies were not found in the literature for Turkey. In this study, we aim to evaluate antipsychotic drug use pattern in people with psychotic disorder living in board and care facilities in Turkey.

METHODS

The patients admitted to the Sivas Numune Hospital psychiatry outpatient clinic for examination or control visit during November 1, 2012–May 31, 2013, the patients who stayed in board and care facilities, and the patients with psychotic disorders according to the Diagnostic and Statistical Manual of Mental Disorders, Forth edition (26) were included in the study. All patients had used APDs for at least for one month. The association between antipsychotic use pattern and demographic features and diagnosis was evaluated. Use of more than one APD for at least one month at a specified dosage range was considered as APPP use. APDs that were considered were Olanzapin 5 mg, ketiapin 200 mg, risperidon 2 mg, haloperidol 5 mg, klorpromazin 200 mg and above. Cumhuriyet University Medicine Faculty Ethical Committee approved the study (decision number: 2013-03/47). Sivas Numune Hospital Administration approved the required documents. Information regarding the study was given to patients and legal consultants, and their written informed consent forms were received.

Statistical Analysis

Data were evaluated with Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL, USA) 16.0 program. Chi-square test was used for categorical comparisons of the groups; t test was used to compare mean values. P<0.05 was considered as significant.

RESULTS

Two hundred patients staying in board and care facilities were evaluated. The demographic characteristics and clinical characteristics of the patients and associations with mono or polytherapy use were presented in Table 1.

The ratio of APMT use was 38%, use of two APDs was 34%, and use of 146 more than two APDs was 28% (Table 2). Sixty-one percent patients used

biperiden plus antipsychotic drugs, 15% patients used low dose clorpromazin plus antipsychotic drugs, and 8% patients used mood-stabilizer drugs plus antipsychotics.

Olanzapine is the most preferred drug for monotherapy, followed by quetiapine and risperidone (Table 3). Although 28% of patients with monotherapy used biperiden, patients with polytherapy who used four to five APDs used biperiden at a rate of 100% (Table 3,4).

35% of the patients used depot APDs (n=69, Zuc=53, Ris=14, Flu=2); however, 7% of them used monotherapy (Table 3,4,5,6). The most preferred doublet APD was olanzapin–ketiapin combination (13%). The incidence of first and second generation APD use was 50% (n=34), second generation APD combination use was 44% (n=30), and doublet use of first generation APD was 4% (n=3) (Table 5).

The incidence of clozapine use was 3% (4 APMT, 2 APPP) (Table 3,5,6). Low rate of clozapine combination is remarkable as preferred too few in polytherapy. Polytherapy drugs mentioned in Table 4 and 6 are examples of the overdose of APD. In addition, it is remarkable that the frequency of APPP administration increased as the depot APD administration increased.

DISCUSSION

According to the study results, 62% of the patients with psychotic disorder living in board and care facilities have used multiple antipsychotic drugs. APPP use was determined as common in young patients, suicide attempt cases, frequently hospitalized patients, patients with higher Clinical Overall Impression scores, and patients with schizophrenia and schizoaffective disorders. Olanzapine–quetiapine was the most preferred combination as a doublet APD, and olanzapine was the most preferred agent for single APD use. Typical–atypical APD combination was the most preferred combination (50%) as a doublet APD. Depot APDs were frequently used with other APDs. Single depot APD was rarely used. Anticholinergic drug requirement was increased if several APD agents were used. According to studies performed in our country with hospitalized

Table 2. Mono and polytherapy drug uses and combination drug use

Drug use pattern	Number (%)	Combined drugs			Diseases	
		BIP	CPZ	MS	SCH-SAD	NOS-PD
Mono	76 (38)	21	7	6	50	26
Doublet	68 (34)	55	12	6	57	11
Triplet	42 (21)	31	9	6	41	1
Four-five	14 (7)	14	1	1	13	1
Total	200 (100)	121 (61)	29 (15)	16 (8)	161	39

BIP: biperiden; CPZ: chlorpromazine; MS: mood-stabilizer; SCH-SAD: schizophrenia-schizoaffective disorder; NOS-PD: not otherwise specified psychotic disorder

Table 3. Single antipsychotic drug use

Drugs	Number	Combined drugs			Diseases	
		BIP	CPZ	MS	SCH+SAD	NOS PD
OLZ	25	6	3	2	13	12
QUET	18	2		1	14	4
RIS	18	8	2		9	9
ZUC-dep	4	1			4	
CLOZ	4	1	1	3	4	
HAL	3	3			3	
ARI	2		1		1	1
PALI	1				1	
RIS-cons	1				1	
Total	76	21	7	6	50	26

