Neonatal myocardium is more sensitive to ischemia than the adult one

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Background

Bioelectrical impedance spectroscopy is a non-invasive method to determine alterations in tissue structures during ischemia, which is now applied to neonatal hearts for the first time world wide. Neonatal and adult hearts were examined at different temperatures (35°C and 25°C) during ischemia to analyze distinctive organ specific changes in appropriate impedance spectra (Fig. 1).

Methods

Isolated ischemic hearts of landrace piglets (NEO, n=9) and adult pigs (ADULT, n=9) were examined at 35°C and 25°C. Mean age of NEO was 7 days (35°C) and 4 days (25°C) and of ADULT 2.8 and 2.6 months, respectively. After harvesting of every heart an epicardial probe (Fig. 2b/c) was placed on the left ventricle parallel to the LAD and continuous measurements of bioelectrical impedance were performed within a frequency range from 100 Hz to 1 MHz, using a computer controlled Solartron 1260 Impedance Analyser and ImpDAQ V1.03 iba e.V. Software. The measurements included absolute impedance, its real (Re) and imaginary parts (Im) and the resulting phase angle (φ).

All hearts were incubated at constant temperatures (35°C, 25°C) and humidity (30%) for 24 hours. Furthermore, morphology was evaluated by ultrastructural analyses (Fig. 4).

Results

A sigmoid curve of the phase angle could be seen in both neonates and adults (Fig. 3a). Significant differences between NEO and ADULT were evident, especially at 35°C (e.g. p=0.009 after 4hrs). The maximal changes of the phase angle indicating the measured impedance were much higher in both neonatal groups (35°C: -24.74, 25°C: -28.22) in comparison to the adults (35°C: -21.12, 25°C: -24.34). At 25°C the onset of the impedance increase occurred later in NEO and ADULT groups compared with 35°C data. Ultrastructural analyses showed first reversible, later irreversible injuries (Fig. 4).

Fig. 3: (a) Phase angle and (b) ESI of ischemic neonatal and adult myocardium at 35°C and 25°C, respectively.

The Extracellular Space Index (ESI) as a marker for the ischemia-induced oedema was calculated (Fig. 3b) according to the following equation:

\[ \text{ESI} = \frac{\text{Re} (Z) \text{ at } 1 \text{ MHz} [\Omega]}{\text{Re} (Z) \text{ at } 300 \text{ Hz} [\Omega]} \]

It decreased from 54.9% (NEO) and 51.3% (ADULT), respectively, to 10.4% (NEO) and 13.5% (ADULT) at 35°C after 5 and 7 hours. At 25°C ESI decreased from 60.1% (NEO) and 52.5% (ADULT) to 8.4% (NEO) and 8.8% (ADULT) after 9 hours.

Fig. 4: Ultrastructure of the (a, c) adult and (b, d) neonatal myocardium after 60 minutes of ischemia at 35°C and 25°C. Magnification 1:7900.

Conclusions

1. Atraumatic measurements of bioimpedance provide an insight in intraischemic changes of myocardial membranes and extra-cellular space.
2. At high frequencies (> 1kHz) current conduction (Im) through tissue is mainly determined by tissue structures (extra- and intracellular compartments and cell membranes).
3. At low frequencies (< 1kHz) Re is influenced by a decrease of extracellular space, an increase of extracellular ion density and the closing of gap junctions.
4. Neonatal myocardium is much more sensitive to ischemia-induced alterations, since irreversible myocardial injury occurs faster than in adult tissue.
5. It’s important to further expand our knowledge of neonatal myocardium during ischemia and thereby of intraoperative myocardial protection.

References


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