Will all drugs be prescribed with a pre/probiotic in future?

by: Dr Hamid Merchant

Our gut microbiota contains trillions of microorganisms, including at least 1000 different species of known bacteria with more than 3 million genes. The majority of drugs are still taken orally and we know that drug response varies significantly between individuals. We also see differences in the type and the magnitude of adverse effects that people observe from the same medication. This can be attributed to the likely interaction of drugs with microbiota during their voyage through the gut. A recent study from Zimmermann and colleagues in Nature examines the ability of gut microbiota to chemically modify drugs into super active or potentially toxic substances which may be the reason for the variability in response between individuals and the severe adverse effects observed in some. The gut harbours such a diversity of microbiota that it contains 150 times more microbial genes than the body's own genetic material. This consequently produces a bank of microbial enzymes in the gut which can potentially breakdown the chemical structure of drugs administered into the gut. The study investigated over 20 thousand drug-microbial interactions and studied over six thousand compounds produced by the microorganisms in the presence of a specific drug. The chemical modification of drugs by the bacterial enzymes lead to the activation of some drugs (for instance sulfasalazine) but also caused inactivation (e.g., digoxin) or even toxification of others (sorivudine/brivudine, irinotecan). It can be argued that drugs that are administered orally should have been absorbed from the upper gut and therefore will never arrive in the colonic region to interact with bacteria. However, the reality is that many drugs do not absorb fully from the small intestines and a significant fraction usually ends up reaching colon and hence interacts with the bacteria in most of the cases.

This new study has also identified some interesting drug targets for bacterial attack explaining that the drugs possessing a particular chemical group in their structure are most likely to be attached by a particular group of bacteria. This knowledge will be very useful for predicting the susceptibility of drugs to potential microbial attack. This could potentially enable rational strategies to manipulate an individual's gut microbiota in their favour to prevent the formation of undesirable drug by-products. To manipulate one's microbial profile, faecal transplants have been in use since long in parts of the world but was not received very well by the public as many people find this weird or disgusting. You may recall the story of 'Super poo donors' in the BBC news last year. Faecal transplantation has since been used in some NHS trusts to treat a type of chronic diarrhoea caused by a pathogenic bacteria called *Clostridium difficile* (the C. diff) in patients where the standard antibiotic treatment had failed.

Probiotics, on the other hand, contain millions of live 'good bacteria' which have been very popular in the food industry, the most common is the probiotic yoghurts. Their efficacy is often a major concern as most of the bacteria or their active metabolites will not survive the harsh acidic conditions of the stomach and may not reach alive or intact to the colon (the bottom of the gut). Some novel colonic delivery technologies such as Phloral™ have shown promising evidence in clinical trials that can be adapted to safely deliver desired probiotics to the colon.

Prebiotics, on the other hand, are substances which normally human gut cannot digest (like fibre) but are consumed by the 'good bacteria' and therefore promotes beneficial microbial population in the colon over the opportunistic harmful bacteria. Pre and/or probiotics can, therefore, alter the microbial profile of an individual's gut. Therefore, it is not impossible that in the future all drugs are prescribed with a form of pre and/or probiotics to improve the safety and efficacy of drugs tailored to the needs of the individual patients.