Frequency of the antipsychotic therapy acute side effects in the treatment of acute psychosis

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Abstract

Antipsychotic drugs produce a wide spectrum of physiological actions. Some of these effects differ among the various classes of antipsychotics. This medications have indications in the treatment of acute psychotic disorders. The main goal of this investigation was to determine the incidence and prevalence of the neuroleptic therapy acute side effects. The reason for this epidemiological investigation performing was the lack of knowledge of the exact neuroleptic therapy side effects incidence. Qualitative study on this problem has not been performed yet. Antipsychotic therapy side effects prevalence rate according to the literature data is ranging from 24% to 74%. Different prevalence rate is a consequence of different antipsychotic drug usage, different drug administration method and different side effects identification.

On account of all these facts, we put the hypothesis on the correlation between the antipsychotic therapy and occurred side effects.

Our experiment included all patients hospitalised from December 31st 1999 to January 31st 2000 in Intensive Care Unit of Biological Psychiatry Department of Psychiatric Clinic in Sarajevo. All patients were divided in three groups according to the applied therapy. All of them met ICD-10 criteria for schizophrenia (F20-29). During our study the following examinations were performed: psychiatric interview, BRPS, scale of side effects, psychophysiological tests, general clinical impression, scale of appetite, carbon hydrate needs scale. Psychiatric and statistical evaluations were done as well. The evaluation of our examination is showing successful results in all groups of patients. The improvement of psychopathological symptoms was insignificant. Reported side effects were minimal with low incidence rate and relatively high prevalence rate. Statistical tests were calculated from the obtained data after what the null hypothesis was rejected. Consequently, an alternative hypothesis was confirmed and it indicated that the acute side effects incidence and prevalence were within the range of expectation.

Intensity of the recorded side effects was moderate to mild.

On the basis of the obtained data, it has been concluded that applied antipsychotic agents did not induce more psychophysiological function impairments in the treated patients. Psychophysiological functions remained in physiological range limits and their changes were not significant.

Neuroleptic therapy side effects were minimal, meaning no toxic signs or therapy discontinuations were recorded.

Keywords: schizophrenia, antipsychotic agents, acute side effects, incidence, prevalence, intensity of side effects.

Introduction

It is difficult to define schizophrenia. The differ schizofrenia from other psychotic conditions, sometimes, is not clear. Schizohrenia is, may be, a group of related syndromes rather than single disorder. Division of schizophrenia into acute and chronic syndromes can be useful.

The predominant clinical features of the acute syndrome are delusions, hallucinations and interference with (often known as "positive" symptoms). The main features of the chronic syndrome are apathy, lack of drive and social withdrawal (so-called "negative" symptoms). (Jablensky, 1995; Karno i Norquist, 1995).

There is evidence for some degree of genetic predisposition towards schizophrenia and environmental factors are also thought to contribute. The pathophysiological mechanism of schizophrenia is unclear and several hypotheses have been proposed. Since antipsychotic drugs block dopamine receptors in the midbrain it has been suggested that dopaminergic system overactivity may be involved. Most commonly schizophrenia begins in adolescence and early adulthood and has an annual incidence of about 0, 1 to 0, 5 per 1000. The prognosis for schizophrenia is general worse than for other psychiatric disorders and many patients develop a chronic illness with repeated relapses and varying degrees of recovery between episodes. The best prognosis is patients in who the schizophrenia is of sudden onset with a definite precipitant and who have florid acute symptoms with marked mood changes and who previously were well adjusted.

Treatment of schizophrenia consists mainly of a combination of social therapy and antipsychotic drugs. Drug treatment should de individualized for each patient with

close monitoring. Negative symptoms tend to respond less well to drug therapy than do positive symptoms.
A useful generalization is that low-potency antipsychotic are sedative and strongly antimuscarinic and antiadrenergic but are less likely to cause acute extrapyramidal symptoms than the high-potency agents with exhibit a reversed pattern of adverse-effects. Sedative and muscarinic effects usually diminish with continued use, although sedative effects may be useful for behavioral control in acute illness (Martindale, 1999).
Antipsychotic medications are indicated in the treatment of acute psychotic disorders. The main goal of this investigation was to determine the incidence and prevalence of the neuroleptic therapy acute side effects. The reason for this epidemiological investigation performing was the lack of knowledge of the exact neuroleptic therapy side effects incidence. Qualitative study on this problem has not been performed yet. Antipsychotic therapy side effects prevalence rate according to the literature data is ranging from 24% to 74%. Different prevalence rate is a consequence of different antipsychotic drug usage, different drug administration method and different side effects identification (Loga i Fišeković, 2000).

No systematic reporting and evaluating system for documenting these adverse effects has evolved. Even the recognition of an adverse effect may be difficiult in an individual case (Meyler's, 2000); for example, akathisia may be difficult to differentiate from exacerbation of the illnes and often has a deleterious effect on compliance (Van Putten, 1974).

Definition of side effects:
Each unexpected appearance during application of drug, diagnostical and preventive
agents in usual doses is called side effects.
It is very hard to predict when side effects appear, because antipsychotic are drugs with large width (for chlorpromazine amounts 25 to 5000 mg daily).

Evaluation of side effects:
During the experiment following examinations were done:

- psychiatric interview,
- BRPS- Brief Psychiatric Rating Scale
- scale of side effects,
- psychophysiological tests,
- global clinical impression
- scale of appetite and carbon hydrate needs scale.

Scale of side effects:

- anxety
- sleep
- drowsnes
- dry mouth
- tachycardia
- blurred vision
- muscle pain
- sweating
- tremor
- vertigo
- dizziness
- dysuria
- dyspepsia
- nauzea
- pruritus
- constipation
- vomiting

Physiological parameters:

- blood pressure (sitting and standing position),
- pulse rate (sitting and standing position)
- pupil's size (normal and indirect light),
- digit symbol test,
- length of handwriting,
- scale of appetite
- carbon hydrate needs scale

Clinical global impresion (CGI):

- *Severity of symptoms*
- *Change of illnes state*
- *Effects of treatment*
- *Side effects*

Basic Goal
To determine prevalence and incidence of acute side effects in treatment with antipsychotic drugs during one month.

