Original Paper

The Effect of Switching to Long-Acting Injection (LAI) Antipsychotic Therapy on Patients with Schizophrenia

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ABSTRACT: Material and method: We analyzed 362 patients with schizophrenia admitted during 2016 in an acute psychiatric ward and in a chronic psychiatric ward, diagnosed with paranoid or other schizophrenia, according to DSM-IV-TR, which, after remission of the symptoms of the acute episode, they benefited from antipsychotic therapy only in oral formulation. For some of these patients we instituted maintenance therapy with depot formulas. Patients were followed for up to two years. Results: Comparing the level of adherence to therapy, we found a statistically significant improvement, from 42.96% to 76.30%. Although we estimate that adherence to LAI therapy is over 90%, almost a quarter of patients have given up this type of treatment at some point due to side effects. Carrying out the comparative analysis of the number of hospitalizations per year, from the past and from the follow-up period, as well as of the scores registered at the scales used (PANSS, CGI, GAS, WHOQOL), in dynamics, we demonstrated the appearance of statistically significant changes. Conclusions: the administration of antipsychotic therapy through LAI-type depot formulas can improve the therapeutic adherence of the patient with schizophrenia, thus improving the evolution of the disease and the quality of life.

KEYWORDS: *Schizophrenia, antipsychotic therapy, LAI, PANSS, WHOQOL.*

Schizophrenia, first named by Eugen Bleurer in 1911, but described since antiquity, is a disabling disease that affects 1% of the general population, and has become a symbol of psychiatric diseases, of profound behavioral and personality disorders [1,2].

ICD characterizes schizophrenic disorders by characteristic distortions of thought and perception and inadequate and weakened affects. Both clarity of consciousness and intellectual capacity are maintained, although knowledge deficits over time are not excluded [3].

ICD-10 highlights the most important psychopathological phenomena [4,5]:

- echo and/or theft of thought;
- influence or transmission of thoughts
- deplexive perception
- delusional ideas of control, influence or passivity
- commentive or insulting auditory hallucinations,
- thought disorders
- negative symptoms

The DSM-5 diagnostic criteria for schizophrenia are as follows [6,7]:

A. Two (or more) of the following criteria, each manifesting a sufficient period of time within 1 month (or less if the treatment is effective). At least one of them must be (1), (2) or (3):

1. Delusional ideas;
2. Hallucinations;
3. Disorganized speech (eg. frequent derailment or inconsistency);
4. Intense disorganized or catatonic motor behavior.
5. Negative symptoms (eg decreased expression of emotions or abolition).

B. A significant period of time from the onset of the disorder, the level of functioning in one or more important areas such as: professional, interpersonal or self-care is well below the level reached before the onset

C. Signs of the disturbance are maintained continuously for at least 6 months. This 6-month period should include at least one month of

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symptoms (or less if the treatment is effective) that meet Criterion A.

It is accepted that the evolution of schizophrenia may continue or is episodic, with stable or progressive deficit, with complete or incomplete remission.

Antipsychotics are widely used in the management of patients with schizophrenia. After Deniker and colleagues accidentally discovered in 1953 the soothing effect of chlorpromazine on laboratory animals [8], and the hypothesis that a cataleptic effect of butyrophenone was a condition for neuroleptic efficacy led to the discovery of haloperidol [9], the first atypical antipsychotic, clozapine, was introduced in the 1970s [10].

In the years that followed, newly discovered antipsychotic molecules were placed in the same "atypical" group, although there was no consensus on the atypicality of these drugs. The apparition of this second-generation of antipsychotics has enlarged the use of this type of drugs, being more effective in treating certain symptoms and having less adverse effects than the first generation. Although better tolerated, even atypical antipsychotics are associated with metabolic, and even cardiovascular or neurological side effects, which has a negative impact on the adherence to treatment by patients.

Because of the diverse side-effects, the schizophrenia patients' adherence to therapy is rather low, with an estimated 50% of patients not adhering to treatment. Therapeutic compliance and adherence represent the degree of concordance between the indications and prohibitions requested by the doctor and their following by the patient, in practice. Estimated rates of non-adherence in schizophrenia are about 50%, [11,12] ranging from 4% (observed in a depot drug study) to 72% [13] or even 74% [14,15].

Atypical antipsychotics are D2, (D2, D3, D4), and D1, D5 dopaminergic receptor antagonists, having an affinity for 5HT2 serotonergic receptors, as well as for receptors of other systems, such as histaminergic, muscarinic and nicotinic receptors [16]. They have multiple actions, at the cortical mesencephalic, and hippocampal level, and have antipsychotic action on both positive (hallucinations, delusions, disorganized language, disorganized catatonic or blatantly disorganized behavior) and negative symptoms (affective flattening, anhedonia, allergy, abolition, social withdrawal).

Atypical antipsychotics tend to have a higher tolerance and safety profile compared to neuroleptics, with extrapyramidal symptoms having a lower frequency, as well as the rest of the side effects, which can contribute to increased adherence and therapeutic compliance. They also have the following advantages-compared to neuroleptics they rarely give extrapyramidal phenomena or late dyskinesia, thus eliminating the need to prescribe anticholinergics that tend to affect memory; they also have little expressed cataleptigenic effect. However, they have some important side effects: moderate extrapyramidal damage-low probability of inducing EPS, weight gain, which can trigger or aggravate diabetes, sexual dynamics disorders, decreased libido, hyperprolactinemia (D2 antagonist activity), nonspecific changes of ST, flattening or reversal of the T wave, orthostatic hypotension, syncope, tachycardia, sleepiness, anticholinergic symptoms (dryness of the oral mucosa, blurred vision, constipation).

