Systematic review of prophylactic vs rescue surfactant

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Authors' objectives
To undertake a systematic review of the effectiveness of prophylactic compared with rescue surfactant, in the treatment and prevention of respiratory distress syndrome (RDS) in premature babies.

Searching
The studies were identified by a search of MEDLINE, through the author's personal knowledge of published findings, and by contacting researchers in the field and the National Perinatal Epidemiology Unit. No search terms or coverage years are given.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were included.

Specific interventions included in the review
Prophylactic treatment: surfactant given on initial resuscitation, and certainly within minutes of birth, down an endotracheal tube.

Rescue treatment: surfactant given to an intubated baby several hours after birth when RDS has been diagnosed. Specific surfactants included BLES, Infasurf and Curosurf.

Trials studied different doses and the catheter technique.

Participants included in the review
The premature babies in the included studies ranged from 24 to 32 weeks. Babies with malformations, rupture of membranes and infection were excluded. The mean gestational age ranged from 26.9 to 31 weeks, and the mean birth weight ranged from 962 to 1,608 g.

Outcomes assessed in the review
Neonatal mortality, total mortality, pneumothorax, pulmonary interstitial emphysema, X-ray grade at 6 hours (grades 3 to 4), number receiving oxygen at 28 days, number receiving oxygen at 36 weeks, all brain haemorrhages, intraventricular haemorrhages (grade 3 and 4), periventricular leukomalacia, patent ductus arteriosus, necrotising enterocolitis, retinopathy of prematurity.

How were decisions on the relevance of primary studies made?
The author does not state how the papers were selected for the review, or how many of the reviewers performed the selection.

Assessment of study quality
The author does not state that validity was assessed.

Data extraction
The author does not state how the data were extracted for the review, or how many of the reviewers performed the data extraction.

Methods of synthesis
How were the studies combined?
A meta-analysis was conducted using the Cochrane Collaboration review manager software (RevMan version 2.1a, 1995). For severity of RDS, a narrative review was undertaken.

How were differences between studies investigated?
The author does not state how differences between the studies were investigated.

**Results of the review**

Six RCTs (2,520 babies) were included.

Neonatal mortality: the odds ratio (OR) was 0.55 (95% confidence interval, CI: 0.41, 0.73) in favour of prophylactic compared to rescue surfactant. This corresponds to a 39% reduction in the incidence of neonatal death.

Total mortality (results from 4 trials): OR 0.59 (95% CI: 0.42, 0.82), corresponding to a 36% reduction in the incidence of total death.

Pneumothorax: OR 0.60 (95% CI: 0.40, 0.88), corresponding to a 39% reduction in the incidence of pneumothoraces.

Pulmonary interstitial emphysema: OR 0.51 (95% CI: 0.32, 0.79), corresponding to a 45% reduction in incidence.

X-ray grade (3 or 4) at 6 hours (results from 3 trials): OR 0.54 (95% CI: 0.38, 0.77) in favour of prophylactic compared to rescue surfactant.

There were no statistically significant differences in the other outcomes which were compared using meta-analysis.

All trials showed improvement in gas exchange and severity of RDS with the use of a prophylactic surfactant.

There was no evidence that prophylactic surfactants had a deleterious effect in any of the trials.

The babies treated prophylactically required about 70% more doses of surfactant than the rescue group. However, the babies in the rescue group who were treated with surfactant received an average of 1.5 doses, compared with 1.2 in the prophylactic group.

**Cost information**
The costs of surfactant treatment for each extra life saved, for those surfactants marketed in the UK, are approximately: ALEC, £1,050; Exosurf and Survanta, £2,142; and Curosurf, £2,800.

**Authors’ conclusions**
Compared with rescue surfactant, prophylactic surfactant significantly reduces neonatal mortality when given at birth to babies of less than 32 weeks’ gestation.

**CRD commentary**
This was a well-written review with clear objectives, which provided detailed information about the intervention, participants and study design for all the individual studies.

However, there was limited information on the review methodology such as the inclusion and exclusion criteria. The search was limited, with no information regarding dates and search terms, and it was unclear whether any attempt was made to identify unpublished studies. Validity does not appear to have been assessed, and there appears to be no details about how decisions were made. Insufficient detail was given about the way in which studies were combined, and it is unclear whether a fixed-effect or random-effects model was used in the meta-analysis. Differences between the studies were not investigated, although it is clear from the tables that such differences existed. The confounding effect of the use of antenatal steroids was not considered in the meta-analysis, although details were given for the individual studies. The results, therefore, should be interpreted with caution.
The author's additional conclusions, regarding the generalisability of the results to surfactants not considered in the review, do not reflect the evidence presented.

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