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TABLE OF CONTENTS

HEADER	1
ABSTRACT	1
PLAIN LANGUAGE SUMMARY	2
BACKGROUND	3
OBJECTIVES	3
METHODS	3
RESULTS	5
DISCUSSION	6
AUTHORS' CONCLUSIONS	6
ACKNOWLEDGEMENTS	6
REFERENCES	7
CHARACTERISTICS OF STUDIES	8
DATA AND ANALYSES	12
Analysis 1.1. Comparison 1 Early vs late CDP, Outcome 1 Use of IPPV.	13
Analysis 1.2. Comparison 1 Early vs late CDP, Outcome 2 Mortality (time not specified).	14
Analysis 1.3. Comparison 1 Early vs late CDP, Outcome 3 Mortality at 28 days.	14
Analysis 1.4. Comparison 1 Early vs late CDP, Outcome 4 Pneumothorax.	15
Analysis 1.5. Comparison 1 Early vs late CDP, Outcome 5 Duration of oxygen in survivors (days).	15
Analysis 1.6. Comparison 1 Early vs late CDP, Outcome 6 Use of IPPV below 1500 g.	16
Analysis 1.7. Comparison 1 Early vs late CDP, Outcome 7 Use of IPPV 1500 g or more.	16
Analysis 1.8. Comparison 1 Early vs late CDP, Outcome 8 Mortality (time not specified) below 1500 g.	16
Analysis 1.9. Comparison 1 Early vs late CDP, Outcome 9 Mortality (time not specified) 1500 g or more.	17
Analysis 1.10. Comparison 1 Early vs late CDP, Outcome 10 Bronchopulmonary dysplasia.	17
Analysis 1.11. Comparison 1 Early vs late CDP, Outcome 11 Retinopathy of prematurity.	17
Analysis 2.1. Comparison 2 Early vs late CDP - excluding Krouskop 1975 (quasi-random), Outcome 1 Use of IPPV.	18
Analysis 2.2. Comparison 2 Early vs late CDP - excluding Krouskop 1975 (quasi-random), Outcome 2 Mortality (time not specified).	18
WHAT'S NEW	19
HISTORY	19
CONTRIBUTIONS OF AUTHORS	20
DECLARATIONS OF INTEREST	20
SOURCES OF SUPPORT	20
INDEX TERMS	20

[Intervention Review]

Early versus delayed initiation of continuous distending pressure for respiratory distress syndrome in preterm infants

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jho@pc.jaring.my.**Editorial group:** Cochrane Neonatal Group**Publication status and date:** New search for studies and content updated (no change to conclusions), published in Issue 3, 2010.**Citation:** Ho JJ, Henderson-Smart DJ, Davis PG. Early versus delayed initiation of continuous distending pressure for respiratory distress syndrome in preterm infants. *Cochrane Database of Systematic Reviews* 2002, Issue 2. Art. No.: CD002975. DOI: [10.1002/14651858.CD002975](https://doi.org/10.1002/14651858.CD002975).

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ABSTRACT

Background

The application of continuous distending pressure (CDP) has been shown to have some benefits in the treatment of preterm infants with respiratory distress syndrome (RDS). CDP has the potential to reduce lung damage particularly if applied early before atelectasis has occurred. Early application of CDP may better conserve an infant's own surfactant stores and consequently be more effective than CDP applied later in the course of RDS.

Objectives

To determine if early compared with delayed initiation of CDP results in lower mortality and reduced need for intermittent positive pressure ventilation in preterm infants with RDS.

Search methods

The standard search strategy of the Cochrane Neonatal Review Group was used. This included searches of the Oxford Database of Perinatal Trials, Cochrane Central Register of Controlled Trials (CENTRAL, The Cochrane Library, Issue 3, 2006), MEDLINE (1966 to September Week 4, 2006), previous reviews including cross references, abstracts, conference and symposia proceedings, expert informants, journal hand searching mainly in the English language.

The electronic search was updated in November 2009.

Selection criteria

Trials which used random or quasi-random allocation to either early or delayed CDP in spontaneously breathing preterm infants with respiratory distress syndrome.

Data collection and analysis

Standard methods of the Cochrane Collaboration and its Neonatal Review Group were used, including independent assessment of trial quality and extraction of data by two authors.

Main results

In six studies on a total of 165 infants, early CDP was associated with a significant reduction in subsequent use of intermittent positive pressure ventilation (IPPV), (typical RR 0.55, typical RD -0.16, NNT 6), but there was no evidence of effect on overall mortality. There was

no evidence of effect on the rates of pneumothorax (five studies) or bronchopulmonary dysplasia (one study). Early CDP resulted in a reduction in duration of oxygen therapy in the single study reporting this outcome.

Authors' conclusions

Early application of CDP has a clinical benefit in the treatment of RDS in that it reduces subsequent use of IPPV and thus may be useful in preventing the adverse effects of this treatment. However, many of the trials were done in the 1970s and 1980s and re-evaluation of the strategy of early CDP in the era of antenatal steroid use and early surfactant administration is indicated focusing on administration methods.

PLAIN LANGUAGE SUMMARY

Early versus delayed initiation of continuous distending pressure for respiratory distress syndrome in preterm infants

Premature babies often lack the substance, surfactant, a detergent like substance produced by the lung. This causes their lungs to fail to expand properly at birth, and breathing in requires a big effort. If left untreated, breathing difficulty progressively worsens and it may cause damage to the lung. Continuous distending pressure (CDP) improves the expansion of the lung making it easier for the premature baby to breath. It is applied through a face mask, or into the nostrils or by a partial vacuum outside the chest. When applied early, it may also reduce the lung damage that causes chronic lung disease. Different ways of using CDP were assessed in six controlled trials (four randomized), and it was found that fewer infants who received early CDP had to go on to be treated with intermittent positive pressure ventilation. No adverse effect of early use of CDP was found in these trials. However, there were several limitations to information from the studies, as the number of infants was small and the mean age ranged from seven to eighteen hours old when CDP was applied. Practice has changed from when these studies were done. CDP interventions are applied earlier, and surfactants are commonly given as well. Corticosteroids are given to the fetus before birth (antenatally) to prepare their lungs for birth.

BACKGROUND

Description of the condition

Primary surfactant deficiency is responsible for respiratory distress syndrome (RDS) in preterm infants (Avery 1959). This deficiency in surfactant results in low lung volumes, poor lung distensibility and atelectasis. The resulting hypoxia leads to increased pulmonary vascular resistance and right to left shunting (Gribetz 1959; Evans 1991). This exacerbates existing ventilation-perfusion abnormalities. The disease is also characterised by alveolar-capillary leakage, pulmonary oedema, and alveolar cell injury (Barter 1960). These lead to the formation of hyaline membranes seen on histological examination of diseased lungs.

