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Utjecaj farmakogenetičkih varijanti na učinkovitost i podnošljivost antidepresivne terapije: iskustva pacijenata

/ *The Influence of Pharmacogenetic Variants on the Efficacy and Tolerability of Antidepressant Therapy: Patient Experiences*

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Uvod: U suvremenom pristupu liječenju usmjerenom na pacijenta, ishodi liječenja koje prijavljuju pacijenti (PRO) imaju sve važniju ulogu u procjeni učinkovitosti i podnošljivosti terapije. Budući da odražavaju iskustva pacijenata vezana uz simptome, nuspojave lijekova (ADR) i opće zdravstveno stanje, PRO je vrijedan dodatak kliničkim pokazateljima. Ciljevi: Ispitati per-

Introduction: In the modern patient-centered approach to treatment, patient-reported outcomes (PROs) play an increasingly important role in assessing the effectiveness and tolerability of therapy. Since they reflect patients' experiences related to symptoms, adverse drug reactions (ADRs), and overall health status, PROs are a valuable complement to clinical indicators. Objectives: To ex-

cepciju bolesnika o učinkovitosti i sigurnosti antidepresivne terapije te istražiti povezanost farmakogenetičkih (PGx) varijanti s prijavljenim ishodima liječenja i nuspojavama. Materijali i metode: Istraživanje je obuhvatilo 123 psihička bolesnika koji su ispunili upitnik o aktualnim simptomima i mogućim nuspojavama antidepresivne terapije. U 49 bolesnika bili su dostupni farmakogenetički (PGx) profili (ABCB1, ABCG2, COMT, CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, CYP3A4/5 i SERT), a dodatno je analizirana njihova povezanost s ishodima liječenja i prijavljenim nuspojavama. Rezultati: Među 49 bolesnika, sertralin je bio najčešće propisivan antidepresiv (85,7 %), a nakon njega escitalopram (8,2 %). Većina bolesnika primala je kombiniranu terapiju (81,6 %). Najčešće prijavljene nuspojave bile su mučnina (51,0 %), omaglica (10,2 %) i suhoća usta (8,2 %). Fenotipovi CYP2C19 bili su pretežno brzi ili normalni metabolizatori, dok su CYP2D6 i CYP2B6 najčešće bili normalni ili intermedijarni metabolizatori. Funkcija SERT (5-HTTLPR) najčešće je bila normalna ili snižena. Eksploratorna analiza Fisherovim egzaktnim testom pokazala je nominalnu povezanost između CYP2B6 i mučnine, CYP2C19 i omaglice te CYP2B6 i suhoće usta. Zaključak: Integracija PGx profila i PRO ishoda omogućuje individualizaciju pristupa propisivanju antidepresivne terapije, smanjujući potrebu za propisivanjem metodom „pokušaja i pogreške“. Istraživanje je financijski podržano projektom *Artificial Intelligence for Personalised Medicine in Depression – ArtiPro* (ERA PerMed).

amine patients' perceptions of the effectiveness and safety of antidepressant therapy and to explore the association of pharmacogenetic (PGx) variants with reported treatment outcomes and adverse effects. Materials and methods: The study included 123 psychiatric patients who completed a questionnaire on current symptoms and possible adverse effects of antidepressant therapy. Pharmacogenetic (PGx) profiles (ABCB1, ABCG2, COMT, CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, CYP3A4/5, and SERT) were available for 49 patients, and their association with treatment outcomes and reported adverse effects was additionally analyzed. Results: Among the 49 patients, sertraline was the most commonly prescribed antidepressant (85.7%), followed by escitalopram (8.2%). Most patients received combination therapy (81.6%). The most frequently reported adverse effects were nausea (51.0%), dizziness (10.2%), and dry mouth (8.2%). CYP2C19 phenotypes were predominantly rapid or normal metabolizers, while CYP2D6 and CYP2B6 were most often normal or intermediate metabolizers. SERT (5-HTTLPR) function was most commonly normal or reduced. Exploratory analysis using Fisher's exact test showed a nominal association between CYP2B6 and nausea, CYP2C19 and dizziness, and CYP2B6 and dry mouth. Conclusion: Integration of PGx profiles and PRO outcomes enables an individualized approach to prescribing antidepressant therapy, reducing the need for "trial-and-error" prescribing. The study was financially supported by the project *Artificial Intelligence for Personalised Medicine in Depression – ArtiPro* (ERA PerMed).