Paranoid Schizophrenia - Clinical and Therapeutic Correlations

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Schizophrenia is a serious psychosis that appears in young adult, usually chronic, characterised by signs of mental dissociation and incoherent delirious activity that determines the breaking of the contact with the exterior world. The primary objective of this study is to compare the efficiency of Haloperidol and Risperidone. The study consisted in enrolling, evaluating and the clinical and therapeutic following of 125 patients hospitalised at the Clinic Hospital of Psychiatry..., in Galai, between 2000 and 2015. They were divided into 4 equal sub-lots according to the medication received. The modern treatment consists in the administration of atypical neuroleptics, such as: Risperidone, Olanzapine, Clozapine, etc. These substances proved their efficiency in the negative and affective symptoms together with the increase of therapeutic compliance due to the absent secondary effects. The precocious diagnostic, the modern anti-psychotic treatment from its first manifestations and maintained in order to avoid relapse, improve greatly the prognostic in the long run.

Keywords: schizophrenia, genetic factor, dilemma of the modern anti-psychotic psychiatry

The concept of *schizophrenia* has been used since 1911 by E. Bleur (*schizei = divide* and *fren=spirit)* after he created the concept in 1908. In 1911 he published in "Handbuch der Psychiatrie by Aschaffenburg, the important paper: Dementia praecox oder die Gruppe der Schyophrenie saying that: I call the precocious dementia schizophrenia because, as I hope to prove, the division of various psychological functions is one of its most important characteristics.

As for the polygenic model, it is supported by Gottesman and Shields (1982). He agrees to the high risk in the families with more than one person with schizophrenia and with high risk among the relatives of 1st degree in the more severely ill, compared to the ill less affected.

Another important symptom is the poor one, comprising the alteration of the logical value, the disorganization of the affective life and the productive symptom represented by the delirious experiences. Thus, the patient faces troubles of perception, visual illusions, troubles of thinking, delirium, troubles of language and affection, will and psychomotricity and, not least, troubles in the consciousness itself.

Psycho-Pharmacologic Treatment of Schizophrenia in Clinical and Ambulatory Assistance

(Clinic study - Risperidone versus Haloperidol in the treatment of the patients with schizophrenia)

The *primary* objective of this study is to put in balance the efficiency of Haloperidol and Risperidone.

Work hypothesis **–** We emitted the idea that important differences may exist in the average efficiency of the Risperidone and Haloperidol in the treatment of î schizophrenia, represented by the variations of efficiency and tolerance, the main criterion of measurement being the necessity to stop the treatment because of some reason.

Experimental part

Material and method

The study was based on enrolling, evaluating and the clinical and therapeutic following of 125 patients hospitalised at the Clinic Hospital of Psychiatry..., in Galai, between 2000 and 2015.

The patients were divided into 4 equal sub-lots according to the medication they received:

-LOT 1-Haloperidol

-LOT 3-Risperidone

The criteria of *inclusion* for this study were: - males or females aged 18-67; - diagnostic of schizophrenia (any sub-type) according to ICD-10 for at least 1 year; - who have PANSS score >70;-CGI-S >=4; - EKG route (12 derivations) – normal morphologic aspect; - who signed the information agreement after having been explained the purpose and procedures requested by the protocol; - capacity of understanding.

The criteria of *exclusion* were: - pregnant or breastfeeding woman; - if they had the diagnostic of syndrome of addiction to alcohol or other substances; - history with allergy to Haloperidol, Risperidone, Olanzapine, solanum or their excipients; - history with positive results in the serologic tests for the virus of hepatitis B, C and HIV; - suicidal ideation or violent tendencies during the period of medication titration; - hospitalised against their will; - history with neuroleptic malign syndrome; - history with glaucoma with closed angle; - any unbalanced somatic affection;- any untreated cardiovascular, respiratory, neurologic, renal, hepatic, endocrinology, hematologic or immunologic problems; etc.

