

PSYCHOPHARMACOLOGICAL APPROACH TO THE TREATMENT OF ADOLESCENTS IN THE FIRST PSYCHOTIC EPISODE

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Summary

Introduction. The first psychotic episodes in adolescents represents a great challenge in the psychopharmacologic and diagnostic point of view. Atypical antipsychotics are the first line treatment of children and adolescents with psychotic disorders. Typical antipsychotics are used as second-line treatment.

Objective. The aim of the study was to assess, analyze and present data on psychopharmacologic treatment of first psychotic episodes in adolescents who were hospitalized at the Clinic for Mental Disorders “Dr Laza Lazarevic” in the Clinical department for older adolescents.

Method. The research was conducted as a retrospective naturalistic study conducted in the period from 01.07.2012. to 08.30.2014. The sample consisted of 60 hospitalized patients with a first psychotic episode. The therapy administered at discharge was recorded. The survey instrument was a closed questionnaire composed for this article. Data analysis was performed by means of descriptive statistics.

Results. Out of 60 patients incidence of those treated with typical antipsychotic was 40 %, atypical 33.33 %, while the incidence of combined therapy with typical and atypical was 26.67 %. The average length of treatment of patients on monotherapy typical antipsychotic was 28.79 days (\bar{X} = 28.79), atypical 24.15 (\bar{X} = 24.15) and a combination of typical and atypical 27.44 (\bar{X} = 27.44). Hallucinations show a better response to typical antipsychotics, while delusions respond about the same in both drug groups.

Conclusion. Successful treatment of initial psychotic episode, especially among adolescents, is crucial for minimizing the consequences for the personal and social functioning. In relation to the course of the disease, duration of treatment and side effects, atypical antipsychotics have the advantage over the first-generation drugs, as has been shown by the results of the study.

Key words: adolescent, first psychotic episode, typical antipsychotic, atypical antipsychotic

INTRODUCTION

Psychopharmacological approach to the treatment of adolescents in the first psychotic episode presents a considerable challenge. Psychosis at an early age can manifest in a more rapid clinical picture in relation to psychotic episode which first occurs in adulthood. Diagnosing and determining the adequate psychopharmacological treatment plan can be complicated due to the difficulty in differentiating between the primitive forms of cognitive reasoning such as magical thinking, which often occurs in children and adolescents, and real symptoms such as delusions [1]. The clinical picture is often less clear, since the development of personality is stopped or slowed due to the progression of the disease [2, 3]. Good therapeutic efficacy during the first episode may delay or prevent the development of a complete clinical picture of a psychotic disorder [4]. Although there are a number of guides on the use of antipsychotic drugs in adult patients, the same cannot be applied in adolescents. Pharmacotherapy of psychotic disorders in adolescents is specific in both pharmacodynamic and pharmacokinetic aspects compared to adult patients [5]. As a rule, in patients with the first psychotic episode the experience of the previous response to therapy is not available. Deciding on the therapy for these patients must be based on the results of research, and not on the current experience the administration a particular drug had [6]. Studies have shown that the outcome of the first two years of treatment can predict the future course of a disease [7].

There are relatively few epidemiological studies on the first psychotic episodes in adolescents. It is known that the inci-

dence of psychoses, especially schizophrenia increases during adolescence, predominantly in men compared to women [8]. In more than 40 % of cases, the first psychotic episode occurs between 15 and 18 years of age [6], which is a period of great importance in relation to the development of personality and obtaining a social role [9].

The aims of treating psychotic episodes are withdrawal of the symptoms, relapse prevention, establishing remission and achieving functional recovery and social reintegration [2]. In the treatment of first psychotic episodes antipsychotics should be introduced very cautiously, because of the higher risk of extrapyramidal symptoms, applying the lowest effective dose of medication (lower dose in the standard dosage range).

In clinical practice, atypical antipsychotics, antagonists of serotonin and dopamine, are the first-line treatment of children and adolescents with schizophrenia. They have been suggested to be more efficient in the reduction of positive and negative symptoms of schizophrenia and to carry a lower risk of extrapyramidal symptoms. In addition, atypical antipsychotics such as quetiapine, ziprasidone and aripiprazole are also antagonists of serotonin and dopamine, which are used in clinical practice for children and adolescents with psychotic disorders who do not respond to other atypical antipsychotics. Typical antipsychotics, such as haloperidol and chlorpromazine are used as the second-line treatment, although the use of chlorpromazine is more favorable due to a lower risk of occurrence of dystonic reaction [10].