Intermittent positive pressure ventilation (IPPV) without a positive end expiratory pressure was the first mode of assisted ventilation used for the treatment of RDS in preterm infants. When it became evident that low lung volume was a consequence of the disease, continuous distending pressure was developed as a means of increasing lung volume and improving oxygenation (Gregory 1971). Positive end expiratory pressure was also found to improve oxygenation in ventilated infants (Herman 1973; Cotton 1998).

Description of the intervention

The application of continuous distending pressure (CDP) either as continuous negative distending pressure (CNP) or continuous positive airway pressure (CPAP) has been shown to have some benefits in the treatment of preterm infants with RDS (Ho 2002). It was not clear whether the effectiveness of CDP is modified by birth weight or gestational age. However, in babies < 1000 g or < 28 weeks there may be insufficient respiratory drive for them to cope with CDP. Continuous distending pressure applied as nasal CPAP has been established in post-extubation care (Davis 2003).

How the intervention might work

CDP improves lung function by reducing the work of breathing, normalizing lung volumes and improving ventilation-perfusion mismatch (Cogswell 1975; Saunders 1976; Richardson 1978; Cotton 1980; Field 1985; Harris 1996). CDP also conserves surfactant (Wyszogrodski 1975; Verder 1994). It splints the airways during expiration and thus reduces atelectasis in the surfactant-deficient lung (Miller 1990). It therefore has the potential to reduce lung damage seen in RDS, particularly if applied early before alveolar collapse occurs. Surfactant, a proven treatment for RDS, is more effective if applied early (Soll 2001; Yost 1999) suggesting the hypothesis that CDP by virtue of its properties may also be more effective if applied early.

Why it is important to do this review

The purpose of this review is to establish whether the early application of CDP has any benefit over later application in preterm infants with RDS. An earlier review on this subject has been done (Bancalari 1992).

OBJECTIVES

To determine if early compared with delayed initiation of CDP results in a lower mortality and reduced need for intermittent positive pressure ventilation in preterm infants with RDS.

Subgroup analyses were planned a priori on the basis of weight (with subdivisions at 1000 g and 1500 g) and gestation (with subdivisions at 28 and 32 weeks), the type of CDP (CPAP or CNP) and according to whether surfactant was used. Sensitivity analyses based on trial quality were also planned.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised or quasi-randomised controlled trials

Types of participants

Preterm infants (i.e. those < 37 weeks) with respiratory distress syndrome breathing spontaneously at trial entry prior to the application of any assisted ventilation other than for resuscitation at birth.

Types of interventions

Early CDP (commencing at randomization) delivered by nasal prongs, mask, single nasopharyngeal tube, endotracheal tube or a continuous negative pressure delivered via a pressure chamber enclosing the thorax, compared with a policy of delayed CDP [initiated at FiO₂ (fraction of inspired oxygen) of approximately 0.6 or more] compared to standard care.

Types of outcome measures

Primary outcomes

1. Failure - death or use of intermittent positive pressure ventilation (IPPV) prior to hospital discharge.
2. Mortality (first 28 days of life and prior to discharge).
3. Use of IPPV prior to discharge.

Secondary outcomes

1. Air leak (pneumothorax, pneumomediastinum, or pulmonary interstitial emphysema).
2. Intraventricular haemorrhage (IVH) (any or grades 3 or 4).
3. Necrotising enterocolitis (NEC) [Bell criteria stage 2, (Bell 1978)].
4. Retinopathy of prematurity (ROP) (any or stage 3 and greater).
5. Bronchopulmonary dysplasia (BPD) (oxygen dependency at 28 days).
6. Chronic lung disease (CLD) (oxygen dependency at 36 weeks postmenstrual age).
7. Long-term growth and neurodevelopmental outcome (cerebral palsy and abnormal mental development < 2 SD below the mean on a standardised score).

Search methods for identification of studies

The standard search strategy of the Cochrane Neonatal Review Group was used.

Electronic searches

The search included the Oxford Database of Perinatal Trials, Cochrane Central Register of Controlled Trials (CENTRAL, The Cochrane Library, Issue 3 2006), and MEDLINE (1966 to September week 4, 2006; all languages). The MEDLINE search terms used were newborn, neonate, respiratory distress

syndrome, hyaline membrane disease, continuous distending pressure, continuous distending airway pressure, continuous positive airway pressure, continuous positive transpulmonary pressure, continuous transpulmonary pressure, continuous inflating pressure, continuous negative distending pressure, continuous negative pressure or continuous airway pressure.

In November 2009, we updated the search as follows: MEDLINE (search via PubMed), CINAHL, EMBASE and CENTRAL (*The Cochrane Library*) were searched from 2006 to 2009. Search terms: respiratory distress syndrome OR hyaline membrane disease OR continuous distending pressure OR continuous distending airway pressure OR continuous positive airway pressure OR continuous positive transpulmonary pressure OR continuous transpulmonary pressure OR continuous inflating pressure OR continuous negative distending pressure OR continuous negative pressure OR continuous airway pressure. Limits: human, infant and clinical trial. No language restrictions were applied.

Updated search found no new trials. No changes to conclusions.

Searching other resources

The search included previous reviews including cross-references and abstracts.

Clinical trials registries were also searched for ongoing or recently completed trials (clinicaltrials.gov; controlled-trials.com; and who.int/ictpr)

Data collection and analysis

The standard methods of the Cochrane Neonatal Review Group Guidelines were employed.

Selection of studies

All randomized and quasi-randomized controlled trials fulfilling the selection criteria described in the previous section were included. Two reviewers reviewed the results of the search and separately selected the studies for inclusion.

Data extraction and management

Two reviewers extracted the data independently.

Assessment of risk of bias in included studies

Identified trials were reviewed independently by each reviewer for methodological quality. Criteria used for assessment of quality were blinding of randomization, blinding of treatment, completeness of follow-up and blinding of assessment of outcomes. Agreement was reached by consensus. This information was entered into the "Characteristics of Included Studies" Table.

For the updated review in 2009, the Risk of Bias table was completed. The two review authors independently assessed the risk of bias for each study using the criteria outlined in the Cochrane Handbook for Systematic Reviews of Interventions. Any disagreement was resolved by discussion.

The Risk of Bias table addressed the following questions:

1. Sequence generation: Was the allocation sequence adequately generated?

For each included study, we described the method used to generate the allocation sequence as: adequate (any truly random process e.g. random number table; computer random number generator); inadequate (any nonrandom process e.g. odd or even date of birth; hospital or clinic record number); or unclear.

