**Important data on effects of late hypothermia**

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An important hypothermia-study has just been published by Laptook and the NICHD group1. 168 newborn term infants who failed the 6h time-window for HT were recruited by 21 centers over 8 years into a trial of hypothermia versus normothermia if they were >6h and <24h old. Survivors were examined at 18-22 months with Bayley III examination. Data was available in 157 including 18 who died (78 HT - 19 with poor outcome, 79 NT - 22 with poor outcome). Clearly any difference between HT and NT must be small, and is not significant (p≈0.75). However, the authors conclude that “among term infants with hypoxic-ischemic encephalopathy hypothermia initiated at 6 to 24 hours after birth compared with noncooling resulted in a 76% probability of any reduction in death or disability”.

In Bayesian analyses, the probability of treatment effect (the posterior probability distribution) is estimated incorporating also a prior probability distribution, if such can be constructed from prior knowledge. In the present case there is no available data from trials or pilot studies with time of recruitment larger than 6 hours post partum. Most of the results in the paper are presented from an analysis using a ‘neutral’ prior (assuming no treatment effect in the median, relative risk = 1.0). However, the authors may freely choose both the shape and the width of the prior distribution. They have chosen an informative prior, a log-normal with SD = 0.35. Other priors could have been used as well.2

However, in the present case there is additional relevant prior information from experimental studies on animals (fetal sheep3 and 7d neonatal rats4). The information obtained in these studies is very clear and similar in the two very different species. The therapeutic effect of cooling diminishes linearly with the time of start of cooling and is zero after 9 hours post insult. On this background the results presented by Laptook et al1 appear to confirm that the results from these two animal species of no effect of late cooling are also valid for newborn humans.

One of the main conclusions in the paper, that “The probability that death or disability in cooled infants was at least 1%, 2%, or 3% less than noncooled infants was 71%, 64%, and 56%, respectively” when hypothermia was initiated 6 to 24 hours after birth, is highly speculative and should not be used as argument for change in the current cooling advice.

References

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