OBJECTIVE

The aim of this study is to assess, analyze and present data on psychopharmacologic treatment of psychotic disorders in adolescents who were hospitalized at the Clinic for Mental Disorders “Dr Laza Lazarevic” in the Clinical department for older adolescents in the first psychotic episode. The result provides insight into the current approach of the treatment of these patients and could provide important information for planning and developing strategies for treatment as well as pointing out the limitations and dilemmas in the treatment of adolescents in the first psychotic episode.

METHOD

Our research was conducted as a retrospective naturalistic study carried out at the Clinic for Mental Disorders “Dr Laza Lazarevic” in the Clinical department for older adolescents in the period from 01.07.2012. to 08.30.2014. when the first 60 hospitalizations of patients with psychotic episode occurred.

Criteria for inclusion of patients in this study were:

- The patient was hospitalized at the, Clinic for Mental Disorders “Dr Laza Lazarevic” in the Clinical department for older adolescents in the period from 01.07.2012. to 30.08.2014.
- The patient was aged between 14 and 18 years including both sexes.
- That the patient was diagnosed according to the International Classification of Diseases (ICD- 10), as psychotic in schizophrenic spectrum of groups F20 to F29

- If the patient was categorized with a level of intelligence satisfactory for regular education
- The patient had no history of addictions and/or has not had contact with psychoactive substances for 3 months previous to the study

The criteria for exclusion of patients from the study were:

- That the patient was previously treated in another psychiatric institution under the above diagnoses.
- The patient was suffering from neurological and somatic diseases.
- If the patient left the clinic on the personal request of parents prior to the diagnosis and treatment.

Parents or legal guardians of patients were provided with a written consent for the use of medical records for the purposes of our study.

Information on psychopharmacologic treatment of the sample were obtained by examining the discharge lists of the patients and prescriptions lists. The therapy administered at discharge was recorded. The survey instrument was a closed questionnaire composed for this research. Medical histories of hospitalized adolescents were used for filling the data in the questionnaire. Data analysis was performed by means of descriptive statistics.

RESULTS

At the Clinic for Mental Disorders “Dr Laza Lazarevic” in the Clinical department for older adolescents in the period from 01.07.2012. to 08.30.2014. sixty hospitalizations of adolescents in the first psychotic episode occurred, which fulfill the conditions stipulated by the design of the study. The average age

of patients was 16.1 ± 0.94 years, of which 22 (36.7%) were females and 38 (63.3%) males. Viewed by diagnosis (ICD-10), there were 58 (96.7%) patients with F23 and 2 (3.3%) patients with F29 diagnosis at discharge.

The methods of descriptive statistics showed that out of 60 patients who were treated with antipsychotics, the incidence of those treated with typical antipsychotic was 40%, atypical antipsychotic 33.33%, while the frequency of the prescribed combination therapy of typical and atypical antipsychotics was 26.67% shown in Table 1 and Figure 1.

The average length of treatment of patients on monotherapy typical antipsychotic was 28.79 days ($\bar{X} = 28.79$),

