

ATTITUDES OF CROATIAN PATIENTS WITH SEVERE MENTAL ILLNESS TOWARDS LONG-ACTING INJECTABLE ANTIPSYCHOTICS

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SUMMARY

Background: It has been shown that patients' attitudes towards long-acting injectable antipsychotics (LAIA) have the influence on the acceptance and use of this type of therapy. The aim of our study was to explore attitudes of patients because, according to our knowledge, there has been no similar research in Croatia thus far.

Subjects and methods: Two questionnaires were given to the total of 100 patients, the first one to patients treated with LAIA (group 1) and the second one to patients treated with oral antipsychotics (group 2).

Results: Significantly more patients treated with LAIA find that good aspects of their medication outweigh the bad ($p=0.014$). Almost one third of patients treated with oral antipsychotics ($n=16$, 32%) quit taking medication when they feel better and 6 patients (12%) very often or often forget to take medication. Larger number of patients treated with LAIA feels much better since they have been taking their medication (group 1=82%, group 2=68%). Almost all patients treated with LAIA would recommend their therapy to other patients (92%), which is not the case with patients treated with oral antipsychotics (58%). 90% of patients decided to take LAIA because of suggestion given by their psychiatrists and 10% were persuaded by their psychiatrists. When given potential advantages of LAIA, 84% of patients said they found very positive the fact that they didn't have to think about taking their medication every day, 82% were fond of LAIA's simplicity, 68% considered positive that their psychiatrists had better control over their treatment and 66% were very content with their recovery.

Conclusion: The larger number of patients treated with LAIA is content with their therapy than patients treated with oral antipsychotics. Patients' attitudes have changed in a way that they don't find LAIA coercive anymore and most of them agreed to that type of therapy on a suggestion given by their psychiatrists.

Key words: psychiatric patients – attitudes - long-acting injectable antipsychotics – LAIA - adherence

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INTRODUCTION

Schizophrenia is a chronic mental disease that manifests with numerous symptoms which are divided in two basic groups: positive (distortion of reality in the form of hallucinations and delusions) and negative (apathy, anhedonia, reduction of socialization). Tendency of modern psychiatry is to identify patients in the earliest stage of disease in order to prevent further progression with adequate therapy. The aim of treating schizophrenia is clinical, social and personal remission and prevention of relapses (Jakovljevic 2014).

Main therapy of schizophrenia are antipsychotics that are available in oral and intramuscular formulations. The treatment of schizophrenia mainly begins with one of the atypical antipsychotics applied in oral form. It is possible to achieve remission in 80% of patients treated with oral antipsychotics in first episode of schizophrenia. However, 80% of them relapse in five years, mainly due to poor adherence (Osborne et al. 2012). 40-60% of patients treated with oral therapy stop taking their medication as it was prescribed within first two years of treatment. There are plenty of reasons for patients' nonadherence. Some patients unintentionally forget to take their therapy, some of them have pro-

blems with understanding the instructions, while some of them knowingly refuse to continue with treatment. Possible causes for discontinuation of treatment could be lack of insight, stigma, fear of dependency and responsibility, preoccupation with side-effects, lack of information but also patients' mental disorganization and personal ambivalence (Jakovljevic 2014). Considering positive correlation between taking long-term therapy and decreased risk of relapses, struggle against patients' nonadherence is the major challenge for modern psychiatry (Ahmadkhanika et al. 2014). Therefore, it was important to develop medication that will be able to unify positive characteristics of oral antipsychotics, give us the possibility to maintain constant drug level in the blood, ameliorate patients' adherence and reduce relapses. For this purpose, long-acting injectable antipsychotics (LAIA) were introduced in the attempt to improve long-term treatment of schizophrenia (Rossi et al. 2012). LAIA are the intramuscular form of antipsychotics that have to be applied every 2-4 weeks in deltoid or gluteal muscle. While conducting this research, there were six LAIA registered in Croatia: haloperidol decanoate, flufenazine decanoate, zuclopenthixol decanoate, risperidone microspheres, paliperidone palmitate and olanzapine pamoate hydrate.

Despite many potential benefits, LAIA are rarely prescribed in clinical practice and their usage is mostly reserved for nonadherent patients and patients with multiple relapses (Lasser et al. 2009). Previous researches showed that percentage of patients treated with LAIA don't go beyond 25% in many countries (Llorca et al. 2013) which indicates that LAIA are still a controversial topic. For this reason, we found it valuable to examine patients' attitudes towards LAIA because, according to our knowledge, there has been no similar research in Croatia thus far.