OLZ: olanzapine; QUET: quetiapine; RIS: risperidone; ZUC-dep: zuclopenthixol depot; CLOZ: clozapine; HAL: haloperidol; ARI: aripiprazole; PALI: paliperidone; RIS-cons: risperidone consta; CPZ: chlorpromazine; BIP: biperiden; MS: mood-stabilizer; SCH-SAD: schizophrenia-schizoaffective disorder; NOS-PD: not otherwise specified psychotic disorder

Table 4. Four and five antipsychotic drugs combination

Drugs	Number	Combined drugs			Diseases	
		BIP	CPZ	MS	SCH+SAD	NOS PD
OLZ+ QUET +HAL+ZUC-dep	2	2			2	
OLZ+RIS+CPZ+ZUC-dep	2	2			2	
OLZ+ QUET +RIS+RIS-cons	1	1				1
OLZ+RIS+HAL+ZUC-dep	1	1			1	
QUET +HAL+CPZ+RIS-cons	1	1			1	
QUET +HAL+CPZ+ZUC-dep	1	1			1	
QUET +RIS+HAL+ZUC-dep	1	1			1	
RIS+HAL+SUL+ZUC-dep	1	1			1	
OLZ+QUET+HAL+ARI+FLU-dep	1	1			1	
QUET+RIS+HAL+CPZ+ZUC-dep	1	1			1	
OLZ+QUET+HAL+CPZ+ZUC-dep	1	1		1	1	
OLZ+QUET+HAL+PALI+ZUC-dep	1	1	1		1	
Total	14	14	1	1	13	1

OLZ: olanzapine; QUET: quetiapine; RIS: risperidone; ZUC-dep: zuclopenthixol depot; CLOZ: clozapine; HAL: haloperidol; ARI: aripiprazole; PALI: paliperidone; RIS-cons: risperidone consta; CPZ: chlorpromazine; SUL: sulpiride; FLU-dep: flufenazine depot; BIP: biperiden; MS: mood-stabilizer; SCH-SAD: schizophrenia-schizoaffective disorder; NOS-PD: not otherwise specified psychotic disorder

Table 5. Doublet antipsychotic drugs use

Drugs	Number	Combined drugs			Diseases	
		BIP	CPZ	MS	SCH+SAD	NOS PD
OLZ+ QUET	9	3			8	1
OLZ+ZUC-dep	8	8	2		7	1
OLZ+HAL	7	7	2		4	3
OLZ+RIS	5	5		2	4	1
OLZ+CPZ	5	4			4	1
OLZ+RIS-cons	4	3	3		4	
OLZ+FLU-dep	1	1			1	
QUET +RIS	6	6	1		4	2
QUET +ZUC-dep	2		1		1	1
QUET +HAL	2	2			2	
QUET +ARI	1	1			1	
QUET +RIS-cons	1			1	1	
QUET +PALI	1			1	1	
QUET +AMI	1	1		1	1	
QUET +ZIP	1			1		1
QUET +CLOZ	1	1			1	
RIS+ZUC-dep	6	6	2		6	
RIS+CPZ	1	1			1	
RIS+AMI	1	1			1	
HAL+ZUC-dep	3	3			3	
HAL+PALI	1	1			1	
AMI+ ZUC-dep	1	1			1	
Total	68	55	11	6	57	11

OLZ: olanzapine; QUET: quetiapine; RIS: risperidone; ZUC-dep: zuclopenthixol depot; CLOZ: clozapine; HAL: haloperidol; ARI: aripiprazole; PALI: paliperidone; RIS-cons: risperidone consta; CPZ: chlorpromazine; AMI: amisulpiride; ZIP: ziprasidone; FLU-dep: flufenazine depot; BIP: biperiden; MS: mood-stabilizer; SCH-SAD: schizophrenia-schizoaffective disorder; NOS-PD: not otherwise specified psychotic disorder

and outpatient schizophrenia patients, the prevalence of APPP use is 38–74% (16,17,18,19,20,27,28,29). APPP use is common almost in every clinical practice. Use of two and more APDs combination is common worldwide for the treatment of schizophrenia and other psychotic disorders (14,30,31). Treatment guidelines never recommend the use of antipsychotic polypharmacy initially; therefore, we should attempt to understand the reason for clinicians prescribing APPP so commonly.

