Psychiatria Danubina, 2011; Vol. 23, No. 1, pp 60–63 *Brief report*

POLYPHARMACY IN THE TREATMENT OF SCHIZOPHRENIC PATIENTS IN THREE UNIVERSITY CENTERS IN THE FEDERATION OF BOSNIA AND HERZEGOVINA (F/BH)

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SUMMARY

Background: *Polypharmacy in psychiatry is becoming the rule rather than the exception. Using more drugs at same time usually occurs where single drugs are considered insufficiently effective.*

Subjects and methods*: The sample consisted of 216 patients: 85 from Sarajevo, and 44 and 87 respectively from Mostar and Tuzla. All schizophrenic patients who were hospitalised in three University Centers of F/BiH (Sarajevo, Tuzla, Mostar) on a particular day are included in the study. This included patients of both sexes (131 (60.65%) males and 85 females (39.35%)), 20-60 ages, who were on antipsychotic treatment with an established diagnosis of schizophrenia by the treating psychiatrist. The research was performed in the year 2004. The census of patients was conducted simultaneously in all three Centers, using a questionnaire in which all routine prescribed antipsychotics were registered, as the common method of the administration, and the doses as well saving as data for other medications that were simultaneously prescribed to the patients that day.*

Results: *Within the total sample the most frequently applied classical antipsychotics were haloperidol, promazine and from the group of new antipsychotics clozapine. The most frequently used other medications were biperidine and diazepam. The administration of all medication was followed through recording of individual doses, daily doses and frequency of administration. There are statistically significant differences regarding the frequency of biperidine use between the centers (p=0.008) .*

Conclusion: *In three University Clinical Centers of the Federation of Bosnia and Herzegovina (Sarajevo, Tuzla and Mostar), the applied rule is that more drugs in the treatment of schizophrenic psychosis and doing polypharmacy is the inevitable approach to treatment. The concept behind the polypharmacy is based on the fact that antipsychotic drugs do not cover all the symptoms of schizophrenic psychosis, and that additional medications may correct iatrogenic side effects caused by antipsychotic drugs. It is expected that the new atypical antipsychotics will treat much broader symptoms of psychosis and will not cause extrapyramidal side effects, as do the typical antipsychotics.*

Key words: *Schizoprenic patients – antipsychotics - polypharmacy (co-adminsitration)*

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INTRODUCTION

Polypharmacy was first described in the psychiatric literature in 1969 (Sheppard et al. 1969). Studies reported variable rates of concurrent antipsychotic prescription depending on the population considered. A study performedin Australia, examining people receiving out-patient treatment for schizophrenia, showed a 13% rate of multiple antipsychotic prescription use (Langan & Shajahan 2010). One Japanese study indicated that the rate of antipsychotic polypharmacy exceeded 90% (Keks et al. 1999). A recent study in the UK showed an intermediate rate of 30%. Despite its common occurrence, the evidence base behind antipsychotic polypharmacy is widely recognised to be limited and its use has been considered both a 'therapeutic option' and a 'dirty little secret' (Ito et al. 1999).

Typical antipsychotics are short in two important performance: poor effect in the treatment of negative schizophrenia symptoms and tendency to cause extrapyramidal side effects. It is considered that 20-30% of schizophrenic patients did not react (nonrespondents) to treatment with typical antipsychotic medications.

Atypical antipsychotics are mostly medications which have a similar structure to already known antipsychotics (close to haloperidol and sulpiride), but others which have a different chemical structure and mechanism of action have been discovered (serotonin and dopamine antagonists) (Jibson at al. 2000).

The aim of this study was to determine which other drugs, alongside with antipsychotics, are administrated to patients (polypharmacy), especially antiparkinsonian medications.

SUBJECTS AND METHODS

The sample consisted of 216 patients: 85 from Sarajevo, and 44 and 87 respectively from Mostar and Tuzla. The research was performed in the year 2004.

All schizophrenic patients who were hospitalised in three University Centers of F/BiH (Sarajevo, Tuzla, Mostar) on a particular day are included in the study. This included patients of both sexes (131 (60.65%) males and 85 females (39.35%)), 20-60 of age, who were on antipsychotic treatment with an established diagnosis of schizophrenia by the treating psychiatrist.

Within the total sample 61.57% patients had diagnosed schizophrenia. In Mostar and Sarajevo this is 100% and 77.65% of patients with confirmed schizophrenia, and Tuzla 26.44%.

Excluded from the study were schizophrenic patients with established comorbidities, patients with a somatic disorder, pregnant and lactating women.