2. Allocation concealment: Was allocation adequately concealed?

For each included study, we described the method used to conceal the allocation sequence as: adequate (e.g. telephone or central randomization; consecutively numbered sealed opaque envelopes); inadequate (open random allocation; unsealed or non-opaque envelopes, alternation; date of birth); or unclear.

3. Blinding of participants, personnel and outcome assessors: Was knowledge of the allocated intervention adequately prevented during the study? At study entry? At the time of outcome assessment?

For each included study, we described the methods used to blind study participants and personnel from knowledge of which intervention a participant received. We assessed the methods as: adequate, inadequate or unclear for participants; adequate, inadequate or unclear for study personnel; and adequate, inadequate or unclear for outcome assessors and specific outcomes assessed.

4. Incomplete outcome data: Were incomplete outcome data adequately addressed?

For each included study and for each outcome, we described the completeness of data including attrition and exclusions from the analysis. We stated whether attrition and exclusions were reported, the numbers included in the analysis at each stage (compared with the total randomized participants), reasons for attrition or exclusion where reported, and whether missing data were balanced across groups or were related to outcomes. We assessed methods as: adequate (<20% missing data); inadequate ($\geq$ 20% missing data) or unclear.

5. Selective outcome reporting: Are reports of the study free of suggestion of selective outcome reporting?

For each included study, we assessed the possibility of selective outcome reporting bias as: adequate (where it is clear that all of the study's pre-specified outcomes and all expected outcomes of interest to the review have been reported); inadequate (where not all the study's pre-specified outcomes have been reported; one or more reported primary outcomes were not pre-specified; outcomes of interest are reported incompletely and so cannot be used; study fails to include results of a key outcome that would have been expected to have been reported); or unclear.

6. Other sources of bias: Was the study apparently free of other problems that could put it at a high risk of bias?

For each included study, we described any important concerns regarding other possible sources of bias (for example, whether there was a potential source of bias related to the specific study design or whether the trial was stopped early due to some data-dependent process). We assessed whether each study was free of other problems that could put it at risk of bias as: yes; no; or unclear.

Measures of treatment effect

Relative risk (RR), risk difference (RD), and number needed to treat (NNT) or number needed to harm (NNH) derived from 1/RD were used for categorical outcomes, and weighted mean difference (WMD) was used for continuous outcomes. For each measure of effect the 95% confidence interval was calculated.

Assessment of heterogeneity

We examined heterogeneity between trials by inspecting the forest plots and quantifying the impact of heterogeneity using the I-squared statistic. If we detected statistical heterogeneity, we planned to explore the possible causes (for example, differences in study quality, participants, intervention regimens, or outcome assessments) using *post hoc* sub group analyses.

Data synthesis

Data were synthesised using the standard method of the Cochrane Neonatal Review Group. Meta-analysis was performed using Review Manager software (RevMan 5), supplied by the Cochrane Collaboration. For estimates of typical relative risk and risk difference, we used the Mantel-Haenszel method. For measured quantities, we used the inverse variance method. All meta-analyses were to be done using the fixed effect model.

Subgroup analysis and investigation of heterogeneity

Subgroup analyses were planned a priori on the basis of weight (with subdivisions at 1000 g and 1500 g) and gestation (with subdivisions at 28 and 32 weeks), the type of CDP (CPAP or CNP) and according to whether surfactant was used. Sensitivity analyses based on trial quality were also planned.

Sensitivity analysis

Sensitivity analysis was performed based on trial methodology (randomized controlled trials were analyzed separately from quasi-randomized studies).

RESULTS

Description of studies

Eight studies involving a total of 251 infants were identified. One of these studies identified was the quasi-random study of [John 1976](#) and co-workers that excluded patients after allocation who died or required mechanical ventilation. Data on excluded patients were not available; thus, treatment effects on none of the primary outcomes specified in this review are available from this study. This study was excluded. One further study, ([Tooley 2003](#)), involving 42 infants was excluded as infants were randomised after intubation and administration of surfactant to extubation and application of nasal CPAP or continued conventional ventilation.

The included studies were all carried out in the pre-surfactant era ([Allen 1977](#), [Gerard 1975](#), [Hegyi 1981](#), [Krouskop 1975](#), [Mockrin 1975](#), [Rowe 1978](#)). All infants required clinical and radiological evidence of RDS for trial entry. The FiO₂ required at entry ranged from 0.3 or more to 0.7 or more. Early CDP was initiated at trial entry and late CDP was initiated if further deterioration occurred at an FiO₂ ranging from 0.5 up to 1.0. This FiO₂ was given to maintain the partial pressure of oxygen of 50 mm Hg in four studies, 60 in one study and 100 in one study. Thus there was considerable variation and overlap in the criteria used for initiating early and late CDP.

Of the six studies included in the review, two used CNP ([Gerard 1975](#); [Mockrin 1975](#)), one used face mask CPAP ([Allen 1977](#)) and three used binasal CPAP ([Hegyi 1981](#); [Krouskop 1975](#); [Rowe 1978](#)). One study ([Hegyi 1981](#)) addressed the overall objectives and was included although the criterion for delayed CDP was based on an FiO₂ of 0.5 rather than the strict 0.6 prespecified. Post hoc the protocol has been altered to make the criteria less narrow by inserting approximately 0.6 or more in the criteria for delayed CDP.

The primary outcome measure for all studies was use of IPPV and mortality. The point in time at which mortality was measured was not specified in any of the studies, although the age of death for each individual death was given in two of the trials. The combined outcome of death before discharge or subsequent use of IPPV was not given in any of the trials. Five studies reported the incidence of pneumothorax ([Allen 1977](#), [Gerard 1975](#), [Hegyi 1981](#), [Mockrin 1975](#), [Rowe 1978](#)), one reported bronchopulmonary dysplasia (undefined) ([Rowe 1978](#)), and one reported retinopathy of prematurity ([Krouskop 1975](#)) as secondary outcomes. One study did a subgroup analysis of mortality on very low birth weight infants ([Krouskop 1975](#)). Duration of oxygen therapy in survivors (time period of survival not stated) was reported in one study ([Allen 1977](#)). This was not a prespecified outcome measure but was included post hoc as it was considered an important secondary outcome.

Risk of bias in included studies

All the studies were controlled trials. Five studies were randomized. Of these five, one ([Gerard 1975](#)) used concealed allocation (sealed envelopes). It was not clear whether the allocation was concealed in the other four studies. One study used random numbers ([Mockrin 1975](#)) and in two other studies the method of randomisation was not stated ([Allen 1977](#); [Rowe 1978](#)). [Hegyi 1981](#) used hospital number to randomize, but the way in which this was done is not clear. The remaining study ([Krouskop 1975](#)) was quasi-random in part. They used a sequential design where the first eight matched pairs were randomized to treatment group using sealed envelopes but subsequent infants were allocated alternately.