SUBJECTS AND METHODS

Subjects

In this research, we included the total of 100 patients, half of them treated with oral antipsychotics and half of them with LAIA. We expressed the number of years of treatment with median of 13,00 with minimum value of 0,10 years and maximum value of 49,00 years. 51 patients (51%) suffer from schizophrenia, 2 patients (2%) from schizotypal disorder, 16 patients (16%) from acute schizophrenia-like psychotic disorder, 14 patients (14%) from schizoaffective disorder, 12 patients (12%) from other non organic psychotic disorders and 5 patients (5%) suffer from bipolar disorder. Other characteristics of the sample are shown in Table 1.

Table 1. Characteristics of the sample

Characteristics of the sample	Patients treated with LAIA (%)	Patients treated with OA (%)
Gender		
Male	54	48
Female	46	52
Age (years)		
≤40	52	50
>40	48	50
Marital status		
Unmarried	68	56
Married	24	26
Divorced	6	12
Widowed	2	6
Education		
Elementary	8	16
Secondary	54	46
Higher	38	38
Employed	68	50
Smokers	46	46
Psychiatrics visits		
>once a week	0	4
- once a week	4	6
>once a month	14	10
- once a month	42	34
<once a month	32	40
- less than once a y.	6	4

* LAIA = long-acting injectable antipsychotics;
OA = oral antipsychotics

In the group of patients treated with LAIA, the lowest number of received doses was 1, the maximum was 240 applications and the median of received doses was 10. The largest number of patients was treated with paliperidone palmitate (n=14, 28%) and olanzapine pamoate hydrate (n=14, 28%). 10 patients were treated with flufenazine decanoate, (20%), 6 patients (12%) with haloperidol decanoate, 4 patients (8%) with zuclopenthixol decanoate, and 2 patients (4%) with risperidone microspheres.

Methods

The research took place in two Croatian hospitals: Department of Psychiatry (University Hospital Center Zagreb) and Psychiatric Hospital „Sveti Ivan“. We created two questionnaires modeled on standardized questionnaires: Drug Attitude Inventory – DAI (Hogan et al. 1983), Rating of medication influences (ROMI) scale (Weiden et al. 1994), Personal evaluation of transitions in treatment - PETiT (Voruganti & Awad 2002). The diagnoses were determined based on medical records.

Questionnaire 1 was given to patients treated with LAIA (group 1) and it consists of two parts. First part is based on sociodemographic data and basic information about disease and treatment. Second part consists of 40 questions of which some are multiple-answer questions. Other questions are statements which patients were evaluating with marks from 1 to 5 to describe their opinion about a given statement (1 - strongly disagree, 2 - disagree, 3 - neutral, 4 - agree, 5 - strongly agree) and they were grouped in four categories: attitudes towards disease and treatment, the advantages of therapy, side effects and motivation for taking medication.

Questionnaire 2 was given to patients treated with oral antipsychotics (group 2). Most of the questions are the same as in questionnaire 1 in order to compare attitudes of these two groups. According to specificity of treatment, we constructed few different questions for patients treated with oral therapy. All patients signed informed consents. The study was approved by the Central Ethics Committee, School of Medicine (University of Zagreb).

Statistical analysis

All the data were analysed in Microsoft Excel (Microsoft, USA). For statistical analysis we used Cran R (R & R" of the Statistics Department of the University of Auckland, New Zealand) and our results are described with descriptive statistics. We used Wilcoxon's test to compare two independent variables and Likert scale was used to measure respondents' attitudes to statements. The internal consistency coefficient (Cronbachs Alpha) of our questionnaire was 0.82.

RESULTS

Attitudes towards disease and treatment

Most of the patients are content or very content with the relationship with their doctor and they have confidence in doctor's choice of medication. There is a slightly larger number of patients treated with oral antipsychotics in comparison with patients treated with LAIA that others have to force to take their medication and there are more patients treated with LAIA who don't find themselves ill. The largest difference in the obtained results is noticeable in question 4 (I think that the good aspects of my medication outweigh the bad.). There are more patients treated with LAIA who strongly agree with this statement (Table 2).

Almost one third of patients treated with oral antipsychotics (n=16, 32%) quit taking medication when they feel better and 6 patients (12%) very often or often forget to take medication.