Treatment: *concomitant medication* **–** pharmacologic treatment used in treating some possible comorbidities can influence the clinic image or can interact with the study medication, modifying its pharmaco-cinetics. Thus, it can be noted any treatment, episodically associated or

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Table 1
CONCOMITANT MEDICATION

Class of medicine	Episodic administration	Chronic administration
Benzodiazepine	yes	yes
Blocking H2	yes	yes
Inhibitors ACE	yes	yes
Antiemetics	yes	no
Antihistaminic	yes	no
Steroids	yes	no
Anti-coughing	yes	no
Thyroid hormones	no	yes
Oral contraceptive	no	yes
Blocking canals of Ca	no	yes
Beta-blocking	no	yes
Class of medicine	**Episodic administration**	**Chronic administration**
Amantadine	no	no
Anticholinergics	no	no
Antiarrhythmics	no	no
Anticonvulsants	no	no
Anti-depressive	yes	no
Anti-psychotic	yes	no
Anticoagulant	no	no
Rezerpine	no	no
Tramadol	no	no
Clonidine	no	no
Tryptophan	no	no
Zolpidem	no	no
Psychostimulants	no	no

administrated chronically. The groups of medicine that can be associated, as well as those that are not allowed during the study are mentioned in the following table. If it is imposed the administration of a substance not allowed, the patient does not continue the study.

At V1 the subjects must be divided into two categories, on taking into account the consumption of benzodiazepine: chronic consumers and occasional consumers. Chronic consumers are those individuals who have received benzodiazepine daily or almost daily in the last two months.

Chronic consumers will remain on a stable dose of benzodiazepine, but the maximal daily dose must not be more than the doses in table 10.2. During the study, it is possible to try and decrease the dose, according to the clinic table. The occasional consumers of benzodiazepine will be excluded, in case the clinic table requires chronic administration after starting the study.

Table 2
EQUIVALENT DOSES OF BENZODIAZEPINE

Benzodiazepine	Equivalent dose (mg/day)
Lorazepam	5
Temazepam	30
Diazepam	20
Oxazepam	30
Flunitrazepam	5
Lormetazepam	3
Chlordiazepoxid	40
Loprazolam	2

Benzodiazepine should not be given less than 8 hours before any psychiatric evaluation!

Period of study I: screening

Visit 1: **(**duration 2-5 days)

The results of the screening tests must be obtained, but also interpreted before V2. It is necessary to observe all the criteria of enrolling at V2, so that the subject could continue their participation in this study.

Period of study II: acute treatment

It is extended on a period of 8 weeks, when the individuals will be evaluated both weekly and every two weeks. During this stage, they receive haloperidol 5 - 10 mg/day, RISPERDAL 2 – 6 mg/day. The efficient daily dose will be set by titration. During visit 7, the patients can leave the hospital and assisted in ambulatory regime if the PANSS score is less than 60.

Period of study III: stage of continuation (V8 – V17)

The study continues in *ambulatory regime* for another 9-10 months in the case of the patients having the PANSS score, less or equal to 60. The visits will take place once a month during this period.

In our study, it becomes important the coupling between multiple categories of events to investigate the relations of causality. Because the number of subjects is low, the samples being small, the repartition of the characteristics studied being normal, and from one visit to the other the number of patients in the sample decreases, we applied the t-Student test. The test means the threshold that separated the descriptive at the beginning of the analytical research.

Results and discussions

The subjects of this study were chosen among the patients hospitalized at the Clinic Hospital of Psychiatry in Galati. The period of choice started in April 2007 and ended in May 2012, when the aimed number of subjects was reached. In total, 124 patients were evaluated, but 20 of them did not meet totally the criteria of inclusion and exclusion. 104 patients were enrolled, who met the criteria of inclusion and exclusion mentioned above and passed the period of screening, but during the visit 2, 4 of them refused to continue the protocol. Repartition in the 4 groups of treatment was done at random, according to the moment of hospitalization.

a. Repartition per sex: 30(60%) females; 20 (40%) men);

b. on lots studied

b.1. Risperidone (17 females-68% and 32 males 32%)

b.2. Haloperidol (13 females-52% and 12 males -48%).

There are no important statistic differences regarding the repartition on sexes of the patients.

In the sub-lot with haloperidol, it is underlined the fact that the repartition on the two sexes of the number of patients is increased in the rural area, the masculine sex being predominant.

