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RETROSPECTIVE ANALYSIS OF ANTIPSYCHOTIC PRESCRIPTION MODELS IN CORRELATION WITH SYMPTOMS OF RESIDUAL SCHIZOPHRENIA. PART 1.

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Abstract

Relevance. The therapeutic models of antipsychotic prescription in residual schizophrenia in highly dependent on various context factors, major – relevant treatment guidelines, local drug legal and registration status, local availability etc. and minor – psychiatrist personal experience, patients individual response and comorbid pathology profile etc. therefore it's almost impossible to track down links between specific treatment model, possible NIDS manifestations or protective antipsychotic effects on negative symptoms in real clinical environment. Nevertheless finding the correlations between specific antipsychotic prescriptions and residual schizophrenia symptoms could highlight possible influence of some antipsychotics on specific symptoms in long term perspective.

Aim – to evaluate correlations between antipsychotic prescription models and negative symptoms profile in patients with residual schizophrenia.

Materials and methods. A study was performed on 60 case histories of patients of Zaporozhye Regional Clinical Psychiatric Hospital who were treated as inpatients with diagnosis of recurrent schizophrenia (ICD-10:F20.5) in time period from 2010 to 2020.

Results. In the first section of a study we gathered clinical data on intensity of main positive and negative recurrent schizophrenia symptoms using as a clinical tools PSS and NSS subscales of PANSS. On the second section our study reveled pool of most common prescribed antipsychotics which are: chlorpromazine, haloperidol, trifluoperazine, clozapine, levomepromazine, chlorprothixene, quetiapine, risperidone, thioridazine, fluphenazine, amisulpride, zuclopenthixol and their various combinations. The third study section was dedicated to analysis of correlations between particular PSS and NSS categories and antipsychotic course experience.

Conclusions. Study have found frequency and correlations of most common antipsychotic prescribed in inpatients with residual schizophrenia in time period between 2010 and 2020. The most frequently chlorpromazine, haloperidol, trifluoperazine, clozapine, chlorprothixene, risperidone and zuclopenthixol and its combinations were prescribed. The concept of "antipsychotic course experience was introduced. Chlorpromazine and haloperidol or risperidone and haloperidol are frequently prescribed as combination, while clozapine and chlorprothixene, chlorpromazine and chlorprothixene, haloperidol and trifluoperazine, chlorpromazine and trifluoperazine have low probability of combined prescription. Positive and negative symptoms of residual schizophrenia correlations with specific antipsychotic course experience were established.

Key words: **residual schizophrenia; negative symptoms; therapeutic models; antipsychotics; antipsychotic course experience.**

Relevance. Antipsychotic therapy became the most perspective option for positive symptoms management in schizophrenia, since their introduction in wide clinical practice in 1952. The history of antipsychotic therapy clinical application produced discussions among specialists and in public space, which resulted in gradual minimization of biological and physiotherapeutic interventions in psychiatry and soon after – to complete denial of their application in favor to pure pharmacotherapy [1, 7].

Conventionally solving the problem of positive schizophrenia symptoms in structure of psychotic exacerbations, antipsychotics failed to introduce any therapeutic impact on negative symptoms, which actually defines the great aim of modern psychopharmacological studies. Furthermore, among modern studies, apart of obvious long-term negative

consequences of antipsychotic therapy as permanent psychomotor violations, there are massive signals on possible antipsychotics amplifying impact on negative symptoms of schizophrenia which could be conceptualized in “Neuroleptic-induced deficit syndrome” (NIDS) presented in permanent loss of affective and motivational personality components, what consonant with traditional understanding of core schizophrenia pathogenesis [2, 6, 7].

The concept of neuroleptic-induced deficit syndrome seems to have large system of theoretical evidences and fits basic rules of pharmacodynamics, but positioned in professional community as highly controversial, what creates a gap in understanding of very nature of conditions sequence between progredient and residual schizophrenia [3, 4, 6, 7].

The therapeutic models of antipsychotic prescription in residual schizophrenia in highly dependent on various context factors, major – relevant treatment guidelines, local drug legal and registration status, local availability etc. and minor – psychiatrist personal experience, patients individual response and comorbid pathology profile etc. therefore it’s almost impossible to track down links between specific treatment model, possible NIDS manifestations or protective antipsychotic effects on negative symptoms in real clinical environment. Nevertheless finding the correlations between specific antipsychotic prescriptions and residual schizophrenia symptoms could highlight possible influence of some antipsychotics on specific symptoms in long term perspective.

Aim – to evaluate correlations between antipsychotic prescription models and negative symptoms profile in patients with residual schizophrenia.

