Review: mild induced hypothermia does not reduce mortality or severe disability in moderate to severe head injury


Q Does mild induced hypothermia reduce mortality and improve long term function in patients with moderate to severe head injury?

METHODS

Data sources: Medline, EMBASE/Excerpta Medica, Cochrane Injuries Group Specialised Register, Cochrane Controlled Trials Register (all to 2001); hand searches of conference proceedings and reference lists of relevant trials and review articles; and investigators in the field.

Study selection and assessment: randomised controlled trials (RCTs) that compared mild therapeutic hypothermia (local or systemic therapeutic cooling [using a fluid filled cooling blanket, a “Bear Hugger” air cooling device, ice water lavage, or combination, or other method] to a target temperature <34–35°C for ≥12 hours beginning on admission to the intensive care unit or when intracranial pressure [ICP] became uncontrollable by conventional management) with control (open or normothermia) in patients with any closed head injury requiring hospital admission. Individual study quality was assessed based on allocation concealment and blinding of outcome assessors.

Outcomes: all cause mortality and death or severe disability (Glasgow Outcome Scale score of severe disability or persistent vegetative state or equivalent measure). Secondary outcomes were complications (pneumonia, coagulopathy, and other serious adverse events) and mean ICP during treatment.

MAIN RESULTS

14 RCTs (n = 1094) met the selection criteria. Allocation was concealed in 5 RCTs and unclear in 9 RCTs; outcome assessment was blinded in 6 RCTs and unblinded or unclear in 8 RCTs. Meta-analysis using a fixed effects model showed that immediate induced hypothermia and normothermia did not differ for all cause mortality (odds ratio [OR] 0.90, 95% CI 0.61 to 1.04), and death or severe disability (OR 0.95, CI 0.56 to 1.00) (table). More patients who received hypothermia developed pneumonia than those who received normothermia (OR 1.95, CI 1.18 to 3.23). None of the studies reported on any of the other secondary outcomes. 1 RCT (n = 33) compared deferred hypothermia with normothermia. The groups did not differ for all cause mortality (OR 0.21, CI 0.04 to 1.05) or risk of pneumonia (OR 1.13, CI 0.18 to 5.93). The deferred hypothermia group had a reduced risk of death or severe disability compared with the normothermia group (OR 0.10, CI 0.01 to 1.00).

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Hypothermia v normothermia for moderate to severe head injury*

<table>
<thead>
<tr>
<th>Outcomes at 3–12 months</th>
<th>Number of trials (n)</th>
<th>Hypothermia</th>
<th>Normothermia</th>
<th>Weighted event rates</th>
<th>RRR (95% CI)</th>
<th>NNT (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All cause mortality</td>
<td>12 (1061)</td>
<td>28%</td>
<td>33%</td>
<td>14% (3–28)</td>
<td>Not significant</td>
<td></td>
</tr>
<tr>
<td>Death or severe disability</td>
<td>9 (746)</td>
<td>50%</td>
<td>57%</td>
<td>12% (0 to 23)</td>
<td>Not significant</td>
<td></td>
</tr>
<tr>
<td>Pneumonia</td>
<td>7 (281)</td>
<td>44%</td>
<td>29%</td>
<td>51% (10 to 108)</td>
<td>7 (4 to 25)</td>
<td></td>
</tr>
</tbody>
</table>

*Abbreviations defined in glossary; RRR, RRI, NNT, NNH, and CI calculated from data in article using a fixed effects model.
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