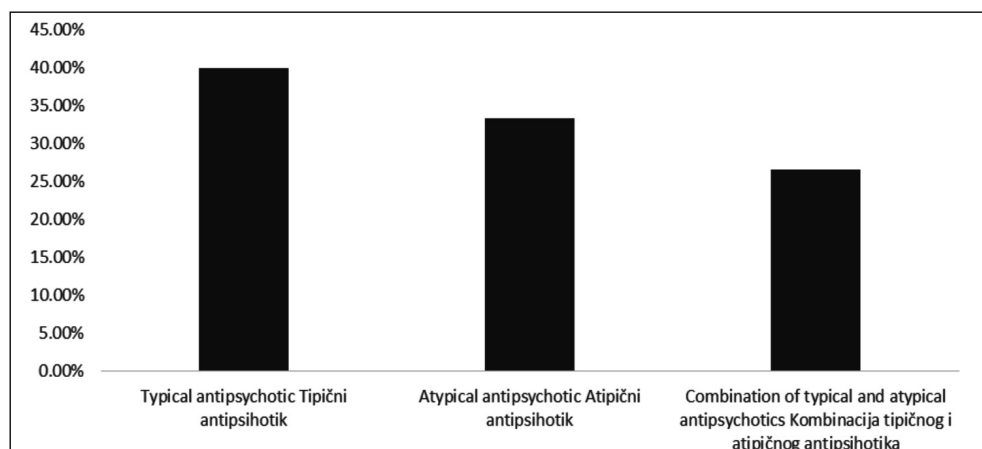
atypical 24.15 days ($\bar{X} = 24.15$) and a combination of typical and atypical 27.44 days ($\bar{X} = 27.44$) shown in Figure 2.

When the results are viewed in terms of clinical signs or prominent manifestations of hallucinations or delusions in relation to the type of applied antipsychotics, the following results:

When hallucinations were present, typical antipsychotics were administered in 26.67%, atypical antipsychotics in 15%, and the combination of drugs in 11.67% of patients. Shown in Table 2. Delusions are reduced using the typical antipsychotics in 36.67%, 31.67% using of atypical antipsychotics and 15% of treated patients received a combination

Table 1. Therapy of study patients on discharge
Tabela 1. Terapija ispitanika pri otpustu

Typical antipsychotic Tipični antipsihotik		Atypical antipsychotic Atipični antipsihotik		Combination of typical and atypical antipsychotics Kombinacija tipičnog i atipičnog antipsihotika	
N	%	N	%	N	%
24	40	20	33,3	16	26,67



Graph. 1. Therapy of study patients on discharge
Grafikon 1. Terapija ispitanika pri otpustu

of drugs. Shown in Table 3. The results obtained in our study were not compared in terms of statistical significance given that the survey was conducted in a short period of time and using relatively small sample.

DISCUSSION

Available literature on pharmacotherapy in children and adolescents with psychosis is critically examining both first and second generation antipsychotics [11]. On the basis of National institute for health and care excellence (NICE)

guide all antipsychotics, which are recommended for use in adults can be applied in children and adolescents with special caution in relation to the age of patients (dose modification) [12]. Administration of depot medication in the population of children and adolescents is not clinically justified.

Also, caution is necessary when administering antipsychotics because the side effects are more pronounced than in adults. It is recommended to start with a low dose of antipsychotic drugs, with a gradual increase in the daily dose. It is important to note that the use of an-

Table 2. Therapy of study patients on discharge in regard to hallucinations
Tabela 2. Terapija ispitanika pri otpustu u odnosu na prisu

Hallucinations Halucinacije	Typical antipsychotic Tipični antipsihotik		Atypical antipsychotic Atipični antipsihotik		Combination of typical and atypical antipsychotics Kombinacija tipičnog i atipičnog antipsihotika	
	N	%	N	%	N	%
Present Prisutne	16	26,67	9	15	7	11,67
Absent Nisu prisutne	8	13,33	11	18,33	9	15

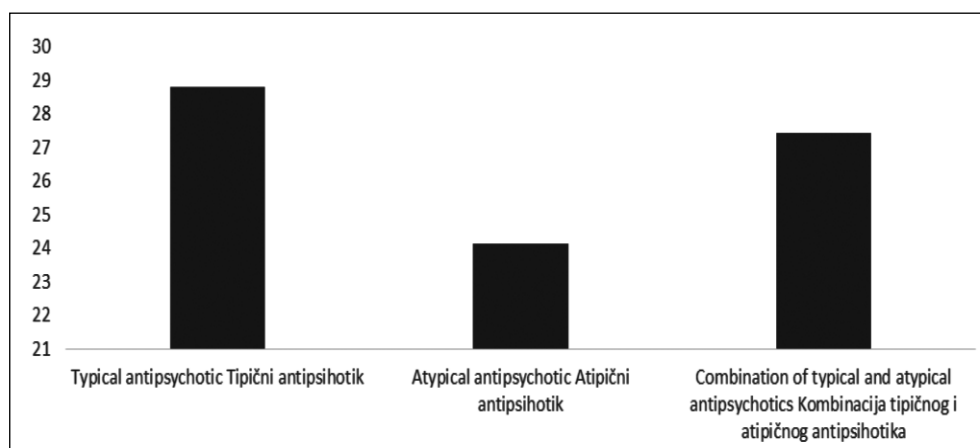


Figure 2. Duration of hospitalisation compared to therapy
Grafikon 2. Trajanje hospitalizacije u poređenju sa terapijom

