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Short Commentary

A Commentary on "Better Treatment Outcomes with Aripiprazole Long-acting Injection in Community and Incarcerated Patients with Serious Mental Illness"

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Dear Editor,

Non-adherence to antipsychotic medication is a primary reason for treatment inefficacy in psychotic patients, particularly those with co-occurring substance use disorders (SUD) or alcohol use disorders (AUD). Poor adherence increases relapse risk, hospitalization rates, treatment costs, and the likelihood of legal issues, perpetuating a "revolving door" cycle of hospitalization and incarceration. In Greece, the impending implementation of Law 5129/2024, effective February 1, 2025, will integrate psychiatric services with the penitentiary system, prompting this study to assess aripiprazole LAI benefits for community and incarcerated patients in Eastern Crete. The findings aim to inform health policy, optimize resource allocation, and support psychiatric reform. As a third-generation antipsychotic, aripiprazole acts as a partial D2 and 5-HT1A agonist and 5-HT2A antagonist, approved by the FDA in 2002 [1]. Its unique mechanism [2] may reduce hyperdopaminergic activity in the mesolimbic system (antipsychotic effect) while enhancing hypodopaminergic activity in the prefrontal cortex, potentially alleviating negative symptoms and cognitive deficits [3-5]. Partial 5-HT1A agonism may also provide anxiolytic benefits [6]. Studies, including a 2015 trial in the UK and Canada, demonstrated aripiprazole's ability to enhance dorsolateral prefrontal cortex (DLPFC) activation during working memory tasks, suggesting improved processing speed [7].

The study enrolled 55 patients: i) Community Patients (n=34): 70.6% male, mean age 42.3 ± 11.9 years, 44.1% with F20.0, 94% with Cluster C personality, 34.1% with psychoactive substance use, mean treatment duration 23.2 ± 18.3 months, ii) Incarcerated Patients (n=21): All male, mean age 37.6 ± 7.7 years, all with F29.0, 57.1% with Cluster B personality, 100% with psychoactive substance use, mean treatment duration 14.5 ± 11.3 months, iii) Significant differences were noted between groups in most demographic and medical history parameters, except for traumatic brain injury, mental retardation, age, and treatment duration.Participants were assessed using the WHOQOL-BREF and CGI-S scales, with outcomes compared pre- and post-aripiprazole LAI treatment over a minimum six-month period.

This study is the first in Greece to evaluate aripiprazole LAI for community patients with psychosis and SUD, and the first in Europe for incarcerated patients with unspecified psychosis and SUD. Observed outcomes may reflect temperamental traits, as noted by Favaretto et al. (2024) [8], which influence psychopathology severity and treatment engagement, especially in dual-diagnosis or Cluster B populations [9]. Our findings confirm significant improvements in quality of life, functionality, and hospitalization rates, aligning with Sampogna et al. (2023) on LAI benefits (10).Aripiprazole LAI also shows promise for AUD, with four community patients achieving abstinence and others reducing consumption. Animal studies support its efficacy in reducing ethanol-related behaviors [11,12]. Further research is needed to quantify cost savings and explore off-label use in AUD.

Ethical approval was granted by the General Hospital of Agios Nikolaos (decision 514/19-07-2023), Scientific Council of the General Hospital of Agios Nikolaos Lasithi of Crete – National Health System of Greece (Prot. No. 10/15-02-2023), 7th Sanitary Region of Crete (Prot. No. 28386/30-06-2023), and Ministry of Public Order (Prot. No. 10456/10-04-2023) under Law 4812/2021, Article 87. The studies were conducted in accordance with the local legislation and institutional requirements.

Based on: 1) Our study under comment, 2) our clinical experience and at the same time on the data of a larger sample that we have already collected and are studying in recent months, we have been led to the conclusion that it would be extremely interesting for our research to study the therapeutic stabilization of our patients in the first three months of treatment with aripiprazole LAI. The recent results to which our constantly evolving research has led us have given us all the important indications of an effective and at the same time faster response to therapy, which could occur before 6 months from the first day of administration of the medication.

Evaluating the results of our studies [13-15] and guided by our clinical examination based on our medical skill and experience, we observe a gradual improvement in the clinical status of patients

(patients in community and incarcerated patients) after the first two months of administration of the Depot antipsychotic therapy, such as their daily functionality, their affective and cognitive response to any form of everyday stimuli [16,17], in combination with the improvement of their quality of life (as evidenced by the systematic medical clinical examination and medical observation of patients, by the management of the crisis in their daily life and by the interactive relationship of the patients with familiar persons in different environments) and the reduction of their hospitalizations due to the hard core of their disease. All these lead us to think about the possibility of having better clinical outcomes and satisfactory indication of stabilization from the treatment even in the first three months.

Such a possibility would provide to patients faster relief from the symptoms of their illness and would reduce more quickly the possibility of dangerous exacerbations of the disease, which are associated with the triggering of inflammatory processes in the body and the sensitization of the immune system. Moreover, such a possibility would reduce the possible threat of the patients' integrity and the integrity of the people around them from clinical manifestations of inappropriate behaviors of the patients that characterize the disease (for example, positive symptoms of the disease). Finally, would encourage the compliance of the patients in the faithful adherence and continuation of their treatment and would restore the general pathogenesis created in their environment by the effects of their illness.

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