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FOCUS ON: TRANSPLANTATION

Donation after cardiac death in the intensive care unit: The role of extracorporeal membrane oxygenation

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SUMMARY

Donor scarcity and the increased need for organ transplantation has prompted the development of an alternative source of donors to the more conventional brain dead donor. Non Heart Beating Donors (NHBD) or Donors after Cardiac Death (DCD) produce organs that have experienced warm ischaemia, which compromises their early function. Extracorporeal membrane oxygenation offers the possibility of minimizing this inevitable damage and extending the range of organs that can be harvested.

1. Introduction

Adverse publicity from the Alder Hey organ retention scandal created problems with multi-organ retrieval in the UK. In 2003 the Department of Health released extra funds to United Kingdom Transplant, which used the money to fund live donor programmes and the relatively new NHBD programmes in different transplant units. As a result the majority of renal transplant units in the UK now have active NHBD programmes.[1] The most straightforward of these donors came from Intensive Care units where a decision was taken to withdraw support (Maastricht category III and IV). There are many ethical issues associated with the connection between the decision to withdraw support and donation.[1] The development of these programmes was difficult because of the tension between the diagnosis of cardiac death with the attendant emotional issues and the pragmatic need to salvage the organs swiftly after death. Cardiac death was defined by the Intensive Care Society following a previous publication by the American Institute of Medicine[2] and was then incorporated into the guidelines on Organ and Tissue donation (http://www.ics.ac.uk/icmprof/standards). A multi-speciality group chaired by Sir Peter Simpson past president of the Royal College of Anaesthetists produced a consensus paper on the definition of death which was published in 2008 and is available on line.[3]

Following these steps, Intensive care staff became more comfortable with NHBD, particularly if they experienced it on their unit. This usually came about as a result of relatives asking about organ donation in relation to an Intensive Care patient where a decision had been made to withdraw support. The Intensive care staff was therefore cajoled into donation after cardiac death and was usually impressed how a tragedy could end on a positive note.

Three years ago the Department of Health set up the National Organ donation taskforce in response to the national shortage of donor organs. The taskforce was aware of two important issues; that this country lagged behind most others in the number of multi-organ donors that were generated per million population and that many potential donors did not donate organs. A national audit of 46,801 ITU deaths had been conducted; of these 42,749 had been on a ventilator prior to death, brain death was confirmed in 2754 and only 1244 actually became multi-organ donors. This meant that 38,583 patients had been ventilated and subsequently died that were either not brain dead or at least not tested (http://www.organdonation.nhs.uk/ukt). Thus the potential impact of NHBD (or Donation after Cardiac Death- DCD- an American term) could be enormous. A similar conclusion was made by Roels[4] using Eurotransplant and a patient record review in Belgium (www.donoraction.org) who stated that if all Belgium hospitals had a policy on NHBD (patchy at present) and 50% of potential donors were realised then the donation rate would rise to 66/million population which is roughly double the best current European rate (Spain- >30/million). Now the recommendations from last year's National Organ Donor taskforce are being implemented and there is a consequent expansion in the number of Transplant Coordinators. There has been an expansion in the number of cadaveric donors and transplants from cadaver donors have increased year on year from 2005. There were 753 donors and 2195 transplants in 2005 and 885 donors and 2539 transplants in 2008. However there were 579 transplants from NHBD in 2008–9, which was a 35% increase on 2007–8 (http://www.organdonation.nhs.uk/ukt/statistics/statistics.jsp), which means that the majority of this

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expansion has been via the NHBD programmes rather than brain stem dead donors (Donation after Brain Death-DBD). Whilst the expansion in the number of donors is to be applauded as it means that many more transplants have occurred, the distribution of organs transplanted in recipients has changed (ie more kidneys are transplanted relative to pancreas/liver/heart/lung). The reason for this can be appreciated by considering the process of Non Heart beating donation.

2. Current normal practice during non heart beating donation

Once a decision is taken regarding withdrawal of support for a sick Intensive Care patient the Transplant Coordinator is normally contacted to determine whether the subject would be a suitable donor. After consent is obtained from the next of kin the donation team travels to the hospital and usually goes straight to the theatre to wait. The actual process of 'withdrawal' depends upon the patient (level of support), the local practice, and the intensivist's preference (with discussion with relatives) though some guidelines are available (http://www.ics.ac.uk/icmprof/standards). However following withdrawal of support a series of changes occur to the patient (hypotension, hypoxia, hypercapnoea, acidosis etc) the magnitude of which determines whether or not cardiac arrest ensues. During this period all the subject's organs are affected which carries some implications for subsequent function. After cardiac arrest and apnoea the current UK guidelines specify that a continuous 5 min period of cardiac standstill must elapse and death is declared at the end of this period. This is to ensure that there has been irreversible ischaemic damage to the brain; consequently there can be no possibility of cerebral resuscitation even if the heart was to start again. This period of time has also been chosen to ensure that the heart cannot start again. This is obviously because if someone was to be defined as dead after cardiac arrest if their heart was to restart they couldn't be dead by that definition! This point is the start of the "warm ischaemic period". Anaerobic metabolism and lactic acidosis is inevitable from the moment of withdrawal of the patients 'support' and is magnified from the point of cardiac standstill up until effective organ preservation commences. After death is declared cold perfusion can proceed and organ retrieval can occur.[1] In the Intensive care situation this usually means the body is rapidly transferred to theatre where a laporotomy is performed and cannulae are placed in the aorta and cava. Occasionally femoral cut down is performed and the cannulae placed on the Intensive care unit. The problem of this approach is that cooling is not very effective and this is important as the metabolic requirements of organs are halved for each 10 °C drop in temperature.[5] If the organs are kept warm without oxygen then anaerobic metabolism continues leading to a build up of lactic acid (Fig. 1).

