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Remote Post-Conditioning (RPC) in renal transplantation

Submission date	Recruitment status	[_] Prospectively registered
02/08/2011	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
19/09/2011	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
29/01/2018	Urological and Genital Diseases	

Plain English summary of protocol

Background and study aims
In end-stage renal failure the usual functions of the kidney stop working. A kidney transplant is the best treatment, but it is important to find ways in which we can improve kidney function and prolong the survival of the transplanted kidney. Immediately after transplantation there is unavoidable inflammation that can reduce kidney function. This is influenced by many factors but could be reduced by using new techniques that directly target this response. The aim of this study is to find out whether a technique called remote postconditioning (RPC) can improve the function of the kidney after transplantation. Remote postconditioning (RPC) is a simple technique that activates the body's natural defences, rather like warming up before exercising to prevent injury. We can use this to target the inflammatory response in the kidney after transplantation. The treatment involves restricting the blood flow to the leg during surgery to convey the protective effect to the transplanted kidney. We do this by inflating a blood pressure cuff placed around the lower leg in short sequenced cycles to restrict the blood flow.

Who can participate?
Patients aged 18 or over receiving a kidney transplant.

What does the study involve?
To determine whether RPC improves kidney function after transplantation participants are randomly allocated into one of the two groups. One group undergoes the RPC procedure, in which a blood pressure cuff is inflated to restrict the blood flow to the leg while the patient is under general anaesthetic during the transplant operation. For the other group the blood pressure cuff is inflated but not enough to restrict the blood flow to the leg. After transplantation participants receive the normal treatment and care associated with receiving a kidney transplant and the surgery will not be altered in any way, regardless of the group that the patient is in. In addition to normal tests to assess kidney function, various other tests will be used to measure the effects of RPC. During surgery a flow monitor is used to monitor the blood flow into the kidney immediately after transplantation. This is removed before the end of the operation and does prolong the operation in any way. Blood samples are taken to measure kidney function. Extra samples are also collected to measure the inflammatory response. Many of these are obtained at the same time as routine sampling to limit the number of times that patients are asked to give a sample. If possible, samples of urine are also collected to measure

the level of kidney injury. Biopsies (samples) of the kidney are taken at various times after transplantation to determine injury and recovery and are part of normal practice. A small amount of extra tissue is taken during the biopsy for later analysis. Two extra samples will also be taken 30 minutes after transplantation and then within the first 3 days. Participants are also required to attend the normal clinic visits at weekly intervals for the first month after transplantation, then at 1, 2 and 3 months for routine patient assessment.

What are the possible benefits and risks of participating?
Participants will experience no additional effects to their lifestyles, other than that which is expected following transplantation. There are no long-term risks associated with RPC. The procedure causes a brief absence of circulation to the lower leg which can cause some discomfort but this is quickly reversed after completion. However, as the study will be performed while the patient is under general anaesthetic, no discomfort will be felt. This technique has been used in other studies with the blood pressure cuff being applied to the either the upper arm or leg and is known to cause no lasting harm or symptoms. The kidney biopsy procedure is of low risk but complications such as bleeding can occur in a small number of cases (5-8%).

Where is the study run from?
University Hospitals of Leicester NHS Trust Leicester General Hospital (UK).

When is the study starting and how long is it expected to run for?
August 2011 to August 2014.

Who is funding the study?
University Hospitals of Leicester NHS Trust and University of Leicester (UK)

Who is the main contact?
Sarah Hosgood
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Contact information

Type(s)
Scientific

Contact name
Prof Michael Nicholson

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
UHL 11035

Study information

Scientific Title
A double-blinded randomised controlled trial of Remote Post-Conditioning in renal transplantation

Acronym
RPC

Study objectives
Remote Post-Conditioning (RPC) can improve post transplant function and graft survival in renal transplant recipients

Ethics approval required
Old ethics approval format

Ethics approval(s)
National Research Ethics Service East Midlands, Leicester, 06/05/2010, ref: 11/EM/0130

