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Renal Protection Against Ischaemia Reperfusion in Transplantation

REPAIR

PATIENT INFORMATION LEAFLET

We would like to invite you to consider becoming involved in a research project. This information sheet is designed to explain what will be required if you agree to take part.

RECIPIENT

VERSION 5, 3rd November 2009
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Why have I been approached?

You have been scheduled for a living donor transplant, either as the donor or recipient. We are performing a clinical trial in living-donor transplantation and have approached you to see if you would be interested to take part.

What is the aim of the study?

We are interested in new ways to reduce damage to the kidney during a transplant. In this clinical trial we wish to determine if a simple technique of inflating a blood pressure cuff over the arm of the donor and recipient for short periods before the operation can reduce damage to the kidney during transplantation.

Why is this study being done?

Kidney transplantation is the best treatment for kidney failure and it is becoming increasingly common for a close relative (the donor) to give a kidney to a patient with kidney failure (the recipient). This operation, referred to as living-donor transplantation, accounts for about a third of all transplants in the UK. Surgery on the donor and recipient is carefully managed, but during the operation there is a risk that the kidney might be damaged. This is because the process of removing a kidney from the donor inevitably cuts off its blood supply, and even though this is for a short period of time, a small degree of damage occurs. It may be possible to make the kidney better able to tolerate periods of reduced blood flow. Any intervention that decreases kidney damage during a transplant may be of great value and might improve the recovery of kidney function after the operation, with possible long-term benefits.

What procedure is being tested in this trial?

We wish to test whether a simple procedure, the application of a blood pressure cuff to the arm of the donor and the recipient before a kidney transplant, can help protect the donor kidney from the harmful effects of the transplant.

How might inflating a blood pressure cuff on the arm help the kidney?

We, and others, have shown that reducing the blood flow to the arm for a short period of time can protect the heart, lungs, and kidney from injury caused by an interruption of the blood supply. The temporary stoppage of blood to the arm activates a reflex that makes internal organs more resistant to the harmful effects of low blood flow. This reflex is called remote ischaemic preconditioning (RIPC for short). We have already showed in a small clinical trial that this technique improves kidney function after transplantation. We now want to perform a large study in 400 patients throughout the UK and two centres in Holland, which will establish whether this technique will be truly valuable to patients.

What will happen during this study?

The blood pressure cuff will be similar to the one that is used to measure blood pressure. The blood pressure cuff will be inflated continuously for a five minute period, after which it will be deflated for five minutes. This cycle of inflation, followed by deflation, will be performed four times in total. This is a safe procedure that we have carried out in hundreds of people without causing any harm. No drugs are being tested in this study, merely the effects of the cuff inflation. The only other changes from the normal transplant procedure will be the collection of extra blood and urine samples for additional analysis. There will also be a detailed measurement of kidney function 12

months after surgery (see below). You will also need to attend the out-patient clinic at 3 months and 12 months after transplant.

Will the blood pressure cuff be used in the donor and recipient?

Yes. In this way we hope to activate the protective reflex in the donor before the kidney is removed, and also activate the reflex in the recipient, in preparation for the kidney transplant.

Will all patients undergo the blood pressure cuff treatment?

No. There will be four separate groups. One group will undergo the cuff inflations immediately before surgery. This group is called the early RIPC group. A second group will undergo the inflation procedure 24 hours before surgery, referred to as the late RIPC group. A third group will undergo cuff inflations both 24 hours and immediately before surgery, and this group will be known as the dual RIPC group. There will be a fourth group, the control group, who will receive a sham cuff inflation, which will not be enough to reduce blood flow to the arm and activate the RIPC reflex.

How will my treatment be decided?

This will be done by the play of chance using a computerised system. This is a routine step in many clinical trials that is essential to ensure that the results of the trial are valid.

Will I know which treatment I will receive?

No. This study will be a blinded trial, so neither the patients nor most of the investigators at each transplant centre will know which group each patient is in. Each volunteer will therefore undergo two cuff inflations, the first 24 hours before surgery, the second immediately before surgery. These will either be two real cuff inflations, two sham inflations or one of each, depending on which group the patient is in.

How will the treatment be scheduled?

This will be very straightforward so as to minimise any inconvenience. The day before the transplant the donor and recipient will be asked to come to the transplant unit. A standard blood pressure cuff will be applied to the donor's and recipient's arm. It will be inflated to either above blood pressure for a period of five minutes (active treatment) or to 40 mmHg (sham treatment). The cuff will then be deflated for a period of five minutes and the procedure repeated three times (i.e. four inflations – a total time of forty minutes). The next day in the hour before surgery the process will be repeated.

Is there any risk?

