



FOCUS ON RESEARCH

PROTECTING THE LIVER FROM INJURY DURING SURGERY

Researchers

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Aim

Liver surgery is now an important treatment for liver cancer. Despite improvement in technique, it still has a risk of death of around 5%. Any method which trains the liver to withstand surgery better should improve the safety of this important operation.

We examined one of the ways in which liver cells naturally protect themselves from injury using an enzyme called HO-1 (Heme Oxygenase-1). We subsequently studied whether HO-1 could be switched on (activated) by a drug in patients having liver surgery.

Project Outline/Methodology

Liver cells were prepared from liver removed from patients undergoing liver surgery. These cells were tested in the laboratory, replicating the damaging environment that occurs during liver surgery. Cell behaviour was tested in normal cells and cells where HO-1 had been switched on.

A clinical trial was then performed in patients undergoing liver surgery. In this trial, patients were randomised to receive either a drug to switch on HO-1 (heme arginate) or placebo (saline). The level of HO-1 in the patients was measured both in the liver and in the bloodstream. The patients were followed up for the duration of their hospital stay to identify any complications.

Key Results

The drug (heme arginate) was found to strongly switch on HO-1 in human liver cells. Cells treated with the drug produced high levels of 'anti-inflammatory' chemicals. Blood cells treated with the drug were able to protect liver tissue from damage.

In the clinical trial, the same drug was found to strongly induce HO-1 both in circulating blood cells and in the liver. There were no deaths in either group, no adverse effects were noted following administration of the drug.

Conclusions

This study demonstrated that a drug (heme arginate) can be used to induce HO-1 both in the laboratory and in patients. It further shows that this drug can be safely used in patients undergoing major surgery.

What does this study add to the field?

This study demonstrates for the first time that HO-1 can be induced by a drug in human liver and circulating cells. There is a wealth of laboratory evidence that HO-1 has therapeutic potential, but to date that has not been exploited in patients because of the lack of a suitable drug.

Implications for Practice or Policy

Further clinical trials are required before this can be applied to routine use. However, if subsequent trials confirm the effects seen in this study, and are able to replicate the results shown in the laboratory, HO-1 could be used to improve surgical outcomes in liver surgery, solid organ transplantation and major vascular and heart surgery.

Where to next?

This trial establishes that a drug can be used to induce HO-1 in the liver in humans. The next stage is to perform further trials to see if this can be used to improve outcomes for patients undergoing liver surgery. This may make liver surgery safer, or enable it to be offered to more people.

This research can be applied to other areas. Another study is currently underway in patients having a kidney transplant and a further study is gathering preliminary evidence for a possible role in patients having heart attacks. Further trials in liver surgery and liver transplantation are under development.

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