typsychotics in children and adolescents is not on the indication list described in the patient information leaflet. For this reason it is important to inform parents / guardians, as well as children and adolescents that even though the given drugs are not recommended for use in children they are essential in the treatment. Therefore, it is often said that children use licensed medication - antipsychotics, for an unlicensed indication - for treatment of psychosis in children and adolescents, which is why the informed consent of a parent or guardian is very important [13].

According to guidelines atypical antipsychotics are first choice drugs in the treatment of adolescents with psychotic episodes. Drugs such as risperidone, olanzapine and clozapine differ from classical antipsychotics in terms of fewer predominance D2 receptor antagonism and are considered to be effective in reducing symptoms of psychosis, with a reduced risk of extrapyramidal symptoms [14]. Recently published case studies and larger controlled studies have demonstrated efficacy of risperidone in the treatment of psychosis in adolescents with the same potency that typical antipsychotics have, such as haloperidol. Antipsychotics such as quetiapine, ziprasidone and aripiprazole

are used in clinical practice on adolescents who do not respond to other atypical antipsychotics [15]. On the other hand, certain studies showed no significant differences in treatment efficacy between risperidone, olanzapine and quetiapine in the six-month followed treatment [16]. According to international studies typical antipsychotics should represent a second line of treatment. However, low-potent antipsychotic drug such as chlorpromazine may be more suitable for adolescents, because of the reduced possibility of the occurrence dystonic reactions [17].

The results of our study have shown that remission with reduction of psychotic phenomenology, agitation and behavioral discontrol in 60 patients treated with antipsychotics, was achieved using typical antipsychotic haloperidol, chlorpromazine or fluphenazine, in 40% of cases, atypical antipsychotic risperidone, clozapine or olanzapine in 33.33% of patients, while the frequency of the prescribed combination therapies of typical and atypical antipsychotic was 26.67%. These results could be explained by the fact that the use of typical antipsychotics remains dominant in the management of psychotic phenomenology, especially in emergency psychiatric care units when it

Table 3. Therapy of study patients on discharge
Tabela 3. Terapija ispitanika pri otpustu

Delusions Sumanute ideje	Typical antipsychotic Tipični antipsihotik		Atypical antipsychotic Atipični antipsihotik		Combination of typical and atypical antipsychotics Kombinacija tipičnog i atipičnog antipsihotika	
	N	%	N	%	N	%
Present Prisutne	22	36,67	19	31,67	15	25
Absent Nisu prisutne	2	3,33	1	1,67	1	1,67

is necessary to achieve rapid therapeutic effect in terms of eliminating psychomotor agitation and sedating the patient [18]. Department in which the survey was conducted primarily deals with urgent psychiatric conditions in terms of agitation, disorganized behavior and aggressiveness, and the results of the research in terms of more frequent use of typical antipsychotics may explain this fact. Also a non-compliant patient, especially with psychotic phenomenology limits the possibility of applying per oral medications, and requires the use of drugs that can be administered parenterally, which are in our country, for now, only available in the form of typical antipsychotics. According to results of our research, reduction of hallucinations is better achieved using typical antipsychotics while delusions respond about the same in both first and second generation. The differences in therapeutic response may be based upon the fact that delusional contents can basically have hallucinatory experiences that respond better to typical antipsychotic drugs, but still delusional contents in relation to hallucinatory phenomenology give greater priority to the second generation.

After the initial stage of treatment and achieved reduction of symptomatology, further treatment, according to protocols, included pharmacotherapy of atypical antipsychotic monotherapy or combination of typical and atypical which indicated that the faster therapeutic effect and recovery is achieved primarily using atypical antipsychotics, which is in line with the current therapeutic guidelines.

