Strategies and Logic of Controlled automated reperfusion of the whole body following Circulatory arrest: The CARL-therapy

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Objective:

Ischemia/Reperfusion injury (IRI) occurs in patients with circulatory arrest (CA) followed by cardiopulmonary resuscitation (CPR) causing high mortality and neurologic sequela. Limiting IRI of the whole-body and the brain could therefore be a goal in the treatment of these patients. Hence a therapeutic regimen called “controlled automated reperfusion of the whole body (CARL)” has been evolved in an animal model now been successfully applied also in humans affected by CA.

Method:

Chronic experimental setting of n=200 pigs in 20 different groups, undergoing either 15 or 20 minutes of unprotected normothermic ischemia. Different conditions of reperfusion have been evaluated, focusing on mortality and neurologic recovery within 7 consecutive days. A therapeutic regimen regarding optimized reperfusion conditions has been extracted from the results and implemented in human use.

Results:

In selected experimental groups, survival and neurologic recovery after 15 minutes CA rates up to 100% with corresponding numbers of 90% survival and 90% neurologic recovery after 20 min CA. Application of CARL in n=13 patients with extremely prolonged CPR (duration: 51-120 min) allowed survival and complete cerebral recovery in 6/13 patients.

Conclusion:

Counteracting IRI by controlling conditions and the reperfusion solution may be an important key to improve survival and neurologic recovery in patients with CA. A therapeutic regimen called CARL has been evolved to meet this demand. First clinical results are in line with the extensive expertise from preceding animal experiments showing beneficial effects for the affected patients. Another clinical trial is currently under development and will start including patients in the year 2018.

CPR before CARL: 51-120 minutes

Reperfusion Strategy: CARL

<u>Pulsatile high pressure/flow</u>	<u>Immediate hypothermia</u>
<u>Immediate heparinization</u>	<u>Hyperosmolaric fluids</u>
<u>Avoid Vasopressors and inotropes</u>	<u>Normoxic</u>
<u>Hyperosmolaric reperfusion</u>	<u>Hypocalcemic</u>
<u>pH-stat</u>	<u>Balanced Hematocrit</u>

References: :

Garcia-Dorado et al, Cardiovasc Res. 2006
Taunyane et al, EJCS 2016
Trummer et al SJTREM, 2017

Conflict of Interest:

G. Trummer, C. Benk, C. Scherer and F. Beyersdorf are affiliated with Resuscited GmbH