Even though in ICD-10 are present the following clinical forms of schizophrenia: paranoid, hebefrenic, catatonic, post-schizophrenic depression, non-differentiated, residual and simple, in the lot studied there were 52% patients with paranoid schizophrenia, 34% of them met the symptoms

Lot				Environment		Total
				U	R	R+U
Haloperidol	Sex	F	Number	5	7	12
			% of F	42.7%	57.3%	100.0%
		B	Number	4	9	13
			% of B	31.8%	68.2%	100.0%
	Total		Number	9	16	25
			% of total	36.0%	64.0%	100.0%
Risperidone	Sex	F	Number	5	3	8
			% of F	62.7%	37.3%	100.0%
		B	Number	3	14	17
			% of B	18.6%	81.4%	100.0%
	Total		Number	8	17	25
			% of total	33.0%	67.0%	100.0%

Table 3
PROVENANCE

			Type of schizophrenia			Total
			hebefrenic	catatonic	paranoid	
Sex	F	Number	4	7	9	20
		% of F	20%	35%	45%	100.0%
	B	Number	4	10	16	30
		% of B	10%	33,3%	56,6%	100.0%
Total		Number	8	17	25	50
		% of F+B	14%	34%	52%	100.0%

Table 4
TYPE OF SCHIZOPHRENIA

of catatonic type and only 14% presented the signs and symptoms specific to the hebefrenic syndrome, with a preponderance of 60% in males compared to 40% in females.

Out of the total of the lot analysed, 83% of the patients are smokers, while 17% do not smoke. These notes underline once again that the patients with schizophrenia are heavy smokers. As in the normal population, the consumption of tobacco in the patients with schizophrenia is matched with the males and with the younger generations. The smokers with schizophrenia have twice to three times more misfortune in the present and abuse or an addition also to other junk substances compared to non-smokers.

Addiction to alcohol implies the existence of a percentage of 30-60% of the patients with schizophrenia during their life according to the studies that have been published lately, while in the case of our lot we can notice a percentage of 23.4% patients that consume alcohol. An explanation for this fact could be the design of the study, which mentions the periodic contact of the patient with the doctor, often enough.

According to the data in the table below, we can notice that the minimal and maximal age was between 20 and 65 years old, with an average of 42.5, respecting thus the criteria of inclusion for the patients.

On each lot separately we record the following values (table 7).

If both parents suffer from schizophrenia, the child's risk increases to 15-50%. Children whose biological parents are healthy, but whose adoptive parents suffer from schizophrenia have a risk of getting ill of only 1% - risk identical with that of the adult population. In our study, it is noticed that 24% of the patients enrolled have hereditary-collateral antecedents, percentage near the theoretical estimations.

Even when the treatment is missing, the percentage of obesity tends to increase in the patients with schizophrenia. This fact can be due to low self-care, inappropriate nutrition, but also a sedentary life. The atypical antipsychotics try to induce more growth in weight than the normal neuroleptics, as it can be noticed also in the case of the results in our lot. In the lots that received risperidone, it is recorded a growth in weight of 2.2 kg respectively of the average weight between the beginning of the protocol and its end. The phenomenon can be prevented by warning the patients and by instructing, possibly – with a nutritionist's support, on a diet and physical exercises.

			Alcohol		Total
			0	1	0
Sex	F	Numbed	20	10	30
		% of F	66.6%	33.3%	100.0%
	B	Numbed	26	4	30
		% of B	85.7%	14.3%	100.0%
Total		Numbed	46	14	60
		% of F+B	76.6%	23.4%	100.0%

Table 5
CONSUMPTION OF ALCOHOL

	N	Minimal	Maximal	Average	Standard deviation
Age	100	20	65	42.5	12.452

Table 6
DESCRIPTIVE STATISTIC

Lot	Average	No. Patients	DS
Haloperidol	45.12	25	11.980
Risperidone	37.13	25	9.472
Total	41.44	100	11.452

Table 7

			Lot		Total
			Haloperidol	Risperidone	
AHC	0	Number	23	17	40
		% of AHC	31.2%	24.7%	100.0%
	1	Number	4	6	10
		% of AHC	14.0%	32.4%	100.0%
Total		Number	25	25	50
		% of AHC	25.0%	25.0%	50%

Table 8
HEREDITARY-COLLATERAL ANTECEDENTS

	G1 (initial)	DS	G2 (1 month)	DS	G3 (6 months)	DS	G4 (1 year)	DS
Risperidone	71.1	7.5	71.2	6.7	7123	5.4	71.7	8.7
Haloperidol	69.1	6.7	68.1	5.5	73.3	6.5	71.1	7.8

Table 9
EVOLUTION OF WEIGHT UNDER TREATMENT

Glycaemia

Another parameter that is investigated during the study was measuring the patients' glycaemia. It is known that FDA has recently requested (2003) that six of the most used atypical antipsychotics (olanzapine, risperidone, clozapine, aripiprazole, quetiapine, ziprasidone) should be marked with notification regarding the high risk of hyperglycaemia and diabetes.