Secondary Goal
Total score acute side effects is reduced with regular selection and correct doses antipsychotic drug.

Taking in account all those facts, we put hypothesis between antipsychotic therapy and occurred side effects.

Null hypothesis
Antipsychotic drugs don' t cause side effects.

Hypothesis II (alternative)
Incidence and prevalence of recorded acute side effects were within the expected limits found
in literature.

Hypothesis III (alternative)
Only some antipsychotic cause acute side effects.

Method

Study is clinical-pharmacological, epidemiological, prospective and randomized. All parameters are taking on day starting the antipsychotics therapy and regularly every seven-day after.
Psychiatrists in the Intensive care unit of the Department of Psychiatry of the Clinical Center University of Sarajevo generally used typical antpsychotics because they are cheaper then atypical antpsychotics.
Our experiment had included all patients were hospitalized from 31.12. 1999. to 31. 01. 2000. in the Intensive care unit of the Department of Biological psychiatry of the Psychiatric Clinic in Sarajevo. Patients were divided in three groups according to used neuroleptics. All of them met criteria ICD-10 for schizophrenia (F20-29). The demographic data of three group patients were homogeneous.

Inclusion criteria:

- Patients of male and female sex, aged from 18 to 65 years
- Patients these met ICD-10 criteria for schizophrenia (F20-29)
- Patients who use antipsychotic therapy

Exclusion criteria:

- Patients who collaborate
- Children, pregnant and breast feeding women

Non-inclusion criteria:

- Patients without determined schizophrenic psychosis (F20-F29).
- Patients who do not use antipsychotic therapy

All patients treated with antipsychotic agents were the sample of our investigation. The drugs applied during our investigation were chosen by M. D., specialist in psychiatry, who ordinates in Intensive Care Unit of Biological Psychiatry Department of Psychiatric Clinic in Sarajevo.

Instruments of research:

- Psychiatric interview
- Brief Psychiatric Rating Scale-BPRS
- Adverse effects scale
- Psychophysiological tests
- CGI

Results and discussion

Patients were divided in three groups (25) according to the used neuroleptics:
I group- treated with single phenothiazine
II group- treated with combination of phenothiazines
III group- treated with phenotiazine and buthirophenone

Average daily doses of neuroleptics are presented in tab. 1.

The most used antipsychotic was promazine, and after it are: chlorpromazine, haloperidol and
fluphenazine. The commonest combination was chlorpromazine, haloperidol and promazine, and promazine with haloperidol.
Age of patients are presented in graph 1.

Graph. 1. Age of patients

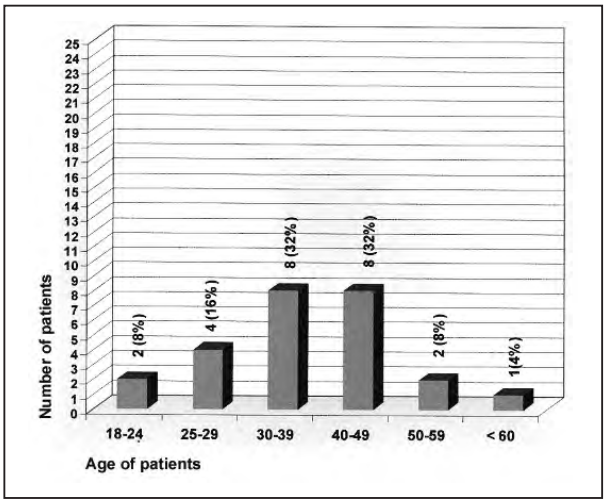
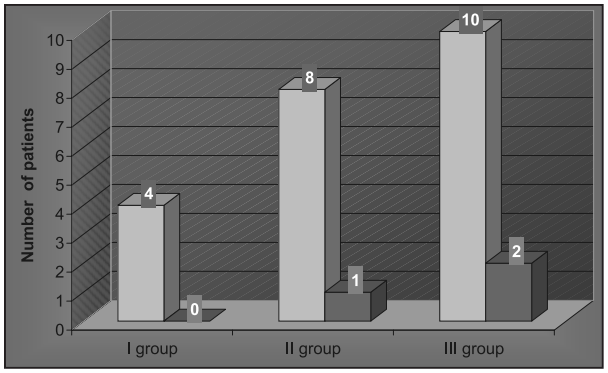


Table 1. Average daily doses of neuroleptics

Drug	Average daily doses	No. of patients
promazine	244 mg	16
fluphenazine	5 mg	1
fluphenazine decanoat	25 mg/ per month	7
haloperidol	6,78 mg	8
haloperidol decanoat	50 mg/ per month	5
levomepromazine	266 mg	3
chlorpromazine	236 mg	15
thioridazine	75 mg	1

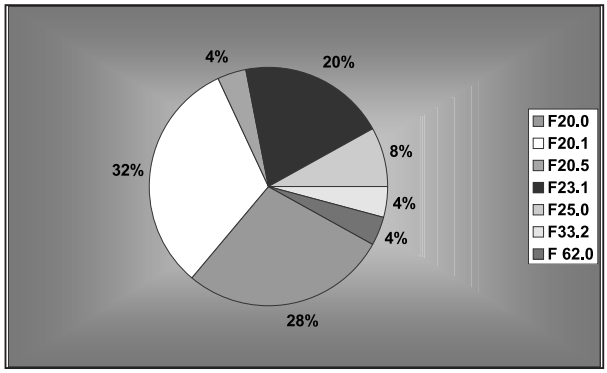
The same number of patients was monitored in patient group aged from 30 to 39 and from 40 to 49 years (32%) while the smallest number of patients were older than 60 years (4%).

