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Pharmacogenetic Testing in the Treatment of Major Depressive Disorder

Brianna Strube
University of North Dakota

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Brianna Strube, PA-S
Department of Physician Assistant Studies, University of North Dakota School of Medicine & Health Sciences
Grand Forks, ND 58202-9037

Abstract

- Major depressive disorder (MDD) is one of the most prevalent psychiatric disorders in the United States and is a large cause of disability. Antidepressants take weeks/months to become effective which can lead to noncompliance. Treatment has a high failure rate which increases medical costs and leads to decreased patient outcomes.
- Pharmacogenetic testing is the practice of analyzing genetic differences to predict a patient's response to medications to improve efficacy and decrease adverse side effects. The purpose of this study was to investigate if pharmacogenetic-guided treatment, specifically in the use of antidepressants in MDD, has resulted in improved patient outcomes. Additionally, the cost effectiveness was also analyzed.
- The review of literature was conducted by systematically searching the online databases PubMed and PsycINFO, and explored studies that compared the current standard of care to pharmacogenetic-guided treatment in adult patients with MDD aged 18-75.
- The results indicated improved compliance and prognosis for patients with MDD using pharmacogenetic-guided treatment versus the current standard of care. Studies also showed cost effectiveness of pharmacogenetic-guided treatment by decreasing medical costs by having fewer clinic visits, less changes in prescriptions, less sick leave taken, and decreased hospital costs.

Introduction

- There is variability in the pathophysiology of depression and not all details are known. Despite recent advances in the use of antidepressants, interindividual variability to treatment remains a serious problem. As patients continue to fail medication regimens, the likelihood of responding to subsequent treatment decreases to 18%. Furthermore, depression has one of the highest instances of mortality from suicide.
- Pharmacogenetic testing has been developed to test a set of preselected psychiatric genes to provide a composite phenotype and accompanying interpretative report. By predicting the drug response of an individual, it may be possible to increase the success rate of antidepressant use and reduce the incidence of adverse side effects.

Statement of the Problem

Major depressive disorder is associated with a high prevalence of therapeutic failure, adverse side effects from medications, and a high recurrence rate. Response to antidepressants take an extended length of time which leads to noncompliance and increased medical costs due to additional follow-up visits and prescription costs.

Research Questions

- **In adult patients with a diagnosis of major depressive disorder, does utilizing pharmacogenetic testing to determine antidepressant use result in improved patient outcomes?**
- **Is pharmacogenetic testing for the patient with major depressive disorder cost effective?**

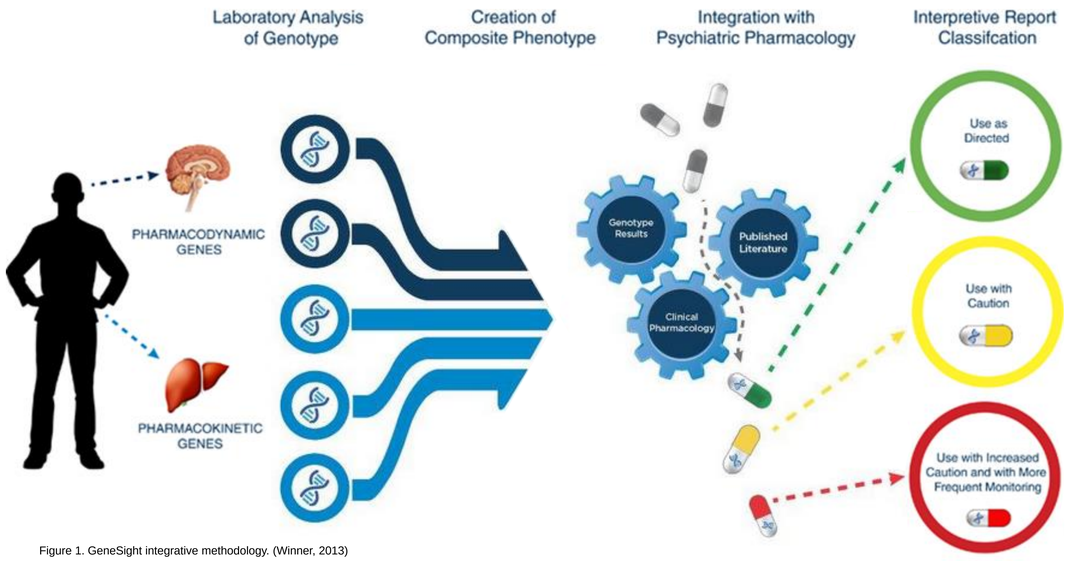

Figure 1. GeneSight integrative methodology. (Winner, 2013)