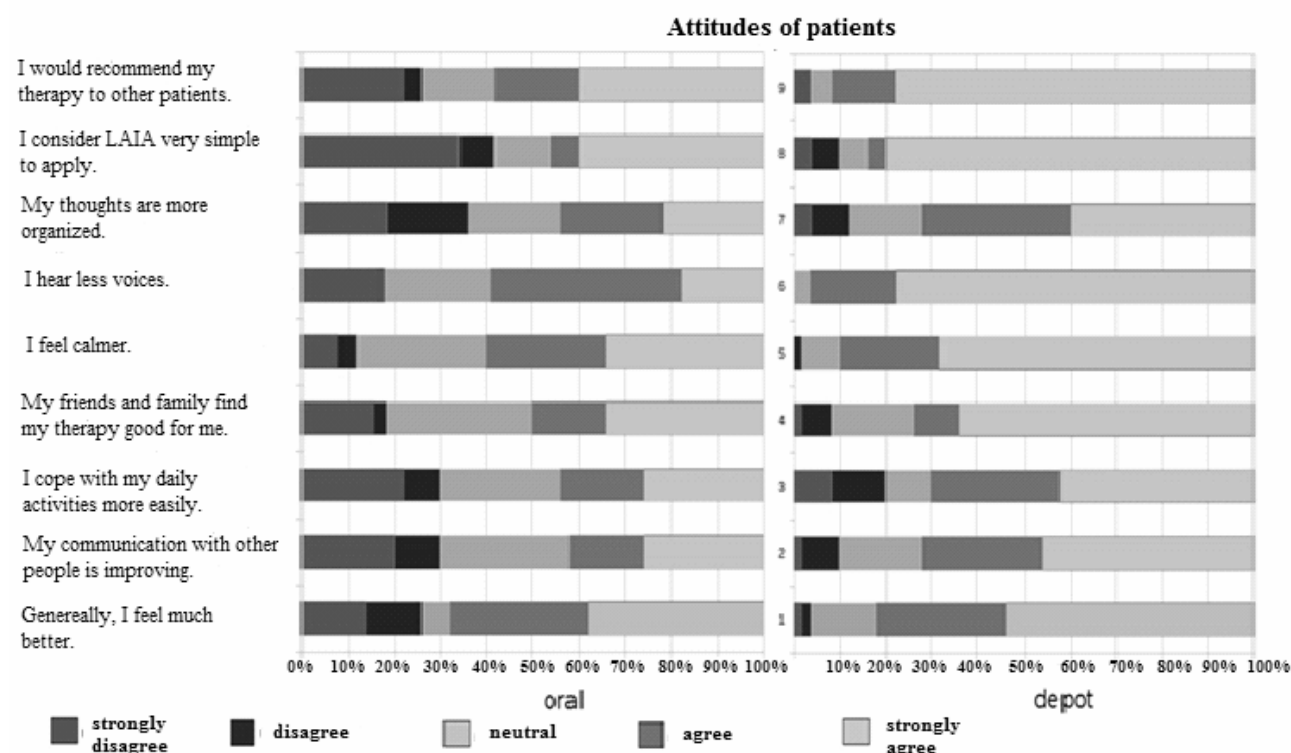
The advantages of therapy

Significantly larger number of patients treated with LAIA feels much better, notices their communication with other people is improving, copes with their daily activities more easily, hears less voices (those who had hearing hallucinations), feels calmer and their thoughts are more organized since they have been taking their medication. There is also a larger percentage of patients treated with LAIA that are relating their recovery directly to their medication. More patients treated with LAIA think that their friends and family find their therapy good for them. Majority of patients treated with LAIA consider their treatment very simple to apply and almost half of the patients treated with oral therapy claim that getting injection once a month would be more simple for them. Almost all patients treated with LAIA would recommend their therapy to other patients, which is not the case with patients treated with oral antipsychotics (Table 3, Figure 1).

Table 2. Attitudes towards disease and treatment

Attitudes towards disease and treatment	Patients treated with LAIA (%)	Patients treated with OA (%)	p
I have confidence in my doctor's choice of medication	92	84	0.023
Others have to force me to take my medication	4	16	0.061
I don't find myself ill	34	24	0.503
I think that the good aspects of my medication outweigh the bad	76	58	0.014
I am very content with the relationship with my doctor	90	84	0.519

* LAIA = long-acting injectable antipsychotics; OA = oral antipsychotics; p = p-value = level of significance