The major indication of common APPP use is probably the clinical severity. However, according to previous studies, clinical severity is valid factor only for the hospitalized patients and not for outpatients (5,20,32). APPP does not increase antipsychotic effect or does not decrease clinical severity more than APMT. Furthermore, APPP causes more side effects (33,34). In our study, APPP use was common in young patients, suicide attempt cases, and frequently hospitalized patients; therefore, it may be directly associated with the overall clinical severity. However, we do not have any evidence that shows that APPP use is a solution for clinical severity. In our study, we were unable to determine whether appropriate APMT dose was used. Six out of 161 schizophrenia patients (3%) had used clozapine. Only four of these six patients had already used monotherapy. Therefore,

we can conclude that this clinical practice is not consistent with the scientific recommendations.

Antipsychotic polypharmacy use was 62% in our sample, and was not consistent with the treatment algorithm recommendations. Treatment algorithms generally recommend using APPP after clozapine trials. While four of 76 APMT patients used clozapine, only two of 124 APPP patients with psychotic disorder used clozapine. These results show that clozapine is not appropriately used in clinical settings. However, clozapine plus another APD is recommended as combination therapy in treatment algorithms, and usually preferred in some clinical settings (8,25,35). According to another study performed in Turkey (20), clozapine is used rarely (7%), and is not included in APPP regimes. In general, we can conclude that sufficient dose of APMT, at least clozapine, is not administered in APPP patients and treatment algorithms are not followed. If APPP is preferred, the most compatible APDs should be combined. Given the cost–expense profile and side effect risk, more than two APD may be more harmful to patients. APPP are generally administered in higher (over) dosages, and therefore, increases the side effects as compared with APMT (1,5).

Table 6. Triplet antipsychotic drugs uses

Drugs	Number	Combined drugs			Diseases	
		BIP	CPZ	MS	SCH+SAD	NOS PD
OLZ+HAL+ZUC-dep	6	5	1		6	
OLZ+ QUET +ZUC-dep	4	2		1	4	
OLZ+ QUET +RIS-cons	3	2	1	1	3	
OLZ+RIS+ZUC-dep	3	3			3	
OLZ+ QUET +RIS	2	1		1	2	
OLZ+HAL+CPZ	1				1	
OLZ+ARI+ZUC-dep	1				1	
OLZ+PALI+ZUC-dep	1	1	1		1	
OLZ+KLOR+RIS-cons	1				1	
OLZ+QUET+AMI	1				1	
OLZ+RIS+RIS-cons	1	1	1		1	
OLZ+RIS+HAL	1	1		1		1
OLZ+CLOZ+AMI	1				1	
QUET +HAL+ZUC-dep	3	3	1		3	
QUET +RIS+HAL	2	2			2	
QUET +AMI+ZUC-dep	1	1			1	
QUET +RIS+RIS-dep	1	1			1	
QUET +PALI+ARI	1				1	
QUET +HAL+ZUC-dep	1	1	1	2	1	
RIS+AMI+ZUC-dep	3	3			3	
RIS+HAL+ZUC-dep	3	3	3		3	
RIS+HAL+CPZ	1	1			1	
Total	42	31	9	6	41	1

OLZ: olanzapine; QUET: quetiapine; RIS: risperidone; ZUC-dep: zuclopenthixol depot; CLOZ: clozapine; HAL: haloperidol; ARI: aripiprazole; PALI: paliperidone; RIS-cons: risperidone consta; CPZ: chlorpromazine; AMI: amisulpride; BIP: biperiden; MS: mood-stabilizer; SCH-SAD: schizophrenia-schizoaffective disorder; NOS-PD: not otherwise specified psychotic disorder

In conclusion, treatment guidelines suggest that multiple antipsychotics should be the last choice in resistant patients, and they may be used for a short time during antipsychotic switching. However, we observed that multiple antipsychotics are preferred frequently in our sample patients staying in board and care facilities. Our study is the first APD use pattern study performed in this patient population. More than one-fourth of these patients had used more than two APDs at the same time. In our study, the disease was more severe in the APPP group. Even though multiple antipsychotic drug use increase the risk of side effects, and more drugs are needed to relieve side effects, drug-drug interactions increase, treatment compliance impairs, and mortality rate increases (14), polypharmacy is used increasingly. Controlled studies are required to elucidate the reasons and to solve the problems regarding polypharmacy. However, the studies show that APPP is used without enough APMT trial period at sufficient dosages (30,36). APPP in outpatient group has not been predicted at psychopathology levels (37). Two-third of the patients did not experience psychopathology alterations, and furthermore, the incidence of weight gain decreased when APPP use switched to APMT use (38). We should clarify the reason for the clinicians preferring APPP so easily, and educate doctors to be careful and avoid prescription of hazardous APPP.

In our study, the data were obtained from patients, patient files, and hospital attendants. Therefore, the most important limitation of our study was access some information. The other limitations were that we could not evaluate side effects associated with drugs, and we could not understand the reasons of prescribing polypharmacy.

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