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[Intervention Review]

Hypothermia for neuroprotection in adults after cardiopulmonary resuscitation

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ABSTRACT

Background

Good neurological outcome after cardiac arrest is difficult to achieve. Interventions during the resuscitation phase and treatment within the first hours after the event are critical. Experimental evidence suggests that therapeutic hypothermia is beneficial, and several clinical studies on this topic have been published. This review was originally published in 2009; updated versions were published in 2012 and 2016.

Objectives

We aimed to perform a systematic review and meta-analysis to assess the influence of therapeutic hypothermia after cardiac arrest on neurological outcome, survival and adverse events.

Search methods

We searched the following databases: the Cochrane Central Register of Controlled Trials (CENTRAL; 2014, Issue 10); MEDLINE (1971 to May 2015); EMBASE (1987 to May 2015); the Cumulative Index to Nursing and Allied Health Literature (CINAHL) (1988 to May 2015); and BIOSIS (1989 to May 2015). We contacted experts in the field to ask for information on ongoing, unpublished or published trials on this topic. The original search was performed in January 2007.

Selection criteria

We included all randomized controlled trials (RCTs) conducted to assess the effectiveness of therapeutic hypothermia in participants after cardiac arrest, without language restrictions. We restricted studies to adult populations cooled by any cooling method, applied within six hours of cardiac arrest.

Data collection and analysis

We entered validity measures, interventions, outcomes and additional baseline variables into a database. Meta-analysis was performed only for a subset of comparable studies with negligible heterogeneity. We assessed the quality of the evidence by using standard methodological procedures as expected by Cochrane and incorporated the GRADE (Grades of Recommendation, Assessment, Development and Evaluation) approach.

Main results

We found six RCTs (1412 participants overall) conducted to evaluate the effects of therapeutic hypothermia - five on neurological outcome and survival, one on only neurological outcome. The quality of the included studies was generally moderate, and risk of bias was low in three out of six studies. When we compared conventional cooling methods versus no cooling (four trials; 437 participants), we found

that participants in the conventional cooling group were more likely to reach a favourable neurological outcome (risk ratio (RR) 1.94, 95% confidence interval (CI) 1.18 to 3.21). The quality of the evidence was moderate.

Across all studies that used conventional cooling methods rather than no cooling (three studies; 383 participants), we found a 30% survival benefit (RR 1.32, 95% CI 1.10 to 1.65). The quality of the evidence was moderate.

Across all studies, the incidence of pneumonia (RR 1.15, 95% CI 1.02 to 1.30; two trials; 1205 participants) and hypokalaemia (RR 1.38, 95% CI 1.03 to 1.84; two trials; 975 participants) was slightly increased among participants receiving therapeutic hypothermia, and we observed no significant differences in reported adverse events between hypothermia and control groups. Overall the quality of the evidence was moderate (pneumonia) to low (hypokalaemia).

Authors' conclusions

Evidence of moderate quality suggests that conventional cooling methods provided to induce mild therapeutic hypothermia improve neurological outcome after cardiac arrest, specifically with better outcomes than occur with no temperature management. We obtained available evidence from studies in which the target temperature was 34°C or lower. This is consistent with current best medical practice as recommended by international resuscitation guidelines for hypothermia/targeted temperature management among survivors of cardiac arrest. We found insufficient evidence to show the effects of therapeutic hypothermia on participants with in-hospital cardiac arrest, asystole or non-cardiac causes of arrest.

PLAIN LANGUAGE SUMMARY

Cooling the body after resuscitation following cardiac arrest

Review question

In this review, we asked whether people resuscitated from cardiac arrest benefit when their bodies are cooled to a temperature of 34°C or lower.

Background

Population and outcomes

Around 30% to 50% of all people with coronary heart disease suffer sudden cardiac death at some stage of their illness. Sudden cardiac death means that the heart and subsequently the circulation stop. If these people are not resuscitated, brain cells begin to be irreversibly damaged, and subsequently the person dies. After resuscitation, treatment within the first few hours is critical for avoiding or limiting brain damage. One form of therapy that may help to prevent cell damage consists of cooling the body for several hours after successful resuscitation to 34°C or lower.

Intervention

We compared people who had their bodies cooled to 32°C to 34°C or below after resuscitation with people who were not cooled following successful resuscitation.

Search date

Evidence is current to May 2015.

Study characteristics

We included in our analysis six studies (1412 people overall), four of which (437 people) examined effects of cooling the body by conventional methods after successful resuscitation for cardiac arrest. One study that used haemofiltration (cooling the blood externally - similar to dialysis) as the cooling method and one study in which cooling to 33°C was compared with temperature management at 36°C were treated separately in the review.

Study funding sources

The study that used external cooling was supported by a dialysis-related company. Of the five studies included in the main analysis, two received funding from government or non-profit organizations; three studies did not provide information on funding.

Key results

When we compared people whose bodies were cooled to 32°C to 34°C after resuscitation versus those whose bodies were not cooled at all, we found that 63% of those receiving cooling would suffer no, or only minor, brain damage, while only 33% of those not cooled would suffer no, or only minor, brain damage. Cooling had an important effect on simple survival, with or without brain damage: 57% would survive if their bodies were cooled compared with 42% if their bodies were not cooled at all. No serious side effects occurred, but cooling the body

was associated with increased risk of pneumonia (49% vs 42% of those studied) and increased risk of low concentrations of potassium in the blood (18% vs 13%).

Quality of the evidence

Some studies had quality shortcomings including small numbers of participants and use of inadequate methods to balance participants between intervention and control groups. However, when differences between studies are acknowledged (heterogeneity), it is clear that these shortcomings had no major impact on the main results.