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Letter to the Editor

# Long-acting injectable antipsychotics treatment during COVID-19 pandemic – A new challenge

Non-adherence is an important factor in therapeutic failure, which is frequently correlated with disease progression. This phenomenon is common in most diseases that require chronic treatment (cardiovascular, metabolic, degenerative, etc.) (Timmerman et al., 2016). In the case of mental illness and schizophrenia in particular, non-adherence (total or partial) reaches up to 75% of cases, being rather the rule than the exception (Kane et al., 2013a; Dobber et al., 2018; Kishimoto et al., 2013a). Medication non-adherence is associated with poor outcomes, more hospital readmissions, and increased costs of care in schizophrenia (Winton-Brown et al., 2017; Haddad et al., 2014).

Poor medication adherence is multifactorial, is caused by the lack of insight (the individual does not want to be treated because he/she does not consider himself/herself ill), or persistent psychotic symptoms. In contrast, cognitive deficits and causes related to the evolution of the disease are important factors in the individual's motivation for taking medication (Lacro et al., 2002).

Strong evidence of the superiority of long-acting injectable antipsychotics (LAIs) over oral antipsychotics (OA) in relapse prevention and reducing mortality in schizophrenia is demonstrated in many studies (Taipale et al., 2018). LAIs have been shown to be more effective in persons under 35 years of age. Avoiding treatment abandon, LAIs determined more frequently remission and recovery than OA (Kishimoto et al., 2013b; Kane et al., 2013b). Efficiency has been proven in the prevention of relapses also in the catatonic forms (Ifteni and Teodorescu, 2017). Experts considered that LAIs should be introduced as early as possible for better outcome in schizophrenia (Stahl, 2014).

Despite its proven effectiveness and favorable cost-benefit ratio, LAIs are still underused world-wide due to different reasons including economic (high cost), mistrust, fear, stigma and outdated concepts (Taylor et al., 2018). On the part of the patients, the refusal is related in particular to the mode of administration (injection), the control of the treatment (the feeling that they no longer decide), the administration protocols (in specialized centers, post injection monitoring in the case of olanzapine pamoate, etc.) (Yeo et al., 2017).

To all these, new restrictions or limitations of prescription and administration caused by COVID-19 pandemic are now are added.

In order to limit the possibility of contamination, authorities in many countries, including Romania, have recommended limitation or restriction of access to hospitals, which remain strictly intended for emergencies only. General practitioners, but also psychiatrists, have limited the number of interactions with patients and have started a difficult process for online consultations. In addition to benefits, issues regarding ethics, confidentiality, accessibility, etc. are present. Online consultations cannot capture many aspects of psychiatric pathology and are often impossible in cases with low income or in rural or isolated areas.

Delayed supply in pharmacies caused by the restriction or cancellation of the export of medicines or sanitary equipment in the context of a COVID-19 is another barrier.

As a result, a significant number of patients with schizophrenia have been (or will soon be) undergoing treatment with less expensive, easy-to-obtain, and manageable oral antipsychotics. In our psychiatric setting (public hospital with 150 beds for acute patients), the number of LAIs prescriptions decreased dramatically (49% for risperidone LAI and 90% for olanzapine LAI) from December 2019 to March 2020 (Table 1).

The switch from LAIs to OA was requested by patients or caregivers to reduce the number of trips to pharmacies, medical offices or public mental health centers.

For most forms of intramuscular administration, manufacturers and experts have recommended that the treatment be done by specialized medical personnel (physicians or nurses) in centers with experience to avoid any problems. Administration at home is not recommended.

Human natural anxiety related to this unique phenomenon in the last hundred years is added. Conspiracy theories in media have a major impact on patients with schizophrenia but not only.

We will probably see in the coming days or weeks many patients in clinical remission switched from LAI to OA.

Future mirror-image studies will show the consequences of this switch. The effect size will be directly proportional with duration of the pandemic and the restrictions imposed. No-one can anticipate the duration of COVID-19 pandemic and this situation can be prolonged.

What can we do to prevent relapses with its dramatic consequences, especially in patients who have been undergoing LAIs for years and have not experienced relapses for a long time, some even considering themselves to be “cured”? What would be the best standard of care in these situations? Proposed measures such as increasing the dose, delaying the next injection, or administration by the pharmacists or family members imposed important risk: stress, pain, too superficial or too profound injection, inadequate site of injection (deltoid or gluteal), etc.

We must continue to advocate for improved access to long-acting antipsychotics for the people with previous non-adherence as well as for the young patients at the early stages of schizophrenia, even in this difficult period.

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#### Declaration of competing interest

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**Table 1**
The evolution of LAIs prescription before and after declaration of COVID-19 pandemic.

| Type of LAIs | Number of prescriptions before WHO declared COVID-19 pandemic | | | | Number of prescriptions after WHO declared COVID-19 pandemic | Reduction of LAIs prescriptions |
|---|---|---|---|---|---|---|
| | December 2019 | January 2020 | February 2020 | 3 months average | March 2020 | |
| aripiprazole | 30 | 33 | 35 | 32.66 | 10 | 70% |
| paliperidone | 22 | 27 | 30 | 26.33 | 5 | 81% |
| olanzapine | 19 | 21 | 20 | 20.00 | 2 | 90% |
| risperidone | 35 | 41 | 40 | 38.66 | 20 | 49% |

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