The census of patients was conducted simultaneously in all three Centers, using a questionnaire in which were registered the antipsychotics used, the method of administration, doses, as well as data on other medications that are simultaneously prescribed to the patients that day.

Table 1. Application of other medications (antiparkinsonian drugs, anxiolitics, antidepressants) (overview by cities)

		Center					
		Sarajevo		Tuzla		Mostar	
		N	%	N	%	N	%
other medications	biperidine	12	20.3	9	8.8	32	54.2
	nitrazepam	20	33.9	27	26.5		
	diazepam	9	15.3	24	23.5	10	16.9
	paroxetine	4	6.8	11	10.8		
	amitriptyline	6	10.2	8	7.8		
	carbamazepine	5	8.5	1	1.0	6	10.2
	bromazepam			9	8.8		
	biperiden (ampul.)					10	16.9
	maprotiline			6	5.9		
	phenytoin			1	1.0		
	vaproic acid			1	1.0		
	phenobarbital	1	1.7	2	2.0		
	levodopa					1	1.7
	fluoxetine	2	3.4				
	sertraline			1	1.0		
	clomipramine			2	2.0		
Total		48	100.0	69	100.0	40	100.0

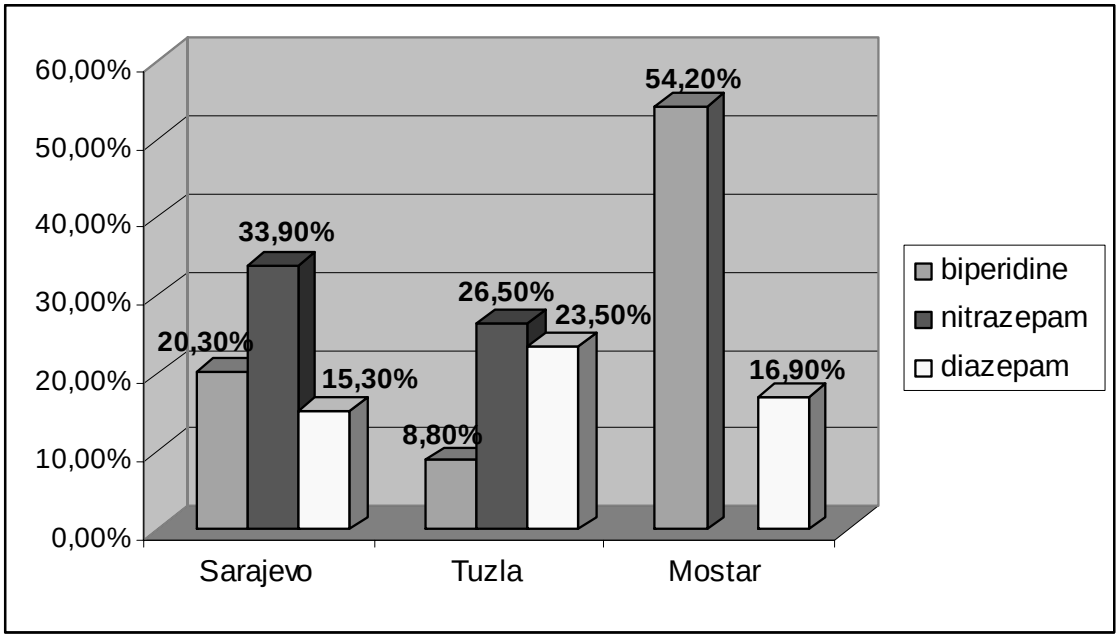

Figure 1. Most frequent other medications

RESULTS

The research results are presented in tables, and this time only concomitant therapy is listed.

Among other medications most frequently administered in Sarajevo was nitrazepam in 20 cases (33.9%), as well as in Tuzla in 27 cases (26.5%). In Mostar the most frequent medication is biperidine in oral and parenteral form in 32 cases which is in more than half of the treated patients, or ten cases (16.9%) (Table 1 and Figure 1).

In Sarajevo 38 patients (44.7%) did not receive treatment with other medications, and 37 (43.5%) patients were treated with only one of the group of other medications. Prescription of two medications from the group of others occurred among 10 patients (11.8%).

Eighteen patients in Tuzla (20.7%) were not treated with other medications, and forty patients (50.6%) were treated with only one medication from the groups of others. Prescription of two medications from the group of others occurred in 17 cases (19.5%). A combination of three other medications was used in 8 cases (9.2%).

