Boehringer Ingelheim Veterinary Scholars Program – France

Vet school : Ecole Nationale Vétérinaire d'Alfort

Total liquid ventilation and cardiopulmonary resuscitation

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

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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). 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 ultra-fast and systemic cooling 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, in particular for the treatment of hypoxic-ischemic encephalopathy. To achieve this goal, experiments will be conducted in newborn piglets undergoing experimental anoxia. The candidates will be involved in this program, through experimentations in *in vivo* animal models of cardiac arrest and resuscitation.

Examples of references from the laboratory

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