Study design
Double-blinded randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Kidney injury after transplantation

Interventions

Patients will be randomised to either receive RPC during transplantation or the standard transplant with sham procedure

Intervention Type
Procedure/Surgery

Primary outcome measure
Live donor:
1. Slow graft function measured by creatinine fall in the first 24 hours and Area under the curve (AUC) serum creatinine over the first 7 days post transplant
2. Graft function rates: incidences of delayed graft function and primary non-function
3. Glomerular filtration rate (eGFR) and serum creatinine levels: 1 and 3 months
4. Graft survival
5. Patient survival
6. Episodes of rejection within the first 3 months (cell and antibody mediated)

Deceased donor:
1. Slow graft function measured by creatinine fall in the first 24 hours and Area under the curve (AUC) serum creatinine over the first 7 days post transplant
2. Graft function; incidences of delayed graft function and primary non-function
3. Glomerular filtration rate (eGFR) and serum creatinine levels: 1 and 3 months
4. Graft survival
5. Patient survival
6. Episodes of rejection within the first 3 months (cell and antibody mediated)

Secondary outcome measures
Live and deceased donor:
In addition, we wish to further understand the mechanisms by which remote postconditioning (RPC) conveys its protective actions.

1. The renal blood flow into the kidney in the immediate post transplant phase will be measured using a Doppler flow probe. The renal vascular resistance will be calculated from the kidney weight and renal arterial blood flow
2. Mediators of RPC: Nitric oxide levels and adenosine levels determined by ELISA using plasma samples taken from the renal vein 30 minutes after reperfusion and from peripheral venous samples (see blood sample protocol)
3. Markers of ischaemic injury: Neutrophil gelatinase-associated lipocalin (NGAL)- small protein that is increased with ischaemic injury, KIM-1, Oxidative damage (protein carbonyl, Lipid peroxidation, DNA damage), Inflammation; levels of cytokines (IL-1, IL-©¬, IL-2, IL-6, IL-8, IL-10, TNF-¥á), determined using plasma and urine samples
4. Measure the level of repair: Determination of up and down regulated genes using gene array analysis in renal biopsies. The presence of genes such as those involved in apoptosis (anti-apoptotic Bcl-2), Protection [Hemeoxygenase-1 (HO-1) and Heat shock protein (HSP)] and fibrosis will be validated by RT-PCR.
5. Histological changes: Biopsies will be stained with H&E for histological scoring, immunohistochemistry techniques to determine injury and Sirius red (an extracellular matrix stain) to measure interstitial fibrosis

Overall study start date
21/08/2011

Completion date
21/08/2014

Eligibility

Key inclusion criteria
1. Age greater than or equal to 18 years
2. Patients receiving a primary or secondary renal allograft from a live or donation after Brain Stem Death (DBD donor)
3. Patients with second transplants must have maintained their primary graft for at least six months after transplantation (with the exception of graft failure due to technical reasons)
4. Signed written informed consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
80

Key exclusion criteria
1. Blood type ABO incompatible live donor transplants
2. Donation after cardiac death donors
3. Patients with severe peripheral vascular disease
4. Patients on ATP-sensitive potassium channel opening or blocking drugs

Date of first enrolment
21/08/2011

Date of final enrolment
21/08/2014

Locations

Countries of recruitment
England

United Kingdom

Study participating centre

Leicester General Hospital
Leicester
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LE5 4PW

Sponsor information

Organisation
University of Leicester (UK)

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Sponsor type
University/education

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ROR
https://ror.org/04h699437

Funder(s)

Funder type
University/education

Funder Name
University Hospitals of Leicester NHS Trust (UK)

Funder Name
University of Leicester (UK)

Alternative Name(s)

UoL

Funding Body Type
Private sector organisation

Funding Body Subtype
Universities (academic only)

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/08/2015		Yes	No