FRAMEWORK FOR A MANUSCRIPT SUBMITTED TO THE WORLD CONGRESS OF PHARMACOVIGILANCE AND DRUG SAFETY

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RESEARCH TOPIC

The relationship between certain pharmacogenes and SSRI-induced adverse drug events among patients in an era of COVID-19.

PROBLEM STATEMENT:

The Food and Drug Administration (FDA, 2018) stated that 125,000 people die annually because of complications arising from adverse drug reactions. Adverse drug reaction is a leading cause of death in the United States (Wester et al. 2008). The problem is worthy of a solution because the loss of human lives can hurt a family, community, and country. Antidepressants are the third most commonly prescribed medications in the United States, of which Selective Serotonin Reuptake Inhibitors (SSRI's) are a significant class (Fuentes et al. 2018). Some frequent adverse drug events associated with SSRI's include insomnia, nervousness, restlessness, headache, dry mouth, and sexual dysfunction (Lucire& Crotty, 2011). These adverse effects sometimes lead to discontinuation of the drug, prolonged illness, and sometimes death.

The emergence of the novel strain of coronavirus (COVID-19) has influenced our approach to research, pharmacotherapy, and patient outcome. For example, coronavirus impacts how the human body metabolizes drugs, including antidepressants (Streetman, 2020). Specifically, coronavirus affects immunological and hematological systems such that some patients will metabolize drugs quite differently. Hence, it is needful to know how pharmacogenomics can help patients and health providers in selecting the most appropriate drug and dose for vulnerable patients.

SIGNIFICANCE

This study is significant because a well-guided selection of drugs for therapy will minimize the likelihood of an adverse drug reaction. Antidepressants currently have a myriad of side effects and potential adverse drug reactions. There is a possibility of more adverse drug reactions in patients with COVID-19.

SUMMARY OF EXISTING FINDINGS

Several studies support the fact that some genes influence antidepressants' outcomes (Altar, Hornberger, Shewade, et al. 2013). Such genes include CYP2D6, CYP2C19, CYP2C9, CYP1A2, CYP3A4, HTR2A, and SLC6A4. Also, different people metabolize drugs in different ways (Solomon, Cates & Li, 2019). Likewise, Streetman (2020) suggests that coronavirus could impair the metabolism of antidepressants in humans regardless of existing variables that undermine the relationship between specific genes and antidepressant-induced adverse drug events.

.TYPE OF STUDY

We plan to use a secondary dataset for this quantitative study. We propose a case-control study. The cases will be COVID-19 survivors who experienced adverse drug reactions, including insomnia, after taking specific antidepressants. The controls will comprise of COVID-19 survivors who did not experience adverse drug reactions but received the same antidepressant drug. The proposed dataset is the Mayo Clinic Genetic Dataset. The sample size for the study will be representative of the United States in as many ways as possible. The study will characterize the clinical (disease states), demographics (age, sex, and race) as well as the genetic characteristics of the cases and then compare them with the controls. The genetic biomarker of interest in these patients will be cytochrome P450 genes and serotonin transporter genes. These genes include CYP2D6, CYP2C19, CYP2C9, CYP1A2, CYP3A4, HTR2A, and SLC6A4. We chose these biomarkers because the literature suggests that the biomarkers are associated with adverse drug events when patients take SSRI antidepressants.

RESEARCH QUESTIONS

1. What is the relationship between age and SSRI-induced adverse drug events among COVID-19 survivors?

2. What is the relationship between sex and SSRI-induced adverse drug events among COVID-19 survivors?

3. What is the relationship between race and SSRI-induced adverse drug events among COVID-19 survivors?

4. How does the use of pharmacogenetics testing for specific genetic biomarkers vary among COVID-19 survivors who experience adverse drug events due to SSRI's?

DEPENDENT VARIABLE

Our proposed dependable variable is "SSRI-induced adverse drug event." This variable will be identified by the presence of relevant ICD-10 code in the Mayo Clinic dataset. The ICD-10 codes include those for insomnia, sexual dysfunction, nervousness, restlessness, headache, and dry mouth.

INDEPENDENT VARIABLE

Our proposed independent variable will be the presence of pharmacogenes such as CYP2D6, CYP2C19, CYP2C9, CYP1A2, CYP3A4, HTR2A, and SLC6A4. This variable will be identified through the medical records and existing protocol of the hospital and attending physician.

COAVARIATES

The proposed covariates in this study include age, sex, race, geographical location, and socioeconomic status.

DATA ANALYSIS PLAN

The variables in the data will be analyzed with logistic

regression. The aim is to understand the relationship between the dependent and independent variables, as discussed earlier. The result of this study will be ready by the end of 2020.

References

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