Literature Review

- Altar et al. (2015) found subjects who entered the study on red category medications showed 61.5% less improvement in depressive symptoms over 8–10 weeks compared with those prescribed yellow (t = 3.15; P = 0.002), green (t = 2.22, P = 0.02) or yellow ± green category medications (t = 2.97, P = 0.003).
- Hall-Flavin et al. (2013) found the pharmacogenetic guided group experienced greater percent improvement in depression scores from baseline on three depression instruments (HAMD-17, P < 0.0001; QIDS-C16, P < 0.0001; PHQ-9, P < 0.0001) compared with the unguided group. Using repeated measures analysis for all participants who completed the 8-week study, a greater reduction of symptoms was observed for guided group participants compared with unguided group participants for HAMD-17 (P < 0.001), QIDS-C16 (P < 0.001), and PHQ-9 (P = 0.002) (Figure 2). Significantly greater response rates (i.e. >50% reduction in score from baseline) were found in the guided group versus the unguided group at week 8 as determined with QIDS-C16; 44.4% of participants in the guided group responded versus 23.7% in the unguided group. HAMD-17 and PHQ-9 showed nearly identical results.
- Winner et al. (2013) determined that the likelihood of response and remission was greater than double in the GeneSight guided group measured by HAMD-17 at week 10. Mean percent improvement in symptoms on HAMD-17 was higher for the GeneSight group over treatment as usual (30.8% vs 20.7%; p=0.28).
- Singh (2015) found that subjects receiving genetically guided prescribing had a 2.52-fold greater chance of remission (p<0.0001).
- Fagerness et al. (2014) found that individuals with assay-guided treatment were significantly more medication adherent (P = 0.002) than patients with standard treatment and demonstrated a relative cost savings of 9.5% in outpatient costs over a 4-month follow-up period, or $562 in total savings.

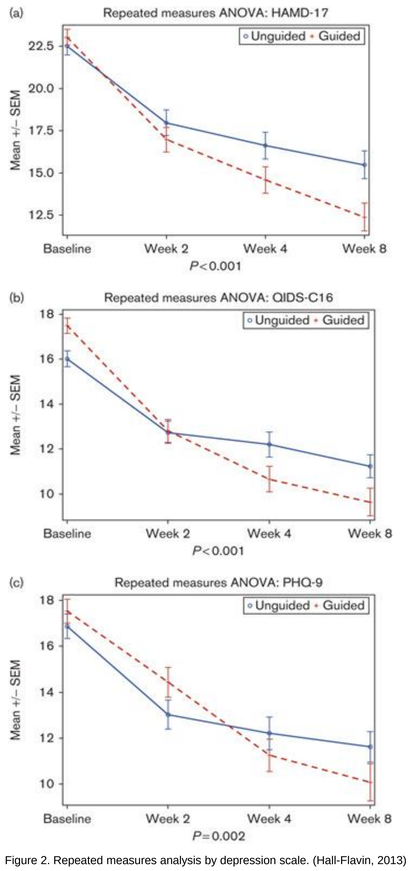

Figure 2. Repeated measures analysis by depression scale. (Hall-Flavin, 2013)

Discussion

In summary this research found

- **Pharmacogenomic-guided treatment has shown effectiveness and improved patient outcomes when compared to the current standard of treatment.**
- **The utility of this genetic information as it pertains to clinical decision making, treatment effectiveness, and cost savings has shown benefit for patients with moderate to severe depression who have failed prior treatment.**
- **Pharmacogenetic testing provides significant cost savings, while simultaneously improving adherence in a difficult to treat psychiatric population. Patients who had pharmacogenetic-guided treatment had improved outcomes in addition to decreased cost to the patient by having fewer clinic visits, less changes in prescriptions, lessened and shorter sick leave taken, and decreased hospital costs.**

Applicability to Clinical Practice

- As a newer topic in the medical field, efforts are needed to improve clinicians' knowledge of pharmacogenetic testing in order to facilitate its successful integration into clinical practice.
- Pharmacogenetic testing can aid in directing treatment towards a more effective approach.
- Medicare Part B and Veterans Affairs cover pharmacogenetic testing if deemed medically necessary.
- Pharmacogenetic testing is a relatively new concept, but has been proven to have advantages over the current treatment of MDD. It offers providers an effective resource to provide improved outcomes for patients with MDD requiring pharmacotherapy.

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