Graph. 2. Sex of patients



Groups II and III had similar sex structure (88.9%, respectively 83.3% of men and 11.1%, respectively 16.7% of women. Group I consisted of only of men (100%).

Graph.3. Diagnoses



Diagnoses presented in Graph 3 are: hebephrenic psychosis (32%), regressive paranoid schizophrenia (28%), acute polymorphic psychotic disorders with schizophrenic symptoms (28%).

The demographic data of three group patients were homogeneous.

Evaluation symptoms of psychopathology

Table 2. Total BRPS (0 day)

Group	I group	II group	III group
α	77.25	80.89	87.58
SD	11.09	14.08	6.92
t-test	← -0.45 (p=0.66) →		
		← -1.44 (p=0.17) →	
	← -2.24 (p=0.04*) →		

Table 3. Total BRPS (7 day)

Group	I group	II group	III group
α	66.5	72.89	78.17
SD	12.39	17.0	12.59
t-test	← -0.67 (p=0.52) →		
		← -0.82 (p=0.42 →	
	← -1.61(p=0.13) →		

Significant differences regarding psychopathologic symptoms were noticed on the null day between treated groups I and III 0 (p=0.04*).

Table 4. Total BPRS (Difference 0/7 day)

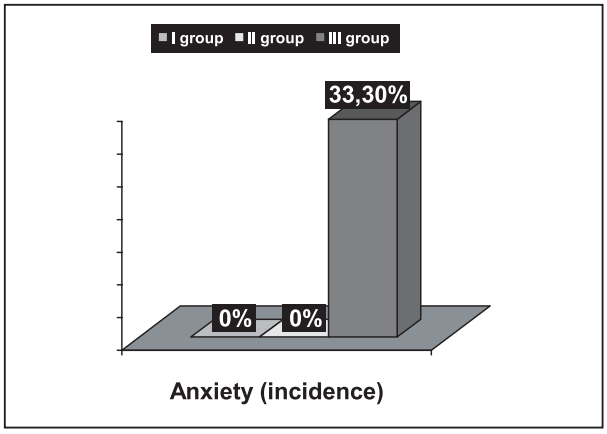
Group	α	SD	t-test
I group 0 day	77.25	11.09	1.29 (p=0.24)
I group 7 day	66.5	12.39	
II group 0 day	80.89	14.08	-1.09 (p=0.29)
II group 7 day	72.89	17.0	
III group 0 day	87.58	6.92	2.27 (p=0.03*)
III group 7 day	78.17	12.59	

Psychopathologic symptom improvement was observed in all groups at the end of observation period with significant improvement registered in group III (p = 0.03*). Psychopathologic symptom stabilisation was obtained in very short time and applied antipsychotic therapy completely reached all examination goals:

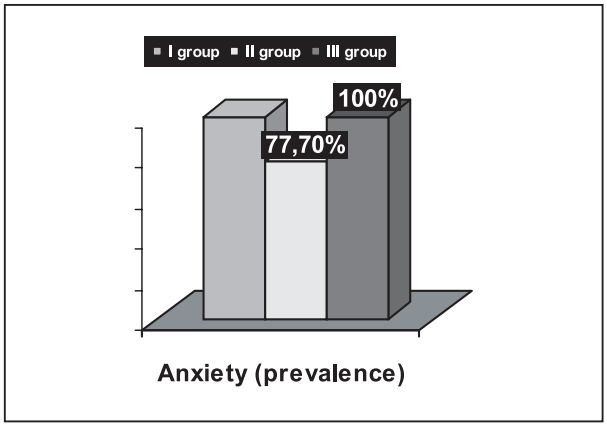
- dereistic thinking reduction
- alleviation of psychomotor unrest
- hallucination control (Loga, 1999).

