Research programming - pharmacogenomics

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KEYWORDS

pharmacogenomics, biomarkers, psychotropics

Over the past few years, collaboration between the CPNP Research and Program Committees has resulted in high quality, membership driven research programming at the Annual Meeting. Input is requested from all CPNP committees but this collaboration, in particular, has led to the development of focused programming fulfilling a need for members who either work primarily in a research setting or want to keep abreast of the ever-changing field of psychopharmacology research. One of the logistical difficulties of this type of collaboration is the CPNP programming timeline. It is not long after the Annual Meeting that the following year's offerings are being determined. With the focus of both committees and commitment to excellence in programming, this project has been a great success. The collaboration has led to a two hour track of programming ranging from 'Incorporating Health Services Research into Practice' to this past year's 'Pharmacogenomics for the Neuropsychiatric Pharmacist'. As the offerings are many at the Annual Meeting, CPNP thought a brief review of what was discussed in this most recent two hour track was in order for all members.

A PRIMER

During the first hour of the two hour track, Dr. Jeffrey R. Bishop from the University Of Illinois College Of Pharmacy gave a thorough primer to help the audience better understand the sources of genetic variability and how they might contribute to drug outcomes in psychiatry. Additionally, common study designs used in pharmacogenomics studies were reviewed. A well-organized review of definitions, background and nomenclature set the stage for a discussion of genetic variation as it relates to SNPs, gene expression and genotyping technologies. The various study designs reviewed included cross sectional studies, post hoc analyses of DNA collected from clinical trials and effective/pragmatic clinical trials. Examples of these studies included carbamazepine-associated hypersensitivity, olanzapine treatment response related to genetic variability in the type-3 metabatropic glutamate receptor gene and warfarin/clopidigrel, respectively. Examples of scientific advances related to genome-wide association studies in psychopharmacology were also reviewed.

Additionally, Dr. Bishop discussed the dramatic increase over the last 25 years of drug labeling that mention human genomic biomarkers as well as labels with pharmacogenomics information included in boxed warnings, warnings, dose/administration and drug interactions. Much of this increase relates specifically to medications used in psychiatry with 26 of 105 labels referring to pharmacogenomics biomarkers and 22 of 65 labels referring to the other pharmacogenomics information listed above involving psychiatric medications.

PHARMACOGENOMICS IN PRACTICE

Dr. Daniel Mueller, Associate Professor at the University of Toronto and Head of the Pharmacogenomics Research Clinic Centre for Addiction and Mental Health followed Dr. Bishop with a discussion of the work his group has conducted analyzing liver gene variants to assess poor or rapid metabolizer status in order to help predict dosage and response, as well as avoid side effects of antipsychotics and antidepressants. It is the struggle to find maximum response with minimum side effects that is the main goal of Dr. Mueller's pharmacogenomics lab.

Much of his work centers on CYP2D6 and CYP2C19 activity status. He first reviewed a study evaluating OCD patients who were treated with a variety of antidepressants and then evaluated by chart review for response (using the Clinical Global Improvement (CGI) scale) and additionally were evaluated for 2D6 metabolizer status. He observed that impaired CYP2D6 metabolizer status was significantly associated with non-response in this population. He presented specific cases from the study of patients who, given their metabolizer status a priori, might have led to a better treatment choice earlier in therapy. He then reviewed a survey study that his clinic performed to evaluate provider and patient acceptance of genotyping services. Metabolizer status was determined for both CYP2D6 and CYP2C19 metabolizer frequencies and recommendations were given based on genotype, as would be done in clinical practice. Physicians reported that the information was useful, they and their patients were satisfied with the service and that they believed that genetic testing would become common in psychiatric drug treatment.

Finally, Dr. Mueller turned his attention to the pharmacogenetics of antipsychotic-induced weight gain. He discussed a review of studies that found a strong correlation between a 5HT2C-759C/T polymorphism and increased weight gain among patients receiving an antipsychotic. He also described work his lab has done studying the effect of Neuropetide Y (NPY), one of the most potent orexigenic peptides. Specifically, a combined analysis of three gene variants (SNP rs16147, rs5573 and rs5574) was significantly associated with antipsychotic-induced weight gain.

The presentations from Drs. Bishop and Mueller highlighted the importance of pharmacogenomics in psychiatric pharmacy practice, providing a thoughtful review of pharmacogenomics principles and exciting research in this ever-growing field. For those who would like to hear the presentations in their entirety, look for future notification of their availability at CPNP University via your CPNP Weekly Updates.

How to cite this editor-reviewed article
Overman J. Research programming - pharmacogenomics. Ment Health Clin [Internet]. 2012;1(12):305-6. Available from: http://dx.doi.org/10.9740/mhc.n109224