Data Studio

1:00–2:30pm, Wednesday, 18 November 2020
Videoconference:
https://stanford.zoom.us/j/98567770260?pwd=QlA4MEJVeVZXZTF1RjhGSHVNR2FNQT09
Password: 489313

Investigator: **Hector Fabio Bonilla** Medicine/Infectious Diseases

Title: The Impact of Aripiprazole on Chronic Fatigue Syndrome

Summary:

The Data Studio Workshop brings together a biomedical investigator with a group of experts for an in-depth session to solicit advice about statistical and study design issues that arise while planning or conducting a research project. This week, the investigator(s) will discuss the following project with the group.

Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) is a chronic, debilitating illness of unknown etiology. An ME/CFS diagnosis is based solely on symptoms with case definitions made by expert consensus. According to the most recent Institute of Medicine (2015) case definition, the core symptoms of ME/CFS include debilitating fatigue, unrefreshing sleep, post-exertional malaise, and cognitive dysfunction or orthostatic intolerance. Up to 85% of patients with ME/CFS report cognitive impairment symptoms which include difficulty with memory, attention, and information processing.

Although the cause of the illness is unknown, a growing body of evidence suggests that ME/CFS involves inflammation of the brain which includes changes in inflammatory cytokines in both plasma and cerebrospinal fluid correlated with the severity of symptoms. Studies using positron emission tomography (PET) show evidence of activated microglia or astrocytes in various regions of the brain in ME/CFS patients.

Dopamine D2 receptor agonists have been shown to mediate neuroinflammation, microglial activation, and cell death in animal models and humans (4-6). This suggests that dopamine-modulating drugs may lead to clinical improvement in fatigue and cognitive symptoms in ME/CFS. Given the lack of approved drugs for treating this condition, we are interested in exploring the potential benefit of low doses of Aripiprazole.

In a retrospective study, we reviewed the medical records of 101 patients who met the criteria for an ME/CFS diagnosis according to three separate case definitions (Fukuda, CCC, and IOM) and who received off-label Aripiprazole. Medical records were included for individuals evaluated in the clinic at least twice, representing periods before and after the use of the medication. The age range was from 18 to 84 years old (mean 51 y), with a gender distribution of 67% female and 33% male, and the duration of illness was from 1 to 54 years (median 10 years). The daily oral dose of Aripiprazole ranged from 0.2-2.0 mg/day (mean 0.94 mg/day). During each clinic visit, patients were asked to rate their symptoms on a scale of 0-10.

Of the 101 patients taking Aripiprazole, 75/101 (74%) experienced an improvement in one or more categories: fatigue, brain fog, unrefreshing sleep, and frequency of post-exertional malaise (PEM) episodes. Twelve individuals (12%) had no observable difference in symptoms at the maximum dose of 2 mg, and 14 individuals (14%) reported worsening of symptoms or onset of side effects that led to discontinuation of the drug. These results suggest that Aripiprazole may effectively reduce symptoms of ME/CFS and warrants further investigation in a randomized clinical trial.

Questions:

1. Is this the best study design to address the efficacy of Aripiprazole on patients with ME/CFS?
2. How can we select the appropriate dose of Aripiprazole to use in the study? In our retrospective study, the dose to which the patients responded ranged from 0.25-2 mg, and the mean was 1 mg.
3. Are there other techniques to assess fatigue (efficacy of Aripiprazole)?
4. What would be an acceptable sample size to reach statistical significance?
5. What type of statistical methods will be used for the analysis?
6. Based on available data, can one define a clear-cut inclusion/exclusion criterion that eliminates the risk of underlying depression being the cause of drug effect?
7. If not, then how can one modify the trial protocol and statistical analysis plan to measure the confounding effect depression as comorbidity?

Zoom Meeting Information

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Join from PC, Mac, Linux, iOS or Android:
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For more information about Data Studio:

http://med.stanford.edu/dbds/resources/data-studio.html