Side effects and their intensity, incidence and prevalence are described below

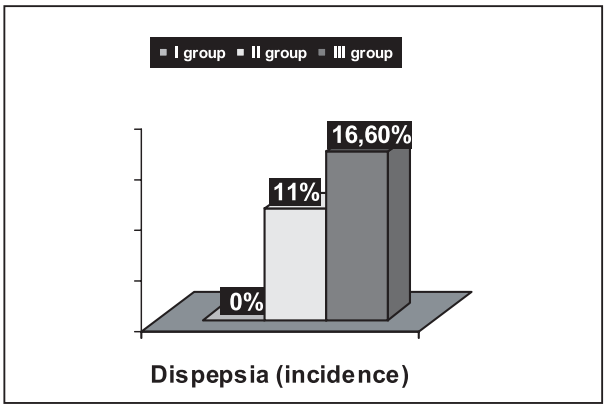
Graph. 4. Anxiety-incidence



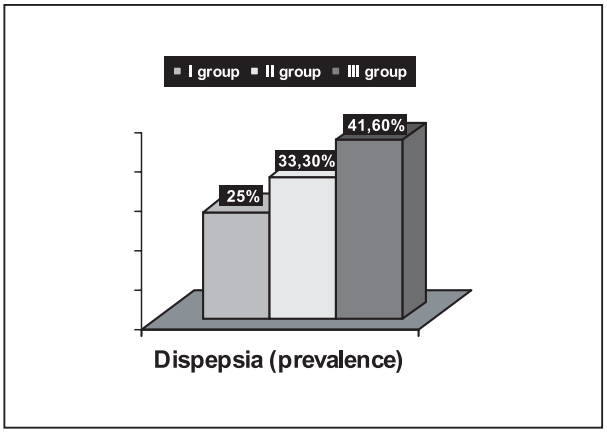
Graph. 5. Anxiety-prevalence



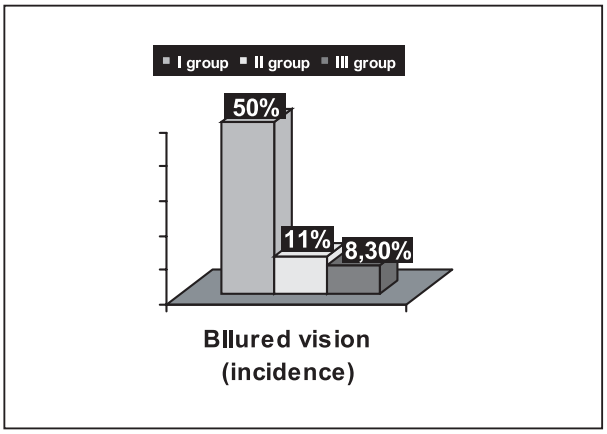
Graph. 6. Dyspepsia-incidence



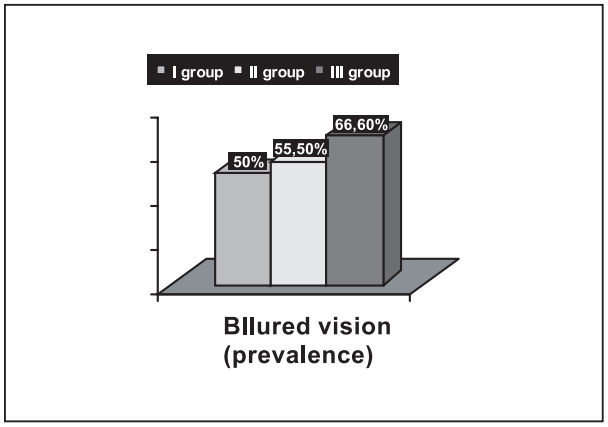
Graph. 7. Dyspepsia-prevalence



Graph. 8. Bllured vision-incidence



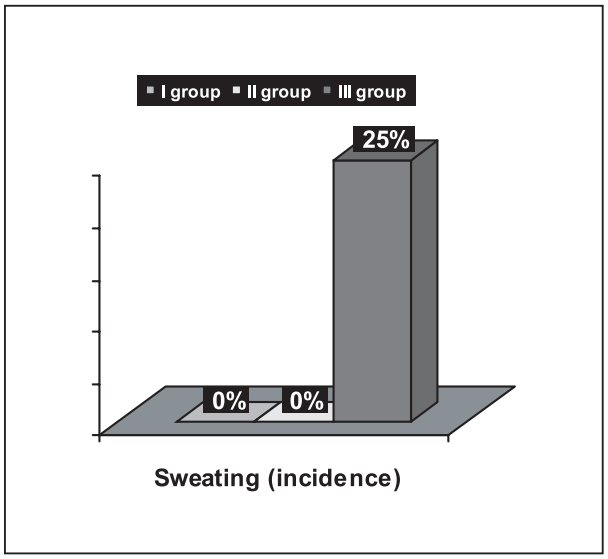
Graph. 9. Bllured vision-prevalence



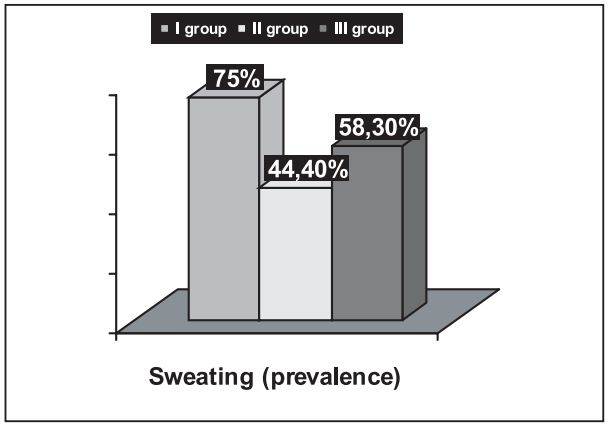
Various antipsychotic drugs, particularly low-dose phenothiazines and thioxanthenes, commonly cause blurred vision secondary to their anticholinergic activity. This is primarily a nuisance, except in the rare patient with closed-angle glaucoma.
Of more concern are two distinct types of adverse effects in the eye, witch may be produced by various antipsychotic drugs: lenticular and corneal deposits and pigmentary retinopathy.

Non-phenothiazines appear to have minimal propensity to cause oculocutaneous reactions and may be preferred when these problems have occurred during treatment with phenothiazines, although the patients should still be closely monitored. Pigmentary retinopathy, witch can seriously impair vision, is specifically associated with thioridazine, and has occurred more often with high and prolonged dosage (e.g. 1200-1800 mg/day for weeks to months) (Shah i sur., 1998).

