The link between drug therapy and kidney failure in transplant patients

September 11 2015

New research will help scientists and medical professionals to better understand the long-term complications caused by an immunosuppressant drug used to treat thousands of kidney transplant patients.

Cyclosporin A (CsA) is administered to kidney transplant patients to improve and maintain the survival of the new functioning organ (or graft) by suppressing the immune system. This increases the body's chances of accepting the new kidney but the immunosuppressant therapy has been associated with acute and chronic nephrotoxicity (the poisonous effect of some substances on the kidneys). It can also lead to secondary complications such renal scarring and fibrosis (the formation of excess connective tissue during the body's repair process).

Scientists from the University of Lincoln, UK, have now been awarded a research grant of £70,000 by the Petroleum Technology Development Fund to explore these complications. The aim is to improve graft survival rates and reduce the levels of kidney failure in transplant patients.

The research will be led by Professor Paul Squires and Dr Claire Hills, biomedical scientists from the University of Lincoln's School of Life Sciences.

Dr Hills said: "Currently, in the UK alone, there are around 7,000 patients waiting for a kidney transplant. Most of these patients will be on

dialysis, at a cost to the NHS of around £193m per year. If all of these patients were to receive a transplant, the approximate cost would be £41m per year, representing a saving to the NHS of £152m per year. According to the Department of Surgery, graft survival is 90% in the year immediately after the transplant, but this falls to 67% after five years and 41% after 10 years when using a kidney from a deceased donor. Most of this tissue loss can be attributed to fibrosis and renal scarring, often attributable to immunosuppressant treatments such as CsA.

"For transplant patients, progression into kidney failure is directly connected to the degree of fibrosis in and around the kidney. We believe that exposure of tubule kidney cells to high concentrations of CsA initiates a number of changes which lead to the accumulation of fibrotic material in the kidney - ultimately causing failure of the newly transplanted kidney in some patients on CsA therapy."

Through their new research, which will support a PhD Studentship for Mr Omololu Fagunwa from the Nigerian Petroleum Technology Development Fund, Dr Hills and Professor Squires aim to explain how CsA mediates renal fibrosis in the kidney, and therefore identify potential targets in future drug design while providing mechanisms to help graft survival.

Their preliminary studies have confirmed that exposure of the kidney's renal tubular cells to CsA leads to physical and structural changes characteristic of early tubular injury. Ultimately, as cells undergo this process they begin to secrete fibrotic molecules, which together contribute to impaired behaviour, loss of cell function and scarring of the kidney.

The three-year study will build on Professor Squires and Dr Hills' previous work exploring ways of preventing renal damage in diabetes

sufferers.

Provided by University of Lincoln