There was no blinding of the intervention or the outcome assessment in any of the studies. There was complete follow-up of randomised patients in all studies. Only two studies stated how many of the potentially eligible infants were entered ([Gerard 1975](#), [Hegyi 1981](#)).

Effects of interventions

Six studies ([Allen 1977](#); [Gerard 1975](#); [Hegyi 1981](#); [Krouskop 1975](#); [Mockrin 1975](#); [Rowe 1978](#)) involving 165 infants met the entry criteria and were included in the analysis.

PRIMARY OUTCOMES

Use of IPPV (Outcome 1.1):

None of the six individual trials showed that early vs delayed CDP caused a significant reduction in the requirement for IPPV. However, the meta-analysis of all six trials supports a reduction in use of IPPV in the early CDP group that was statistically significant and clinically important [typical RR 0.55 (0.32, 0.96), RD -0.16 (-0.28, -0.03), NNT 6 (4, 33)].

Subgroup analyses by type of CDP was done for the four studies using CPAP and the two studies using CNP. Early CDP caused a significant reduction in use of IPPV in the two studies using CNP

[typical RR 0.12 (0.02, 0.85), RD -0.36 (-0.58, -0.14), NNT 3 (2, 7)], but not in the four studies using CPAP [typical RR 0.77 (0.43, 1.38), typical RD -0.08 (-0.23, 0.08)].

Mortality (Outcome 1.2):

Mortality (explicitly specified as mortality prior to discharge) prior to discharge was not reported in any of the studies. For mortality (time not specified) there was no significant effect of early CDP in any of the six individual trials or in the pooled estimate [typical RR 0.68 (0.34, 1.38), typical RD -0.07 (-0.18, 0.04)]. In the subgroup analysis by type of CDP there was no evidence of effect on mortality.

Mortality at 28 days (Outcome 1.3):

There was no significant effect of early CDP on mortality at 28 days in the two studies that reported this [typical RR 0.93 (0.13, 6.81)].

Failure

None of the trials reported failure as we defined it, i.e. death or subsequent use of IPPV.

SECONDARY OUTCOMES

There was no significant effect of early CDP on the rate of pneumothorax (outcome 01-04) (five trials) or BPD (Outcome 01-10) at 28 days (one trial, [Rowe 1978](#)). The number of days on oxygen (Outcome 01-05) in survivors, assessed in one trial ([Allen 1977](#)), was reduced in the early CDP group [MD -1.70 (-3.27, -0.13)]. A further study ([Rowe 1978](#)) found no difference in the time spent in FIO₂ > 0.3 or > 0.7. The outcomes IVH, NEC, and CLD at 36 weeks were not reported in any of the studies nor was there follow up assessment of physical growth, neurodevelopmental outcome or cerebral palsy in any of the studies. One study ([Krouskop 1975](#)) reported no cases of ROP (Outcome 01-11) in either group. In subgroup analysis by type of CDP there was no evidence of effect on pneumothorax.

Subgroup Analysis by Birthweight (Outcome 1.8):

One study ([Krouskop 1975](#)) did a subgroup analysis by birthweight using subgroups < 1500 g and 1500 g or more. There were no deaths in either group for infants 1500 g or more. Among infants <1500 g there was no significant effect of early CDP in use of IPPV [typical RR 1.00 (0.45, 2.23)] or mortality [typical RR 1.00 (0.45, 2.23)], but only a very small number of patients were analysed.

Sensitivity Analysis

Excluding the quasi-random study of Krouskop did not change the conclusion that early compared with delayed CDP reduces use of IPPV.

DISCUSSION

The results of this review suggest that in preterm infants with RDS, early compared with delayed application of CDP is effective in reducing subsequent use of IPPV. This is clinically important, as IPPV is associated with increased costs and adverse effects.

However, caution is required in interpreting these results as the sample size is small and the studies were all performed in the pre-surfactant era when the use of antenatal steroids was not common. These interventions could reduce baseline risk and hence the effect size that CDP may have on RDS. The mean birth weight and gestation of the treatment groups ranged from 1545 to 2113

g and 31 to 34 weeks, considerably higher than the major group of infants receiving treatment for RDS in current practice. The age at application of early CDP ranged from a mean of 7.1 to 18 hours, later than what would currently be considered early intervention for the treatment of RDS ([Narendran 2003](#); [Tooley 2003](#)). In addition there was wide variation in the criteria used for initiating early and late CDP and some overlap between the intervention and control groups as well as no blinding of treatment or outcome assessment.

We have included any type of CDP irrespective of the mode of delivery. Included trials used CNP and CPAP delivered by face mask or nasal prongs. In this review the studies using CNP showed a reduction in treatment failure but this was not seen in the studies using CPAP. Airway resistance is increased with CPAP compared with CNP so this difference may be plausible. Indeed recently differences in efficacy between CPAP devices have been described ([De Paoli 2003](#)) and direct comparison of CNP with other methods of applying CDP may be warranted.

Pneumothorax occurred in more than 10% of infants in the CDP subgroup. This is higher than would be expected today ([Verder 1999](#)). There was no evidence of effect of early CDP on the rate of pneumothorax. The one small study that looked at BPD did not find any effect but there is insufficient evidence to draw any conclusion. The rates of ROP, NEC and post discharge outcomes were not reported in any study.

AUTHORS' CONCLUSIONS

Implications for practice

There is some evidence that early application of CDP has a clinical benefit in the treatment of RDS in that it reduces subsequent use of IPPV and thus may be useful in preventing the adverse effects of this treatment.

However the applicability of these findings to the current practice of neonatal intensive care is uncertain given that the trials in this review were all conducted in the pre-surfactant era when antenatal steroid usage was uncommon and infants were higher birth weights, gestations and older than those currently treated for RDS.

Implications for research

Revaluation of the strategy of early CDP in the era of antenatal steroid and surfactant administration is indicated. However, as CDP is now a standard practice the main thrust for research in this area should be towards establishing the preferred mode, level of pressure and timing of CDP use. These studies should also attempt to answer the question about the preferred timing, dose and mode of administration of surfactant when used in conjunction with CDP.

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REFERENCES

References to studies included in this review

Allen 1977 {published data only}

Allen AP, Reynolds EOR, Rivers RPA, Le Souef PN, Wimberley PD. Controlled trial of continuous positive airway pressure given by face mask for hyaline membrane disease. *Archives of Disease in Childhood* 1977;**52**:373-8.

