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Outcomes in Treatment of Major Depressive Disorder: Pharmacogenomic Testing vs. Treatment as Usual

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Abstract

- The goal of this scholarly project was to evaluate the efficacy of pharmacogenomic testing (PGx) versus treatment as usual (TAU) in the treatment of major depressive disorder (MDD). According to Huang & Lin (2015), MDD is characterized by multiple signs and symptoms consisting of mood, vegetative, cognitive, and even psychotic behaviors that may cause substantial impairment in the functioning and quality of life in an affected individual. This literature review consisted of articles found in PubMed, Cochrane, and PsychINFO which were extensively reviewed. Articles prior to 2008 were excluded due to the ever-changing landscape of PGx testing. In this review, 18 articles and studies were analyzed. This review found favorable outcomes when treatment was guided by PGx versus TAU while examining response and remission rates. Although data varied, cost effectiveness suggested some positive results with PGx although further investigations are needed due to limitations and lack of studies. Despite many favorable outcomes, more evidence of the effectiveness of PGx is needed to make a concrete recommendation that PGx guided treatment is superior to TAU. Information in this review will help clinicians decide if this is an appropriate option for the treatment of MDD. With continued research and ongoing studies this biotechnology is becoming more available to the mainstream.
- *Terms and mesh headings: depression, major depressive disorder, pharmacogenomics, pharmacogenetics, treatment as usual, pharmacotherapy, medication, selective serotonin reuptake inhibitors, antidepressant, psychiatry and Patient Health Questionnaire (PHQ-9)*

Introduction

- According to the Diagnostic and Statistical Manual of Mental Disorders (5th ed.; DSM-5; American Psychiatric Association, 2013), “major depressive disorder (MDD) is characterized as a serious illness that causes a person to feel deeply sad (or wholly absent of feeling) most of the day, nearly every day, for at least two weeks” Depression is the leading cause of disability in the United states with an average of 400 million disability days each year. According to Greenberg at al. (2015), this is a much higher number than other mental and physical conditions.
- Pharmacogenomics is the study of how genes affect an individual’s response to medications. Pharmacogenomic testing can be utilized to see what medications may be the most effective for a patient with the least amount of side effects. Though the utilization of PGx appears beneficial in choosing a medication tailored to a patient’s specific genes, the clinician should continue to keep age, lifestyle, side effects, cost, and comorbid factors in mind while using pharmacogenomics. MDD continues to be a significant health condition that impacts people regardless or devoid of age, race, or gender. Comorbidities are often associated with depression which can make appropriate management difficult. The goal of the clinician is to treat these patients with the best possible medication choice while mindful of side effects, cost, and outcomes.
- This project focused on medication management rather than other treatment modalities. Treatment as usual (TAU) with medication management is usually based on practice guidelines and the clinicians own experience with certain medications that they believe will help control current symptoms. The purpose of this article is to evaluate whether PGx demonstrates improved clinical outcomes compared to TAU.

Statement of the Problem

- Treatment of depression remains a difficult issue in primary care as well as psychiatric medicine. Many of these patients require multiple medication trials prior to finding a drug that works to control their symptoms without causing unfavorable side effects. This process may cause prolonged suffering with depression as well as a decrease in quality of life and productivity. The cost and time strain of attempting multiple medications continues to be a burden on the patient as well as the medical community.
- Studies on pharmacogenomic testing for MDD are needed to demonstrate which medications may have higher efficacy and lower cost for both the patient and health care community. Medications are uniquely metabolized based on multiple genetic variants which pharmacogenomic testing can help identify. One consideration to remember while reviewing these finding is that many medications are not able to be analyzed with metabolism and genetic variances at this time, therefore only medications included in the pharmacogenomic testing databases are explored.

Research Question

- In patients with MDD, are medications guided by pharmacogenomic testing in the treatment of MDD more effective in achieving response and remission of symptoms compared with TAU based on depression assessment scales?
- In patients with MDD, does medication management guided by pharmacogenomic testing improve cost effectiveness in the management of disease compared to TAU?

