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Clinical Paper

Feasibility study of immediate pharyngeal cooling initiation in cardiac arrest patients after arrival at the emergency room☆

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ABSTRACT

Aim: Cooling the pharynx and upper oesophagus would be more advantageous for rapid induction of therapeutic hypothermia since the carotid arteries run in their vicinity. The aim of this study was to determine the effects of pharyngeal cooling on brain temperature and the safety and feasibility for patients under resuscitation.

Methods: Witnessed non-traumatic cardiac arrest patients ($n = 108$) were randomized to receive standard care with ($n = 53$) or without pharyngeal cooling ($n = 55$). In the emergency room, pharyngeal cooling was initiated before or shortly after return of spontaneous circulation by perfusing physiological saline (5 °C) into a pharyngeal cuff for 120 min.

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Results: There was a significant decrease in tympanic temperature at 40 min after arrival ($P = 0.02$) with a maximum difference between the groups at 120 min (32.9 ± 1.2 °C, pharyngeal cooling group vs. 34.1 ± 1.3 °C, control group; $P < 0.001$). The return of spontaneous circulation (70% vs. 65%, $P = 0.63$) and rearrest (38% vs. 47%, $P = 0.45$) rates were not significantly different based on the initiation of pharyngeal cooling. No post-treatment mechanical or cold-related injury was observed on the pharyngeal epithelium by macroscopic observation. The thrombocytopaenia incidence was lower in the pharyngeal cooling group ($P = 0.001$) during the 3-day period after arrival. The cumulative survival rate at 1 month was not significantly different between the two groups.
Conclusions: Initiation of pharyngeal cooling before or immediately after the return of spontaneous circulation is safe and feasible. Pharyngeal cooling can rapidly decrease tympanic temperature without adverse effects on circulation or the pharyngeal epithelium.

1. Introduction

Mild hypothermia is known to ameliorate poor neurological outcomes after resuscitation in humans,[1,2] with clinical[3] and laboratory[4] data suggesting that early achievement of hypothermia is one of the most important factors for good neurological outcomes. However, rapid intravenous infusion of cold fluid, which is considered the technique for the fastest induction of hypothermia, may increase rearrest rates even after return of spontaneous circulation (ROSC) initiation.[5] Furthermore, nasal cooling, which is used for intra-arrest cooling, may cause serious epistaxis and periorbital emphysema.[6] Therefore, a technique that can be initiated before or shortly after ROSC without adverse effects is needed.

The bilateral common carotid arteries run near the pharynx and upper oesophagus. Therefore, cooling the pharyngeal region decreases brain temperature by cooling the blood in the carotid artery.[7] We developed a pharyngeal cooling system in which cold saline (5 °C) is perfused into a pharyngeal cuff. The pharyngeal cooling can be initiated before or shortly after ROSC. In a cardiac arrest animal model, pharyngeal cooling was initiated simultaneously with chest compression without having adverse effects on ROSC and pharyngeal epithelium.[7,8]

The primary aim of the present study was to determine the safety and feasibility of pharyngeal cooling in patients with non-traumatic cardiac arrest; the effects of particular interest were ROSC success and rearrest rates. The second aim was to identify the complications associated with the use of pharyngeal cooling, e.g., mechanical damage or cold-related injury to the pharyngeal epithelium. The third aim was to determine the effects of cooling on the tympanic and core temperatures during the initial 2-h period after arrival at the hospital.

2. Methods

2.1. Study design

This study was a multicentre, randomized, controlled clinical trial performed in 19 emergency medical centres in Japan between June 2009 and October 2013. The protocol was determined by a scientific advisory committee, in which emergency departments from seven universities in the Chugoku–Shikoku area in Japan participated, and was approved by the institutional review board of each participating centre. This study is registered at http://www.umin.ac.jp/ctr/index.htm (UMIN000002224 and UMIN000008506).

Originally, the present study was financially supported by the Ministry of Health, Labour and Welfare of Japan and was intended to determine the effect of pharyngeal cooling on tympanic temperature. In July 2010, the institutional review board at Okayama University Medical School recommended discontinuation of this work because of the apparent decrease in tympanic temperature in the pharyngeal cooling group. In December 2011, after approval by the institutional review board, the research was resumed to examine the effect of pharyngeal cooling on survival with the same protocol and was supported by Daiken Medical Co. Although the sample size (108 cases) was much smaller than the size required to evaluate survival (692 cases), the study was terminated owing to the end of the planned experimental period.

Written, informed consent was obtained before enrolment when the family of the patient was present. However, if the family of the patient could not be located, the need for written, informed consent was waived, and consent was obtained as soon as possible. Randomization assignments were generated with block sizes of 4 in a 1:1 allocation to groups receiving standard care with or without pharyngeal cooling. The emergency physician in each participating centre checked the eligibility of patients and, when a patient was eligible, telephoned the allocation centre.

2.2. Patients

The eligibility criteria included the following: aged 16–89 years and witnessed cardiogenic cardiac arrest or witnessed non-cardiogenic cardiac arrest with resuscitation by medical personnel, including emergency services, within 15 min after collapse. Both in-hospital and out-of-hospital cardiac arrests were included. The exclusion criteria included the following: traumatic cardiac arrest, core body temperature <34 °C upon arrival at the emergency room, or pharyngeal or oesophageal disorder.

2.3. Treatments

Patients were resuscitated according to the 2005 or 2010 American Heart Association (AHA) Guidelines, depending on the date of admission. Immediately after arriving at the emergency room, pharyngeal cooling was initiated during chest compression or immediately after ROSC, if ROSC was achieved before arrival, and continued for 2 h unless the tympanic temperature decreased to <32 °C. Although it was encouraged to initiate whole body cooling following 2 h of pharyngeal cooling, the decision regarding timing and the technique were up to each facility based on their current standard care practice, i.e. infusion of cold fluid, ice pack, body surface cooling, or percutaneous cardiopulmonary support. Resuscitation measures were continued for at least 30 min after arrival at the emergency room.

2.4. Pharyngeal cooling

The pharyngeal cooling system (Daiken Medical Co., Osaka, Japan) was composed of a disposable pharyngeal cooling cuff (size #4 for 50–70 kg body weight) and circulator (Fig. 1). The cuff was made of vinyl chloride, designed to fit the upper oesophagus and pharynx and inserted using a manoeuvre similar to that for a