Emergency aid for overdoses

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Every minute counts in the event of an overdose. ETH professor Jean-Christophe Leroux and his team have developed an agent to filter out toxins from the body more quickly and efficiently. It can also be used for dialysis in patients suffering from hepatic failure.

To date, antidotes exist for only a very few drugs. When treating overdoses, doctors are often limited to supportive therapy such as induced vomiting. Treatment is especially difficult if there is a combination of drugs involved. So what can be done if a child is playing and accidentally swallows his grandmother's pills? ETH professor Jean-Christophe Leroux from the Institute of Pharmaceutical Sciences at ETH Zurich wanted to find an answer to this question. "The task was to develop an agent that could eliminate many different toxic substances from the body as quickly as possible," he says.

Leroux and his team knew that lipid emulsions can bind to drugs when injected into the blood stream. The researchers pursued this approach in their own studies, developing an agent based on liposomes, which are tiny bubbles with a lipid membrane as an outer layer. Instead of an intravenous injection, the agent is used as a dialysis fluid for so-called peritoneal dialysis. This method of dialysis is less common than haemodialysis, which is mainly used as a long-term form of treatment of kidney failure.

"Washing" toxic substances out of the body

In the case of haemodialysis, the blood is "washed" in a machine at the

hospital, whereas peritoneal dialysis involves eliminating toxic substances from within the body. The peritoneum serves as a dialysis membrane. The dialysis fluid is passed through a catheter into the abdominal cavity where it rids the body of toxins through the highly perfused peritoneum. In the case of the new dialysis liquid developed by the ETH researchers, the toxic compounds find their way into the core of the liposomes. Once the solution is loaded with toxins, it is drained out of the abdominal cavity through the catheter. The researchers were able to demonstrate that the new agent is especially effective at this. "Our peritoneal dialysis fluid can extract up to a hundred times more toxins than conventional alternatives," reported the ETH professor.

Their efforts are based on the principle that peritoneal dialysis is an especially attractive method for the emergency treatment of overdoses. Unlike haemodialysis, it does not require sophisticated equipment and can even be employed away from specialized hospitals.

New applications for peritoneal dialysis

Until now, however, peritoneal dialysis has only filled a specific niche. No more than 10 percent of all dialysis patients worldwide use this method, and it is almost never used for overdoses. One reason for this is that cleaning the blood using peritoneal dialysis and currently available dialysis agents has often been less effective than haemodialysis. Secondly, there is a greater risk of infection. The catheter insertion point can become inflamed, and bacteria can infiltrate the abdominal cavity through this opening. Doctors therefore opt for peritoneal dialysis only for a minority of patients whose blood needs to be cleaned due to renal failure caused by toxic metabolic products.

The findings of the ETH researchers may help to discover new applications for peritoneal dialysis in two respects: in the course of their research, Leroux and his team were pleased to find that their dialysis

fluid rids the body of both drug residues as well as toxic metabolic products.

Treatment of serious liver diseases

The researchers' findings are especially promising for treating serious liver disease. Leroux has no doubt that there is a need for this because in addition to hepatitis and severe alcoholism, being overweight or obese can lead to liver disease. Given that obesity rates are constantly increasing in the western world, this is quite literally becoming a weightier issue all the time.

The dialysis fluid appears to be especially effective for liver diseases involving the accumulation of ammonia in the blood. Experiments in rats have shown that the substance effectively eliminates toxic ammonia. For example, it might be possible to provide effective emergency aid to infants who are born with metabolic disorders such as urea cycle disorder. "If a baby is not treated within a few hours of birth, there is already a hazard of irreparable brain damage," explains Leroux. Peritoneal dialysis is well-suited for newborns, because venous access for haemodialysis is difficult and there is a high risk of thrombosis.

Following these promising findings, Jean-Christophe Leroux's team now hopes to further develop the agent for actual medical applications. If everything goes as planned, the first clinical trials will be possible within the next five years.

More information: Foster V, Signorell RD, Roveri M, Leroux JC: Liposome-supported peritoneal dialysis for detoxification of drugs and edogenous metabolites. *Science Translational Medicine* 2014. 6: 258ra141, DOI: 10.1126/scitranslmed.3009135

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