The values of glycaemia are slightly increased for the lots of patients that received haloperidol and risperidone. It has been known for a long time that patients with schizophrenia are exposed to a much higher risk of diabetes (5-6 times more) than the general population.

Correlations of the medication with the need to be associated to adjuvant medication (Sedative, Hypnotic, Anxiolytic, Normotimizant)

If we analyse separately the association of the medication on each lot, we obtain (table 10).

By a process of crossed analysis (cross-tab), we can notice the relation between the type of associated medication and the number of patients that received it (tables 11, 12).The symptomatic treatment was adapted to the specific of each case, with hypno-inducing medication. It involved the pharmacological properties of the associations of substances and the patient's general clinical aspect and their preferences; this fact results from the following graphic (table 13).

Lot	Sedative	Hypnotic	Anxiolytic	Normotimizant
Haloperidol	17	15	17	18
Risperidone	15	14	14	15
Total	32	29	31	33

Table 10

			Lot		Total
			Haloperidol	Risperidone	
Sedative	0	number	8	10	43
		% of Sedative	16.2%	25.6%	100.0%
	1	number	17	15	57
		% of Sedative	31.6%	24.5%	100.0%
Total		number	25	25	100
		% of Sedative	25.0%	25.0%	100.0%

Table 11

			Lot		Total
			Haloperidol	Risperidone	
Hypnotic	0	number	12	11	23
		% of Hypnotic	29.7%	27.0%	100.0%
	1	Number	13	14	27
		% of Hypnotic	22.2%	23.8%	100.0%
Total		number	25	25	50
		% of Hypnotic	25.0%	25.0%	100.0%

Table 12

			Lot		Total
			Haloperidol	Risperidone	
Anxiolytic	0	Number	6	13	19
		% of Anxiolytic	18.9%	32.4%	100.0%
	1	Number	17	14	31
		% of Anxiolytic	28.7%	20.6%	100.0%
Total		Number	25	25	50
		% of Anxiolytic	25.0%	25.0%	100.0%

Table 13

			Lot		Total
			Haloperidol	Risperidone	
Normo timizant	0	Number	8	9	17
		% of Normotimizant	18.4%	26.3%	100.0%
	1	Number	17	16	33
		% of Normotimizant	29.0%	24.2%	100.0%
Total		Number	25	25	50
		% of Normotimizant	25.0%	25.0%	100.0%

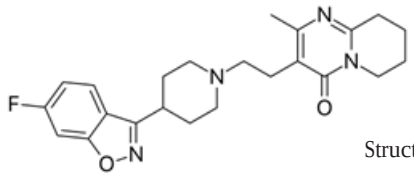
Table 14

Identical to the hypno-inducing treatment, the anxiolytic symptomatic treatment was adapted on the specificity of the case. We notice the significant association (in percentage of 28.7%) for the lot of patients who followed the treatment with Haloperidol, indicating that at least a part of the anxious symptoms could be imposed on the profile of side effects of the classical antipsychotic (table 14).

The symptomatic medication with Orthotics products was suggested for the component of aggressiveness (including the intropunitive tendencies), the decrease of affective oscillations, even though not so obvious in the context of the negative symptoms affect though the life quality, as well as for the counteraction of the secondary effects of the antipsychotics. It explains the increased coupling of the ortotimising medication with the classical antipsychotic (Haloperidol).

Risperidone

Chemical formula $C_{23}H_{27}FN_4O_2$



Structural formula

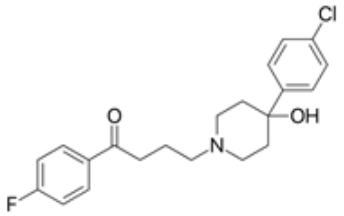
For the treatment of the acute and chronic schizophrenia, it is indicated the Risperidone, where the positive symptoms (hostility, suspicion, hallucinations, delirium, troubles of thinking) and/or negative symptoms (social estrangement and emotional withdrawal, reduced vocabulary, affective flattening) are predominant.

Risperidone reduces, at the same time, the affective symptoms (depressions, guilt, anxiety) combined with schizophrenia. It is thus noticed in the graphic above the evolution of the average scores for the scale PANSS, which was at the beginning of the research around the value 81 continuing until visit 8, where it is recorded an average value of 72. Between V9 and V14 the positive symptoms and the negative symptoms evaluated by the scale PANSS decrease in intensity, reaching thus an average value of 61, value that remains approximately until the end of the protocol.

