Resuscitation of newborn infants with 21% or 100% oxygen: an updated systematic review and meta-analysis
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CRD summary
This review concluded that there was a significant reduction in the risk of neonatal mortality and a trend to towards a reduction in risk of severe hypoxic ischaemic encephalopathy in newborns resuscitated with 21% oxygen compared to those given 100% oxygen. Despite poor reporting of some aspects of the review process, this conclusion is probably reliable.

Authors' objectives
To compare the efficacy of 21% and 100% oxygen in the resuscitation of newborn infants.

Searching
MEDLINE, EMBASE and Cochrane Central Register of Controlled Trials were searched up to March 2008. Search terms were reported. Experts were consulted and abstracts, conference proceedings and symposia were searched. Authors of some studies were contacted.

Study selection
Randomised controlled trials (RCTs) or quasi-randomised controlled trials (quasi-RCTs) that assessed 21% or 100% oxygen in the resuscitation of depressed newborn babies (defined as those felt by the attending clinician to require ventilatory intervention with either a bag and mask or an endotracheal tube and typically had apnea and a heart rate under 80 to 100 beats per minute) were eligible for inclusion. There were no restrictions on gestational age or birth weight. The primary outcome was neonatal death. The secondary outcome was the presence of stage two or three hypoxic ischaemic encephalopathy.

RCTs in the review enrolled only term or near-term infants; quasi-RCTs included babies with birth weight as low as 1,000g. Mean gestational age ranged from 35.3 to 40.5 weeks and mean birth weight from 2,319g to 3,536g.

Three authors selected the studies through consensus.

Assessment of study quality
Randomisation and blinding were assessed and the studies classed as highest quality (randomised and blinded), intermediate quality (randomised but unblinded) and lowest quality (quasi-randomised and unblinded). The authors did not state how many reviewers performed this assessment.

Data extraction
Data were extracted to permit the calculation of relative risks (RR) with 95% confidence intervals (CI). Authors were contacted for missing data where necessary.

The authors did not state how many reviewers performed the data extraction.

Methods of synthesis
Pooled relative risks with 95% CI were calculated using a fixed-effect meta-analysis. Numbers needed to treat (NNT) with 95% CI were calculated. Statistical heterogeneity was assessed using the $I^2$ statistic and visual inspection of forest plots. Subgroup analyses were performed for randomised and quasi-randomised studies.

Results of the review
Ten studies (n=2,133) were included in the review: six RCTs and four quasi-RCTs. Three studies were double-blinded.
Neonatal mortality: Pooled analysis of all trials showed a statistically significant reduced incidence of neonatal mortality in the groups treated with 21% oxygen (RR 0.69, 95% CI 0.54 to 0.88, NNT 25, 95% CI 16 to 100; 10 trials). Subgroup analyses of RCTs and quasi-RCTs showed comparable results. The RCT analysis produced a relative risk of 0.32 (95% CI 0.12 to 0.84; six RCTs).

There were no statistically significant differences between the groups in incidence of stage two or three hypoxic ischaemic encephalopathy. But both the overall analysis and the subgroups of RCTs and quasi-RCTs showed directions of effect that favoured 21% oxygen.

Authors’ conclusions
There was a significant reduction in the risk of neonatal mortality and a trend to towards a reduction in risk of severe hypoxic ischaemic encephalopathy in newborns resuscitated with 21% oxygen.

CRD commentary
The review question and the inclusion criteria were clear. Three relevant databases and other sources were searched, which reduced the chances of relevant studies being omitted. The authors reported using some measures to reduce reviewer bias and error in the selection of studies, but not at other stages of the review process. Two key aspects of trial validity were assessed and the synthesis was informed by the criteria of randomisation. The use of meta-analysis and pre-planned subgroups was appropriate.

The authors’ conclusions reflect the results of the review and, despite poor reporting of some aspects of the review process, are probably reliable.

Implications of the review for practice and research
Practice: The authors stated that, until further data are available, use of 100% oxygen should be avoided in the resuscitation of depressed newborn term or near-term infants. Resuscitation with room air appeared safe and may be of great benefit in both high- and low-income countries. Oxygen should be readily available for use in infants who do not respond to resuscitation with room air.

Research: The authors stated that there was a need for appropriately powered studies with longer-term follow-up to assess developmental sequelae in newborns resuscitated with room air compared to those given 100% oxygen. Further studies were needed to assess the best means of resuscitating low birthweight babies and the benefits of 30% and 40% oxygen in different groups should be assessed.

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Other publications of related interest
Saugstad OD, Ramji S, Vento M. Resuscitation of depressed newborn infants with ambient air or pure oxygen: a meta-analysis. Biology of the Neonate 2005; 87:27-34

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