Gerard 1975 {published data only}

Gerard P, Fox WW, Outerbridge EW, Beaudry PH, Stern L. Early versus late introduction of continuous negative pressure in the management of the idiopathic respiratory distress syndrome. *Journal of Pediatrics* 1975;**87**:591-5.

Hegyi 1981 {published data only}

Hegyi T, Hiatt IM. The effect of continuous positive airway pressure on the course of respiratory distress syndrome: The benefits of early initiation. *Critical Care Medicine* 1981;**9**:38-41.

Krouskop 1975 {published data only}

Krouskop RW, Brown EG, Sweet AY. The early use of continuous positive airway pressure in the treatment of idiopathic respiratory distress syndrome. *Journal of Pediatrics* 1975;**87**:263-6.

Mockrin 1975 {published data only}

Mockrin LD, Bancalari EH. Early versus delayed initiation of continuous negative pressure in infants with hyaline membrane disease. *Journal of Pediatrics* 1975;**87**:596-600.

Rowe 1978 {unpublished data only}

Rowe JC, Guthrie RD, Hinkes P, Prueitt J, Murphy J, Woodrum DZ, Hodson WA. Time of initiation of CPAP in HMD (Abstract). *Pediatric Research* 1978;**12**:533.

References to studies excluded from this review

John 1976 {published data only}

John E, Thomas DB, Burnard ED. Influence of early introduction of continuous positive pressure breathing on the course of hyaline membrane disease. *Australian Paediatric Journal* 1976;**12**:276-80.

Tooley 2003 {published data only}

Tooley J, Dyke M. Randomized study of nasal continuous positive airway pressure in the preterm infant with respiratory distress syndrome. *Acta Paediatrica* 2003;**92**:1170-4.

Additional references

Avery 1959

Avery ME, Mead J. Surface properties in relation to atelectasis and hyaline membrane disease. *American Journal of Diseases of Children* 1959;**97**:517.

Bancalari 1992

Bancalari E, Sinclair JC. Mechanical ventilation. In: Sinclair JC, Bracken MB editor(s). *Effective Care of the Newborn Infant*. Oxford: Oxford University Press, 1992:200-20.

Barter 1960

Barter RA, Maddison TG. The nature of the neonatal pulmonary hyaline membrane. *Archives of Disease in Childhood* 1960;**25**:460.

Bell 1978

Bell MJ, Ternberg JL, Feigin RD, Keating JP, Marshall R, Barton L, Brotherton T. Neonatal necrotizing enterocolitis. Therapeutic decisions based upon clinical staging. *Annals of Surgery* 1978;**187**:1-7.

Cogswell 1975

Cogswell JJ, Hatch DJ, Kerr AA. Effects of continuous positive airway pressure on lung mechanics of babies after operation for congenital heart disease. *Archives of Disease in Childhood* 1975;**50**:799-804.

Cotton 1980

Cotton RB, Lindstrom DP, Kanarek KS, Sundell H, Stahlman MT. Effect of positive-end-expiratory-pressure on right ventricular output in lambs with hyaline membrane disease. *Acta Paediatrica Scandinavica* 1980;**69**:603-6.

Cotton 1998

Cotton RB. Pathophysiology of hyaline membrane disease (excluding surfactant). In: Polin RA, Fox WW editor(s). *Fetal and Neonatal Physiology*. 2nd Edition. Philadelphia: WB Saunders, 1998:1165-74.

Davis 2003

Davis PG, Henderson-Smart DJ. Nasal continuous positive airways pressure immediately after extubation for preventing morbidity in preterm infants. *Cochrane Database of Systematic Reviews* 2003, Issue 2. [DOI: [10.1002/14651858.CD000143](https://doi.org/10.1002/14651858.CD000143)]

De Paoli 2003

De Paoli AG, Davis PG, Faber B, Morley CJ. Devices and pressure sources for administration of nasal continuous airway pressure (NCPAP) in preterm neonates. *Cochrane Database of Systematic Reviews* 2003, Issue 3. [DOI: [10.1002/14651858.CD002977](https://doi.org/10.1002/14651858.CD002977)]

Evans 1991

Evans NJ, Archer LN. Doppler assessment of pulmonary artery pressure and extrapulmonary shunting in the acute phase of hyaline membrane disease. *Archives of Disease in Childhood* 1991;**66**:6-11.

Field 1985

Field D, Milner AS, Hopkins EK. Effects of positive end expiratory pressure during ventilation of the preterm infant. *Archives of Disease in Childhood* 1985;**60**:21-68.

Gregory 1971

Gregory GA, Kitterman JA, Phibbs RH, Tooley WH, Hamilton WK. Treatment of the idiopathic respiratory distress syndrome with continuous positive airway pressure. *New England Journal of Medicine* 1971;**284**:1333-40.

Gribetz 1959

Gribetz I, Frank NR, Avery ME. Static volume-pressure relations of excised lungs of infants with hyaline membrane disease, newborn and stillborn infants. *Journal of Clinical Investigation* 1959;**38**:2168-75.

Harris 1996

Harris TR, Wood ER. Physiologic principles. In: Goldsmith JP, Karotkin EH editor(s). Assisted ventilation. 3rd Edition. Philadelphia: WB Saunders, 1996:21-68.

Herman 1973

Herman S, Reynolds EOR. Methods of improving oxygenation in infants mechanically ventilated for severe hyaline membrane disease. *Archives of Disease in Childhood* 1973;**48**:612-7.

Ho 2002

Ho JJ, Subramaniam P, Henderson-Smart DJ, Davis PG. Continuous distending pressure for respiratory distress syndrome in preterm infants. *Cochrane Database of Systematic Reviews* 2002, Issue 2. [DOI: [10.1002/14651858.CD002271](https://doi.org/10.1002/14651858.CD002271)]

Miller 1990

Miller MJ, DiFiore JM, Strohl KP, Martin RJ. Effects of nasal CPAP on supraglottic and total pulmonary resistance in preterm infants. *Journal of Applied Physiology* 1990;**68**:141-6.

Narendran 2003

Narendran V, Donovan EF, Hoath SB, Akinbi HT, Steichen JJ, Jobe AH. Early bubble CPAP and outcomes in ELBW preterm infants. *Journal of Perinatology* 2003;**23**:195-9.

Richardson 1978

Richardson CP, Jung AL. Effects of continuous positive airway pressure on pulmonary function and blood gases of infants with respiratory distress syndrome. *Pediatric Research* 1978;**12**:771-4.

Saunders 1976

Saunders RA, Milner AD, Hopkin IE. The effect of CPAP on lung mechanics and lung volumes in the neonate. *Biology of the Neonate* 1976;**29**:178-81.