Between V10 and V16, the average scores of the global clinical impression continue to decrease until 3, signifying a favourable evolution of the patients who followed the medication with Risperidone.

Because of the alpha-blocking action of Risperidone, orthostatic hypotension can appear, especially during the titration of the dose. Based on that, it was carefully prescribed to patients with cardiovascular diseases (heart failure, dehydration, hypovolemia or cerebrovascular diseases, driving troubles, myocardial infarction), and the dose was titrated gradually.

Because Risperidone is a medicament with antagonistic properties on the dopaminergic receptors, it was followed the induction of late dyskinesia marked by involuntary movements, mainly of the tongue and/or face, as it can be noticed in the graphics below, on knowing that the appearance of the extrapyramidal symptoms is a risk factor for the appearance of the dischineziei late dyskinesia.



Structural formula

Haloperidol

Chemical formula $C_{21}H_{23}ClFNO_2$

It represents a neuroleptic from the category of the butirophene derivatives, which inhibit the fixation and accumulation of catecholamines in the central nervous system. With a wide range of antipsychotic activity and exercising a sedating effect in the states of marked agitation and aggressiveness of the patients, it reduces the symptoms of restlessness, anxiety and hostility. The evolution of the scores PANSS for that lot starts from an average of 82 at the beginning of the research, but the rate of the decrease is lower than in the case of the other antipsychotics followed.

The extrapyramidal symptoms that appear during the chronic treatment with Haloperidol are represented by: trembling, muscular tension, other Parkinsonism symptoms that can decrease in intensity or can disappear spontaneously, until the reduction of the doses or the temporary interruption of the medication. At times, in order to have control on these symptoms, it was useful the use of anti-Parkinsonism medicine during the study, as it can be noticed in the graphics below. The anti-Parkinsonism treatment is not administered routinely, but only when it is necessary, because it reduces the efficiency of Haloperidol.

As the other antipsychotic medicine, Haloperidol can determine the appearance of late dyskinesia, especially in the chronic treatment, in the old patients – especially females – treated with increased doses. The involuntary movements of the tongue, face, mouth and cheeks are separate, as it can be seen in the graphic presenting the AIMS scale. A premature sign of late dyskinesia is the fine movement of the tongue. In Haloperidol AIMS total overlaps on AIMS facial.

By using this scale, apart from the general quantification of the level of life quality and the satisfaction in the ill with schizophrenia, we also succeeded in finding the fields of global interest where there is a deficit of functioning, in view of interfering in the subsequent psychosocial assistance.

The main objective of the research consisted in evaluating and comparing the potential the two antipsychotics. The main instrument used in the comparative evaluation of the efficiency of these two antipsychotics followed was the score PANSS. We considered as useful also the application of the scale of general clinic impression because, even if there is an agreement between the score PANSS and the score CGI, the overlapping is not complete. In the case of the research of a high number of individuals, there is an important index of overlapping, fact that is not investigated if we examine lots that are not numerous. We made comparisons between Haloperidol and an antipsychotic of the second generation, but also for each antipsychotic between the score from V1 and the score at the end of the treatment. It can be noticed during our research a positive evolution of the CGI score, while in the PANSS score some minor modifications are produced, attesting for the persistence of the schizophrenic phenomenology.

The general clinical opinion was influenced in some individuals by the improvement of some symptoms such as insomnia, agitation or anxiety; even though they can be found in the PANSS evaluation, they do not influence a lot the total score. Moreover, the score CGI marks the global clinic aspect in the moment of the evaluation, and that's why it is recommended to mention it in the source documents after the exam is over for that visit. The number of points is between 1 and 7, and it is often difficult to classify the patient between two scores, the probability of error being increased. The periodic evaluation of the symptoms of schizophrenia by means of the PANSS scale offers the possibility to identify the therapeutic answer. We considered as therapeutic answer in individuals who presented at least the same value of the score PANSS from base-line or its slight decrease.

The variables of increased efficiency include the points according to PANSS, but also CGI. The point of PANSS type could be comprised between 70 and 120 points, the highest indicating a tougher psychopathology, from 1 to 7, while the high numbers of points indicated a higher severity and intensity of the disease.