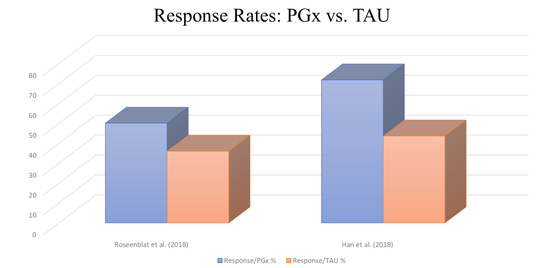
Literature Review

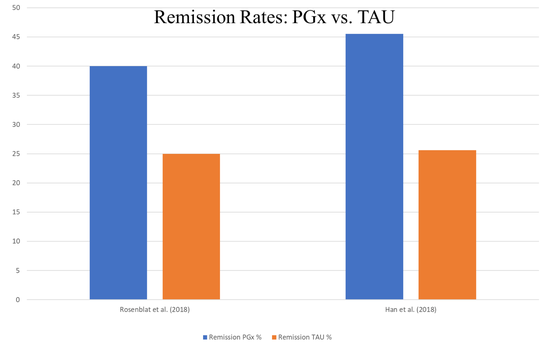
Pathophysiology of Major Depressive Disorder

- The Diagnostic and Statistical Manual of Mental Disorder (5th ed.; DSM-5; American Psychiatric Association, 2013) is widely used by clinicians and researchers alike to classify specific mental disorders. According to the DSM-V, major depressive disorder (MDD) is diagnosed by having five out of the following nine symptoms. Depressed mood most of the day which occurs nearly every day, diminished interest or pleasure in almost all activities, significant weight loss categorized as 5% of body weight in a month, insomnia or hypersomnia, psychomotor agitation or retardation, fatigue or loss of energy, feelings of worthlessness or excessive inappropriate guilt, diminished ability to think or concentrate, or recurrent thoughts of death/suicide or suicide attempt. Five of these nine symptoms must be present nearly every day, during a two-week time frame. These symptoms need to cause significant stress with social and occupational impairment. Also, these episodes may not be attributable to the physiologic effects of a substance or another medical condition (American Psychiatric Association, 2013).

Pharmacogenomic testing to aid in the treatment of MDD

- In the meta-analysis performed by Rosenblat, Lee, and McIntyre (2018), the authors focused on response and remission rate of MDD based on TAU and PGx guided treatment. The PGx group had a response rate of 50% compared to the unguided group at 36%. The pooled relative risk (RR) for treatment response comparing guided versus unguided treatment was 1.36 or a 95% confidence interval in favor of guided treatment and a (p=0.0006). The pooled RR for remission was 1.74 or 95% confidence interval and a (p=0.02) which demonstrates statistical significance. The remission rates of the guided treatment group were 40% when compared to the unguided group at 25%, respectively.





Cost Effectiveness of Pharmacogenomic Testing

- In a study by Benitez, Cool, and Scotti (2018), the authors evaluated administrative claims by health plan members who were treated for psychiatric conditions with PGx vs. TAU. These included prescriptions, office visits, inpatient, and outpatient services. A major healthcare insurance provider which consisted of over 25 million members was used. Payments were evaluated for 24 months, pre and post treatment. Although only records were reviewed, plan member records evaluated had to be at least 18 years old and on a commonly prescribed psychotropic medication starting within the past 180 days and without other known history of psychotropic medication use. These could be members who received TAU or PGx. Statistical significance was evaluated by measuring the pre and post treatment cost controlling demographics and comorbid conditions. They analyzed 205 members treated by PGx and 478 with TAU. There was no significant difference in the cohorts when age and gender were observed. Although over the period studied the healthcare costs in both groups did rise, the TAU increase was higher at $23,132 versus $17,627 (p=0.0004). The cost of the PGx test was taken into consideration during these analyses. It was noted that the reduced spending was mostly saved by a decrease in outpatient services received.

Discussion

- Studies have shown some promise in the use of pharmacogenomic testing for the treatment of MDD. MDD may affect a person in many different aspects of their life whether it be emotionally, physically, or financially. As the use of pharmacogenomic testing in the treatment of MDD continues to be explored, the very complicated disease process of MDD that may stem from multiple variances in genes must be considered. After reviewing the literature, the use of PGx may have a positive impact in the treatment of MDD when compared to TAU. As advances continue, this will help guide treatment and reduce the cost associated with the treatment and management of MDD.

Applicability to Clinical Practice

- As we strive to make mental health topics less taboo, the treatment of these diseases will surely increase. With new advances such as PGx, guided treatment will continue to be evaluated and hopefully show positive outcomes for those suffering from such conditions.
- Treatment of MDD can be quite challenging whether it be by psychiatry or family medicine. Being able to review an individual’s genetics and how they may react and/or metabolize a drug should eliminate time and cost while improving the patient’s mental health. Many of these studies show that utilizing PGx has shown greater improvement in depression rating scores, less cost associated with treatment, and improved quality of life.
- Exploring and testing the effects of BDNF, cortisol, inflammatory markers, and Vitamin D levels have revealed some common links between a person’s overall health and MDD. As PGx continues to evolve it is likely that we will see more studies evaluating the CYP450 system to better understand the metabolism of many of these drugs. As some insurance companies are now covering some or all costs of these tests, it is presumed that they will become more readily available and providers will receive proper education on the utilization of PGx.

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