Local Head and Neck Cooling Leads to Hypothermia in Healthy Volunteers

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Introduction

Therapeutic hypothermia is a promising neuroprotective strategy for awake patients with acute ischemic stroke [1]. Animal studies have suggested that the benefit of cooling is larger the earlier this therapy is started [2]. For this reason, cooling may be more effective when initiated already before the patient arrives at the hospital. While the rapid infusion of cold saline and devices for external cooling have been tested successfully in patients after cardiac arrest [3], data on prehospital cooling in suspected stroke are lacking. In contrast to survivors of cardiac arrest, the majority of acute stroke patients is awake and nonsedated. Furthermore, the diagnosis can be misleading in the initial situation and an acceptable benefit-risk ratio must be considered for the cooling method. Up to date, data on the safety of the rapid-saline-infusion method are preliminary [4] and concerns arise from serious fluid overload with respiratory deterioration [5]. In this study, we tested the feasibility, safety and temperature effects of a commercially available cooling cap, covering the surface of the head and neck in healthy volunteers.

Methods

This study was approved by the local ethics committee of the Medical Faculty, University of Erlangen-Nuremberg. The head and neck cooling device (HVM Medical, Rothenburg, Germany) contains free-floating cooling gel with a central portion, covering the head with the exception of the face, and 3 flaps, 1 for the dor-
sal cervical region and 2 for both carotid triangles (fig. 1). Prior to its use, the device is kept at 4°C. Inclusion criteria for the present study were an unremarkable medical history with absence of any active disease, fever, infection or any medication within 4 weeks prior to participation. After obtaining written informed consent, 10 healthy volunteers lay down on an examination couch and were connected to a multimodal monitoring system (Infinity Gamma-Series, Dräger Medical, USA), including continuous ECG, blood pressure and pulse oximetry. A temperature probe (Temprecise, Arizant Healthcare, Inc., USA) was inserted into the rectum. Tympanic temperature was measured with an electronic thermometer (Genius 2 tympanic thermometer, Tyco Healthcare Group, Mansfield, USA). The volunteers rated the perception of frostiness and overall discomfort on a visual analogue scale ranging from 0 (not any) to 10 (maximum). Shivering was quantified from 0 to 3 as described previously [6]. Environmental temperature was set constantly to 23°C and the volunteer’s body was covered with a blanket to avoid heat loss from the trunk and extremities. An initial resting phase of 20 min prior to cooling allowed adaptation to the local environment. After treatment completion, the measurements were continued for another 30 min. A standardized questionnaire was used to assess any adverse events within 24 h by telephone.

Data were processed using the PASW Statistics 18 (SPSS Inc., USA) software package. Normality of distribution was tested using the Shapiro-Wilk and Kolmogorov-Smirnov tests. Data are summarized as means and standard deviations or medians and interquartile ranges (IQR), if they were not distributed normally. Physiologic data were tested for significant differences by repeated-measures ANOVA. The level of significance was set a priori at p = 0.05. If applicable, the Greenhouse-Geisser correction was used.

Results

Four women and 6 men (median age = 35 years, IQR = 28–42 years) with a median body weight of 80 kg (IQR = 67.3–95.3 kg) and a body mass index of 25.3 (IQR = 23.3–30.1) participated in the study.

No serious adverse events, no cardiac arrhythmias, no blood pressure crises or intolerable discomfort occurred during the treatment. Moreover, no shivering was noticed. For the perception of frostiness, a maximum score of 4.5 (IQR = 2–6) was reached on the visual analogue scale after 10 min (IQR = 10–12.5 min). The maximum value for discomfort was 3 (IQR = 2–4) after 50 min. Four test persons complained of moderate headache or pain in the neck during treatment. In 1 case, moderate occipital headache started 3 h after treatment completion. All symptoms had resolved completely during follow-up. No other adverse events occurred.

