School : Ecole Nationale Vétérinaire d'Alfort

Title : Total liquid ventilation and cardiopulmonary resuscitation (Apply here)

Laboratory : Inserm U955, Team 3 (UMRs UPEC-ENVA; Head : Pr Berdeaux)

Principal investigator : Renaud Tissier

Scientific background

In humans, "sudden death" or out-of hospital cardiac arrest is a major public health issue. When patients are rescued and resuscitated with appropriate pre-hospital cares, the clinical recovery still remains very poor. *In fine*, less than one third of the resuscitated patients admitted at hospital really benefit from a full neurological recovery. The induction of a moderate hypothermia (32-34°C), so called "therapeutic hypothermia", is the only well admitted treatment able to improve significantly the medical prognostic for those resuscitated patients. Such a benefit has also been clearly demonstrated in animal models and might involve a reduction of the cellular metabolism and a decrease in neurotoxic metabolites and mediators release (glutamate, interleukine 1β). Two main multicentric clinical trials demonstrating the ability of therapeutic hypothermia to improve survival and neurological recovery in comatose survivors of shockable cardiac arrest (ventricular fibrillation). On such experimental and clinical bases, the international guidelines for the treatment of adult patients after out-of-hospital cardiac arrest include the use of therapeutic hypothermia (32-34°C during 12-24 hours). However, several experimental studies have reported that such a benefit depends on the rapidity of institution of hypothermia.

In this context, the present laboratory has investigated since several years a strategy able to induce an ultra-fast cooling of the body using total liquid ventilation of the lungs (TLV) with perfluorocarbons. These liquids use the lungs as a thermal bio-exchanger with concomitant maintenance of normal gas exchanges. Using a prototype of liquid ventilator, the team has shown that it was possible to reduce the blood temperature to 32°C within less than 5-10 min in an experimental model of myocardial infarction in laboratory animals. In these conditions, myocardial infarct size was considerably reduced, as well as ventricular mechanical dysfunctions and biochemical abnormalities at the level of mitochondria. In a model of cardiac arrest induced by ventricular fibrillation, therapeutic hypothermia induced by TLV has also demonstrated its ability to reduce significantly the neurological and cardiac outcomes. The laboratory is currently aiming at transferring TLV towards its clinical usefulness in humans. To achieve this goal, experiments are conducted using TLV in large animals (pigs). The candidates will be involved in this program, through experimentations in animal models of cardiac arrest and resuscitation.

Examples of references from the laboratory

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