Atypical antipsychotics available in Romania are: Clozapine, Olanzapine, Quetiapine, Risperidone, Paliperidone (metabolite of risperidone, with the same receptor profile), Ziprasidone, Amisulprid, Aripiprazole (considered by some authors to be third generation AP). Of them, Olanzapine, Risperidone, Paliperidone and Aripiprazole have depot formulas, together with the typical antipsychotic Fluanxol.

Together with structured or semi-structured clinical interviews, operational diagnostic scales are currently the main way of diagnosing and evaluating positive and negative symptoms (PANSS). In addition to their usefulness in monitoring the severity of symptoms (GAFS), scales are also used to monitor the therapeutic response (CGI-S and CGI-I) and assess the quality of life (WHOQOL). Regardless of the reason for applying these scales-clinical evaluation or scientific research, these scales must meet certain criteria of validity and reliability, their usefulness largely depending on the time chosen for administration [17].

Aim

The aim of the research is to determine the extent to which prolonged-release injectable formulas, which require a bi-monthly or monthly injection, can increase the quality of life of patients with schizophrenia and the impact on their relatives, as they can lead to better treatment compliance.

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Materials and Method

The initial research was performed on 248 patients hospitalized in the clinics of the Craiova Clinical Neuropsychiatric Hospital, and 114 patients from the Dumbrăveni Chronic Psychiatric Hospital, hospitalized during 2016, diagnosed mainly with paranoid schizophrenia according to DSM-IV-TR, who were previously treated with antipsychotic therapy only in oral formulation.

The study was approved by the Ethics Committee of the University of Medicine and Pharmacy of Craiova. All the subjects recruited were volunteers, and they have participated to the study following the informed consent.

We used socio-demographic variables (age, area of residence, marital status, education level etc.) and other parameters that describe the evolution of the disease (type and age of onset, hospital admissions, aggressive behavior, therapy adherence etc.), together with different clinical and diagnosis scales, in order to identify the patients' features that are linked to a negative course of the disease.

PANSS-Positive and Negative Syndrome Scale-was developed in 1987 by Stanley Kay's team, being the most widely used scale for evaluating the clinical response to antipsychotic drug therapy, with many authors considering it the "gold standard" in evaluating treatment effectiveness. PANSS is composed of 30 elements organized in three independent subscales: the scale of positive symptoms, which includes 7 items, the scale of negative symptoms -7 items and general psychopathology that allows the assessment of comorbidities and which includes 16 items, with a total score that can vary from 30 to 210 points [18]. These evaluation subscales have a good and independent distribution in relation to each other [18].

WHOQOL-World Health Organization-Quality of Life evaluates quality of life, with QOL defined as "the perception of individuals about their positions in life in the context of the culture and value systems in which they live and their goals, expectations, standards and concerns" [WHOQL Group 1995]. This scale contains 26 items that analyze four major areas: physical health, mental health, social relations and the environment. Two other items measure QOL and general well-being.

Clinical Global Impression (CGI0 scale, with its items CGI-S-symptom severity and CGI-I-improvement from initial evaluation, and Global Assessement of Functioning (GAF) scale are used in evaluating the therapeutic response and the patient's functionality before and after the administration of the therapeutic protocol [19,20].

Following the analysis of the data collected, we found that patients with a more serious condition are those in rural areas, who have not graduated high school, who are unmarried or widowed, without occupation, with more than one hospitalization per year in the last 10 years, with insidious onset, possibly at a younger age, with a history of hetero-aggressive behavior (which correlates with a deficient level of integration) and with non-therapeutic adherence.

In order to have an objective measure of the relationships between the rather qualitative components of the patient profile, which were quantified by scores used to assess patients' mental and general health and scales analyzing stress levels or patients' quality of life, we used Spearman correlation test to measure the degree of concordance between them.

As a conclusion to this analysis of the correlation coefficients, we can state that, for the evaluation of the patients' condition, the most suitable variables are the number of hospitalizations per year, the PANSS score, the GAFS score and the WHOQOL score.

As a result of establishing the profile of patients who are in a worse condition and who could benefit most from changing therapy, or who have an acceptable condition but who could have a significant improvement in their quality of life, we decided to change the traditional therapy, oral, with atypical antipsychotics and, to a lesser extent, typical antipsychotics, with atypical antipsychotics administered in depot form, as LAI-long-acting injection. For some of the initial patients, after the remission of the symptoms of the acute episode, we decided to switch to maintenance therapy with depot formulas. A limitation of the initiation of LAI therapy was also represented by the age of the patients, various studies showing that, at advanced ages, the modification of the therapy is not justified. Because of this, patients older than 55 years were excluded from depot therapy.

Following the explanation of the benefits, but also of the possible side effects, a number of 135 patients, representing 37.29% of the total, agreed, directly or through legal representatives, to change their current medication with the equivalent or the nearest AP drug, which also has a depot form.

Raw data were stored in Microsoft Excel files, then they were processed using the

XLSTAT add-on for MS Excel (Addinsoft SARL, Paris, France). Because we compared sets of paired data (initial values versus final values) of numeric variables that do not have a normal, Gaussian distribution, we were forced to use the Wilcoxon signed-rank test. Being a test that compares the distribution of values rather than the average value, the descriptive statistic results are expressed as median value and interquartile range (25%-75%).