Graph. 10. Sweating-incidence

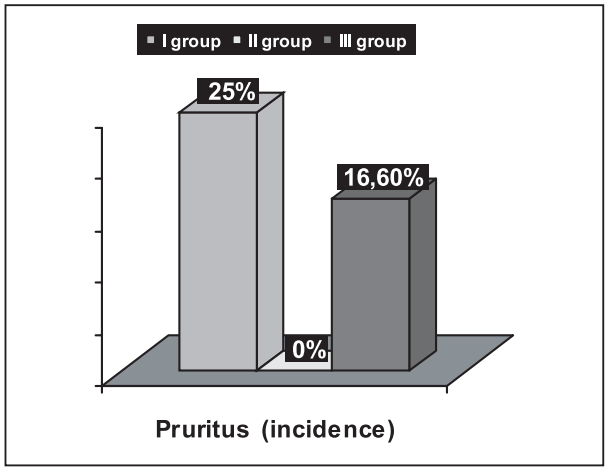


Graph. 11. Sweating-prevalence

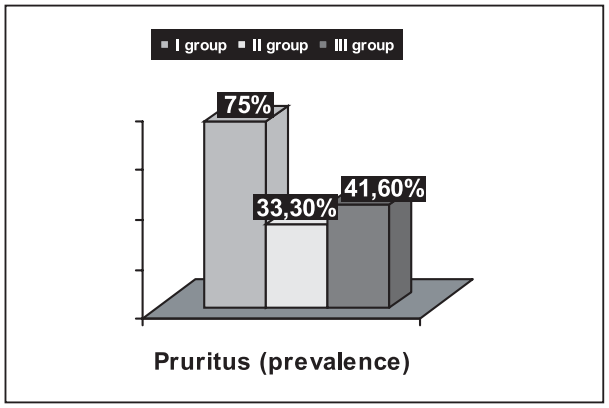


Antipsychotic drugs interfere with the temperature regulatory function of the hypothalamus, and also peripherally with the sweating mechanism, resulting in poikilothermy. This can result in either hyperthermia or hypothermia, depending on environmental temperature. Clozapine often cause a benign and transient increase in body temperature early in treatment
(Tremeau i sur., 1997).

Graph. 12. Pruritus-incidence

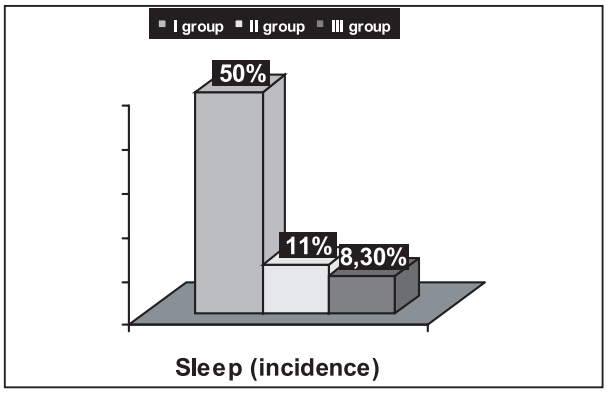


Graph. 13. Pruritus-prevalence

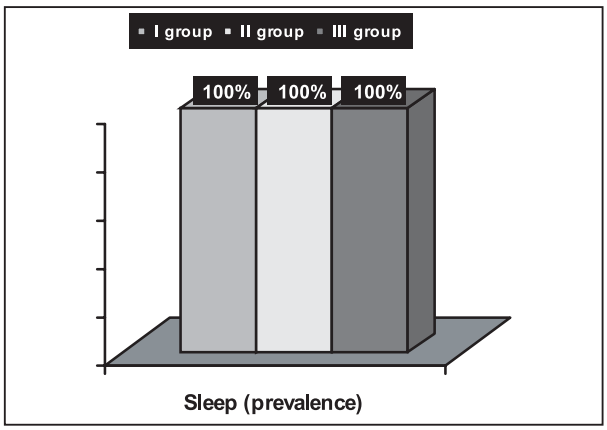


Many cutaneous reactions have reported with antipsychotic drugs, including urticaria, abscess after intramuscular injection, rashes, photosensitivity or exaggerated sunburn, contact dermatitis, and melanosis or blue gray skin discoloration. Skin rashes are usually benign. Chlorpromazine is most often implicated (incidence 5-10%)(George i sar., 2000). Sedation is commonly adverse effects antipsychotic therapy. In mainly patients sedation cause low potention antipsychotic such as chlorpromazine, but and other antipsychotic. This side effects is most frequently in initial phase of tretment (Davis i sar.,1989).

