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Original article

A Hemodynamic, Metabolic and Histopathological Study of a Heterotopic Auxiliary Swine Liver Graft With Portal Vein Arterialization ☆

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ABSTRACT

Background: Auxiliary heterotopic liver transplantation with portal vein arterialization (AHLT-PVA) is a model that has been hardly studied, despite its therapeutic potential.
Methods: Hemodynamic and biochemical characterisation was carried out during graft implantation, in a pig-to-pig model (n=15 AHLT-PVA). Furthermore a histopathological study was performed to establish microscopic alterations due to PVA.
Results: Reperfusion of the arterialized graft produced an increase in heart rate (HR) vs baseline (P=.004) and vs inferior vena cava clamping phase (P=.004); and a decrease in systemic vascular resistance vs cava clamping phase (P=.021). At the end of implantation, cardiac output remained elevated (P=.001), likewise HR remained increased vs baseline phase (P=.002). Mean arterial pressure decreased with cava clamping, but was not affected by the reperfusion of the graft, nor the skin closure. The histopathological study at 3, 10, and 21 days post-PVA revealed that functional liver structure was maintained although it is common to find foci of perilobular necrosis on day 3 (P=.049), and perilobular connective tissue proliferation at day 10 (P=.007), vs native liver.

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Conclusions: The described arterialized liver graft model minimises the number of vascular anastomoses vs previously described models. It is hemodynamically and metabolically well tolerated and the double arterial vascularisation of the graft does not cause significant changes in liver histology.

Estudio hemodinámico, metabólico e histopatológico de un modelo porcino de trasplante auxiliar heterotópico hepático con arterialización portal

Palabras clave:
Trasplante auxiliar heterotópico hepático
Arterialización portal
Anastomosis vascular
Estudio histopatológico
Respuesta hemodinámica
Valoración bioquímica

RESUMEN

Introducción: El trasplante auxiliar heterotópico hepático con arterialización de la vena porta (TAHH-AVP) es un modelo poco estudiado a pesar de su potencial terapéutico. El objetivo del estudio es valorar la respuesta hemodinámica y bioquímica durante el implante y analizar la repercusión de la arterialización portal en la funcionalidad y morfología hepática.

Métodos: Se realizó un estudio hemodinámico y bioquímico durante el implante auxiliar en un modelo porcino (n = 15 TAHH-AVP). Además, se analizaron las consecuencias de la arterialización portal sobre la arquitectura hepática mediante un estudio ultraestructural.

Resultados: La reperfusión del injerto arterializado aumentó la frecuencia cardiaca (FC) respecto a los valores basales (p = 0,004) y a la fase del pinzamiento de la vena cava (p = 0,004) y disminuyó las resistencias vasculares sistémicas respecto a la fase del pinzamiento de la vena cava (p = 0,021). Al final del implante, el gasto cardiaco permaneció elevado (p = 0,001), al igual que la FC respecto a la fase basal (p = 0,002). La presión arterial media disminuyó con el pinzamiento venoso, pero no se vio afectada ni por la reperfusión del injerto ni por el cierre de la piel. Todas las muestras histológicas obtenidas a los 3, 10 y 21 días conservaron su morfología y arquitectura hepáticas. Si bien se observaron algunos focos de necrosis perilobular el día 3 (p = 0,049) y proliferación conectiva perilobular el día 10 (p = 0,007), respecto al hígado nativo.

Conclusiones: El trasplante del injerto hepático arterializado descrito minimiza el número de anastomosis vasculares respecto a los modelos previamente publicados, presenta una buena tolerancia hemodinámica y metabólica, y la arterialización portal del injerto no produce cambios significativos en la histología hepática.

Introduction

Orthotopic hepatic transplant (OHT) is the treatment of choice for chronic terminal hepatic diseases.[1–3] Although auxiliary hepatic transplant (AHT) has more restricted indications, it may be an alternative to OHT in certain situations, such as: (a) non-cirrhotic metabolic hepatopathologies, or sudden potentially reversible liver failure in which recovery of the native liver is possible[4–9]; (b) extremely small liver grafts[10,11] and (c) even in xenotransplant, as a bridging solution until a compatible human graft becomes available for OHT.[12]

Portal vein arterialisation (PVA) is a technical variant that when associated with auxiliary heterotopic hepatic transplant (AHHT) makes it possible to conserve the native hepatic hilus intact, preventing the phenomenon of competition for the portal flow between the two livers, while supplying the native liver with optimum conditions for its potential regeneration.[13–18] However, portal vein arterialisation will subject the hepatic portal territory to high pressure arterial flow.

The aim is to analyse the hemodynamic, electrolytic and acid base balance alterations which occur in a porcine model of AHHT-PVA during implant in the recipient, and to analyse the histopathological changes that arise in the graft.

Method

Animals

15 AHHT-PVA were performed on female crossed Large White and Landrace pigs. The donors weighed 12 kg and the recipients weighed 25 kg, as did those used for hemotherapeutic resources. Crossed agglutination tests were used to determine donor-recipient compatibility.[19]

All of experimental protocols were approved by the Ethics Committee of our University, which is responsible for the application of Directive 2010/63/EU. The animals were anaesthetised with isofluorane (1.5%–2%) and fentanyl (0.03–0.05 mg/kg/h).