Evaluation of the Impact of Lai Therapy on Patients

Analyzing the initial therapy of the patients in the entire study group, we found that almost 75% of them (73.20%) benefited from a pharmacological therapy consisting in the combination of an antipishotic (AP), in most cases atypical, a benzodiazepine and a thymostabilizer, and 13.26% of them had two antipsychotics in combination, 6.08% had PA and thymostabilizer, 4.7%-AP and benzodiazepines, and 2.76% were patients in the first episode without medication.

The most common drug combinations of antipsychotics were:

- quetiapine with aripiprazole
- amisulprid with aripiprazole
- aripiprazole with convulex
- clozapine with olanzapine

Mention should also be made of the frequent associations of:

- aripiprazole with benzodiazepines /thymostabilizer
- haloperidol+benzodiazepines

Table 1. Types of antipsychotics used in LAI therapy.

LAI	Aripiprazole	Paliperidone	Risperidone	Fluanxol	Olanzapine	Total
Patients	45	35	24	20	11	135
Percent	33.33%	25.93%	17.78%	14.81%	8.15%	100%

For LAI therapy, in most cases we opted for aripiprazole, due to the rarer side effects, followed, as a benefit/risk ratio, by paliperidone and risperidone. For some patients, who had a long history of typical antipsychotic therapy, fluanxol was chosen. The least commonly used depot drug was olanzapine, as its most common side effects, weight gain and sedative effect, are that they have less adherence to therapy (Table 1, Figure 1).

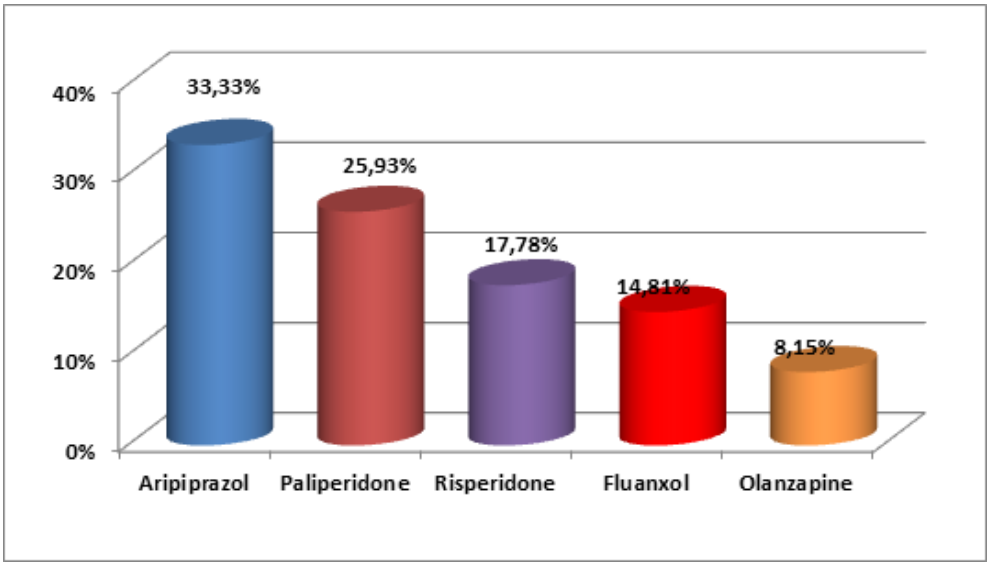

Figure 1. Types of antipsychotics used in LAI therapy.

Table 2. The distribution by sex and area of residence for the LAI group.

LAI group	Rural	Urban	Total
Female	42 (62.69%)	25 (37.31%)	67 (100.00%)
Male	31 (45.59%)	37 (54.41%)	68 (100.00%)
Total	73 (54.07%)	62 (45.93%)	135 (100.00%)

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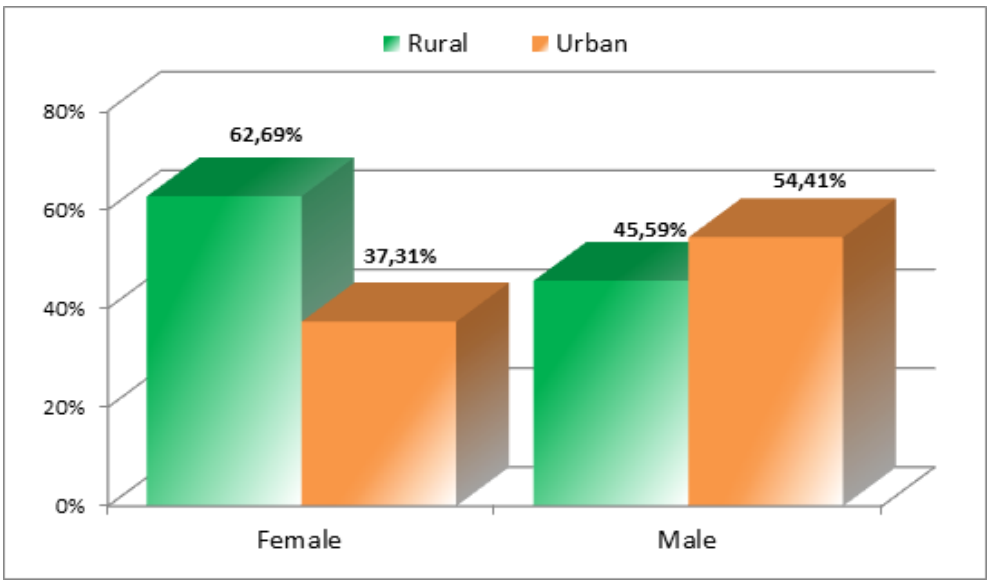

Figure 2. The distribution by sex and area of residence for the LAI group.

