Letter

Prehospital therapeutic hypothermia in cardiac arrest: will there ever be evidence?

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Bruel and colleagues nicely demonstrate that the infusion of 2 l cold saline during resuscitation is a feasible, effective, and safe measure to induce therapeutic hypothermia in out-of-hospital cardiac arrest [1]. Therapeutic hypothermia was induced in 33 eligible advanced life support patients before primary survival was foreseeable, and was continued in 11 patients after intensive care unit admission. The authors conclude that a large randomised trial should be performed.

The design of future trials on therapeutic hypothermia, however, seems challenged by the fact that withholding this treatment in a control arm might be considered unjustifiable from an ethical point of view. In the prehospital setting, such a trial would require a large number of study patients to demonstrate an additional benefit. This is due to the fact that both a spontaneous decline in body core temperature occurs, especially in the no-flow and low-flow phase, and that the overall gain of time (typically around 45 min) may be considered marginal against the background of most published data, indicating that target temperatures cannot be reached until about 6 to 8 hours later [2,3]. Given the optimistic view that prehospital cooling increases the number of favourable neurological outcomes from 55% [4] to 60%, about 750 patients would have to be included in a given randomised trial.

Nevertheless, although we totally agree with Bruel and colleagues that the intervention is safe and feasible, and that a clear biological rationale for the earliest possible induction of therapeutic hypothermia exists [2-5], we doubt that a prospective randomised trial on additional prehospital cooling is feasible and justifiable. We may have reached another boundary of evidence-based medicine.

Authors’ reply

Cédric Bruel, Jean-Jacques Parienti, William Marie, Xavier Arrot, Cédric Daubin, Damien Du Cheyron, Massimo Massetti and Pierre Charbonneau

We would like to thank Schefold and colleagues for their interest in our article [1]. Two issues are discussed in their correspondence. First, they questioned the ethical rationale of a randomised study in which the control group would not receive out-of-hospital therapeutic hypothermia (which is not yet standard practice) [6]. We believe the findings of our small pilot feasibility study should not be overinterpreted, particularly regarding safety issues, because we presented no control group. For this reason, it is our view that the potential benefit in terms of neurologic outcome, if any, should be evaluated in a randomised controlled study.

The second issue raised by Schefold and colleagues is the small effect size and thus the large sample size required to demonstrate significant improvements. Recent animal models by Nozari and colleagues [7] and Zhao and colleagues [8] demonstrate the benefit on survival if hypothermia is induced during cardiopulmonary resuscitation. This finding supports the concept that postresuscitation injury processes begin immediately after the return of spontaneous circulation, and that cooling during advanced life support may serve as a useful therapeutic approach to improve survival.

Although we do not share Schefold and colleagues’ opinion that the gain of time on cerebral disease is marginal [9], we agree that the potential improvement would be small, in terms of clinical outcome. For this reason, a multicentre international randomised study may be necessary.
Competing interests
The authors declare that they have no competing interests.

References