New ideas - Transplantation

A new disposable perfusion machine, nuclear magnetic resonance compatible, to test the marginal organs and the kidneys from non-heart-beating donors before transplantation

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Abstract

This article is the first report about our new hypothermic pulsatile perfusion machine (HUG’s HPP-machine) for kidney perfusion. This machine will be used for 31P NMR spectroscopy. The aim is to obtain scores of viability of marginal kidneys and those from non-heart-beating donors (NHBD) before transplantation using HPP as it has been demonstrated necessary in these situations. The most predictable test is the ratio of phosphomonoester on inorganic phosphorus (PME/PI) that can be obtained from 31P spectroscopy. The machine has been built to allow perfusion of kidneys in the range of that performed with the traditional Belzer, Mox-Waters machines and others, but compatible with the magnetic fields of the MRI apparatus used for 31P NMR spectroscopy. In this publication, the technical aspects of this new aerobic HPP-machine compatible with MRI is presented.

Keywords: Hypothermic pulsatile perfusion; 31P NMR; Non-heart-beating donor (NHBD); MRI compatibility

1. Introduction

The kidneys from marginal donors and from non-heart-beating donors (NHBD) present a high rate of primary non-function and delayed graft function [1, 2]. The use of these organs is necessary to increase the possibilities of transplantation. To make optimal use of this potential organ supply, the ischemic injury that occurs after a period of warm ischemia needs to be reversed [3–5].

It has been demonstrated that hypothermic pulsatile perfusion (HPP) can restore energetic cellular level in damaged kidneys due to long warm ischemic time, that is the rule in marginal kidneys and in the case of NHBD.

Breton and colleagues [6] have first shown that the ratio of phosphomonoester on inorganic phosphorus (PME/PI) in the kidney is correlated with graft function after transplantation. The dosage of PME/PI is obtained by the NMR spectroscopy of 31P. Until now, nobody has been able to correlate HPP and NMR spectroscopy together, because of the impossibility to perfuse in the tunnel of the MRI apparatus. 31P NMR spectroscopy will be realized in a classical MRI apparatus transformed for the tests with a specific P-coil.

We have developed a HPP-machine compatible with NMR spectroscopy, which means that it is MRI compatible. Naturally our machine works in agreement with the other standard HPP machines e.g. Belzer or Mox-Waters and others that are generally used for kidney perfusion.

This machine is specially devoted to the perfusion of kidneys removed by the ‘en-bloc’ technique. As demonstrated, ‘en bloc’ kidney perfusion is preferable to minimize the damage to the vessels that is associated with perfusion of kidneys separately; what is more, it is less expensive.

2. The HPP-machine (HUG’s HPP-machine)

The machine is composed of three parts:
1. The drive module, with automatic feedback control of pressure
2. The ‘umbilical cord’ connecting the drive module and the perfusion module
3. The module of perfusion and its ‘igloo’

Only this configuration can warrant hypothermic pulsatile perfusion in the tunnel of the MRI apparatus; the perfusion module performs the NMR compatible element (Fig. 1).

2.1. Module 1: the drive module

In this machine, the driver is O2, the flow is 6 l/min. The flow of O2 lets the pulsatile pump function on the perfusion module. The pump is capable of delivering a perfusate flow of 0–360 ml/min. Systolic pressure is stopped at 40 mmHg and the pressure is allowed to decrease until the diastolic pressure is reached (15 mmHg) and the pump starts again. It is a soft perfusion as described by Lledo Garcia and...
colleagues [7]. Consequently, the pulsation rate (1–60/min) depends directly on the vascular resistance (VR) (Fig. 1).

The drive control is obtained with the direct measure of the perfusion pressure at organ’s level. The feedback is controlled by a pressostat acting on the delivery of O₂.

2.2. Module 2: the ‘umbilical cord’

The ‘umbilical cord’ is necessary to connect the inside and the outside of the Faraday-cage around the MRI apparatus (Fig. 1).

It is composed of two tubes of 7 m length, one for the O₂ driver and the second for the pressure control. It is connected to the drive module and at time of perfusion the second end is connected directly to the module of perfusion. Its material is compatible with NMR and with the magnetic fields.