Analyzing the distribution by sex and area of residence for the group that received LAI therapy (Figure 2, Table 2), we found that there is a significant difference between the distribution of women and men in regard to area of residence, with p Chi square=0.046, women being in a greater percent from rural areas (62.69%), while men are closer to the distribution of the general population (54.41% of the urban area, compared to 54% of the urban area in the general population).

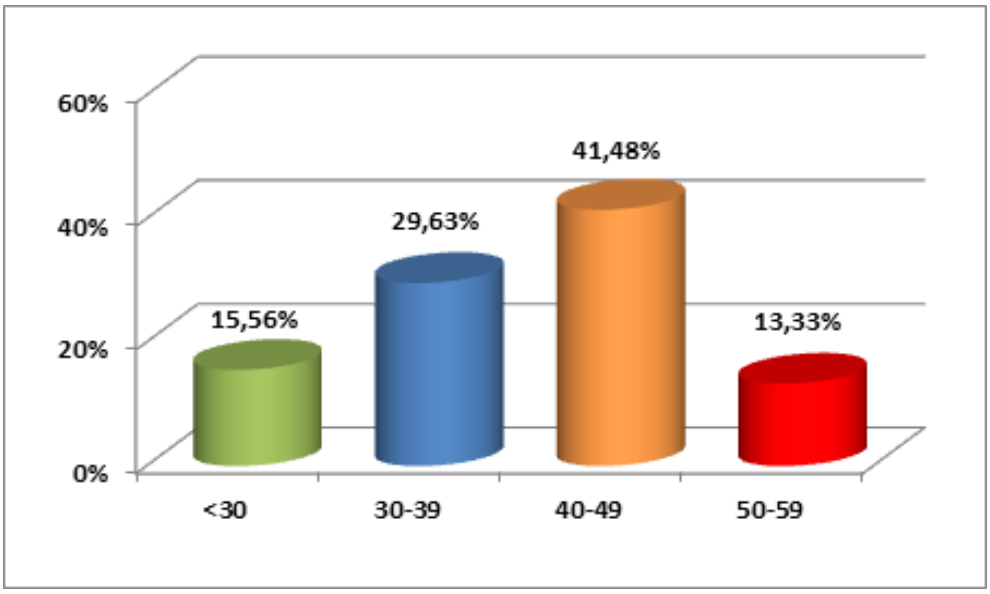

Figure 3.The age distribution for the LAI group.

As replacement therapy with LAI-type formulas is not recommended for elderly patients, there is a limitation of the age distribution, with most patients being aged 40-49 years (41.48%) and 30-39 years (29, 63%). Because we introduced LAI therapy only in people under 55 years of age, it is observed that younger people, under 30 years of age, are more common in this group (15.56%) than in the initial study group (Figure 3), and in greater number than those over 50 years of age (13.33%).

The distribution according to marital status did not differ significantly from that of the initial study group, most patients being unmarried, over 70% of them; only the frequency of married patients is higher, 22.96% compared to 17.68%, and less are divorced or widowed, an effect of not using LAI therapy in the elderly.

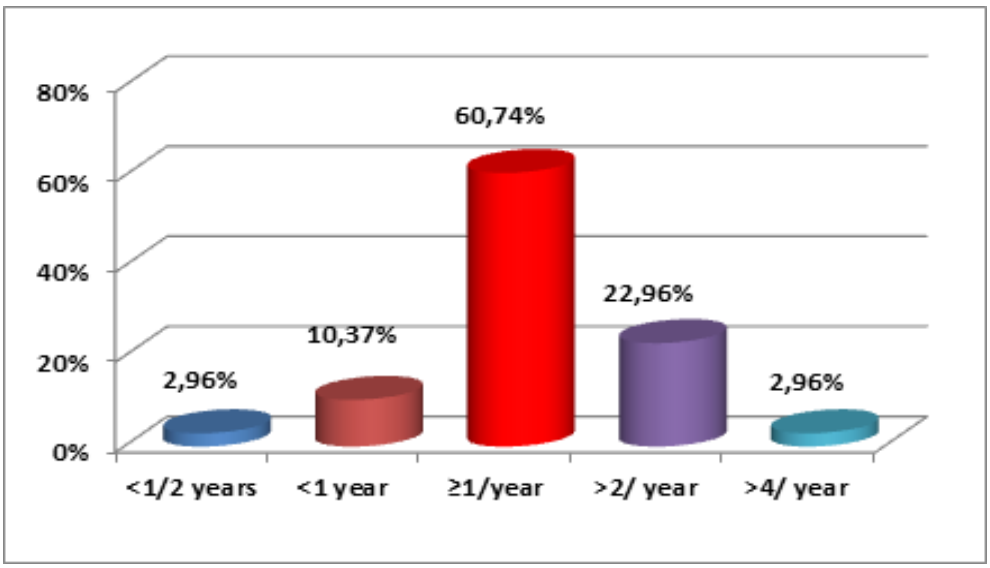

Figure 4. Distribution according to the number of previous admissions per year.