* LAIA = long-acting injectable antipsychotics

Figure 1. Likert scale - Attitudes of patients

Table 3. The advantages of therapy

The advantages of therapy	Patients treated with LAIA (%)	% of them relate their recovery to LAIA	Patients treated with OA (%)	% of them relate their recovery to OA	p
Generally, I feel much better	82	-	68	-	0.035
My communication with other people is improving	72	94	42	71	0.002
I cope with my daily activities more easily	70	86	44	59	0.021
My friends and family find my therapy good for me	74	-	50	-	0.003
I feel calmer	90	89	60	77	0.0001
I hear less voices	96.3	76.92	58.82	40	0.002
My thoughts are more organized	72	83	44	73	0.003
I consider LAIA very simple to apply	84	-	46	-	1.53E-5
I would recommend my therapy to other patients	92	-	58	-	3.46E-5

LAIA = long-acting injectable antipsychotics; OA = oral antipsychotics; p = p-value = level of significance

Table 4. Side effects

Side effects	Patients treated with LAIA (%)	% of them relates their side effects to LAIA	Patients treated with OA (%)	% of them related side effects to OA	p
I often feel side effects	14	-	28	-	0.745
I am often excessively tired	26	23	30	87	0.335
I often have headache	0	-	8	0	0.454
I often feel dizzy	4	0	14	43	0.347
I often experience involuntary movements	8	25	20	60	0.127
I often have tremor	8	0	32	50	0.021
I often have excessive salivation	12	17	24	83	0.483
I often have a feeling of stiffness	20	30	46	74	0.016
I often have nausea	2	0	0	-	0.977
I have gained weight	52	27	54	81	0.726

LAIA = long-acting injectable antipsychotics; OA = oral antipsychotics; p = p-value = level of significance

Considering the fact that it is necessary to see a psychiatrist to take LAIA, most of the patients feels more secure with LAIA therapy because they know they won't forget to take it (n=39, 78%) and they think in that way their psychiatrist has better insight into their treatment (n=42, 84%). 35 patients (70%) are not afraid of worsening of disease since they have been taking their therapy.

Side effects

Seven patients (14%) treated with LAIA and 14 patients (28%) treated with oral antipsychotics often feel side effects of their therapy. The least number of patients define headache, dizziness and nausea as a side effect. Side effects like tremor, involuntary movements, stiffness, slowness and excessive salivation appear in both groups of patients, but there is a larger percentage of patients treated with oral antipsychotics that are relating their side effects directly to their therapy. There is a similar number of patients in both groups that are excessively tired or have gained weight since they have been taking their medication. There is also a larger

percentage of patients treated with oral therapy that are relating these side effects directly to their therapy (Table 4). Only two patients treated with LAIA report administration site rash.

Motivation for taking medication

The main motivation for most of the patients to take their medication is a fear of experiencing exacerbation of their disease but as well a belief that they can prevent worsening of the disease by taking drugs. There are fewer patients who are taking their medication because their family wants them to or because of the fear of rehospitalization (Table 5).

Specific attitudes about LAIA – multiple-answer questions

45 patients (90%) decided to take LAIA because of suggestion given by their psychiatrists and 5 patients (10%) were persuaded by their psychiatrists. Only small number of our patients (12%) took suggestion from their families and 1 patient (2%) from his general practitioner.

Table 5. Motivation for taking medication

Motivation for taking medication	Patients treated with LAIA (%)	Patients treated with OA (%)	p
I don't want to experience exacerbation of my disease	86	74	0.316
I take medication because my family want me to	46	44	0.728
I have a fear of rehospitalization	50	36	0.131
I believe I can prevent deterioration of my disease by taking drugs	70	68	0.542

LAIA = long-acting injectable antipsychotics; OA = oral antipsychotics; p = p-value = level of significance

When they were asked why did they decide to take LAIA, Most of the patients answered it was because they wanted to get better (n=44, 88%) and because they found getting injection once in 2-4 weeks more simple (n=34, 68%). Sixteen patients (32%) agreed to take LAIA because of the fear of rehospitalization and the same number of patients chose that type of therapy because oral therapy was inadequate for them. Worsening of the disease was a reason for choosing LAIA for 17 patients (34%). When given potential advantages of LAIA, 42 patients (84%) said they found very positive the fact that they didn't have to think about taking their medication every day, 41 patients (82%) were fond of LAIA's simplicity, 34 patients (68%) considered positive that their psychiatrists had better control over their treatment and 33 patients (66%) were very content with their recovery since they had been taking LAIA. When patients had to choose between potential disadvantages of LAIA, 25 (50%) of them didn't consider any of the offered statements as a disadvantage. 13 patients (26%) found negative pain at the injection spot. 11 patients (22%) considered negative that they had to take their medication in hospital. 9 patients (18%) found problematic the impossibility of immediate discontinuation of their therapy in case of occurrence of side effects.