Side effects - There are frequently mentioned in the literature the side effects of the antipsychotics, but their administration is a disputed topic. And that is due to the fact that it is not enough to simply register the side effects. Their evaluation needs a classification by scales accepted by most researchers. That's why we used in our study the scales AIMS, SAS and BARS for side effects, variants destined to the research in the degree of tolerance to antipsychotics. By means of these scales AIMS, SAS and BARS we evaluated the side effects of the antipsychotics studied, by using a semi-structured interview, following point by point each item and writing down the possible clinical observations of the medical staff or the data in the observation files. The evaluation of the side effects during each visit allowed marking the tolerance to the two antipsychotics studied on short term (V2 – V8), but also on long term (V8 – V17).

These side effects depend directly on the dose administered. The side effects noticed in the antipsychotics were anticholinergics (somnolence, hazy sight, dry mouth, constipation, urinary retention), histaminic (somnolence, tiredness, weight gain) or antiadrenergic (postural hypotension and dizziness).

Since Risperidone presents a potential to induce the extrapyramidal symptoms less compared to the classical neuroleptics, it has a lower risk of inducing late dyskinesia compared to the Haloperidol in the case of our research. In three cases, there were the following extrapyramidal symptoms: akathisia, acute dystonia, tremor, bradykinesia, rigidity, hypersalivation. They were in most cases light and reversible after diminishing the dose and/or administrating the Antiparkinsonian medication. Sometimes, after administrating Risperidone, it was noticed the orthostatic hypotension in two patients. The most common symptoms appeared during the study in the patients who received Risperidone were: insomnia, agitation, headache, anxiety.

The concept of *life quality* is newly approached in the class of health and, at the same time, in the class of mental health.

PANSS scale, the general clinic impression or other instruments in the same class reduces the perspective on the ill as simple medical case. In the usual psychiatric practice, the ill are approached from the complex bio-psycho-social perspective, concept that was launched and promoted by the School of Psychiatry in Socola. In order to enlarge the vision on each case followed in evolution, we applied to the ill a scale of self-assessment. This scale allows the recording of some complete dimensions that

overlap partially on the symptoms of schizophrenia, as an advantage being the reporting of the ill of the impact of schizophrenia and medication in the social life.

The physical disabilities and tiredness are often invoked by patients. The psycho-social factors are equally important: minimal social support social minim, poor financial resources, low access to health services. Age is related in a negative way to the physical functioning, the frequency of pains, general health. In general, the results suggest an affectation of the life quality, especially for the individuals with material difficulties who suffer from schizophrenia.

In general, Risperidone registered the upper scores regarding improvement.

A special role in the therapy of the individual with schizophrenia has the nurse specialised in psychiatric nursing. In the case of the patients in ambulatory, the compliance was measured by questioning regarding the doses of antipsychotic administrated daily between two visits.

After the patient leaves the hospital or after the visit in the psychiatric cabinet in the ambulatory, it is good to write down the treatment on a piece of paper where to mention exactly the doses and the moments of the day when they must be given. Whenever it is possible to discuss with the family, they will be informed with the development of the treatment, because family can be a factor of strengthening the compliance. Other elements that could increase the compliance are lack of addiction, administration of antipsychotic in unique dose, prefiguring of the risks and side effects. It is useful to strengthen the idea that the antipsychotic treatment is given in the long run, even if the symptoms have disappeared, so it is not a treatment given only *when required*.

Conclusions

The modern treatment with atypical antipsychotics is superior from the point of view of the efficiency and return compared to the classical antipsychotics because of the following reasons: - the atypical antipsychotics act on the affective symptoms (depression, anxiety), which is may be conducive to diminishing the rate of suicide associated often with schizophrenia; - the atypical antipsychotics act on the symptoms of cognitive dysfunction; - the patients' compliance is very good, most of them maintaining the treatment; - in the case of the atypical antipsychotics, the side effects are minimal or lack;- the atypical antipsychotics act on the positive but also negative symptoms.

The results of the treatment are noticed in a short time (1-3 months) and in a high percentage of patients (for example Rispolept is very rapid in the control of the acute stage, the same decrease of the positive symptoms being determined by Rispolept-4 mg/day in 14 days, compared to 4 weeks that are used for Haloperidol 20 mg/day; - the atypical antipsychotics are the major opportunity to diminish the costs of health care and, at the same time, they improve the life quality of those who suffer, offering them a chance to be reintegrated in the society.

The precocious diagnostic, the modern antipsychotic treatment from the first manifestations and maintained in order to avoid relapse improve greatly the prognostic in the long run.

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Manuscript received: 11.01.2017