Materials and methods. A study was performed on 60 case histories of patients of Zaporozhye Regional Clinical Psychiatric Hospital who were treated as inpatients with diagnosis of recurrent schizophrenia (ICD-10:F20.5) in time period from 2010 to 2020. Gender distribution is 43 (71,7%) male and 17 (28,4%) female patients. Mean study-relevant age is 55,0±13,1 years, mean disease experience is 31,2±13,1 years, mean clinical manifestation age is 24,1±8,9 years.

Main methods of a study are clinical data evaluation using criteria and diagnostic categories of “Positive and negative syndrome scale” and statistical analysis.

Study has retrospective design and performed in 3 sections:

1) analysis of intensity levels of schizophrenia recurrent manifestations among study contingent to generate symptom profile;

2) analysis of typical antipsychotic prescription models among study contingent to evaluate the variety of possible impact of antipsychotic prescriptions on schizophrenia recurrent manifestations;

3) analysis of correlations between antipsychotic prescription models and recurrent symptom profile.

Results. In the first section of a study we gathered clinical data on intensity of main positive and negative recurrent schizophrenia symptoms using as a clinical tools PSS and NSS subscales of PANSS (tab. 1 and 2).

Table 1

PSS scores

Tag	Symptom	M	m
P1	Delusions	2,1	0,5
P2	Conceptual disorganization	4,3	0,3
P3	Hallucinations	1,9	0,5
P4	Excitement	2,4	0,4
P5	Grandiosity	1,3	0,2
P6	Suspiciousness/persecution	2,1	0,4
P7	Hostility	2,1	0,3

It was found that positive symptoms generally not pronounced (have average intensity of “week”) what is typical for residual schizophrenia with one exception of conceptual disorganization [of thinking] what is conventionally recognized as component of cognitive symptoms which are “false positive” (result of function loss).

Table 2

NSS scores

Tag	Symptom	M	m
N1	Blunted affect	4,3	0,2
N2	Emotional withdrawal	3,9	0,4
N3	Poor rapport	3,9	0,3
N4	Passive/apathetic social withdrawal	3,6	0,3
N5	Difficulty in abstract thinking	3,5	0,3
N6	Lack of spontaneity and flow of conversation	3,0	0,3
N7	Stereotyped thinking	2,3	0,4

It was found that negative symptoms are evenly dominant in contingent (being on “moderate” or “pronounced” level).

For pharmacotherapy data systematization the concept of “*Antipsychotic course experience*” (ACE) have been introduced. ACE represents systematic prescription of specific antipsychotic (or specific combination of several antipsychotics) during single inpatient treatment cycle (in average from 3 to 6 weeks) which resulted in positive clinical effect and become acceptable stereotype of further treatment.

On the second section our study reveled pool of most common prescribed antipsychotics which are: chlorpromazine, haloperidol, trifluoperazine, clozapine, levomepromazine, chlorprothixene, quetiapine, risperidone, thioridazine, fluphenazine, amisulpride, zuclopenthixol and their various combinations.

For current analysis enough clinical data was gathered for chlorpromazine, haloperidol, trifluoperazine, clozapine, chlorprothixene, risperidone and zuclopenthixol (tab. 4).

Table 4

Most common antipsychotic prescription rates

ACE (substance)	Abb.	n	%
Chlorpromazine	CHZ	29	48,3
Haloperidol	HPD	40	66,7
Trifluoperazine	TFP	31	51,7
Clozapine	CZP	36	60,0
Chlorprothixene	CPX	44	73,3
Risperidone	RPD	31	51,7
Zuclopenthixol	ZPX	25	41,7

Analysis of ACE correlations (tab. 5) used to found general local rules of combined antipsychotic prescription among chosen drugs.

Table 5

Antipsychotic prescription correlations

ACE	CPZ	HPD	TFP	CZP	CPX	RPD
Chlorpromazine (CPZ)	1					
Haloperidol (HPD)	0,42	1				
Trifluoperazine (TFP)	-0,01	-0,29	1			
Clozapine (CZP)	0,15	0,12	0,02	1		
Chlorprothixene (CPX)	-0,29	-0,08	0,03	-0,49	1	
Risperidone (RPD)	0,05	0,25	-0,10	0,10	-0,05	1
Zuclopenthixol (ZPX)	0,10	-0,11	0,15	0,08	0,07	-0,05

It was found that moderate positive correlations are present for CPZ and HPD prescription rates (r=0,42) what reflects traditional incisive treatment scheme for hallucinatory-paranoid psychotic condition where CPZ used for agitation management and HPD for hallucinations reduction. Weak positive correlation found between RPD and HPD prescription rates (r=0,25) what reflects trend of RPD usage for replacement of CPZ by atypical antipsychotic in “CPZ+HPD” treatment scheme which was popular before RPD was introduced in wide clinical practice.