Blocking the blood supply to the arm for five minutes will not cause any damage. You will feel the upper arm being squeezed and when the cuff is deflated you might feel a tingling sensation, but this is not harmful. This procedure has been used on several hundred patients (including children) and in healthy volunteers without any harmful effects on the arm.

Will blood and tissue samples be collected?

Yes. These are detailed below. It is important for you to understand that these samples will be considered as a gift and may be used in future research. This also applies to DNA samples.

Blood samples before and after the blood pressure cuff treatment

A small sample (1 table spoonful) of blood will be taken before and after the sequence of cuff inflations, 24 hours before surgery and the morning of surgery. These samples will be kept for analysis at a later date, but this will depend on the main result of the trial. We think that it may be useful to measure the response of genes, proteins and other metabolic pathways in these samples, but at a later date. These samples are optional.

Blood and urine samples before and after surgery

These will be in addition to your normal care. Samples will be used to measure whether the RIPC reflex alters your response to the surgery. We will ask for four samples of blood (about 1 table spoonful each time) before and in the first 5 days after transplantation. In addition we will collect 4 urine samples (about 2 table spoonfuls each time) from you before and in the first 5 days after surgery.

Samples taken from the transplanted kidney

We would like permission to collect unwanted specimens of kidney tissue for laboratory analysis. These will be small pieces of blood vessel that would ordinarily be discarded by the surgeon. In addition in some centres it will be routine to perform a biopsy of the kidney during the operation. If there is any tissue not needed after the biopsy has been analysed we would like to collect and keep this for analysis at a later time. These analyses will help understand how the RIPC reflex actually works in patients.

Samples taken during follow-up

In one of the centres (Royal Free Hospital) blood samples will be taken at 1, 3, 6, 12 and 18 months after surgery for studies of immune cell function. These samples will be of about 2 table spoonfuls. This will require a visit to the Royal Free Hospital to have this blood taken.

Are there any risks or discomforts?

Most of the blood samples will be obtained using the standard drips already in place. No extra needles or drips are necessary. The total volume of blood required for the study amounts to 65mls. You will not notice any effect of this extra amount of blood that we will take. We aim to collect as many of these samples simultaneously with routine sampling.

Are there any other additional tests?

As mentioned above, we plan to precisely measure kidney function 12 months after transplantation. At the Royal Free Hospital this is not measured routinely. We will use an established way to measure kidney function, using a substance called iohexol. At 12 months from the transplant operation we will schedule an outpatient visit where kidney function will be measured after injecting iohexol. Iohexol is used for this purpose in many kidney centres, and by measuring the concentration of iohexol in the blood we can derive accurate information about the kidney function. Iohexol (about 5 teaspoons full) is injected through a drip into one of the veins in the arm, and 4 blood samples are taken over the next 4 hours. Iohexol can cause irritation to the vein, and rarely patients are allergic to it. If you have an iodine allergy, you should not take part in the study, as iohexol contains iodine.

What are the potential benefits?

There may not be any benefits to you. It is possible that your new kidney might have better function after the operation. This could be due to the fact that the kidney sustains less damage during the transplantation procedure, but we cannot be certain of this. That is why we are doing this study.

Who will have access to the research information?

Only the researchers and a representative of the Research Ethics Committee will have access to the data collected during the study. The trial is being run by the Trials Coordination Group at the London School of Hygiene and Tropical Medicine, who will be in charge of collecting and analysing the data. An independent Data Monitoring Committee will also have access to the data to ensure that the trial is being run as planned and that there are no safety concerns.

What are the arrangements for compensation?

An independent Research Ethics Committee who believes that it is of minimal risk to you has approved this research. However, research can carry unforeseen risks and we want you to be informed of your rights in the unlikely event that any harm should occur as a result of taking part in this study.

This research is covered by a no-fault compensation scheme, which may apply in the event of any significant harm resulting from involvement in this study. Under this scheme it would not be necessary for you to prove fault. You also have the right to claim damages in a court of law. This would require you to prove fault on the part of the Hospital/Institute and/or any manufacturer involved.

Do I have to take part in this study?

You do not have take part in this study if you do not want to. If you decide to take part you may withdraw at any time without giving a reason. If you decide, now or at a later date that you do not wish to participate in this research project, that is entirely your right, and will not in any way prejudice any present or future treatment.

Who do I speak to if a problem arises?

If you have any complaint about the way in which this research project has been, or is being conducted, please, in the first instance discuss them with your local researcher. If the problems are not resolved he/she will escalate your concerns through the local research governance procedures.

Details of how to contact the researchers

Dr ********** is contactable via the transplant unit at ********* Ext *****