[To go on your hospital Trust's Headed paper]

ProMISe

Patient Information Sheet

Protocolised Management In Sepsis (ProMISe): a multi-centre, randomised controlled trial of the clinical and cost-effectiveness of early, goal-directed, protocolised resuscitation for emerging septic shock

Introduction

We would like to invite you to take part in a clinical trial which considers the benefit of early, goal-directed, protocolised resuscitation compared to usual resuscitation in patients with severe sepsis or septic shock.

Before you decide, it is important that you understand why the trial is being done and what it involves. One of our team will go through the information sheet with you and answer any questions you have. Please feel free to talk to others about the trial if you wish and please don't hesitate to ask us if there is anything that is unclear.

Background

The usual resuscitation for severe sepsis in the United Kingdom involves treatment with antibiotics, fluids given into a vein, and medication to support the blood pressure, the heart and lung function. In the United States (US), a trial performed at one hospital found that usual resuscitation for severe sepsis worked better with a treatment plan guided by central blood oxygen levels during the first six hours of hospital treatment. This treatment plan is early, goal-directed, protocolised resuscitation.

What is the purpose of this trial?

When a person has a severe infection, their body may react by producing an 'inflammatory response', which can damage important organs, such as the heart and lungs to the point where they no longer function properly. When infection causes organ failure, it is called severe sepsis. If severe sepsis results in low blood pressure, it is referred to as septic shock.

The purpose of this trial is to investigate whether early, goal-directed, protocolised resuscitation results in more people recovering from severe sepsis or septic shock when compared with usual resuscitation. Early, goal-directed, protocolised resuscitation is a structured series of steps or elements that must be initiated as soon as possible, and completed over a six-hour period. This is referred to as the 'trial protocol' in the rest of the document. Usual resuscitation is less structured in that the doctor may provide some of the same elements, but does not necessarily follow a structured series of steps or elements in a time dependent manner.

The trial, which took place in the US (see background), showed that early, goal-directed, protocolised resuscitation is better than usual resuscitation, but this trial only involved a small number of patients, and therefore, more research is needed. Doctors don't know if early, goal-directed, protocolised resuscitation will be better than usual resuscitation, so this trial will help to determine if early, goal-directed, protocolised resuscitation should be used routinely in this country.

Why have I been asked to take part in the trial?

You are eligible to participate in this trial because you have severe sepsis or septic shock, and have been admitted through the Emergency Department in your hospital.

Do I have to take part?

Joining the trial is entirely voluntary. Once you have read this information sheet, if you agree to take part, we will ask you to sign a consent form. You are free to withdraw at any time, without giving a reason, and this will not affect the standard of care you receive.

What will happen to me if I take part?

In order to find out which of the resuscitation methods is best, each patient will be put into one of two groups (early, goal-directed, protocolised resuscitation or usual resuscitation). The results will be compared to see which one is better.

ProMISe is a 'randomised controlled trial', which means that, each patient is randomly put into one of the two groups. The groups are selected by a computer that will decide on a chance basis (as if it were tossing a coin) whether you will receive early, goal-directed, protocolised resuscitation or usual resuscitation. Your progress will be closely followed to see which resuscitation method turns out to be the most beneficial. There is equal likelihood that you will receive either early, goal-directed, protocolised resuscitation or usual resuscitation. Neither you nor the doctor can decide which resuscitation method you will receive.

Whether you receive early, goal-directed, protocolised resuscitation or usual resuscitation, you will be provided with all other standard care as necessary, such as antibiotics or surgery. We will collect information about your progress throughout your hospital stay.

Many people who develop severe sepsis or septic shock routinely require a central venous catheter (CVC). This involves a doctor inserting a tube (catheter) into a large vein, usually in the neck, or near the collarbone to provide drugs, fluids or other products required during standard sepsis treatment. Treatment can include giving fluid into the vein; medications to support the blood pressure and heart; and a possible blood transfusion. The patient may also have an arterial catheter, which is a smaller tube that will be inserted into your artery in the wrist or groin and connected to a monitor to measure blood pressure. Additional treatment to support breathing may include supplemental oxygen and a machine to help the patient breathe.

