Current Status of HBP Research Field

Cases of Basic Research II

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Basic Research What I Did

1. Liver cell viability during ischemia and reperfusion injury in liver
2. Significance of Bioelectrical Impedance during Ischemia-Reperfusion injury
3. Bioelectrical Impedance May Predict Cell Viability During Ischemia and Reperfusion in Rat Liver
4. Impaired Cation Transport May Lead to Bioelectrical Impedance Changes During Hepatic Ischemia

On Going Project

1. New trial to treat hepatocellular carcinoma - Preliminary study for Local hyperthermic treatment under magnetic field
2. Treatment with expandable heat producing metallic stent in inoperable CBD malignancy.

Significance of Bioelectrical Impedance during Ischemia-Reperfusion Injury

Introduction and Aim: During liver resection and liver transplantion, liver is damaged by ischemia-reperfusion injury. Until now, there is no approved method to measure or predict the extent of liver injury during the operation. This is the preliminary study to make the real time monitoring system by quantification of electric impedance and ischemia-reperfusion injury in liver.

Material and Method: Ten Newzealand white rabbits (male 3.5-4.0 kg) were randomly divided into three groups. In experiment 1 (n=5), changes of bioelectrical impedance were observed during ischemia according to frequency (120-100 KHz). In experiment 2 (n=5), changes of bioelectrical impedance were observed during 30 minutes ischemia and reperfuion. In experiment 3 (n=5), we induced 120 minutes ischemia. Liver tissue bioelectrical impedance were measured every 5 mimutes interval with two mono-polar needle coated with platinum using LCR meter (GS-4311B, ANDO, Japan). Cell viability was assessed by metabolic capacity of fatty acid (palmitic acid metabolic rate) and histologic examination (H/E stain) at every 30 minutes interval during 120 minutes ischemia.

Results: Liver bioelectrical impedance was changed significantly ($p<0.05$) during ischemia in lower frequency compared to those of higher frequency. The level of bioelectrical impedance (120 Hz) at pre-ischemia, 5, 10, 15, 20, 25 and 30 minutes after ischemia are 7.3±1.5, 8.3±1.0, 9.6±0.8, 10.5±1.2, 12.0±1.4, 13.6±3.0 and 14.8±3.7, 16.3±4.9 kΩ (Mean±SD), respectively. The level of bioelectrical impedance returned to base line level after reperfusion. The level of bioelectrical impedance (120 Hz) increased gradually after ischemia for 1 hour. After 1 hour, the level of bioelectrical impedance had tendency to maintain plateau. Palmitic acid oxidation rate were not changed significantly during 120 minutes ischemia and there were no significant difference in histologic examination.

Conclusion: We found the possible role of bioelectrical impedance to measure and predict the extent of ischemia-reperfusion injury. But we need further study to clarify the relationship between bioelectrical impedance and ischemia-reperfusion injury and we also need further study to prove causes of bioelectrical impedance change during ischemia-reperfusion injury.

Bioelectrical Impedance May Predict Cell Viability During Ischemia and Reperfusion in Rat Liver

Ischemia and reperfusion (I/R) injury is a major cause of hepatic failure after liver surgery, but there is no direct method to monitor or predict it in real-time during surgery. We measured bioelectrical impedance (BEI) and cell viability to assess the usefulness of BEI during I/R in rat liver. A 70% partial liver ischemia model was used. BEI was measured at various frequencies. ATP content, palmitic acid oxidation rate, and histological changes were measured in order to quantify liver cell viability. BEI changed significantly during ischemia at low frequency. In the ischemia group, BEI increased gradually during 60 minutes of ischemia and had a tendency to plateau thereafter. The ATP content decreased below 20% of the baseline level. In the I/R group, BEI recovered to near baseline level. After 24 hours of reperfusion, the ATP contents decreased to below 50% in 30, 60 and 120 minutes of ischemia and the palmitic acid metabolic rates decreased to 91%, 78%, and 74%, respectively, compared with normal liver. BEI may be a good tool for monitoring I/R during liver surgery. The liver is relatively tolerant to ischemia, however after reperfusion, liver cells may be damaged dependent upon the duration of ischemia.

Key Words: Bioelectrical Impedance; Cell Viability; Ischemia and Reperfusion; ATP

Impaired Cation Transport May Lead to Bioelectrical Impedance Changes During Hepatic Ischemia

Ischemia causes biochemical and physiological changes in tissue, which influence tissue impedance. These changes are manifested as a rise in bioelectrical impedance (BEI), but the mechanism responsible for ischemia-related BEI changes has not been clearly determined. The authors used a LCR meter to quantify BEI changes at 0.12 KHz. Livers were subjected to 70% partial ischemia for 120 minutes, and ATP contents, cation changes in extracellular fluid (ECF; determined using an in vivo intracellular microdialysis technique), hepatocyte sizes, and histological changes were then examined. Liver tissue BEI was found to increase gradually during the first 60 minutes of ischemia and then tended to plateau. During the same period, intracellular ATP contents decreased to below 20% of the baseline level, $[Na^+]$ in ECF decreased from 150.4±3.8 to 97.8±10.6 mmol/l, and $[K^+]$ in ECF increased from 7.5±0.3 to 34.3±5.5 mmol/l during the first 60 minutes of ischemia. Hepatocyte diameter increased by ~20% during the first 60 minutes of ischemia. This study suggests that BEI changes during hepatic ischemia are probably caused by sodium and potassium concentration changes in the ECF due to reduced intracellular ATP contents.

Key Words: ATP; liver; microdialysis; cation