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Newcastle University

Liver disease 'shrunk' by blood-pressure drug

A blood-pressure medicine has been shown to reverse the effects of early-stage liver failure in some patients.

Newcastle University researchers analysed a small clinical trial of losartan, a drug normally prescribed for hypertension, on 14 patients in Spain, who had Hepatitis C.

The illness was at an advanced stage causing fibrosis - scarring in the liver - which would usually have progressed to liver failure.

Half of the patients in the trial saw the scars in their liver shrink allowing the organ to repair itself.

Professor Derek Mann from Newcastle University said: "At the moment we have no proven effective way of treating people with chronic liver disease other than transplantation. This early stage trial has shown that we can shrink liver scarring in some patients and shows promise for a treatment that could make a huge difference to the lives of thousands of people."

The team whose work is published today in *Gastroenterology*, say this early stage trial is promising and they now want to carry out several much larger studies initially involving patients with liver disease caused by obesity and then later alcohol, hereditary and autoimmune diseases.

Mechanism

Liver damage, known as fibrosis, is caused by the unwanted accumulation of excess fibrous connective tissue which is produced and maintained by a specialised cell, the liver myofibroblast.

In chronic liver disease a signalling pathway is created that instructs the liver myofibroblast to stay alive and proliferate. It is this pathway that then causes scar tissue to accumulate, creating the liver damage.

Work carried out in rat and mouse models allowed the researchers to study what was happening inside the liver when losartan, an angiotensin II receptor antagonist drug, was present.

Researchers believe that the drug blocks the signalling pathway so that the liver myofibroblasts die, removing the source of scar tissue. As the scar tissue breaks up, the damaged area of the liver is repaired by the body.

In this research, funded by the Medical Research Council and the British Liver Trust, the Newcastle University researchers discovered a biological marker, NF-kB, was crucial for the activities of scar-forming cells.

Tests on their livers revealed that, before treatment with losartan, half of the patients had a high level of the biomarker NF-kB. After treatment, the level fell indicating that losartan is able to switch off NF-kB with the result that scars are no longer produced or maintained, but instead shrink.

Professor Mann said: "By measuring the amount of active NF-kB in the liver from a biopsy sample, we may be able to tell which patients will benefit from treatment with losartan or similar drugs such as ACE inhibitors. This may prove to be a new treatment for up to half of all liver patients."

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The trial was carried out with patients at the Liver Unit, Institut Clinic de Malalties Digestives i Mataboliques, Hospital Clinic, Insitut d'Investigacions Biomediques August Pi i Sunyer, Barcelona, Spain.

People with liver disease caused by being overweight – though fatty liver disease or NASH (Nonalcoholic Steatohepatitis) – and who are interested in taking part in a future clinical trial should leave their details on tel: 0191 2231900

Paper: Angiotensin II activates IkB kinase phosphorylation of Re1A at Ser536 to promote myofibroblast survival and liver fibrosis

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