



Pharmacomicrobiomics: Another Contributor of Inter-Individual Variations To Drug Response

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INTRODUCTION

Gut-brain axis is now a commonly discussed concept in a variety of clinical contexts, including its well-known importance in neuropsychiatric disorders. Gut microbiota is a diverse population of microorganisms containing bacteria, yeast, protozoa, parasite, helminth, viruses, etc. However, the bacterial population among the above group is most well-characterized as of now. This gut microbiota is considered a vital organ in itself. The number of cells in microbiota outnumber human body cells by 1.3:1.1 This gut microbiota has been implicated to contribute to a variety of functions in the host, including metabolism, immunity, and brain functions like mood, memory, and behavior among several others. The genetic material inside our body is 99% of gut microbiota in comparison to human genes. The human genetic material is stable throughout our life span. However, the genetic material of gut microbiota is dynamic and changes rapidly in response to a variety of external stimuli like age, diet, sleep, stress, exercise, general health condition, consumed medications, etc. Perturbations in gut microbiota have been shown to influence multiple health conditions like metabolic disorders, gastrointestinal diseases, immune-related dysfunctions, cancers, depression, and several other mental disorders.

It has been known for a long time that the consumption of antibiotics can alter the gut microbiota negatively and has consequences on health. However, recently, it was reported that other medications like proton pump inhibitors, metformin, etc. change gut microbiota composition and function, which can impact health status or drug efficacy.²

Personalized medicine is a practice of medicine that uses a person's genetic data to guide the decision regarding prevention, diagnosis, treatment, and outcome. The response of medications in individuals differs greatly in efficacy, side effects, and toxicity. Interindividual differences in response to medicines not only compromises the safety and efficacy of medicines but also causes significant clinical and financial burden. These variabilities in response have been largely explained by pharmacogenetic and pharmacogenomic till now. It is reported that genetic factors can explain about 20–95% of the variability in drug responses.³ However, other factors contribute to this variability in responses.⁴

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The interaction of the gut microbiome and medications is one such factor that can contribute to the inter-individual variability in medication response and tolerability. The microbiome has been implicated in every step of the pharmacokinetics of the drugs like absorption, distribution, metabolism, and elimination. The drug-microbiome interactions are bi-directional, and effects are seen on the pharmacokinetics and pharmacodynamics of drugs as well as on the microbiota itself. Hence, pharmacomicrobiomics is the study of the direct influence of gut microbiota on an individual's response to a specific drug by either directly altering its chemical structure through enzymes, or altering its bioavailability, bioactivity, or toxicity. Additionally, gut microbiota can indirectly result in inter-individual variability of immune therapy in cancer treatment by influencing the host immune response.² Psychotropics have also been implicated in the bi-directional interaction of gut microbiota and drugs.

At the current stage of understanding, the practical application of pharmacomicrobiomics is

limited to theoretical constructs. Clinicians need to be aware of this emerging paradigm and its foreseeable practical implications. This is a new frontier for researchers. Developments are likely to be immensely useful across the medical discipline including mental health.

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