2.3. Module 3: the module of perfusion

This is the disposable piece of the machine. It is the part in contact with the kidneys and with the perfusate (VIASPAN).

The module of perfusion and its cooling box (the igloo) have a maximum size of 40 cm to take place in the ‘tunnel’ of the magnets of the MRI apparatus. Because of the high magnetic field it cannot contain any ferro-magnetic material (Figs. 1 and 2).

The machine has to function for up to 8 h, to obtain functional evaluation of the kidneys, at a temperature between 0–6 °C. For marginal organs, HPP is used for the reanimation of the organs. The literature [8–11] shows that the duration of this reanimation phase needs at least 4–6 h perfusion before noticing a decrease of the vascular resistance (VR). Authors who measure enzymes reflecting tubular damage (e.g. glutathione S-transferase) as a pre-transplant viability test, having a predictive value, generally perfuse for up to 8 h [12, 13]. Other groups continue the perfusion until the transplantation [10]. For that reason we have tested our machine for longer than 8 h. We have perfused kidneys for up to 24 h without any change in the temperature. The module is placed in an ice-box filled with frozen ice (T°: −15 °C). The temperature remains stable even after 24 h of perfusion. The regulation of temperature is obtained only by radiation.

The most important part of the module is the pump that will deliver the perfusate to the organ.

In HPP the evolution of the vascular resistance (VR) [8] during perfusion is monitored. It leaves no possibility to monitor the flow in an NMR-compatible machine so that the generally accepted formula to quantify the VR: P (mean)/Q in ml/min, cannot be used.

In fact, the VR is only an index reflecting the flow that can be delivered to the organs under a definite pressure. The exact value of this ratio is not important; only the evolution of this value during the 8 h of perfusion is important. People working with Belzer, Mox or other machines record directly the flow during perfusion. In our situation, the pump is nearly volumetric so that only its frequency is monitored. When the frequency increases it reflects a decrease of the VR. But, as for everybody, the optimal flow is stated at 0.5 ml/g/min.

Our pulsatile pump stops at 40 mmHg pressure [14] and functions again when diastolic pressure (15 mmHg) is reached. That means that the frequency of the pump is
inversely proportional to the VR at constant pressure. With our machine, the VR becomes the ratio pressure/frequency. The maximum frequency of the device is 60/min. Our pump is a modification of our old ‘Arthopump’ described in 1980 as peristaltic pump [15].

The residual O₂ at the outlet of the pump is used for oxygenation of the perfusate through the porous filter, acting as well as support for the organs. That system allows a pO₂ of 500 mmHg. The perfusion module is placed in an ice box (T: −15 °C) allowing a constant temperature of 0–6 °C during the 8 h of perfusion. Longer perfusion time gives no advantage to ‘restore’ the organs as shown above.

3. Experimental results regarding HPP and MRI compatibilities

Five experiments have been conducted on mini pigs. Kidneys have been removed ‘en-bloc’. Their mean weight was 92 g for the two kidneys. They were perfused on our HPP machine for 8 h. To demonstrate the feasibility of our machine in HPP concept see Fig. 2. During perfusions, the machine and organs have been tested for MRI compatibility (Fig. 3). That allows us to obtain imagery (without contrast medium) of high quality (Fig. 4). We observed during these perfusions a decrease of VR (frequency: mean 8/min – at the beginning – to 18/min after 8 h) for a maximum systolic pressure of 40 mmHg, representing a flow of 0.2 ml/g/min at the beginning to 0.6 ml/g/min after 8 h of perfusion.

4. Conclusion

We present here an aerobic HPP-machine that works on request. At no time of perfusion is the organ forced with a flow to reach a fixed pressure, nor must work under a supposed good pressure be determined as an optimal flow. Consequently the measure of VR that must decrease during the perfusion is different in our machine.

This machine has been built to offer what the organ needs. Naturally, a bad organ is detected because the frequency of the pump is low but this mechanical phenomenon is not sufficient to decide if the organ is viable or not. Other tests, such as PME/Pi are necessary to decide on the future function of the organ. In future presentations we shall correlate these observations with the 31P spectrometry, the best technique that can predict the function of the organ. Actually, the special P-coil necessary for PME/Pi measurement is in development.

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References