The mean rectal temperature at baseline was 37.3 ± 0.3°C, while 3 participants presented with elevated core body temperature of 37.6 or 37.7°C prior to treatment. Under therapy, a drop in rectal temperature occurred (fig. 2) and the mean difference from baseline measured 0.65°C (95% CI = 0.064–1.2°C, p = 0.019; fig. 3) after 60 ± 54 min. The mean tympanic temperature at baseline was 36.4 ± 0.4°C. The lowest values were reached after 36 ± 12 min and the mean difference from baseline measured 1.7°C (95% CI = 0.61–2.7°C, p = 0.001). In all participants, the tympanic temperature dropped below 35.7°C, but never exceeded 33.3°C.

An early drop in heart rate with consecutive slow reincrease occurred during cooling. The minimum was reached after 49 ± 37 min and the mean difference from baseline measured 15 beats/min (95% CI = 0.63–30 beats/min, p = 0.036). Arterial blood pressure measurements (F = 0.45, d.f. = 11, p = 0.926) and pulse oximetry (F = 0.332, d.f. = 10, p = 0.97) revealed no significant changes.

Discussion

Treatment by local cooling on the head and neck led to a drop in tympanic and rectal temperature and the procedure was well tolerated by all participants. Neither serious adverse events nor shivering occurred.

There is a strong association between initial core body temperature and the clinical outcome of patients with cerebral injuries [7]. In acute ischemic stroke, with each 1°C
increase in temperature on admission, the relative risk for death or severe neurologic deficits at discharge rises by the factor of 2.2 [8]. In the present study, a drop in the core body temperature by 0.65°C was observed during treatment in healthy volunteers. Given the strong association mentioned before, this rather small effect should still be of clinical relevance. In addition, the applied intensity of cooling was tolerated well by all participants. Enforcing a larger decrease of the core body temperature might cause serious side effects and shivering, leading to an inappropriate risk profile of this method. However, the cooling cap is developed for the use outside the hospital setting in anticipation of more invasive cooling techniques, e.g. endovascular catheters, under the controlled conditions of an intensive care unit.

At present, there is no sufficient evidence for the assumption that surface cooling at the head could lower the intracranial temperature to a greater extent than the core body temperature, and results from clinical studies are conflicting [9, 10]. However, it was suggested that head caps reduce cerebral temperature mainly in superficial, cortical brain regions, while cooling with neck bands

![Graphs showing time course of tympanic and rectal temperature](image-url)

**Fig. 2.** Time course of tympanic and rectal temperature. (a) Heart rate and mean arterial blood pressure (b) during the treatment phase (0–190 min) and the post-treatment phase (starting at 190 min). Error bars indicate standard deviations. MAP = Mean arterial blood pressure.
could lead to hypothermia also in the deep brain [11], probably delivered through the cranial vessels. Whether the cervical flaps of the cooling devices are capable of mediating similar effects remains hypothetical and requires confirmation by future investigations.

Tympanic and rectal temperature measurements show acceptable agreement in normothermic stroke patients [12]. In the setting of the present study, local cooling is performed with close contact to the external ear. Therefore, tympanic readings may be artificially low and should be interpreted as a surrogate of a local cooling effect at superficial regions, including skin and the external ear. This probably does not reflect intracranial temperature.

**Fig. 3.** Effect of surface cooling of head and neck on rectal temperature, tympanic temperature and heart rate. Data reflect mean lowest values during treatment compared to baseline. *p = 0.05; **p = 0.001.

Exposure of the forehead to a cold stimulus had previously been reported to trigger central vagal activation with reactive bradycardia [13] and an increase in cerebral blood flow [14] in humans. Bradycardia was also noted as a consequence of surface cooling in the present study. Further research is necessary to investigate autonomic changes during treatment with the cooling device.

In conclusion, the investigated method of surface cooling for head and neck is feasible and effective in conscious volunteers. It can be considered as a method for preclinical induction of hypothermia.

### References