The properties of atypical antipsychotics are such that it is expected that the rate of recovery and reintegration will be much higher than the typical antipsychotics despite the fact that in acute treatment no significant distinction between these two groups of drugs [19].

CONCLUSION

Successful treatment of initial psychotic episode, especially among adolescents, is crucial for minimizing the consequences for the personal and social functioning. Control of unusual and conspicuous behavior associated with positive symptoms enables better re-socialization of the patient and involvement in everyday activities. Applying typical antipsychotic during the initial phase of treatment is still an essential part of treatment, due to the potency of drugs, and because of the possibility to administer them in parenteral form. In relation to the course of the disease, duration of treatment and side effects, atypical antipsychotics have the advantage over the first-generation drugs, as showed the results of the study. Clinical department for older adolescents at the Clinic for Mental Disorders "Dr Laza Lazarevic", in addition to interventions in the first psychotic episodes, addresses and early recognition and prevention of psychosis in accordance with applicable guidelines for good clinical practice. Past experience indicates that further research is necessary due to the low rates of remission, narrow therapeutic action of drugs and frequent side effects.

PSIHOFARMAKOTERAPIJSKI PRISTUP TRETMANU ADOLEŠČENATA U PRVOJ PSIHOTIČNOJ EPIZODI

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Kratak sadržaj

Uvod. Prva psihotična epizoda kod adolescenata predstavlja sa dijagnostičke i psihofarmakoterapijske tačke gledišta veliki izazov. Atipični antipsihotici su prva linija tretmana dece i adolescenata sa psihotičnim poremećajem. Tipični antipsihotici se koriste kao druga linija tretmana.

Cilj rada. Cilj istraživanja je sagledavanje, analiza i prezentovanje podataka o psihofarmakoterapijskom tretmanu prve psihotične epizode kod adolescenata koji su hospitalizovani na Odeljenju za starije adolescentne Klinike za psihijatrijske bolesti „Dr Laza Lazarević“.

Metod rada. Istraživanje je sprovedeno kao retrospektivna naturalistička studija obavljena na Klinici za psihijatrijske bolesti „dr Laza Lazarević“ na odeljenju za starije adolescentne u periodu od 01.07.2012. do 30.08.2014. godine. Uzorak je činilo 60 hospitalizovanih pacijenata sa prvom psihotičnom epizodom. Roditelji, odnosno zakonski staratelji bolesnika su dostavili pisanu saglasnost za korišćenje medicinske dokumentacije za potrebe našeg istraživanja. Uvidom u otpusnu listu bolesnika i terapijski karton evidentirana je terapija ordinirana na otpustu. Instrument istraživanja bio je upitnik zatvorenog tipa sastavljen za potrebe ovog rada. Analiza dobijenih podataka obavljena je metodama deskriptivne statistike.

Rezultati. Prosečna starost pacijenata je $16,1 \pm 0,94$ godine, od kojih je 22 (36,7%) ženskog pola i 38 (63,3%) muškog pola. Deskriptivnom statistikom utvrđeno je da od 60 pacijenata koji su lečeni antipsihotikima, učestalost lečenih tipičnim antipsihotikom je 40%, atipičnim 33,33%, dok je učestalost kombinovane terapije tipičnog i atipičnog bila 26,67%. Prosečna dužina lečenja pacijenata na monoterapiji tipičnim antipsihotikom iznosila je 28,79 dana ($X = 28,79$), atipičnim 24,15 ($X = 24,15$) i kombinacijom tipičnog i atipičnog 27,44 ($X = 27,44$). Halucinacije pokazuju bolji odgovor na tipične antipsihotike, dok je redukcija sumanutosti približno ista za obe grupe lekova.

Zaključak. Uspesšan tretman inicijalne psihotične epizode, posebno u populaciji adolescenata, je krucijalan za minimiziranje posledica po lično, socijalno i društveno funkcionisanje. U odnosu na tok bolesti, dužinu lečenja i neželjene efekte, atipični antipsihotici imaju prednost nad prvom generacijom lekova, što je i pokazano rezultatima studije.

Ključne reči: adolescenti, prva psihotična epizoda, atipični antipsihotik, tipični antipsihotik

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