There are large differences from the initial distribution in terms of frequency of previous hospital admissions (Figure 4), because LAI therapy was instituted mainly for patients not adhering to the classic treatment, with oral forms, who had a higher number of hospitalizations due to frequent exacerbations of symptoms. Patients with less than one hospitalization in 4 years were not included in the LAI therapy group (0 of 44), and only a small proportion of those with less than one hospitalizations per two years (4 of 66) or less than one hospitalization per year (14 out of 72), because they either adhered to treatment with oral antipsychotics or had a less aggressive course of the disease. At the other end of the spectrum are patients with more than two or four hospitalizations per year, who, if they gave their consent, were almost entirely transferred to LAI-type atypical antipsychotics therapy (31 out of 35 and 4 out of 6, respectively).

Table 3. Adverse effects recorded after LAI therapy.

Therapy	Sexual dysfunctions		Weight gain		Extrapyramidal symptoms EPS		Hiper-prolactinemia		Akathisia	
Aripiprazol	13	28.89%	1	2.22%	6	13.33%	2	4.44%	7	15.56%
Paliperidone	11	31.43%	12	34.29%	6	17.14%	10	28.57%	4	11.43%
Risperidone	10	41.67%	11	45.83%	8	33.33%	7	29.17%	3	12.50%
Fluanxol	9	45.00%	2	10.00%	8	40.00%	7	35.00%	4	20.00%
Olanzapine	1	9.09%	7	63.64%	2	18.18%	2	18.18%	1	9.09%
Total	44	32.59%	33	24.44%	30	22.22%	28	20.74%	19	14.07%

Analyzing the side effects that were felt by patients treated with LAI-type therapeutic forms (Figure 5, Table 3), we found that the most common allegations were related to disorders of sexual dysfunctions (32.59%) and weight gain (24.44%), followed by extrapyramidal symptoms (22.22%), hyperprolactinemia (20.74%), the rarest effect being akathisia (14.07%). In addition, 3 patients treated with Olanzapine claimed a sedative effect of this drug.

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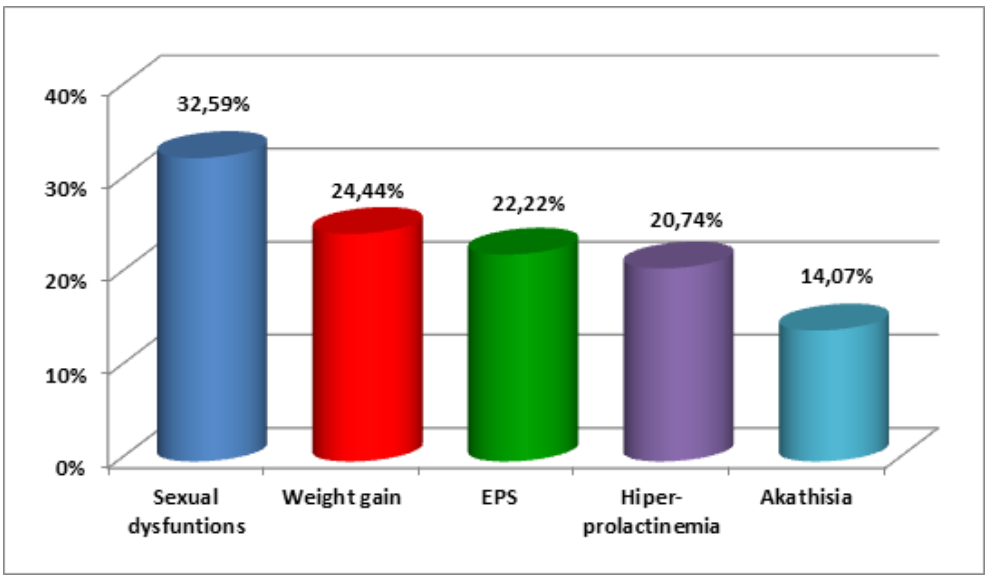

Figure 5. Adverse effects recorded after LAI therapy.

Comparing the level of adherence to therapy, we found a statistically significant improvement, from 42.96% to 76.30% (Table 4). Although we estimated that adherence to LAI therapy will be over 90%, almost a quarter of patients have given up this type of treatment at some point, the main dissatisfaction being related to weight gain and sexual dysfunctions (impotence, anorgasmia, low libido).

Table 4. Changes after LAI therapy.

	Therapy adherence	Social functioning	Aggresive behaviour
Initial	58 (42.96%)	24 (17.78%)	71 (52.59%)
Final	103 (76.30%)	47 (34.81%)	38 (28.15%)

The level of social adaptation and functioning almost doubled, with over a third of patients declaring that they have satisfactory social relationships, simultaneously with the decrease of heteroaggressive manifestations, from 52.59% to 28.15% (Table 4).

These subjective observations, which were found from interviews with patients and their relatives, were related to variables considered objective, such as the number of hospital admissions during the monitoring period of patients recruited to benefit from antipsychotic therapy with depot formulas, or the values recorded at the re- assessment of scales or scores by which patients were clinically evaluated initially.

For example, we observed a highly significant decrease in the number of hospitalizations for patients treated with LAI (Figure 6), the median value decreasing from 1.33 (1-2) to 1 (0.66-1.33).

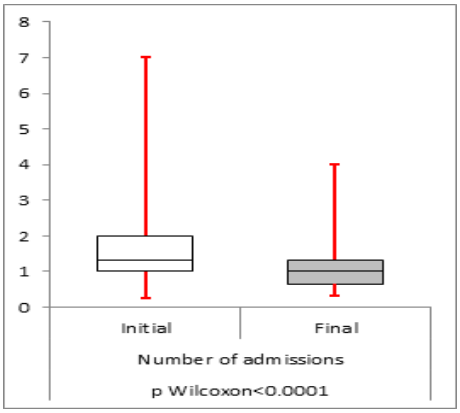

Figure 6. Comparison of the number of admissions per year before and after LAI therapy.