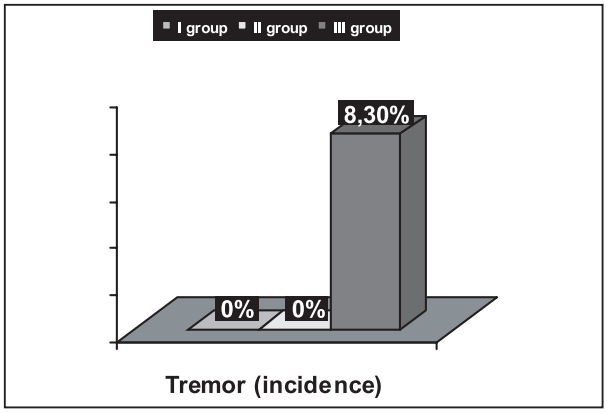
Graph. 14. Sleep-incidence



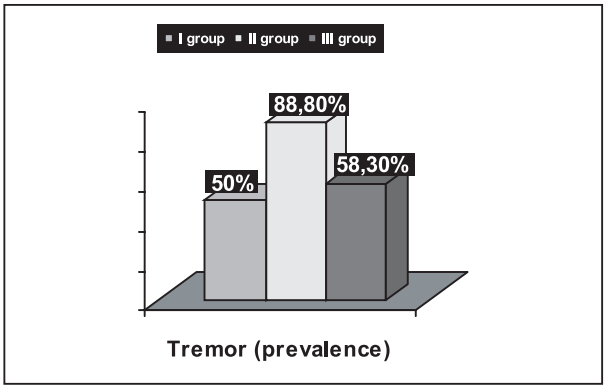
Graph. 15. Sleep-prevalence



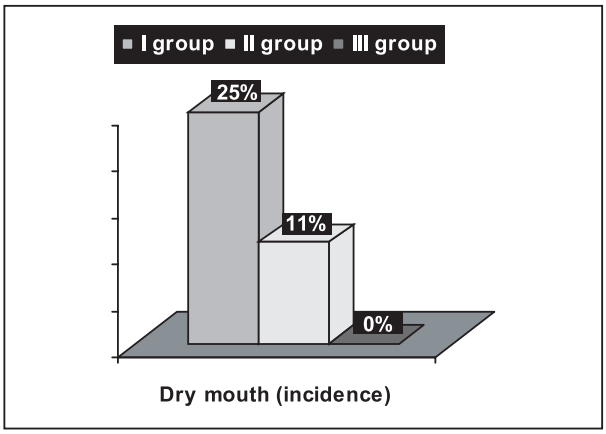
Graph. 16. Tremor-incidence



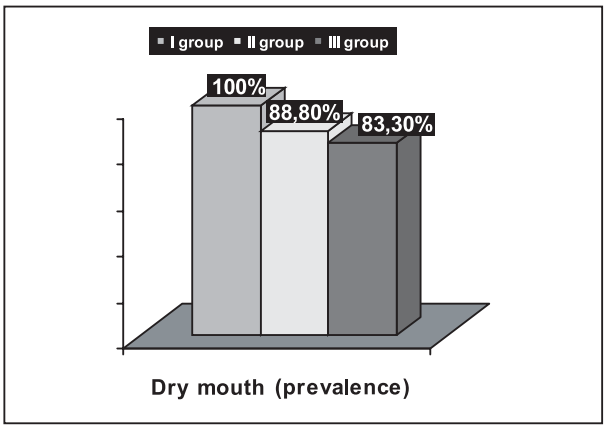
Graph. 17. Tremor-prevalence



Graph. 18. Dry mouth-incidence



Graph. 19. Dray mouth-prevalence



Dry mouth is a commonly reported autonomic adverse effect of antipsychotic drugs and is seen more often with drugs that have prominent anticholinergic properties, such as thioridazine and chlorpromazine. Dry mout is mainly a nuisance, but its persistence may promote dental caries, oral moniliasis, and infective parotitis. When feasible, once daily administration of antipsychotic drugs at bedtime helps to alleviate the problem of dry mouth. In contrast, clozapine, a potent muscarinic, can cause nocturnal hypersalivation (Szabadi, 1997).

Phisiological tests

Pulse rate in sitting and standing position

Table 5. Pulse rate in standing position (0 day)

Group	I group	II group	III group
α	89.25	104	105
SD	12.15	10.15	9.67
t-test	← -2.29(p=0.04*) →		
		← -0.23 (p=0.82) →	
	← -2.66 (p=0.02*) →		

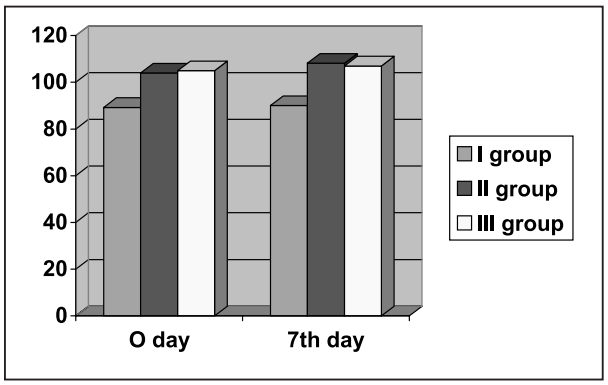
Table 6. Pulse rate in standing position (7 day)

Group	I group	II group	III group
α	90	108.22	107
SD	10.58	11.25	12.10
t-test	← -2.74 (p=0.02*) →		
		← -0.24(p=0.87) →	
	← -2.49(p=0.02*) →		

Table 7. Pulse rate in standing position (difference between 0 and 7th day)

Group	α	SD	t-test
I group 0 day	89.25	12.15	-0.22 (p=0.84)
I group 7 day	90	10.58	
II group 0 day	104	12.33	-0.95 (p=0.37)
II group 7 day	108.22	10.29	
III group 0 day	105	9.88	-0.56 (p=0.59)
III group 7 day	107	11.8	

Graph. 20. Pulse rate in standing position (difference between 0 and 7th day)



Pulse rates measured in patient sitting position on the null and seventh day did not significantly differ between all three groups, as well as intra each group.

Pulse rates measured in patient standing position on the null day showed marked differences between group I and group II, as well between group I and group III.

The highest pulse values were registered in group III while the lowest once were registered in group I. Statistically significant intra group differences between the null and the seventh day were not observed (table 5, 6, 7. and graph. 20).

Hypotension is the most commonly observed cardiovascular adverse effects of antipsychotic drugs, particularly after administration of those that are also potent a-adrenoreceptors antagonist, such as chlorpromazine, thioridazine. A central mechanism involving the lowering of blood pressure. Antipsychotic drugs of high and intermediate potency, such as haloperidol, have minimal a-blocking effects and would be less likely to cause such changes, (a fall of 30 mm Hg) were report orthostatic changes, although in one report with these drugs in 27% and 22% of cases respectively (Simpson et al., 2000). In our investigation changed in pulse rate and blood pressure were not significant.

Pupil's size (normal light)

Table 8. Pupil's size normal light (0 day)

Group	I group	II group	III group
α	2.75	2.39	2
SD	0.5	0.55	0.62
t-test	← 1.12(p=0.29) →		
		← -1.39 (p=0.18) →	
	← 0(p=1) →		

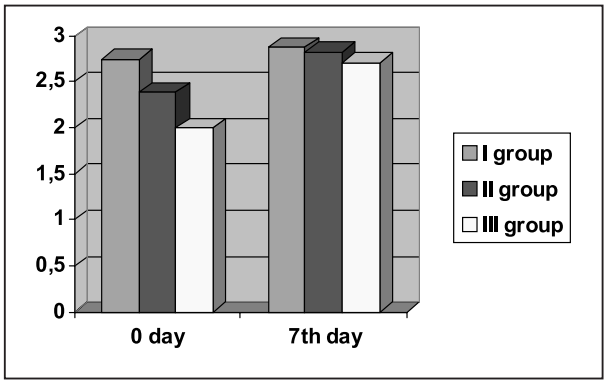
Table 9. Pupil's size normal light (7th day)

Group	I group	II group	III group
α	2.88	2.83	2.71
SD	0.25	0.56	0.49
t-test	← 0.14 (p=0.89) →		
		← 0.54 (p=0.59) →	
	← 0.63 (p=0.54) →		

Table 10. Pupil's size normal light (difference between 0 and 7th day)

Group	α	SD	t-test
I group 0 day	2.75	0.5	-1.0 (p=0.39)
I group 7 day	2.88	0.25	
II group 0 day	2.39	0.55	-2.87 (p=0.02*)
II group 7 day	2.83	0.56	
III group 0 day	2	0.62	0.29 (p=0.78)
III group 7 day	2.71	0.49	

Graph. 21 Pupil's size normal light (difference between 0 and 7th day)



Pupil sizes remained the same (daylight) in all patients during the whole period of examination with the exception of group II patients. Non significant pupil enlargements were observed in group I and group III patients (table 8, 9, 10. and graph. 21.)