Noticeable negative correlations found for CZP and CPX (r = -0,49) and CPZ and CPX (r = -0,25) what in both cases could be explained by dangerous summation of α_1 antagonism effects: hypotension; dizziness, nausea, vomiting, diarrhea, etc.; CPZ and TFP (r = -0,29) and TFP and HPD (r = -0,29) negative correlations could be explained by dangerous summation of sedative effects.

On the third study section it was dedicated on analyze correlations between particular PSS and NSS categories and ACE.

When PSS correlations with ACE (tab. 6) represent aims for specific antipsychotic prescription because positive symptoms are actually becoming a reason to prescribe pharmacological treatment, while NSS correlations with ACE (tab. 7) have complicated origin hypothetically showing cumulative impact (both positive and negative) of long term antipsychotic consumption, natural course of a disease and various comorbid violations – neurological and metabolical which are crucial in contingent of patients with average disease experience more than 30 years.

Table 6

PSS and ACE correlations

PSS	CPZ	HPD	TFP	CZP	CPX	RPD	ZPX
Delusions	0,04	0,10	-0,02	-0,13	-0,05	0,32	0,01
Conceptual disorganization	0,10	0,09	-0,02	0,22	-0,18	-0,04	0,08
Hallucinations	0,16	0,16	0,18	-0,19	0,11	-0,07	0,02
Excitement	0,23	0,07	-0,06	0,07	-0,05	0,11	0,30
Grandiosity	0,02	0,11	-0,03	0,03	-0,01	0,32	-0,20
Suspiciousness/persecution	0,13	-0,03	-0,01	-0,21	-0,05	-0,02	0,22
Hostility	0,11	-0,23	0,04	-0,07	0,04	-0,01	0,35

It was found patients with CPZ ACE have more intensive manifestations of excitement, hallucinations, suspiciousness/persecution, hostility and conceptual disorganization with most relevant aim of excitement. Patients with HPD ACE have more intensive manifestations of hallucinations, delusions and grandiosity with most relevant aim of hallucinations, while hostility have higher intensity. Patients with TFP ACE have more intensive manifestations of hallucinations. Patients with CZP ACE have more intensive manifestations conceptual disorganization corrections and have low probability of prescription in patients with delusions, hallucinations and suspiciousness/persecution. Patients with CPX ACE have more intensive manifestations hallucinations, while higher intensity of conceptual disorganization. Patients with CPX ACE have more intensive manifestations of delusions, grandiosity and excitement. Patients with CPX ACE have more intensive

manifestations of exictment, hostility and suspiciousness/persecution, while have higher intensity of grandiosity.

Table 6

NSS and ACE correlations

NSS	CPZ	HPD	TFP	CZP	CPX	RPD	ZPX
Blunted affect	0,07	0,04	0,11	0,12	-0,12	0,03	-0,01
Emotional withdrawal	0,06	0,03	0,03	0,07	-0,01	-0,10	-0,03
Poor rapport	-0,07	0,11	-0,08	0,10	-0,05	0,04	0,02
Passive social withdrawal	-0,12	0,04	0,01	0,17	-0,17	-0,01	-0,20
Difficulty in abstract thinking	-0,21	-0,02	0,04	-0,10	-0,02	-0,10	-0,14
Lack of conversation flow	-0,09	0,02	-0,02	-0,05	-0,11	-0,12	-0,02
Stereotyped thinking	0,01	-0,04	0,08	-0,01	0,09	-0,10	0,08

It was found that patients who have CPZ ACE have lower intensity of difficulty in abstract thinking and passive/apathetic social withdrawal. Patients with HPD ACE have higher intensity of poor rapport. Patients with TFP ACE have higher intensity of blunted affect, poor rapport and passive/apathetic social withdrawal. Patients with CZP ACE have higher intensity of passive social withdrawal, blunted affect, poor rapport, while have lover intensity of difficulty in abstract thinking. Patients with CPX ACE have lower intensity of blunted affect, passive/apathetic social withdrawal and lack of conversation flow. Patients with RPD ACE have lower intensity of emotional withdrawal, difficulty in abstract thinking, lack of conversation flow and stereotyped thinking. Patients with ZPX ACE have lower intensity of passive social withdrawal and difficulty in abstract thinking.

Conclusions. Study have found frequency and correlations of most common antipsychotic prescribed in inpatients with residual schizophrenia in time period between 2010 and 2020. The most frequently chlorpromazine, haloperidol, trifluoperazine, clozapine, chlorprothixene, risperidone and zuclopenthixol and its combinations were prescribed. The concept of “antipsychotic course experience was introduced. Chlorpromazine and haloperidol or risperidone and haloperidol are frequently prescribed as combination, while clozapine and chlorprothixene, chlorpromazine and chlorprothixene, haloperidol and trifluoperazine, chlorpromazine and trifluoperazine have low probability of combined prescription. Positive and negative symptoms of residual schizophrenia correlations with specific antipsychotic course experience were established.

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