Genetic variation linked to drug-induced liver damage in some patients

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Credit: University of Nottingham

Scientists have discovered an uncommon genetic variation that may identify patients with a higher risk of liver damage associated with a range of commonly-prescribed medications.

The study, published in the journal *Gastroenterology*, has been led by academics at the universities of Nottingham and Newcastle in collaboration with a group of scientists in the US.

The results could lead to new advances in patient care, where doctors could tailor drug prescription to an individual based on their genetic make-up to reduce the risk of liver injury in the future.

Professor Guruprasad Aithal, of The University of Nottingham's School of Medicine, is Head of the National Institute of Health Research (NIHR) Nottingham Digestive Diseases Biomedical Research Unit and

was co-lead investigator on the study.

He said: "This work gives us a better understanding of how individuals' genetic background influences their susceptibility to adverse reactions leading to liver injury.

"This information may help us to identify those who are at risk and eventually help to develop safer medications in the future."

Adverse reaction

Most medicines given to patients to treat or prevent disorders will have a long list of potential side effects, while in reality less than one in 100 people who are taking the medication will suffer a bad reaction.

However, it can be unpredictable and difficult to identify those patients who are likely to be affected and these adverse reactions can occasionally lead to drug-induced liver injury. In the UK, around one in 10 acute liver failures are the result of damage caused by medication.

The study team led a worldwide collaboration aimed at shedding more light on why some patients are more likely to be affected than others.

They analysed the genes in 862 patients who had experienced a severe liver injury in response to taking a range of commonly taken drugs which are generally considered to be safe treatments including blood thinners, anti-fungal medication, medicines to treat high blood pressure and high cholesterol and antibiotics.

These were compared to those in healthy individuals – this is known as a genome-wide association study (GWAS). The occurrence of genetic variations – or differences in DNA – at more than 50,000 DNA bases in the genetic makeup were compared in the two groups to identify variants

which may increase the risk of drug-induced liver damage.

One such variant was found in the HLA A gene. When functioning normally it plays an important role in the immune system, protecting the body from harmful agents. But in patients with an uncommon variation in this gene – HLA A*33:01 - it may instead cause a rogue immune response to a variety of common medication, leading to liver damage.

The identification of a genetic risk factor may lead to the development of new tests to help doctors predict which patients are more likely to have a bad reaction to medications that may lead to liver damage.

It may also be possible to tailor drug prescriptions for individuals based on their genetic make-up to avoid medications with known side effects that are likely to badly impact on their health.

More information: Paola Nicoletti et al. Association of Liver Injury From Specific Drugs, or Groups of Drugs, With Polymorphisms in HLA and Other Genes in a Genome-wide Association Study, *Gastroenterology* (2016). DOI: 10.1053/j.gastro.2016.12.016

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