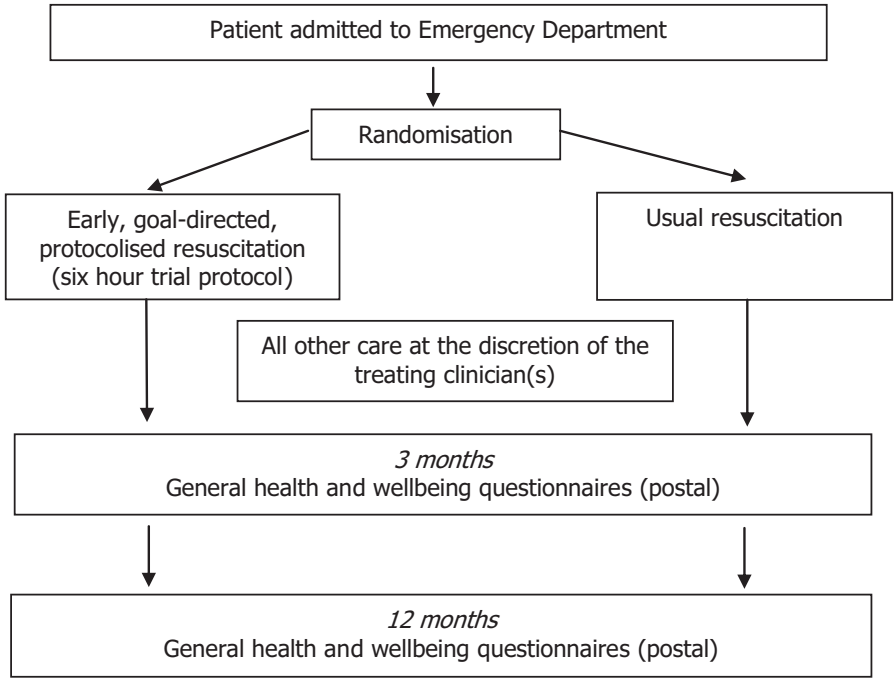
Early, goal-directed, protocolised resuscitation

If you are assigned to receive early, goal-directed, protocolised resuscitation, you will be cared for by the hospital's ProMISe Trial Team in conjunction with the team who will provide your ongoing care. You will receive resuscitation which follows the trial protocol for six hours. All patients will have a specialised CVC placed. The specialised CVC measures the oxygen level in blood returning from the tissues to the heart (central blood oxygen levels). These levels are monitored and treated accordingly. This specialised central catheter is used routinely. Many patients may have an arterial catheter to monitor blood pressure. The treating clinician(s) will use the information from these to treat you, and will include many of the standard sepsis treatments mentioned above, but according to the trial protocol. Each element in the trial protocol is to be given at the discretion of the treating clinician(s). Once a total of six hours of early, goal-directed, protocolised resuscitation has been completed, you will be given standard care at the discretion of the treating clinician(s) in accordance with current best practice.

Usual resuscitation

If you are assigned to receive usual resuscitation, you will continue to be monitored and treated by the hospital's usual clinical team in accordance with the hospital's current standard resuscitation practice. You will often have a CVC and an arterial catheter placed, if the treating clinician(s) deems this is needed for your treatment.

ProMISe patient schedule



What are the possible disadvantages and risks of taking part?

All medical procedures, regardless of trial participation, involve some risk of injury. In addition, there may be risks associated with this trial that are presently unknown or unforeseeable. In spite of all reasonable precautions, you might develop medical complications from participating in this trial. The most predictable risks are from the insertion of a CVC and an arterial catheter. These catheters are commonly inserted as part of usual resuscitation, but the CVC will always be inserted, and the arterial catheter will often be inserted, as part of early, goal-directed, protocolised resuscitation.