Soll 2001

Soll RF, Morley CJ. Prophylactic versus selective use of surfactant for preventing morbidity and mortality in preterm infants. *Cochrane Database of Systematic Reviews* 2001, Issue 2. [DOI: [10.1002/14651858.CD000510](https://doi.org/10.1002/14651858.CD000510)]

Verder 1994

Verder H, Richardson B, Griesen G, Ebbesen F, Albertsen P, Lundstrom K, Jacobsen T. The Danish-Swedish multicentre study group. Surfactant therapy and respiratory distress syndrome. *New England Journal of Medicine* 1994;**331**:1051-5.

Verder 1999

Verder H, Albertson P, Ebbesen F, Griesen G, Robertson B, Bertelsen A, Agertoft L, Djernes B, Natha E, Reinholdt J. Nasal continuous positive pressure and early surfactant therapy for respiratory distress syndrome in newborns less than 30 weeks gestation. *ePediatrics* 1999;**103**:<http://www.pediatrics.org/cgi/content/full/103/2/e24>.

Wyszogrodski 1975

Wyszogrodski I, Kyei-Aboagye K, Taesch HW Jr, Avery ME. Surfactant inactivation by hyperventilation: conservation by end-expiratory pressure. *Journal of Applied Physiology* 1975;**38**:461-6.

Yost 1999

Yost CC, Soll RF. Early versus delayed selective surfactant treatment for neonatal respiratory distress syndrome. *Cochrane Database of Systematic Reviews* 1999, Issue 4. [DOI: [10.1002/14651858.CD001456](https://doi.org/10.1002/14651858.CD001456)]

References to other published versions of this review

Ho 2002b

Ho JJ, Henderson-Smart DJ, Davis PG. Early versus delayed initiation of continuous distending pressure for respiratory distress syndrome in preterm infants. *Cochrane Database of Systematic Reviews* 2002, Issue 2. [DOI: [10.1002/14651858.CD002975](https://doi.org/10.1002/14651858.CD002975)]

Ho 2007

Ho JJ, Henderson-Smart DJ, Davis PG. Early versus delayed initiation of continuous distending pressure for respiratory distress syndrome in preterm infants. *Cochrane Database of Systematic Reviews* 2007, Issue 2. [DOI: [10.1002/14651858.CD002975](https://doi.org/10.1002/14651858.CD002975)]

CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Allen 1977

Methods	Concealment of allocation unclear, no blinding of intervention or outcome assessment, follow-up complete
Participants	24 infants with clinical and radiological RDS not previously ventilated and PaO ₂ < 60 mm Hg on FIO ₂ > 0.6

Allen 1977 (Continued)

Interventions	Face mask CPAP 5-10 cm H2O at allocation vs CPAP or IPPV for PaO2 < 50 mm Hg in FIO2 > 0.95	
Outcomes	Use of IPPV, mortality (time not specified), pneumothorax, days in O2	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	Concealment of allocation unclear.
Blinding? All outcomes	High risk	No blinding of intervention or outcome assessment.
Incomplete outcome data addressed? All outcomes	Low risk	Follow-up complete.

Gerard 1975

Methods	Allocation concealed using sealed envelopes, no blinding of intervention or outcome assessment, complete follow-up	
Participants	23 infants > 1000 g, with clinical & radiological RDS, spontaneously breathing, PaCO2 < 70 mm Hg and FIO2 >0.4 but < 0.8 to maintain PaO2 above 40 mm Hg	
Interventions	CNP 5-12 cm H2O at allocation vs CNP for PaO2 < 100 mm Hg in FIO2 1.0	
Outcomes	Use of IPPV, mortality (time not specified), pneumothorax	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	Allocation concealed using sealed envelopes.
Blinding? All outcomes	High risk	No blinding of intervention or outcome assessment.
Incomplete outcome data addressed? All outcomes	Low risk	Complete follow-up.

Hegyí 1981

Methods	Randomised by hospital number, concealment of allocation unclear. No blinding of intervention or outcome assessment. Complete follow-up	
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Hegyi 1981 (Continued)

Participants	38 (13 study & 25 control) preterm infants with clinical & radiological RDS requiring FIO ₂ 0.3 or greater to maintain PaO ₂ > 50 mm Hg
Interventions	Nasal prong CPAP at 6 cm H ₂ O at allocation vs CPAP at FIO ₂ 0.5 or more to maintain PaO ₂ > 50 mm Hg
Outcomes	Use of IPPV, mortality (time not specified), mortality at 28 days, pneumothorax
Notes	Reason for inequality in group sizes not stated. The way in which the hospital number was used for randomization was not clear.

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	High risk	Randomised by hospital number.
Allocation concealment?	Unclear risk	Concealment of allocation unclear.
Blinding? All outcomes	High risk	No blinding of intervention or outcome assessment.
Incomplete outcome data addressed? All outcomes	Low risk	Complete follow-up.

Krouskop 1975

Methods	Matched on admission for birthweight and age. Allocation randomized for first 8 pairs (sealed envelope), but alternate allocation for rest. No blinding of intervention or outcome assessment. Follow-up complete
Participants	21 infants with clinical and radiological RDS, PaO ₂ < 60 mm Hg in FIO ₂ 0.4 on 2 occasions within 1 hour
Interventions	8-14 cm H ₂ O nasal prong CPAP on allocation vs nasal prong CPAP for PaO ₂ < 60 mm Hg in FIO ₂ 0.7
Outcomes	Use of IPPV, required use of IPPV < 1500 g, required use of IPPV ≥ 1500 g, mortality (time not specified), mortality < 1500 g, mortality ≥ 1500 g
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	High risk	Matched on admission for birthweight and age. Allocation randomized for first 8 pairs (sealed envelope), but alternate allocation for rest.
Allocation concealment?	High risk	Matched on admission for birthweight and age. Allocation randomized for first 8 pairs (sealed envelope), but alternate allocation for rest.
Blinding? All outcomes	High risk	No blinding of intervention or outcome assessment.

Krouskop 1975 (Continued)

Incomplete outcome data addressed? All outcomes	Low risk	Follow-up complete.
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Mockrin 1975

Methods	Random numbers used in allocation, concealment of allocation unclear. No blinding of intervention or outcome assessment. Complete follow-up
Participants	23 infants (10 early and 13 late) with RDS diagnosed on clinical, blood gas and xray evidence), < 24 hours of age, spontaneously breathing and PaO ₂ between 50 and 100 mm Hg on 70% oxygen
Interventions	CNP starting at 8 and increasing as required to 15 cm H ₂ O at allocation vs for PaO ₂ < 50 mm Hg in FIO ₂ 0.7
Outcomes	Use of IPPV, mortality (time not specified), mortality at 28 days, pneumothorax
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Low risk	Random numbers used in allocation.
Allocation concealment?	Unclear risk	Concealment of allocation unclear.
Blinding? All outcomes	High risk	No blinding of intervention or outcome assessment. Complete follow-up.
Incomplete outcome data addressed? All outcomes	Low risk	Complete follow-up.

