Transmyocardial revascularisation

There are an increasing number of patients who have severe angina despite appropriate medical treatment and in whom conventional revascularisation techniques are not possible. This is usually because of distal or diffuse coronary artery disease or both. Many will have had previous revascularisation procedures and a long history of ischaemic symptoms. Diabetic patients and those with hypercholesterolaemia may present with diffuse, distal disease before any revascularisation has been attempted.

Until now the options for these patients have been limited. A few are considered for transplantation. In many left ventricular function is maintained, and moreover, a significant proportion are above the age where transplant is offered. The limited number of donor organs continues to be a problem. Alternative treatments such as transcutaneous nerve stimulators, discussed in a previous editorial, are not widely available and possibly underused. Most patients, therefore, are simply maintained on medical treatment.

There has been considerable recent interest in a new technique called transmyocardial revascularisation (TMR) which aims to improve myocardial blood supply by creating transmural ventricular channels using a high energy (850 W) carbon dioxide laser.

The idea of using conduits from the left ventricular cavity to directly perfuse the myocardium is not new. In reptiles most of the blood supply to the heart is delivered via sinusoids from the ventricular cavity directly into the muscle with little contribution from the epicardial coronary arteries. The creation of new channels, simulating the reptilian circulation may prove a novel way of revascularising the human myocardium. The creation of channels using needles or cannulas was hindered by the fact that scarring tended to close off the channels. The placing of T-tubes within the myocardium with the leg of the tube in the cavity of the ventricle was also unsuccessful because the tubes clotted. Interest in these techniques waned as coronary artery bypass grafting evolved and was successful. Matters have come full circle, now that there seems to be an expanding group of patients refractory to current treatments.

Animal studies

Animal studies using the carbon dioxide laser suggest that transmural myocardial channels may offer protection against acute ischaemia. In dogs Mirhoseini and Cayton used a carbon dioxide laser to create channels from the epicardial surface. When this was done immediately before ligation of the left anterior descending artery it reduced mortality from 83% to 0% compared with a control group in which no channels were created. The advantage of the high energy carbon dioxide laser is that tissue is removed by vaporisation, with high absorption of the carbon dioxide wavelength by biological tissue allowing for precise tissue removal and little in the way of scarring. Some studies have shown that laser channels remain patent for more than two years. Since the channels become lined with endothelium, they may remain patent in the long term. Some have suggested that the laser may act as a stimulus for neovascularisation.

It has been pointed out, however, that there may be important differences between the microcirculation of dogs and humans owing to the rich collateral circulation in dogs. Horvath et al studied sheep, which have little in the way of collateral circulation. They found that infarct size could be markedly reduced, when compared with a control group, when transmural laser channels were created an hour after ligation of the diagonal artery. In a separate experiment they demonstrated the preservation of myocardial contractility at 30 days in laser treated animals and showed histological proof of channel patency. Some, but not all investigators were also able to demonstrate flow through these channels using radioactive microspheres. The amount of flow and whether this is maintained in the long term remains controversial.

Human studies

Initial experience with the laser in human subjects was obtained in combined coronary artery bypass and TMR operations. Mirhoseini et al used the carbon dioxide laser to create channels in ischaemic areas of the myocardium deemed unsuitable for grafting. Subjective improvements in well-being, and more particularly perfusion, are difficult to interpret. This is because areas of myocardium treated with the laser, but not grafted are nonetheless likely to be affected by an improved collateral circulation from grafted areas. Their studies did, however, illustrate that the laser itself was intrinsically safe.

The next stage in the development of TMR was its use as sole treatment for revascularisation. The heart was exposed through a left thoracotomy and with the heart still beating the laser probe was placed directly onto the surface of the heart and the laser fired. No cardiopulmonary bypass was necessary. The laser was synchronised to fire during diastole when the heart is electrically inactive and full of blood. Each laser pulse lasted about 80 milliseconds. Usually 15–40 channels were made. Successful channel creation was confirmed by the appearance of turbulence as seen with transoesophageal echocardiography. The channels themselves were 1 mm in diameter, and epicardial sealing, which is seen shortly after their creation, extends only a few microns into the myocardium. Although individually the channels were small, it was thought feasible that the sum of perfusion occurring through the channels was significant (figure).
The experience with TMR as sole treatment is still limited. In a review of the experience with the first 142 patients in North America results were encouraging. This group was followed up for 12 months after TMR and 73% achieved a reduction of two or more angina classes. Preoperatively 75% were Canadian Cardiovascular Society grade 4 and 23% were grade 3. A high proportion (70%) had unstable angina preoperatively. Some, but not all patients, showed improved perfusion by either myocardial scintigraphy or positron emission tomography. Left ventricular angiography does not consistently show the laser channels. Their size and the limited spatial resolution with conventional angiography probably account for this. Mean perioperative mortality within the first six months of performing the procedure was about 12%. In patients operated on more recently, the perioperative mortality was 5%.

These results should be viewed with some caution. There has been no reported controlled clinical trial to date comparing TMR with either medical treatment or redo coronary artery bypass grafting.

A prospective randomised controlled trial funded by the Medical Research Council is currently underway in the United Kingdom to evaluate TMR as sole treatment for intractable angina in patients unsuitable for conventional revascularisation. Patients are eligible if they have refractory symptoms, if left ventricular ejection fraction is greater than 30%, and if there is demonstrable reversible ischaemia by nuclear perfusion scanning. The primary end point is an improvement in exercise tolerance as measured on the treadmill. Myocardial scintigraphy is being used to detect changes in perfusion. More subjective measures such as anginal symptoms and nitrate consumption are also being collected.

It is hoped that the trial will be able to demonstrate whether TMR is an effective form of revascularisation in these subjects. There appears to be little else on the horizon for these patients who present a difficult therapeutic challenge.