CVC complications

The most common complication is infection which occurs in less than one in 20 patients. The most serious complications are puncture of the lung, causing collection of air into the chest, or puncture of an artery causing blood to collect in the chest. These are rare and occur in less than one in a hundred patients. Other complications include injury to the blood vessel causing bruising and/ or bleeding or a blood clot inside the blood vessel (thrombosis). These are treatable and all patients will be assessed for the presence of any of these complications.

Arterial catheter complications

Complications from arterial catheters are rare, but may include bleeding, infection or a lack of blood flow to tissue supplied by the artery, which is nearly always correctable by removal of the catheter.

Other trial treatments

There are specific risks associated with each of the individual standard treatments used routinely for patients with severe sepsis or septic shock. These treatments are commonly used in critically ill patients and side effects can include:

Fluid infusions: giving fluid into a vein can cause fluid overload where the patient temporarily has too much fluid for their blood vessels and heart to cope with easily. This is reversible by slowing the speed at which the fluid is given, discontinuation, and sometimes by giving other medications.

Blood transfusion: can contribute to fluid overload, cause a reaction to the blood itself (rare) and spread viral disease. All blood is screened prior to administration.

Drugs: medication given to support the heart can cause abnormal heart rhythm or rarely, a decreased blood supply to the heart and extremities.

All patients are monitored closely for development of any side effects from treatments, which will be immediately treated by decreasing the dose or stopping the treatment altogether.

What are the possible benefits of taking part?

We cannot promise that participation in the trial will benefit you during your hospital stay but the information we get from this trial may help improve the way in which we care for patients with severe sepsis or septic shock in the future.

If you receive early, goal-directed, protocolised resuscitation you will be cared for by the hospital's ProMISe Trial Team in conjunction with the team who will provide your ongoing care and may receive closer observation and additional nursing attention. Early, goal-directed protocolised resuscitation may or may not improve your chances of recovery when compared to usual resuscitation; at present there is no evidence to suggest that early, goal-directed, protocolised resuscitation is harmful.

What happens when the trial stops?

Once the trial has finished you will receive usual medical care up to and following discharge from hospital. However, at 3 months and 12 months after recruitment to the trial you will be contacted by post, by a researcher from ICNARC, to ask that you complete some questions on your general health and wellbeing. These questionnaires will take around 15-20 minutes to complete.

What if something goes wrong?

If you are harmed due to someone's negligence or wish to complain about any aspect of the wa you have been approached or treated during the course of this trial, contact the Hospital's Patien Advice & Liaison Service (PALS) for further information.

Will my taking part in this trial be kept confidential?

Yes. We will follow ethical and legal practice and all information about you will be handled in confidence. All information that is collected about you during the course of the trial will be kept strictly confidential. Where possible, any information about you which leaves the hospital will have your name and address removed so that you cannot be recognised from it. As some patients may lose touch with their hospital, we will need to collect important basic information from national records held by the NHS Medical Research Information Service (MRIS). To ensure we identify you correctly on the MRIS database, we will ask the hospital staff for your name, date of birth, post code and NHS number. In addition, ICNARC will also be given your address and telephone number, in order to send the questionnaires (mentioned above) to your home. Your GP will also be notified that you have agreed to participate in this trial. The information will be stored securely and in strict confidence at ICNARC. Procedures for handling, processing, storing and destroying data [add relevant NHS Trust here] and at ICNARC are compliant with the Data Protection Act 1998.

What will happen to the results of the trial?

The trial is estimated to take two years, commencing in late 2010. It is hoped to publish the results by mid 2014. If you would like a copy of the published results, please contact the Principal Local Investigator (details below).

Funding and organisation of the trial

This trial is being funded by the National Institute for Health Research, Health Technology Assessment programme. The trial is being Sponsored and managed by ICNARC.

Who has reviewed the trial

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect your interests. This trial has been reviewed and given a favourable opinion by the North West London Research Ethics Committee 1.

Thank you for taking the time to read this information:

Local research contact details:

Please contact the Consultant leading the trial at your unit for further information:

- [Insert name and contact number of Local Principal Investigator]

Alternate contacts include:

- [Nurse – name and contact]
- ProMISe Team @ ICNARC – 020 7269 9277