Delayed graft function (slow to work) is commoner for the transplanted kidneys from non heart beating donors than it is from brain dead donors simply due to the warm ischaemic period being longer. This is not an issue for renal transplants because the recipients can be supported by dialysis until the kidneys start to work; in addition there does not seem to be any late consequences such as higher chronic rejection rates. Delayed graft function is an issue for vital organs such as the liver and lung; if these organs are transplanted they have to work immediately otherwise the recipient will die.

An increasing number of transplant units are using livers and lungs from such donors. Usually only use the best of donors are used i.e. young, usually with head injuries, with a short 'prodromal' period after withdrawal to death and a short cold ischaemic period. However even with this approach, the liver 'non use' rate is high. If used, the recipients of these liver transplants face a slightly higher regraft rate because of liver dysfunction and a higher incidence of both biliary strictures and hepatic artery stenosis in comparison to livers from brain dead donors.[6]

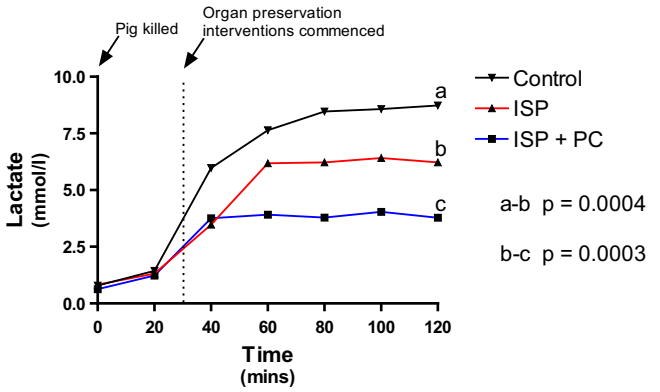

Fig. 1. Tissue lactate levels as determined by microdialysis. The catheter being placed in the kidney in an animal model. The control curve is with no intervention. ISP indicates aortic perfusion and venous drainage only with organ perfusion fluid (in situ perfusion) and PC supplementary peritoneal cooling with cold peritoneal dialysis fluid.[6]

3. Extracorporeal membrane oxygenation (ECMO)

This technique is an adaptation of cardiopulmonary bypass technology that has been used for the treatment of pulmonary (or cardiac) failure in neonates and children for many years. It has been shown to be effective in a number of case series and more recently in two randomised trials, the most recent in adults.[7–10] There is a vast database run by the extracorporeal life support organization (ELSO) that demonstrates efficacy in cardiopulmonary support over many years.[11] ECMO works because warm oxygenated blood is delivered to the patient's tissues despite the severe life threatening dysfunction of either heart or lungs. Some groups have used this technique to allow the perfusion of candidates after cardiac death with warm oxygenated blood thus minimizing the period of warm ischaemia of the abdominal organs prior to retrieval and perhaps optimizing their function.[12,13]

Equipment required: Much of this is already available. A standard centrifugal pump; an oxygenator suitable for cardiac surgery (see Fig. 2); appropriate femoral cannulae (17FG for the artery, 23FG for the femoral vein); a portable heater cooler and a short perfusion loop to allow circulation of the prime which need only be clear fluid. (See Fig. 3, after Magliocca)

Drug use; heparin would have to be given at around the time of death, it will work but is less effective if given up to 30 min after death. The prime (fluid within the ECMO circuit) may contain both lidocaine and phenobarbitone to help prevent any inadvertent cardiac activity after the onset of perfusion if the intra-aortic balloon deflates inadvertently. Madrid and Barcelona have for some time utilised cardiac arrest donors that are admitted through the Accident and Emergency units. Such subjects have generally had a longer period of cardiac standstill than those from the Intensive Care unit (Maastricht category I/II versus Maastricht III/IV).

These units discovered that a high number of these kidney transplants failed and therefore changed their approach to use ECMO to improve graft success rates. With improved renal transplant rates they were emboldened to try vital grafts and though they are quite selective, there are successful liver and lung programmes utilizing/depending on these donors.[14] This has prompted some groups to use this approach for Maastricht III donors from the Intensive Care unit.