DISCUSSION

According to the results of our research, patients treated with LAIA generally have better opinion about their therapy than patients treated with oral antipsychotics. These results are in accordance with previously conducted researches in other countries which are not only showing positive attitudes of patients treated with LAIA towards their therapy but also demonstrating that patients prefer LAIA over oral therapy (Caroli et al. 2011). Considering that complete recovery is based on clinical, social and personal component, it is important to emphasize that patients treated with LAIA achieve statistically significantly higher scores in that part of the questionnaire. Larger number of patients treated with LAIA is feeling much better, calmer and hears less voices which argues for their clinical recovery. Besides, some other unexpected advantages have been noticed thanks to regular contact between the patient and his psychiatrist. Namely, regular contact allows doctor-patient relationship to become more opened with better communication and greater mutual trust which encourages patients to

play a more active role in their treatment instead of their previous passive role. The main purpose of LAIA is to empower patients to control their disease and to help them to regain control over their life (Jakovljevic 2014). Our research showed that there is a larger number of patients treated with LAIA that cope more easily with their daily activities and communicate better with other people which enables them to return to social environment more easily, accomplish successful interpersonal relationships, achieve inner peace and better quality of their life. Caroli et al. (Caroli et al. 2011) also state that LAIA could have a positive impact on patients' ambitions in business, family and social life and create a greater sense of autonomy. Considering that one third of our patients treated with oral antipsychotics are non-adherent with taking medication when they feel better, we find these results as unsurprising, since it is necessary to take drugs regularly to maintain remission.

Since patients have to take their medication in hospital, they feel more secure because it is less possible they would forget to take their therapy. Beside security, there are many reasons why patients choose LAIA, such as desire for recovery, fear of rehospitalization, worsening of the disease and simplicity of application. Patients consider dosing of LAIA once in 2-4 weeks as an advantage, not only because of simplicity of application, but also because they don't have to think every day about taking their medication and potentially hesitate about it. It is interesting that patients treated with oral therapy also say it would be more convenient for them if there was a medication with the same effect which wouldn't have to be taken every day. Researches from other countries show the same results (Wehring et al. 2011). However, there is a problem in insufficient awareness of treatment possibilities within our patients, and according to our results, more than a half of our respondents have never heard about LAIA. It is possible that this is one of the main reasons for low trend of prescribing LAIA. Another possible reason is a fear of needle (Jeong & Lee 2013), but our results don't speak in favour of that (31 patients claim they don't have a fear of needle).

Although Patel et al. (Wehring et al. 2011) state that there is a larger number of patients treated with LAIA than those treated with oral therapy that find their therapy regimen coercive, newer researches emphasize the importance of cooperation between patient and psychiatrist in the choice of therapy after detailed briefing about advantages and disadvantages of all options (James et al. 2012). Our results show that almost all the patients chose LAIA on a suggestion, and

not on a persuasion. According to the states written above, we find these results as a positive progress in approach to the treatment of schizophrenia.

For the matter of side effects, the frequency of their occurrence is similar in both groups of patients, but we find it interesting that there is higher percentage of patients treated with oral antipsychotics that relate their side effects directly to their medication.

Considering attitudes given by patients that favour LAIA, future researches should focus on more detailed examination of attitudes of patients and psychiatrists.

This research has certain limitations. Non-standardised questionnaires were used and testing was performed on a relatively small number of patients, which could potentially result in lower statistical probabilities of certain factors tested on this sample. It is also possible that mental status had an influence on the attitudes of patients towards treatment.

CONCLUSION

The larger number of patients treated with LAIA is content with their therapy than patients treated with oral antipsychotics. Considering the fact that there is much effort put in patient-centered approach, our results show change in patients' attitudes towards LAIA. Patients' attitudes have changed in a way that they don't find LAIA coercive anymore and most of them agreed to that type of therapy on a suggestion given by their psychiatrists. Despite these results, LAIA are still relatively rarely prescribed. According to experiences of our patients, there is no important difference in frequency of occurrence of side effects which we find important because it shouldn't be a limiting factor for future prescribing of LAIA. Precisely because all of this, future researches should be focused on further examination of patients' attitudes toward therapy in order to achieve higher level of awareness that may have a positive impact on trend of low prescribing of LAIA.

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Contribution of individual authors:

Sarah Bjedov: design of the study, collecting data, interpretation of data, writing the paper;
Mirta Ciglar: literature searches, interpretation of data, writing the paper;
Hrvoje Maleković: statistical analysis.

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