Rowe 1978

Methods	Concealment of allocation not clear. No blinding of intervention or outcome assessment. Complete follow-up.
Participants	36 infants with RDS and PaO ₂ < 50 mm Hg in FIO ₂ > 0.4
Interventions	Nasal prong CPAP at allocation vs at PaO ₂ < 50 mm Hg in FIO ₂ > 0.7
Outcomes	Use of IPPV, mortality (time not specified), pneumothorax, bronchopulmonary dysplasia
Notes	Data from conference abstract. Author clarification sought re definition of BPD

Risk of bias

Bias	Authors' judgement	Support for judgement
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Rowe 1978 (Continued)

Adequate sequence generation?	Unclear risk	Method of allocation not clear.
Allocation concealment?	Unclear risk	Concealment of allocation not clear.
Blinding? All outcomes	High risk	No blinding of intervention or outcome assessment.
Incomplete outcome data addressed? All outcomes	Low risk	Complete follow-up.

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
John 1976	Quasi-random study of 42 infants 29 weeks or more with RDS. Deaths and those requiring mechanical ventilation were excluded post-allocation.
Tooley 2003	The study of 42 infants included infants of 25 to 28 weeks gestation who were all intubated at birth, given a single dose of surfactant and positive pressure ventilation then randomised at about one hour of age to extubation to nasal CPAP or to continued conventional IPPV. No criteria for the diagnosis of RDS were given.

DATA AND ANALYSES

Comparison 1. Early vs late CDP

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Use of IPPV	6	165	Risk Ratio (M-H, Fixed, 95% CI)	0.55 [0.32, 0.96]
1.1 CPAP	4	119	Risk Ratio (M-H, Fixed, 95% CI)	0.77 [0.43, 1.38]
1.2 CNP	2	46	Risk Ratio (M-H, Fixed, 95% CI)	0.12 [0.02, 0.85]
2 Mortality (time not specified)	6	165	Risk Ratio (M-H, Fixed, 95% CI)	0.68 [0.34, 1.38]
2.1 CPAP	4	119	Risk Ratio (M-H, Fixed, 95% CI)	0.85 [0.39, 1.86]
2.2 CNP	2	46	Risk Ratio (M-H, Fixed, 95% CI)	0.32 [0.06, 1.74]
3 Mortality at 28 days	2	61	Risk Ratio (M-H, Fixed, 95% CI)	0.93 [0.13, 6.81]
3.1 CPAP	1	38	Risk Ratio (M-H, Fixed, 95% CI)	0.62 [0.03, 14.22]
3.2 CNP	1	23	Risk Ratio (M-H, Fixed, 95% CI)	1.3 [0.09, 18.33]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4 Pneumothorax	5	144	Risk Ratio (M-H, Fixed, 95% CI)	0.84 [0.37, 1.91]
4.1 CPAP	3	98	Risk Ratio (M-H, Fixed, 95% CI)	1.09 [0.39, 3.04]
4.2 CNP	2	46	Risk Ratio (M-H, Fixed, 95% CI)	0.53 [0.13, 2.20]
5 Duration of oxygen in survivors (days)	1	20	Mean Difference (IV, Fixed, 95% CI)	-1.70 [-3.27, -0.13]
6 Use of IPPV below 1500 g	1	8	Risk Ratio (M-H, Fixed, 95% CI)	1.0 [0.45, 2.23]
7 Use of IPPV 1500 g or more	1	13	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
8 Mortality (time not specified) below 1500 g	1	8	Risk Ratio (M-H, Fixed, 95% CI)	1.0 [0.45, 2.23]
9 Mortality (time not specified) 1500 g or more	1	13	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
10 Bronchopulmonary dysplasia	1	36	Risk Ratio (M-H, Fixed, 95% CI)	1.12 [0.08, 16.52]
11 Retinopathy of prematurity	1	21	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Analysis 1.1. Comparison 1 Early vs late CDP, Outcome 1 Use of IPPV.

Study or subgroup	Early CDP n/N	Delayed CDP n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Test for overall effect: $Z=2.11(P=0.04)$					
Test for subgroup differences: Not applicable					
<div style="display: flex; justify-content: space-between;"> Favours early 0.001 0.1 1 10 1000 Favours delayed </div>					

Analysis 1.2. Comparison 1 Early vs late CDP, Outcome 2 Mortality (time not specified).

Study or subgroup	Early CDP n/N	Delayed CDP n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
1.2.1 CPAP					
Allen 1977	0/12	5/12		33.36%	0.09[0.01,1.48]
Hegyi 1981	0/13	1/25		6.37%	0.62[0.03,14.22]
Krouskop 1975	3/10	3/11		17.33%	1.1[0.28,4.25]
Rowe 1978	5/17	2/19		11.46%	2.79[0.62,12.57]
Subtotal (95% CI)	52	67		68.52%	0.85[0.39,1.86]
Total events: 8 (Early CDP), 11 (Delayed CDP)					
Heterogeneity: $\tau^2=0$; $\chi^2=5.06$, $df=3(P=0.17)$; $I^2=40.69\%$					
Test for overall effect: $Z=0.41(P=0.68)$					
1.2.2 CNP					
Gerard 1975	0/11	4/12		26.2%	0.12[0.01,2.01]
Mockrin 1975	1/10	1/13		5.27%	1.3[0.09,18.33]
Subtotal (95% CI)	21	25		31.48%	0.32[0.06,1.74]
Total events: 1 (Early CDP), 5 (Delayed CDP)					
Heterogeneity: $\tau^2=0$; $\chi^2=1.55$, $df=1(P=0.21)$; $I^2=35.28\%$					
Test for overall effect: $Z=1.32(P=0.19)$					
Total (95% CI)	73	92		100%	0.68[0.34,1.38]
Total events: 9 (Early CDP), 16 (Delayed CDP)					
Heterogeneity: $\tau^2=0$; $\chi^2=7.56$, $df=5(P=0.18)$; $I^2=33.86\%$					
Test for overall effect: $Z=1.07(P=0.28)$					
Test for subgroup differences: Not applicable					
<div style="display: flex; justify-content: space-between;"> Favours early 0.001 0.1 1 10 1000 Favours delayed </div>					

Analysis 1.3. Comparison 1 Early vs late CDP, Outcome 3 Mortality at 28 days.

