Title: EFFECT ON NEUROLOGIC OUTCOME AFTER PROLONGED CARDIAC ARREST IN DOGS, OF POST-INSULT HYPOTHERMIA BY CARDIOPULMONARY BYPASS. PRELIMINARY RESULTS.

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Introduction. Cerebral recovery after cardiac arrest (CA) depends on the duration of ischemia and secondary derangements, the postresuscitation syndrome (1). Protection by hypothermia before and during arrest is well established. Cooling early after focal ischemia seems to reduce infarct size (2). Resuscitative hypothermia after global ischemia has not been evaluated, except for anecdotal clinical reports and uncontrolled animal experiments with conflicting results. Hypothermia induced postarrest (when there are cerebral no reflow and prolonged hypoperfusion with hypermetabolism) might mitigate brain damage by reducing $CMRO_2$, stabilizing membranes, slowing free radical reactions and preventing lipid peroxidation. We, therefore, studied hypothermia delivered by cardiopulmonary bypass (CPB) after prolonged CA in our dog outcome model (3, 4).

Methods. 18 male coon hounds of similar weight and age were prepared under light N_2O/halothane anesthesia and subjected to normothermic VF CA of 17 min (no flow). Resuscitation in all was by closed-chest CPB (veno-arterial pumping) including hemodilution (to hct 25%), heparinization, epinephrine, and $NaHCO_3$. After total bypass of 3 min and defibrillation, partial bypass was continued for 4 h, with control of flow, pressure, T and composition of blood. IPPV was continued to 20 h and standardized intensive care to 96 h. A normothermic control group (n=7), a mild hypothermic group (32°C) (n=5), and a moderate hypothermic group (28°C) (n=6) were studied in alternating sequence. Hypothermia was induced immediately with reperfusion, using the CPB heat exchanger at 10°C below body T. Pulmonary artery T of 34±1°C was reached at 3 min of CPB, and 32°C or 28°C at 15-20 min. Arterial blood gases were controlled at levels "normal" at 37°C. During the fourth hour of CPB, uniform slow rewarming to baseline normothermia was achieved. Hct was normalized. After weaning from IPPV at 24 h, outcome was evaluated according to overall performance categories (OPC) #1-#5 (Table 1) and neurologic deficit (ND) scores 0-100% (Table 2).

Results. There were no significant group differences in prearrest variables. CPB management and weaning from CPB and IPPV were according to protocol in all dogs. Tympanic, esophageal, rectal, cutaneous and pulmonary artery T levels were similar and changed simultaneously. Four experiments were eliminated from neurologic outcome evaluation because of cardiopulmonary complications, which led to death at 36-72 h (1/7 after 37.5°C, 1/5 after 32°C, and 2/6 after 28°C). In the survivors there were no major postarrest management problems. The best OPC and ND scores between 24 and 96 h were all abnormal, but showed significantly better mean values in the two hypothermic groups combined vs. the normothermic control group (Tables 1 and 2, *).

Table 1. Best Overall Performance Categories 24-96h (each symbol = one dog)

OPC	37.5°C	32°C	28°C
5 death			
4 coma	o		
3 severe disability	ooooo	+++	**
2 moderate disability		+	**
1 normal			
p vs. 37.5°C			0.05
		*p 0.05	

Table 2. Best Neurologic Deficit (ND) Score 24-96 h (ND 0%=normal; 100%=brain death)

	37.5°C	32°C	28°C
n	6	4	4
ND mean±SD (range)	42±9% (30-55%)	32±7% (25-45%)	31±5% (24-37%)
p vs. 37.5°C			0.05
		*p 0.05	

Discussion. The model used is reliable, since after CPB the 6 normothermic control dogs (and 20 dogs of previous studies with similar insults) all achieved compareble brain damage (OPC 3-4). The statistically significant (although slight and inconsistent) improvement in OPC and ND postarrest achieved by hypothermia, as suggested by these preliminary results, justify cautious optimism. Larger series and mapping of the best level, duration and method of administration of hypothermia are indicated.

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