Four patients in Mostar (9.1%) did not receive any other medication, and 26 (59.1%) were treated with only one from the group of others. Prescription of two other medications occurred in 10 cases (22.7%). Combination of three other medications occurred in three cases (6.8%), while only one patient (2.3%) received four medications from the group of others.

It is evident that in the whole sample (baseline) the majority of patients were treated with only one medication from the group of others -107 (49.5%), after that the most dominant are the patients who did not receive any other medication, these comprised sixty or 27.8% (Table 2).

Table 2. Number of administered other medications

		Center						Total	
		Sarajevo		Tuzla		Mostar		N	%
		N	%	N	%	N	%		
No. of other medications	0	38	44.7	18	20.7	4	9.1	60	27.8
	1	37	43.5	44	50.6	26	59.1	107	49.5
	2	10	11.8	17	19.5	10	22.7	37	17.1
	3			8	9.2	3	6.8	11	5.1
	4					1	2.3	1	0.5
Total		85	100.0	87	100.0	44	100.0	216	100.0

Within the total sample the most frequently applied classical antipsychotics were haloperidol, promazine, and clozapine out of the group of new antipsychotics. The most frequently used other medications were biperidine and diazepam. The administration of all medication was followed by recording of individual doses, daily doses and frequency of administration.

Average frequency of biperidine administration varies in the total sample as well as between the centers (Table 3.).

There are statistically significant differences regarding the frequency of biperidine use between the centers (p=0.008) (Table 4).

Table 3. Frequency of biperidine administration

Center	N	Mean	SD	Std. error mean	95% CI		Minimum frequency of application	Maximum frequency of application
					Lower bound	Upper bound		
Sarajevo	9	1.2222	0.44096	0.14699	0.8833	1.5612	1.00	2.00
Tuzla	9	1.3333	0.50000	0.16667	0.9490	1.7177	1.00	2.00
Mostar	32	1.7188	0.45680	0.08075	1.5541	1.8834	1.00	2.00
Total	50	1.5600	0.50143	0.07091	1.4175	1.7025	1.00	2.00

Table 4. Frequency of biperidine application (ANOVA)

Center	Sum of squares	df	Mean square	F	Sig.
Between centers	2.296	2	1.148	5.382	0.008
Within centers	10.024	47	0.213	-	-
Total	12.320	49	-	-	-

DISCUSSION

The effect of low-dose haloperidol combined with the anticonvulsant carbamazepine was investigated in a 5-week placebo-controlled, double-blind study in acute schizophrenic patients. Weekly ratings showed a clinically pronounced and statistically significant improvement in both the carbamazepine and placebo groups. However, the patients on carbamazepine needed less neuroleptic and anticholinergic medication and experienced fewer side effects compared to the patients on placebo. Moreover, patients in the carbamazepine group showed a clear deterioration after discontinuation of carbamazepine (but maintenance of neuroleptic medication), while the placebo group did not change after discontinuation of placebo. Concomitant treatment with carbamazepine in psychotic patients may help to reduce neuroleptic dosages and unwanted side effects.

Wada et al (1987) has conducted a double-blind, placebo-controlled study in 42 chronic schizophrenic inpatients receiving neuroleptics and antiparkinsonian drugs for longer than 3 months in order to evaluate the need for prolonged antiparkinson drug therapy. Patients were randomly assigned to receive either placebo or biperiden for 4 weeks. All patients were switched to biperiden for 1 week; then, the placebo group was abruptly switched to placebo for the remainder of the trial period. After 1 week, 2 of the 21 (9.5%) placebo-treated patients had symptoms and complaints that required restarting of biperiden. During the 4 week study, 33.3% of both the placebo- and biperiden treated patients experienced mild-to-moderate worsening of symptoms, but none of the patients required early discontinuation of therapy. Based on these results and previous studies, the authors concluded that a trial period for discontinuation of antiparkinsonian drugs should be undertaken in all patients.

CONCLUSIONS

In three University Clinical Centers of the Federation of Bosnia and Herzegovina (Sarajevo, Tuzla and Mostar), the applied rule is that more drugs in the treatment of schizophrenic psychosis and using polypharmacy is the inevitable approach to treatment. This treatment is typical not only for Bosnia and Herzegovina, but also much more widely. The concept behind the polypharmacy is based on the fact that antipsychotic drugs do not cover all the symptoms of schizophrenic psychosis, and that additional medications may correct the iatrogenic side effects caused by antipsychotic drugs. It is expected that the new atypical antipsychotics will treat much broader symptoms of psychosis and will not cause extrapyramidal side effects, as do the typical antipsychotics.

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