Digit symbol test

Table 11. Digit symbol test (0 day)

Group	I group	II group	III group
α	11	21.89	33.67
SD	11.58	16.80	21.72
t-test	← -1.17(p=0.27) →		
		← -1.35(p=0.19) →	
	← -1.97(p=0.07) →		

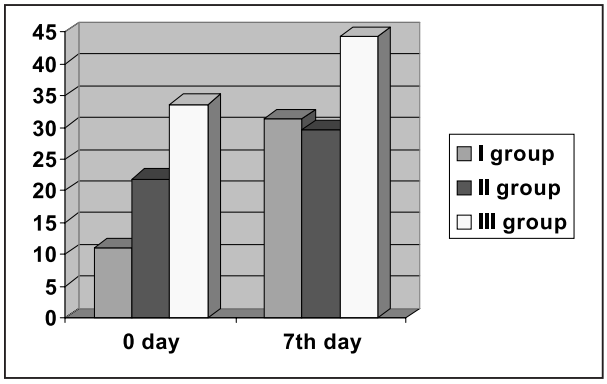
Table 12. Digit symbol test (7th day)

Group	I group	II group	III group
α	31.25	29.56	44.33
SD	27.37	18.91	17.49
t-test	← 0.13 (p=0.89) →		
		← -1.85(p=0.08) →	
	← -1.13(p=0.28) →		

Table 13. Digit symbol test (difference between 0 and 7th day)

Group	α	SD	t-test
I group 0 day	11	11.58	-2.39 (p=0.09)
I group 7 day	31.25	27.37	
II group 0 day	21.89	16.80	-1.41 (p=0.19)
II group 7 day	29.56	18.91	
III group 0 day	33.67	21.72	-2.26 (p=0.05*)
III group 7 day	44.33	17.49	

Graph. 22. Digit symbol test (difference between 0 and 7th day)



There was no statistically significant differences intra and inter treated groups of patients during the whole investigation period, with the exception of group III (p= 0.05) (Table 11, 12, 13. and Graph. 22) Various antipsychotic drugs, particularly low-doses phenothiazines and thioxanthenes, commonly cause blurred visions secondary to their anticholinergic activity (Shah et al., 1998). Although, in this tree group, after used therapy did not changed toward blurred visions.

The extend to which neuroleptic drugs impair mental activity is disputed. A recent study has shown that the more anticholinergic antipsychotic drugs impaired short-term verbal memory (Eitan et al., 1992). One study showed that schizophrenic patients who took neuroleptic drugs had superior information processing compared with unmedicated schizophrenic patients; the authors claimed that neuroleptic drugs probably do not cause, and may actually reverse, slowness of information processing in schizophrenic patients (Simpson et al., 2000). However, a substantial number of schizophrenic patients declare that neuroleptic drugs slow their thinking, cause them to forget, and remove interest thinking, cause them to forget, and remove interest and motivation. These responses to neuroleptic drugs are claimed to be dysphoric and are often associated with drug induced extrapyramidal symptoms, particularly akathisia (Stip, et al., 1996).

The conducted investigation in the Department of Psychiatric showed that the used neuroleptic therapy did not impair cognitive functions of patients, as it can be observed in the Digit symbol test and the test of handwriting.

Scale of appetite

Table 14. Scale of apetite (0 day)

Group	I group	II group	III group
α	4.25	3.33	4.67
SD	3.20	2.78	2.35
t-test	← 0.53(p=0.61) →		
		← -1.19 (p=0.25) →	
	← -0.28(p=0.78) →		

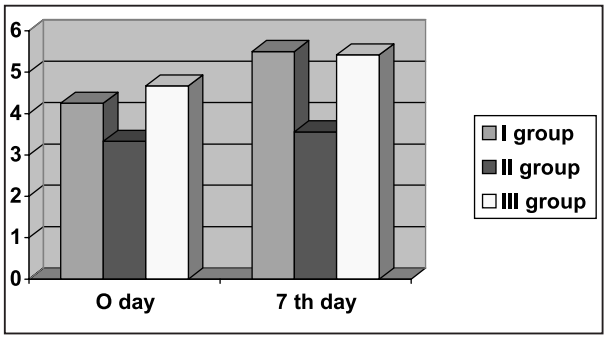
Table 15. Scale of apetite (7 day)

Group	I group	II group	III group
α	5.5	3.56	5.42
SD	2.38	2.40	3.18
t-test	← 1.35 (p=0.20) →		
		← -1.47 (p=0.16) →	
	← 0.05p=0.96) →		

Table 16. Scale of apetite (difference between 0 and 7th day)

Group	α	SD	t-test
I group 0 day	4.25	3.2	-2.61 (p=0.08)
I group 7 day	5.5	2.38	
II group 0 day	3.33	2.78	-0.80 (p=0.45)
II group 7 day	3.56	2.40	
III group 0 day	4.67	2.35	-1.27 (p=0.23)
III group 7 day	5.42	3.18	

Graph. 23. Scale of apetite (difference between 0 and 7th day)



No statistically significant differences regarding appetite were observed between examined groups.

