UTILITY OF MOLECULAR DIAGNOSTIC TOOLS IN IMPROVING PERSONALIZED DOSING OF PSYCHIATRIC DRUGS.

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Determining the correct dose, with the aim to achieve optimal exposure, is very important in psychiatric clinical practice, since underexposed patients are less likely to respond to treatment and since adverse drug reactions likelihood and severity is increased in overexposed patients. CYP2C19 and CYP2D6 enzymes metabolize majority of psychiatric drugs and their genetic polymorphism determines patient's metabolic capacity. The aim was to evaluate the clinical utility of therapeutic drug concentration monitoring and preemptive CYP genotyping. Several retrospective and prospective cohorts of patients, with known CYP genotype and drug levels, were analyzed with the aim to evaluate the association between CYP2C19 and CYP2D6 metabolizer categories on drug exposure, efficacy, and tolerability. Based on 4,700 patients, currently available CYP2D6 metabolizer categorization is not correct and it needs revisions (1). Based on data from 8,379 patients, clinically relevant changes in escitalopram and sertraline exposure are detected in CYP2C19 slow metabolizers, while clinically relevant changes in aripiprazole and risperidone exposure are detected in CYP2D6 slow metabolizers (2). Under standard dosing, almost a half of patients treated with these four drugs are not exposed to optimal drug levels. Since such a substantial amount of patients is wrongly dosed for these four drugs, therapeutic drug monitoring of blood concentration, appropriate metabolizer categorization, and pre-emptive CYP genotyping can improve treatment outcomes for these drugs.

References

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UNAPREĐENJE PERSONALIZACIJE DOZIRANJA PSIHIJATRIJSKIH LEKOVA UZ POMOĆ MOLEKULARNE DIJAGNOSTIKE.

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Utvrđivanje tačne doze leka, sa ciljem da se postigne optimalna izloženost leku, je veoma važna u psihijatrijskoj kliničkoj praksi, zato što subdozirani pacijenti lošije odgovaraju na lek, a predozirani pacijenti bivaju izloženi neželjenim efektima češće i neželjeni efekti su intenzivniji. CYP2C19 i CYP2D6 enzimi metabolišu većinu psihijatrijskih lekova i genetski polimorfizam na odgovarajućim genima određuje metabolički kapacitet pacijenta. Cilj je bio da se oceni klinička korisnost terapeutskog praćenja koncentracije leka i genotipizacije CYP gena. Nekoliko retrospektivnih i prospektivnih kohorti pacijenata, sa poznatim vrednostima koncentracije leka i CYP genotipom su analizirani sa ciljem evaluacije i kvantifikacije uticaja CYP2C19 i CYP2D6 metaboličkih kategorija na izloženost psihijatrijskim lekovima, kao i na efikasnost i sigurnost terapije ovim lekovima. Na osnovu podataka dobijenih na 4.700 pacijenata, trenutno važeća klasifikacija CYP2D6 metaboličkih kategorija nije tačna i potrebno ju je izmeniti (1). Na osnovu podataka dobijenih na 8.379 pacijenata, klinički značajne promene izloženosti escitalopramu i sertralinu su primećene kod CYP2C19 sporih metabolizera, dok su klinički značajne promene izloženosti aripiprazolu i risperidonu primećene kod CYP2D6 sporih metabolizera (2). Pod standardnim doznim režimom, gotovo polovina pacijenata nije izložena optimalnoj koncentraciji ova četiri leka. Budući da je značajan broj pacijenata pod terapijom pogrešnom dozom ova četiri leka, terapeutsko praćenje nivoa leka u krvi, adekvatna kategorizacija metabolizera i CYP genotipizacija pre početka terapije mogu da poboljšaju ishod terapije ovim lekovima.

Literatura

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