Room air resuscitation of the depressed newborn: a systematic review and meta-analysis

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CRD summary
This well-conducted and clearly reported review found that, compared to resuscitation with 100% oxygen, resuscitation with room air is associated with decreased mortality at both 1 week and 1 month. These conclusions are likely to be reliable.

Authors' objectives
To compare the effects of resuscitation with room air and with 100% oxygen on mortality at 1 week and 1 month in asphyxiated newborn infants.

Searching
MEDLINE, EMBASE, CINAHL and the Cochrane CENTRAL Register were searched from inception; the search terms were reported. In addition, the Cochrane Neonatal Group and the journal Pediatric Research were handsearched, the meta Register of controlled Trials was searched for ongoing studies, and conference proceedings were searched using Web of Science and NLM Gateway. All searches were carried out up to August 2005. The reference lists of retrieved studies were screened and experts in the area were contacted for additional relevant studies (including unpublished studies). No language restrictions were applied.

Study selection
Study designs of evaluations included in the review
Randomised or quasi-randomised controlled trials were eligible for inclusion.

Specific interventions included in the review
Studies that compared resuscitation with room air or supplemental oxygen (OxR) were eligible for inclusion. The concentrations of oxygen in the included studies were 21% for room air groups and 100% for OxR groups. The duration of the initial resuscitation was generally 2 minutes and no longer than 10 minutes.

Participants included in the review
Studies of asphyxiated or depressed infants requiring respiratory resuscitation at birth were eligible for inclusion. There were no restrictions in terms of birth weight or gestational age. All studies included asphyxiated newborns. Criteria for asphyxiation (which varied across studies) were one or more of the following: heart rate less than 60 to 100 beats per minute, apnoea, gasping, hypotonia, non-response to external stimuli or nasopharyngeal suction, pale skin and mucous colour, requirement for positive pressure ventilation, pH less than 7.00 to 7.15. The mean gestational age ranged from 37.4 to 40.5 weeks and the mean birth weight from 2,319 to 3380 g. Apgar scores at 1 minute following birth ranged from 3 to 5.

Outcomes assessed in the review
Studies in which death or hypoxic ischaemic encephalopathy (HIE) were evaluated as either primary or secondary outcome measures were eligible for inclusion. Studies had to report previously unpublished data. The outcomes considered in the review were 7- and 30-day mortality, diagnosis of HIE and Apgar scores. Neurological outcomes were determined by detailed examination at 1 month of age.

How were decisions on the relevance of primary studies made?
Two reviewers independently screened studies for inclusion. Any differences were resolved by consensus.

Assessment of study quality
Two reviewers independently assessed the methodological quality of the included studies using the Jadad criteria; the maximum possible score was 4. Any disagreements were resolved through consensus.

Data extraction
Two reviewers independently extracted the data using a standardised form. Any differences were resolved by consensus. Data were extracted on 7-day mortality, 30-day mortality, HIE, Apgar score, gestational age and birth weight. Odds ratios (ORs), together with 95% confidence intervals (CIs), were calculated for dichotomous outcomes.

Methods of synthesis
How were the studies combined?
ORs were pooled using standard meta-analysis methods and using cumulative meta-analysis to investigate the effect of publication date. Publication bias was assessed using a funnel plot.

How were differences between studies investigated?
Differences between the studies were investigated statistically using the chi-squared test.

Results of the review
Seven studies (2,011 infants) were included.

Four studies received a Jadad quality score of zero, while only one received the maximum score of 4. Only 3 studies reported any form of blinding. Four studies based randomisation on day of birth; the remainder randomised at the time of birth after a diagnosis of asphyxia was established.

Mortality in the first week (6 studies) was lower in infants resuscitated with room air than in those resuscitated with OxR (OR 0.70, 95% CI: 0.50, 0.98). There was no evidence of heterogeneity (p=0.939).

Mortality in the first month (5 studies) was also lower in infants resuscitated with room air than in those resuscitated with OxR (OR 0.63, 95% CI: 0.42, 0.94). There was no evidence of heterogeneity (p=0.543).

Publication date did not affect these results.

The incidence of grade II or III HIE (4 studies) was similar between the two groups (OR 0.86, 95% CI: 0.65, 1.14). There was no evidence of heterogeneity (p=0.298).

There was no evidence of publication bias based on funnel plots.

Authors' conclusions
Room air resuscitation is associated with decreased mortality at both 1 week and 1 month compared to resuscitation with 100% oxygen.

CRD commentary
This review addressed a focused question that was supported by defined inclusion criteria. A detailed literature search without language restrictions, and which included attempts to locate unpublished studies, was conducted and it is unlikely that any relevant studies were missed. Appropriate steps were taken to minimise errors and bias at all stages of the review process. Study quality was assessed using appropriate criteria and the results were presented and discussed. Relevant details of the studies were summarised in tables. The pooling of the studies was appropriate and clearly presented, but it is unclear whether random-effects or fixed-effect models were used. This was a well-conducted and clearly reported review, and the authors' conclusions are likely to be reliable.

Implications of the review for practice and research
Practice: The authors stated that room air was the preferred choice for initiating resuscitation in depressed full-term newborns, although definitive recommendations could not be made because of limitations in the methodology and patient populations of the included studies.

Research: The authors stated that large-scale randomised trials are required to assess the potential benefits of room air resuscitation in pre-term infants; such trials should include long term follow-up.
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