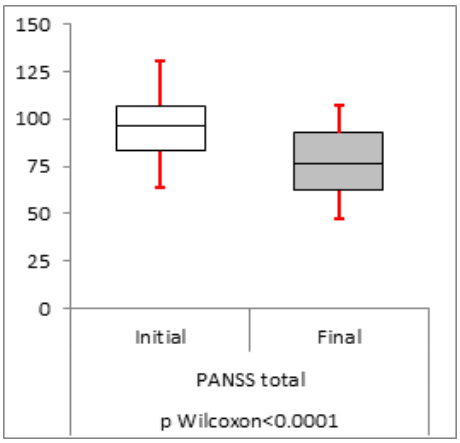

Figure 7. Comparison of total PANSS score before and after LAI therapy.

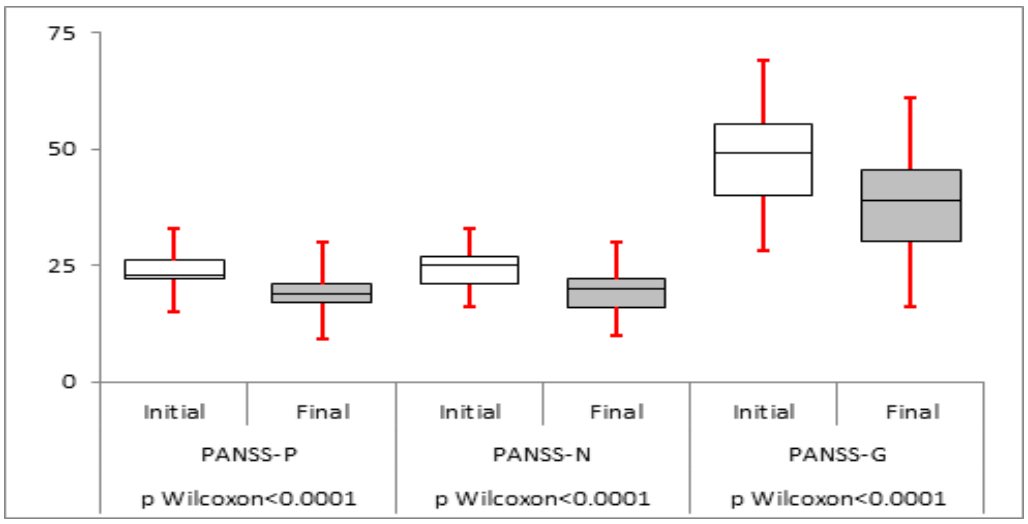

Figure 8. Comparison of the domains of the PANSS score before and after LAI therapy.

When comparing the total PANSS score, we identified significantly higher values (p Wilcoxon <0.001-highly significant difference) at the initial assessment, the median value decreasing from 96 (83-107) to 76 (62-92.75), a similar situation being observed on each of the three domains: P, N, and G (Figure 7, Figure 8).

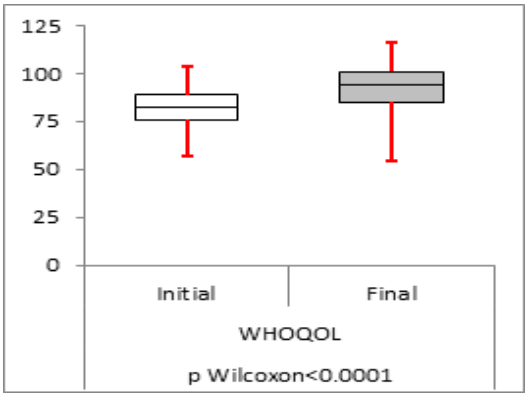

Figure 9. Comparison of total WHOQOL score before and after LAI therapy.

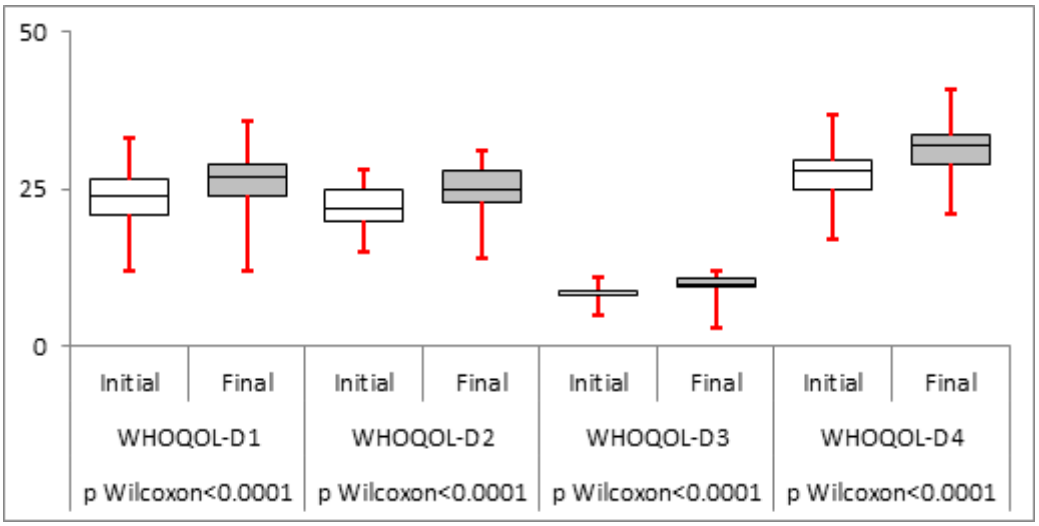

Figure 10. Comparison of the domains of the WHOQOL score before and after LAI therapy.

