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Meagan Shields - University of Calgary

Project: Pharmacogenetic-guided prescribing of selective serotonin reuptake inhibitors in adolescent depression and anxiety

Background:

Depression and anxiety are the second and third causes, respectively, of non-fatal disability among adolescents. Untreated depression and anxiety among youth can have longstanding impacts on educational attainment, substance use, suicidality, and role functioning. Management of these mental disorders include behavioral interventions (e.g., psychotherapy) and medication-based management with selective serotonin reuptake inhibitors (SSRIs). While most SSRIs (fluoxetine, escitalopram, citalopram, sertraline, fluvoxamine) have evidence to support their guideline-based role in treatment of moderate to severe depression and anxiety in adolescents, interindividual response varies greatly. Only 50-66% will respond to medication treatment with SSRIs, while nearly half of people will also experience adverse drug reactions that may result in poorer quality of life and treatment discontinuation. Unfortunately, these medications may also take weeks to determine treatment effects - generally 4-8 weeks for depression, and up to 12 weeks for anxiety – prolonging the time it takes youth to find an effective medication option. Some differences in medication response may be attributed to variability in genes that encode drug metabolizing enzymes, transporters, or receptors – this is referred to as pharmacogenetics (PGx). Trials in adults, pharmacokinetic data, and observational studies in pediatrics suggest that clinical outcomes may be improved with genotype-guided prescribing of SSRIs in adolescent depression and anxiety. This approach uses drug metabolism phenotypes for the enzymes *CYP2B6, CYP2C19*, and *CYP2D6*, determined though genotype analysis of an at-home saliva test. Evidence-based guidelines for PGx-guided prescribing are available from organizations such as the Clinical Pharmacogenetics Implementation Consortium (CPIC) and are intended for use in with other clinical practice guidelines (e.g. the Guidelines for Adolescent Depression in Primary Care; GLAD-PC).
My dissertation research is a randomized control trial that will evaluate PGx-guided prescribing of SSRIs, compared to usual care in adolescents with depression and anxiety disorders. In this trial,

adolescents ages 12-17 years will be randomly assigned to either PGx-guided prescribing, or standard guideline-based (non-genetic) prescribing. These interventions will be facilitated by identically formatted medication reports based on either CPIC (genetic) or GLAD-PC (non-genetic) guidelines sent to the prescribing doctor. The primary outcome of this efficacy trial will be treatment remission after 12 weeks of medication therapy. Secondary outcomes include overall symptom change and medication burden. This trial will provide evidence on the impact of PGx testing among adolescents prescribed SSRIs.

BIO

I am a pharmacist and clinician-scientist in-training at the University of Calgary, in my second year of PhD studies supervised by Drs. Chad Bousman and Mandi Newton (University of Alberta). My dissertation is focused on the use of pharmacogenomics (PGx) in adolescent mental disorders. Broadly, my research interests include PGx implementation, clinical trials of other novel health interventions, and the roles of pharmacists in health care models. I was inspired to pursue patient-oriented research after years of pharmacy practice, with a desire to have a broader impact on health outcomes than I could have as an individual clinician. This led me to complete my MSc. in Pharmacy Practice at the University of Alberta in 2022 under Dr. Sherif Mahmoud, where I studied PGx models in pharmacy practice, implementation methods, and pharmacist training in PGx. I continue to practice as a pharmacist part-time with the Poison and Drug Information Service (PADIS; Alberta Health Services) to maintain my clinical skills. Outside of research and pharmacy roles, I love running, hiking, skiing, cycling, and anything active!


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