Study or subgroup	Early CDP n/N	Delayed CDP n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
1.3.1 CPAP					
Hegyi 1981	0/13	1/25		54.7%	0.62[0.03,14.22]
Subtotal (95% CI)	13	25		54.7%	0.62[0.03,14.22]
Total events: 0 (Early CDP), 1 (Delayed CDP)					
Heterogeneity: Not applicable					
Test for overall effect: $Z=0.3(P=0.76)$					
1.3.2 CNP					
Mockrin 1975	1/10	1/13		45.3%	1.3[0.09,18.33]
Subtotal (95% CI)	10	13		45.3%	1.3[0.09,18.33]
<div style="display: flex; justify-content: space-between;"> Favours early 0.001 0.1 1 10 1000 Favours delayed </div>

Analysis 1.4. Comparison 1 Early vs late CDP, Outcome 4 Pneumothorax.

Analysis 1.5. Comparison 1 Early vs late CDP, Outcome 5 Duration of oxygen in survivors (days).

Study or subgroup	Early CDP		Late CDP		Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
	N	Mean(SD)	N	Mean(SD)			

Test for overall effect: $Z=2.12(P=0.03)$

Favours early -4 -2 0 2 4 Favours delayed

Analysis 1.6. Comparison 1 Early vs late CDP, Outcome 6 Use of IPPV below 1500 g.

Study or subgroup	Early CDP		Delayed CDP		Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
	n/N		n/N				

Krouskop 1975 3/4 3/4 100% 1[0.45,2.23]

Total (95% CI) **4** **4** **100%** **1[0.45,2.23]**

Total events: 3 (Early CDP), 3 (Delayed CDP)
Heterogeneity: Not applicable
Test for overall effect: Not applicable

Favours early 0.2 0.5 1 2 5 Favours delayed

Analysis 1.7. Comparison 1 Early vs late CDP, Outcome 7 Use of IPPV 1500 g or more.

Study or subgroup	Early CDP		Delayed CDP		Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
	n/N		n/N				

Krouskop 1975 0/6 0/7 | Not estimable

Total (95% CI) **6** **7** | **Not estimable**

Total events: 0 (Early CDP), 0 (Delayed CDP)
Heterogeneity: Not applicable
Test for overall effect: Not applicable

Favours early 0.1 0.2 0.5 1 2 5 10 Favours delayed

Analysis 1.8. Comparison 1 Early vs late CDP, Outcome 8 Mortality (time not specified) below 1500 g.

Study or subgroup	Early CDP		Delayed CDP		Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
	n/N		n/N				

Krouskop 1975 3/4 3/4 100% 1[0.45,2.23]

Total (95% CI) **4** **4** **100%** **1[0.45,2.23]**

Total events: 3 (Early CDP), 3 (Delayed CDP)
Heterogeneity: Not applicable
Test for overall effect: Not applicable

Favours early 0.1 0.2 0.5 1 2 5 10 Favours delayed

Analysis 1.9. Comparison 1 Early vs late CDP, Outcome 9 Mortality (time not specified) 1500 g or more.

Analysis 1.10. Comparison 1 Early vs late CDP, Outcome 10 Bronchopulmonary dysplasia.

Analysis 1.11. Comparison 1 Early vs late CDP, Outcome 11 Retinopathy of prematurity.

Comparison 2. Early vs late CDP - excluding Krouskop 1975 (quasi-random)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Use of IPPV	5	144	Risk Ratio (M-H, Fixed, 95% CI)	0.49 [0.26, 0.90]
1.1 CPAP	3	98	Risk Ratio (M-H, Fixed, 95% CI)	0.71 [0.37, 1.36]
1.2 CNP	2	46	Risk Ratio (M-H, Fixed, 95% CI)	0.12 [0.02, 0.85]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2 Mortality (time not specified)	5	144	Risk Ratio (M-H, Fixed, 95% CI)	0.59 [0.26, 1.36]
2.1 CPAP	3	98	Risk Ratio (M-H, Fixed, 95% CI)	0.76 [0.29, 2.00]
2.2 CNP	2	46	Risk Ratio (M-H, Fixed, 95% CI)	0.32 [0.06, 1.74]

Analysis 2.1. Comparison 2 Early vs late CDP - excluding Krouskop 1975 (quasi-random), Outcome 1 Use of IPPV.

Analysis 2.2. Comparison 2 Early vs late CDP - excluding Krouskop 1975 (quasi-random), Outcome 2 Mortality (time not specified).

WHAT'S NEW

Date	Event	Description
22 December 2009	New search has been performed	<p>This review updates the existing review "Early versus delayed initiation of continuous distending pressure for respiratory distress syndrome in preterm infants" published in the Cochrane Database of Systematic Reviews (Ho 2007).</p> <p>Updated search found no new trials.</p> <p>No changes to conclusions.</p>

HISTORY

Protocol first published: Issue 4, 2000

Review first published: Issue 2, 2002

Date	Event	Description
17 September 2008	Amended	Converted to new review format.
4 December 2006	New search has been performed	<p>This review updates the existing review "Early versus delayed initiation of continuous distending pressure for respiratory distress syndrome in preterm infants," first published in The Cochrane Library, Issue 2, 2002 (Ho 2002).</p> <p>The literature search was repeated on October 1, 2006 and no further studies eligible for inclusion were found.</p> <p>The overall conclusions of the review have not changed.</p>

Date	Event	Description
12 February 2002	New citation required and conclusions have changed	Substantive amendment

CONTRIBUTIONS OF AUTHORS

JJH conducted the search with input from DHS. JJH and DHS independently evaluated the trials and extracted the data. JJH entered the data and wrote the paper with input from the other two reviewers.

The recent update (2009) was conducted centrally by the Cochrane Neonatal Review Group staff (Yolanda Montagne, Diane Haughton and Roger Soll) and reviewed and approved by JJH.

DECLARATIONS OF INTEREST

None

SOURCES OF SUPPORT

Internal sources

- Royal College of Medicine Perak, Malaysia.
- Dept Paediatrics, Hospital Ipoh, Malaysia.
- Centre for Perinatal Health Services Research, University of Sydney, Australia.
- Royal Prince Alfred Hospital, Sydney, Australia.
- Royal Womens Hospital, Melbourne, Australia.

External sources

- No sources of support supplied

INDEX TERMS

Medical Subject Headings (MeSH)

*Infant, Premature; Positive-Pressure Respiration [*methods]; Respiratory Distress Syndrome, Newborn [*therapy]

MeSH check words

Humans; Infant, Newborn