PERFLUROCHEMICAL NASOPHARYNGEAL COOLING INDUCES SELECTIVE BRAIN HYPOTHERMIA

Marla R. Wolfson, PhD 1, Daniel J. Malone, MS, Jichuan Wu, MD, PhD, John Hoffman, MS, Allan Rozenberg, PhD Thomas H. Shaffer, PhD 1,3, and Denise Barbut, MD 2

1 Physiols & Pedds, Temple Univ Sch of Med, Phila, PA; 2BeneChill, Inc San Diego, CA; 3Nemours Lung Ct, Al duPont Hosp, Wilm, DE

ABSTRACT

Background: Effectiveness of hypothermic brain neuroprotection depends on how rapidly cooling is induced. The therapeutic hypothermic zone (THZ) is created with whole body surface (WBS) or intravascular methods that are cumbersome and require time. Nasophasyngeal cooling (NPC) involves slow induction and requires heavy personnel activity that is temperature resistant. PFC nasopharyngeal cooling (NPC), on the contrary, is practical and provides early cooling.

Methods: Weanling sheep were cooled without cardiopulmonary restrictions. PFC nasopharyngeal cooling rapidly induced global cerebral cooling by influencing brain cooling rates as a function of PFC/Gas flow ratio directly influenced brain cooling rates.

Results: Brain cooling rates were evaluated (ANOVA) as a function of PFC vs WBS. Whole body surface cooling induced and maintained global cerebral cooling without cardiopulmonary compromise.

Conclusions: NPC nasopharyngeal cooling rapidly induced and maintained global cerebral cooling.

INTRODUCTION

Cerebral hyperthermic events are the leading cause of acute neurologic injury in Asia and, as a result, cause of long-term disability across age worldwide. 3.5°C reduction in brain temperature after this event can improve neurocognitive, cerebral energy, and endopsychological outcomes. The noninvasive effectiveness of cerebral brain cooling has been linked to how rapidly cooling is initiated. Ideally, quickly the brain is cooled, and the rate of tissue that reaches the therapeutic hypothermic zone (33°C). Whole body surface (WBS) or intravascular methods for brain cooling are equipped by equipment, systemic hypothermia, severe response, and consequent neurotrophic instability. Selective head cooling by circulatory cold water cap shows promise. Through neural gradients in brain temperature maps. Due to proximity to the cerebral circulation, the nasopharynx is uniquely suited for selective and hypothermic brain cooling. Low flow rates of nasopharyngeal PFC cooling with oxygen or air limited by low heart capacity and respiratory complications. As an alternative the nasopharyngeal distribution and rapid inotropic properties of nasopharyngeal perfusion-controlled (PFC) increases the heat capacity of respiratory gas, thus should facilitate rapid induction and maintainer of global brain cooling without substantial compromise in systemic temperature.

METHODS

Animal Model

- Normal Weaning Sheep (n = 25; 21-25 kg)
- Ketamine (10 mg/kg) and butorphanol tartrate (1 mg/kg) pre-anesthesia (IM)
- Sodium Pentobarbital (12.5 mg/kg) supplemented by continuous infusion (1.25 mg/kg/hr)

Instrumentation

- Temperature, and systemic arterial blood pressure, heart rate: continuous recordings
- Temperature (Blood Chemistry and Cardio Output) Blanket removed, red and final induction, stability throughout maintenance

Measurements

- Gas Flow = 1 L/min/kg

Protocols

- Regional Cooling Rates, Time to Therapeutic Hypothermic Zone, Brain Cooling Rates as a function of PFC-Gas Flow
- Whole Body Surface Cooling induced and maintained by PFC, Gas Flow rates were evaluated (ANOVA) as a function of WBS vs NP-PFC
- PFC: room temperature and Oxygen flow are independently regulated by same flow rates at pre-defined rates
- Nasal Temperature = 2-5°C with PFC nasopharyngeal cooling rapidly induced and maintained global cerebral cooling without cardiopulmonary compromise.

RESULTS

- With WBS nasopharyngeal cooling, PFC gas flow rates directly influenced brain cooling rates.
- With NPC nasopharyngeal cooling, absolute compartmental cooling rates and brain to systemic temperature gradients were significantly greater than with whole body surface cooling.
- With NPC nasopharyngeal cooling, brain to systemic temperature gradients demonstrated preferential brain cooling relative to vascular and rectal temperature profiles. Vascular and rectal cooling rates were approximately one-half and one-third of brain cooling rate, respectively.
- NPC nasopharyngeal cooling, the therapeutic hypothermic zone was reached within 15 min, whereas whole body surface cooling did not obtain this zone within 3 h.
- NPC nasopharyngeal cooling rapidly induced and maintained global cerebral cooling.

CONCLUSIONS

The principle findings of this study are that the therapeutic hypothermic zone targeted for global brain neuroprotection can be rapidly reached and maintained by PFC nasopharyngeal cooling. This approach maintained brain to systemic temperature gradients with preferential brain cooling relative to vascular and rectal temperature profiles, which concomitant systemic instability. Selective head cooling by circulating cold water cap shows promise through neural gradients in brain temperature maps. Due to proximity to the cerebral circulation, the nasopharynx is uniquely suited for selective and hypothermic brain cooling. Low flow rates of nasopharyngeal PFC cooling with oxygen or air limited by low heart capacity and respiratory complications. As an alternative the nasopharyngeal distribution and rapid inotropic properties of nasopharyngeal perfusion-controlled (PFC) increases the heat capacity of respiratory gas, thus should facilitate rapid induction and maintainer of global brain cooling without substantial compromise in systemic temperature.

HYPOTHESIS

NPC nasopharyngeal cooling will rapidly induce global cerebral hypothermia

OBJECTIVES

- Characterize brain cooling rates as a function of PFC-Gas flow rates.
- Compare brain and systemic cooling rates and temperature gradients during NPC nasopharyngeal cooling to whole body surface cooling.

ACKNOWLEDGMENTS

This study was supported by BeneChill, Inc.

SUMMARY

The principle findings of this study are that the therapeutic hypothermic zone targeted for global brain neuroprotection can be rapidly reached and maintained by PFC nasopharyngeal cooling. This approach maintained brain to systemic temperature gradients with preferential brain cooling relative to vascular and rectal temperature profiles, which concomitant systemic instability. Selective head cooling by circulating cold water cap shows promise through neural gradients in brain temperature maps. Due to proximity to the cerebral circulation, the nasopharynx is uniquely suited for selective and hypothermic brain cooling. Low flow rates of nasopharyngeal PFC cooling with oxygen or air limited by low heart capacity and respiratory complications. As an alternative the nasopharyngeal distribution and rapid inotropic properties of nasopharyngeal perfusion-controlled (PFC) increases the heat capacity of respiratory gas, thus should facilitate rapid induction and maintainer of global brain cooling without substantial compromise in systemic temperature.