

## How to conquer tardive dyskinesia: could pharmacogenetics and therapy drug monitoring be useful tools?

Dino Žujić<sup>1</sup>, Nada Božina, MD, PhD<sup>1</sup>, Mila Lovrić, MD, PhD<sup>1, 3, 4</sup>, Lana Ganoci, MD, PhD<sup>4</sup>, Maja Živković, MD<sup>1, 2</sup>

1 School of Medicine, University of Zagreb, Zagreb, Croatia

2 Department of Psychiatry, University Hospital Centre Zagreb, Zagreb, Croatia

3 Faculty of Pharmacy and Biochemistry, University of Zagreb, Zagreb, Croatia

4 Department of laboratory diagnostics, University Hospital Centre Zagreb, Zagreb, Croatia

### Keywords:

clozapine, paliperidone palmitate, pharmacogenetics, tardive dyskinesia, TDM

### Background:

Tardive dyskinesia is a neurological disorder characterized by involuntary, repetitive movements of the face, tongue, and limbs, which may result from a long-term use of antipsychotics.

### Case presentation:

A 27-year-old male was diagnosed with schizophrenia in 2018. Following his initial hospitalization, he was prescribed a combination of medications, including paliperidone palmitate (150 mg), clozapine (50 mg every other day), amisulpride (100 mg), and lamotrigine (50 mg). From July 2022 onwards, the patient began to experience distressing orofacial dyskinesia symptoms that significantly impeded his daily life. In response, a comprehensive evaluation was conducted, which included CYP genotyping and therapy drug monitoring (TDM). The measurement of 9-OH risperidone plasma concentration revealed an elevated level (296.4 nmol/L), twice the permissible upper limit. Consequently, the dosage of paliperidone palmitate was reduced, while the clozapine dosage was increased. In addition, genotyping analyzes of CYP2D6, CYP3A4/5, CYP2C19, ABCB1, and ABCG2 were performed and showed the patient's intermediate metabolizer status for CYP2D6. Subsequent follow-up assessments exhibited a gradual decline in the 9-OH risperidone concentration, with levels reducing to 83.7 nmol/L after three months and further to 67.5 nmol/L after an additional month. This reduction was attributed to the tapering-down and dosage reduction of the medication. Ultimately, 9-OH risperidone was excluded completely, with a concomitant increase in the clozapine dosage (100 mg). Upon the patient's final evaluation in September 2023, he reported a substantial improvement in his condition, marked by the complete resolution of orofacial dyskinesia symptoms.

### Conclusion:

This case underscores the significance of personalized pharmacotherapy adjustments informed by both clinical and genetic factors in achieving favorable outcomes in the treatment of psychiatric disorders. Today, a good psychiatrist should possess the knowledge to recognize adverse effects, understanding of pharmacogenetics and TDM, and a patient-centered approach to tailor treatments for optimal outcomes.