When comparing the values obtained on the WHOQOL scale, we identified significantly higher values (p Wilcoxon <0.001-highly significant difference) at the final evaluation, evidence of the perceived improvement in quality of life, the median value increasing from 82 (76-89) to 94 (85-101). This observation is also valid on the four domains of which the WHOQOL scale is constituted (Figure 9, Figure 10).

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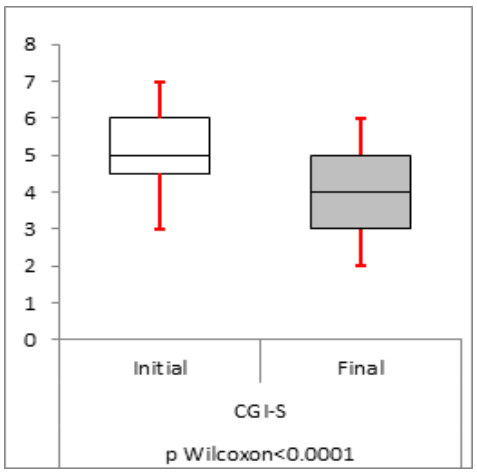

Figure 11. Comparison of CGI-S score before and after LAI therapy.

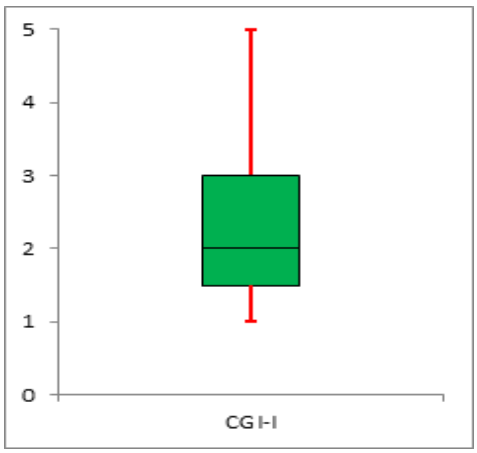

Figure 12. Distribution of CGI-I score after LAI therapy.

The overall clinical evaluation score assessed by the CGI-S scale decreased from 5 (4.5-6) to 4 (3-5), which is also confirmed by the CGI-Improvement values, which are mainly at level 2 ("Much improved") (Figure 11, Figure 12).

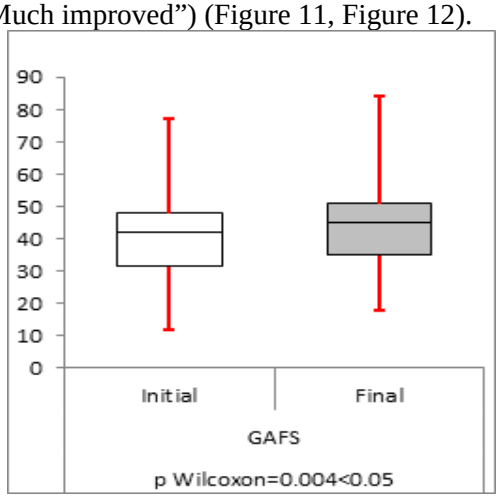

Figure 13. Comparison of GAFS score before and after LAI therapy.

The comparison of the initial general status with the final one via GAFS, from a statistical point of view, showed a significant difference ($p=0.004 <0.05$), although, it did not have a practical impact as high as the scales previously presented, the median value remaining also in the range of 40-60, which shows an average mental deficiency (Figure 13).

Discussions

The degree of damage to the life of the patient with schizophrenia is amplified by the stigma associated with the disease. Decreased functional and cognitive capacity in schizophrenia induces a substantial burden on both the patient and the family or society, involving direct and indirect costs of the disease [21]

LAI, by increasing adherence, and the implicit decrease in the number of hospital admissions, can play an important role in breaking the spiral of desocialization and functional decline in schizophrenia, thus favoring the recovery process [22].

In the present study, in which we mainly included patients who were previously non-compliant, we found an increase in therapeutic adherence from 42.96% to 76.30%. The main causes of discontinuation of LAI treatment were weight gain and the onset of sexual dysfunctions.

A study comparing the level of adherence between LAI and other oral formulas found that patients who received long-acting mediation had an up to 20% higher rate of maintaining the medication throughout the follow-up period, compared to patients treated exclusively with oral antipsychotics formulas [23]. Other studies describe a similar difference in treatment adherence, of almost 17% (49.2% versus 32.3%), between patients treated with LAI and those treated with oral forms in continuous administration [24]. The greater adherence to LAI therapy observed in our research is part of the tendency of studies on this subject to have a very high variability of the results obtained, most meta-analyzes describing this, with most studies proving the superiority of LAI, although others show the exact opposite [25].

Even at a short interval of omission of medication, of only 10 days, patients with schizophrenia are at risk of recurrence and hospitalization. A meta-analysis assessing the risk of relapse after stopping treatment found that 77% of patients relapsed within 1 year and the recurrence rate was 90% after 2 years. By

comparison, the recurrence rate in patients with satisfactory adherence was reported as 18% [26].