Weak appetite of patients was registered in group I on the null day. Appetite of the same group of patients was not statistically increased (p=0.08) on the seventh examination day. The very similar results regarding appetite of patients were registered in group II and group III.

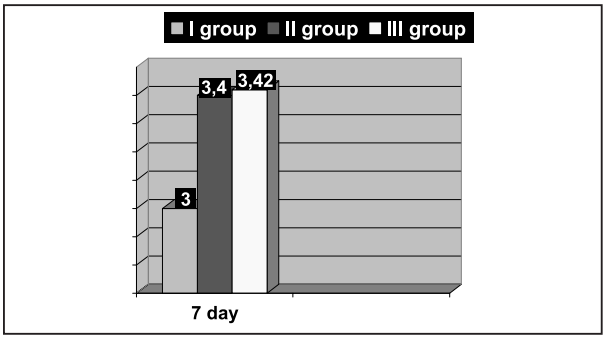
Weight gain is a common adverse effect of neuroleptic drugs. The mechanisms is poorly understood, although a serotoninergic mechanisms has been proposed. A meta-analysis of trials of antipsychotic drugs calculated the following mean weight gains in kg after 10 weeks of treatment: clozapine 4,5; olazapine 4,2; thioridazine 3,2; sertinole 2,9; chlorpromazine 2,6; risperidone 2,1; haloperidol 1,1; fluphenazine 0,43; ziprasidone 0,04; molindone, -0,39; placebo -0,74 (Allison i sar., 1998; Kelly i sar., 1998).

CGI

Table 17. CGI (7th day)

Group	I group	II group	III group
α	3.0	3.4	3.42
SD	0.82	1.13	0.9
t-test	←——— -0.7 (p=0.49) ———→		
	←——— 0.06(p=0.95) ———→		
	←——— -0.82 (p=0.43) ———→		

Graph. 24. CGI (7 th day)



CGI- Symptoms of illness were exceptionally severe in all treated groups. After seven days of the treatment clinically insignificant improvements were observed. Monitoring period was short and therapeutic effects were relatively satisfying. Reported side effects were mild and moderate.

Conclusion

According to the obtained data it has been concluded that applied antipsychotic therapy did not cause more psychophysiological function impairment in treated patients. Psychophysiological functions remained within physiological limits and they were not changed significantly. Neuroleptic therapy side effects were minimal, meaning no toxic signs or therapy discontinuations were recorded.

Sažetak

Antipsihotici posjeduju široki spektar različitih fizioloških djelovanja, a ova dejstva se razlikuju ovisno od klase u koju spada određeni antipsihotik. Ovi lijekovi indicirani su u liječenju akutnih psihotičnih oboljenja. Osnovni cilj našeg epidemiološkog istraživanja, koje je po svom dizajnu prospektivno i kliničko-farmakološko, bio je utvrditi incidenciju neželjenih efekata antipsihotika, ordiniranih kod shizofrenih bolesnika na akutnom psihijatrijskom hospitalnom odjeljenju, jer do danas nije urađena valjana studija u tom pogledu. Prevalencija neželjenih efekata izazvanih neurolepticima, prema literaturnim podacima, kreće se u širokom rasponu od 24% do 74%. Različite stope prevalencije su posljedica različite primijene neuroleptika u istraživanjima, načina njihove aplikacije i metoda detekcije neželjenih efekata. S tim u vezi postavljene su hipoteze o odnosu antipsihotične terapije i pojave neželjenih efekata. Istraživanje je obuhvatilo shizofrene pacijente koji su bili hospitalizirani u periodu od 31.12. 1999. do 31. 01. 2000. godine na Intenzivnoj njezi odjeljenja za biološku psihijatriju Psihijatrijske klinike u Sarajevu. Pacijenti su bili podjeljeni u tri grupe prema ordiniranoj terapiji. Kriteriji uključivanja u pomenute grupe su iziskivali da pacijenti ispoljavaju klinički utvrđenu shizofrenu psihozu (F20-29) prema kriterijima ICD-10. Instrumenti istraživanja su bili psihijatrijski intervju, BPRS, skala neželjenih efekata, fiziološki testovi, procjena opšteg kliničkog utiska i samoocjenske skale (skale apetita i potreba za ugljičnim hidratima). Evaluacija je bila kliničko-psihijatrijska i statistička. Na osnovu procjene rezultata tretmana u sve tri grupe, evidentno je došlo do poboljšanja kliničke slike akutnog pogoršanja bolesti, ali i pojave neželjenih efekata koji su uglavnom bili umjereno izraženi i podnošljivi za bolesnike. Niske stope incidencije i nešto više stope prevalencije uslovile su da se odbaci nulta, a potvrdi alternativna hipoteza, prema kojoj je incidencija i prevalencija akutnih neželjenih efekata u granicama očekivanja. Intenzitet neželjenih efekata bio je umjeren do blago izražen, čime se prihvata osnovna teza ovog rada, a to je da se pravilnim odabirom klasičnih ili tipičnih antipsihotika, kao i njihovim pravilnim doziranjem, smanjuje ukupan skor akutnih neželjeni efekata. Na osnovu procjene fizioloških testova može se zaključiti da primijenjeni antipsihotici nisu u većoj mjeri uticali na psihofiziološke funkcije pacijenata. Znači psihofiziološke funkcije mjerene specifičnim psihofiziološkim testovima su ostale u fiziološkim granicama, tj. ustanovljene promjene nisu imale bitan uticaj na ukupni tretman. To potvrđuje i tezu ovog rada da se pravilnim izborom antipsihotika i pažljivim doziranjem antipsihotične terapije značajnije ne mijenjaju psihofiziološke funkcije pacijenata. Ni u jednom slučaju nije bilo potrebe da se prekine liječenje antipsihoticima, bilo zbog izostanka terapeutske djelotvornosti, ili zbog izraženih neželjenih efekata antipsihotične terapije, odnosno komplikacija u toku liječenja.

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