In a study comparing patients treated with LAI versus haloperidol or oral risperidone, patients treated with LAI had significantly fewer treatment discontinuations (26.0% vs. 70.2%), a lower recurrence rate (9.3% compared to 42.1%), a greater reductions in total PANSS score (-39.7 compared to-25.7), and a higher remission rate (64.0% compared to 40.4%) [27] A follow-up analysis observed remission installed in 64% of LAI-treated patients, which was maintained for 2 years by all but one patient, with early improvement in PANSS symptoms being a significant predictor of remission. In the present study group, we registered a significant decrease in the number of hospital admissions, the median value decreasing from 1.33 (1-2) to 1 (0.66-1.33), so we recorded a lower level of relapse than in the case of oral therapy.

Another study involving inpatients or outpatients, at the onset of schizophrenia, identified, after six months, improvements in baseline values for PANSS, CGI-S and GAFS. The conclusions drawn by the authors are that the use of LAI at the beginning of treatment may reduce discontinuation rates, which could lead to increased efficiency during this critical period [28].

In a study that evaluated patients with a recent onset of schizophrenia showed that, after two years of follow-up, patients who received LAI had significantly lower values of the total PANSS score (47.7 vs. 66.2) and PANSS-N (14.3 vs. 19.4) and PANSS-G (23.4 vs. 32.7), compared to those that received oral AP. Fewer readmissions and a higher remission rate were observed in the LAI group. Reducing negative symptoms and improving personal and social functioning are essential for disease management and recovery. These results show that LAI treatment, compared to oral therapy, right form the onset of schizophrenia, may have an effect on both clinical symptoms and social functioning, improving them [29].

An even more recent study [30], which evaluated the efficacy of risperidone treatment in depot form for one year, showed that the GAFS score improved significantly ($p < 0.001$), by 5.8±0.45 points, between the initial moment (46.4±0.54) and final moment of study (52.2±0.67). Regarding the PANSS score, the initial assessment of the underlying psychotic symptoms identified that, for four items (conceptual disorganization, blunt affect, passive or apathetic social withdrawal, lack of spontaneity and diminished conversational flow), the mean values were moderate in severity. In the end, all scores were mild.

It has been found that aripiprazole LAI therapy can be useful for improving the quality of life, evaluated at baseline and after 3 months of treatment, by QOLS and WHOQOL-BREF [31]. Another study, which compared LAI therapy with aripiprazole versus paliperidone [32], found that the mean scores on all four WHOQOL domains were significantly better in the LAI group with aripiprazole (82.00 versus 66.26 for physical health; 82.62 compared to 60.27 for psychological health; 81.02 compared to 65.41 for social relations; and 85.44 compared to 71.04 for relation to the living environment).

Monthly aripiprazole therapy was associated with a highly significant improvement at one year in positive, negative and general symptoms, as well as a decrease in CGI-S. A gradual improvement in QOL and social and personal functioning was also observed, and therapeutic adherence at the end of the study was 78% [33].

A Korean study, which compared the LAI and oral forms of risperidone, found that at 1-year and 2-year reassessment, patients treated with LAI had lower recurrence rates, higher adherence rates (68% vs. 38%) and longer periods of adherence than patients treated with oral risperidone. Furthermore, patients treated with risperidone LAI showed a greater reduction in the total PANSS score, CGI-S and a better functional improvement, assessed by GAFS. [34].

The level of quality of life, measured using the WHOQOL scale, in patients with schizophrenia, treated with LAI, is significantly higher than that of the normal population, according to a study conducted in Taiwan [35], but the degree of dissatisfaction was slight, suggested that these patients can maintain a satisfactory level of quality of life precisely due to LAI treatment.

All these findings validate the hypothesis of our study, which confirmed at the revaluation from 2 years, a decrease in all subdomains of the PANSS score, a decrease in CGI-S, together with a CGI-I level corresponding to a moderate improvement, as well as a increase of the functional status evaluated by the clinician by the GAFS scale, respectively of the quality of life, on all four domains measured by the

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WHOQOL scale, as it is perceived by the subjects.

Conclusions

1. The initial study showed that the following factors have a negative prognosis of evolution: rural environment, non-graduation from high school, unmarried or widowed marital status, no occupation, more than one hospitalization per year in the last 10 years, insidious onset, possibly at a young age, a history of heteroaggressive behavior (which correlates with a deficient level of integration) and therapeutic non-adherence.

2. For patients who fell into these categories, we decided to modify the traditional, oral therapy with antipsychotics in LAI forms. Depending on the previous medication and possible side effects related to the patients' condition at that time, we decided to administer LAI as follows: Aripiprazole 33.33%, Paliperidone 25.93%, Risperidone 17.78%, Fluanxol 14.81%, Olanzapine 8.15%.

3. Following the administration of LAI, in the next two years we found that the level of adherence increased from 42.96% to 76.30%, the level of social adaptation increased from 17.78% to 34.81%, and the aggressive behavior decreased from 52.59% to 28.15%.

4. The factors that contributed to a suboptimal level of adherence were the perceived adverse effects, the most frequently reported by patients being sexual dysfunctions (32.59%), weight gain (24.44%), extrapyramidal symptoms (22.22%), symptoms associated with hyperprolactinemia (20.74%) and akathisia (14.07). In addition, some olanzapine-treated patients have experienced drowsiness.

5. Following the administration of PA in the form of LAI, we found, at the reassessment, after one or two years, highly significant improvements for the number of hospital admissions, for PANSS – total score, P, N and G, WHOQOL and all subdomains, CGI-S, as well as and significant improvements for GAFS. In addition, the median value reported on the CGI-I scale was "Much improved".

Conflicts of interests

None to declare

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