Strategies for the withdrawal of nasal continuous positive airway pressure (NCPAP) in preterm infants (Review)

Jardine LA, Inglis GDT, Davies MW


www.cochranelibrary.com
# Table of Contents

- **Header** ................................................. 1
- **Abstract** .................................................. 1
- **Plain Language Summary** .................................. 2
- **Background** ............................................... 2
- **Objectives** .................................................. 3
- **Methods** ..................................................... 3
- **Results** ...................................................... 5
- **Discussion** .................................................. 8
- **Authors’ Conclusions** ...................................... 8
- **Acknowledgements** .......................................... 8
- **References** .................................................. 8
- **Characteristics of Studies** ............................... 10
- **Data and Analyses** ......................................... 14
  - Analysis 1.1. Comparison 1 Duration of hospital stay (days), Outcome 1 Off versus Periods off (no cannulae) .................. 15
  - Analysis 1.2. Comparison 1 Duration of hospital stay (days), Outcome 2 Off versus Periods off (plus cannulae) ................. 15
  - Analysis 1.3. Comparison 1 Duration of hospital stay (days), Outcome 3 Periods off - no cannulae versus cannulae ............ 16
  - Analysis 2.1. Comparison 2 Time (from treatment allocation) to successfully coming off NCPAP altogether, Outcome 1 Off versus Periods off (no cannulae) .................................................. 16
  - Analysis 2.2. Comparison 2 Time (from treatment allocation) to successfully coming off NCPAP altogether, Outcome 2 Off versus Periods off (plus cannulae) .................................................. 17
  - Analysis 2.3. Comparison 2 Time (from treatment allocation) to successfully coming off NCPAP altogether, Outcome 3 Off versus Periods off (plus cannulae) .................................................. 17
  - Analysis 3.1. Comparison 3 Duration of oxygen therapy (days), Outcome 1 Off versus Periods off (no cannulae) ................. 18
  - Analysis 3.2. Comparison 3 Duration of oxygen therapy (days), Outcome 2 Off versus Periods off (plus cannulae) ............... 18
  - Analysis 3.3. Comparison 3 Duration of oxygen therapy (days), Outcome 3 Periods off - no cannulae versus cannulae .......... 19
- **History** ..................................................... 19
- **Contributions of Authors** .................................. 19
- **Declaration of Interest** .................................... 19
- **Sources of Support** ....................................... 20
- **Differences Between Protocol and Review** ................ 20
- **Index Terms** .............................................. 20
Strategies for the withdrawal of nasal continuous positive airway pressure (NCPAP) in preterm infants

Luke A Jardine¹, Garry DT Inglis², Mark W Davies²

¹Department of Neonatology, Mater Mother’s Hospital, Mater Medical Research Institute, The University of Queensland, South Brisbane, Australia. ²Grantley Stable Neonatal Unit, Royal Brisbane and Women’s Hospital, Department of Paediatrics & Child Health, The University of Queensland, Brisbane, Australia

Contact address: Luke A Jardine, Department of Neonatology, Mater Mother’s Hospital, Mater Medical Research Institute, The University of Queensland, Raymond Terrace, South Brisbane, Queensland, 4101, Australia. Luke.Jardine@mater.org.au.

Editorial group: Cochrane Neonatal Group.
Review content assessed as up-to-date: 7 October 2010.

Citation: Jardine LA, Inglis GDT, Davies MW. Strategies for the withdrawal of nasal continuous positive airway pressure (NCPAP) in preterm infants. Cochrane Database of Systematic Reviews 2011, Issue 2. Art. No.: CD006979. DOI: 10.1002/14651858.CD006979.pub2.

ABSTRACT

Background

While indications for the use of nasal continuous positive airway pressure (NCPAP) and its associated risks and benefits are extensively investigated, the best strategy for the withdrawal of NCPAP remains unknown. In a survey of Australian and New Zealand Neonatologists, 56% stated that their approach to NCPAP weaning was “ad hoc” (Jardine 2008). At what point an infant is considered stable enough to attempt to start withdrawing their NCPAP is not clearly established. The criteria for a failed attempt at NCPAP withdrawal is also not clear.

Objectives

To determine the risks and benefits of different strategies used for the withdrawal of NCPAP in preterm infants.

Search methods

Searches were made of the Cochrane Neonatal Review Group Specialised Register, MEDLINE from 1966 to June 2010, CINAHL from 1982 to June 2010, and the Cochrane Central Register of Controlled Trials (CENTRAL, The Cochrane Library 2010, Issue 2). Previous reviews (including cross references) were also searched.

Selection criteria

We included all randomised and quasi-randomised controlled trials in which either individual newborn infants or clusters of infants (such as separate neonatal units) were randomised to different NCPAP withdrawal strategies (from the first time they come off NCPAP and any subsequent weaning and/or withdrawal attempt).

Data collection and analysis

We used standard methods of The Cochrane Collaboration and its Neonatal Review Group.
Main results

We identified four potentially eligible studies. Three studies are included in this review. One study showed a significant decrease in the duration of oxygen therapy and a significantly decreased length of stay for babies randomised to a weaning strategy where NCPAP is simply stopped when infants met predefined stability criteria.

Authors' conclusions

Infants who have their NCPAP pressure weaned to a predefined level and then stop NCPAP completely have less total time on NCPAP and shorter durations of oxygen therapy and hospital stay compared with those that have NCPAP removed for a predetermined number of hours each day. Future trials of withdrawing NCPAP should compare proposed strategies with weaning NCPAP pressure to a predefined level and then stopping NCPAP completely. Clear criteria need to be established for the definition of stability prior to attempting to withdraw NCPAP.

Plain Language Summary

Strategies used for the withdrawal of nasal continuous positive airway pressure (NCPAP) in preterm infants

Nasal continuous positive airway pressure (NCPAP) is a form of respiratory support commonly used in the treatment of preterm infants. Potential risks of NCPAP include damage to the nose and leaking of air from the lungs. Infants on NCPAP require more nursing care and the use of extra equipment. However, potential complications of removing NCPAP from babies too early include increasing episodes of forgetting to breathe, increased oxygen needs, increased effort of breathing, the need to restart NCPAP and the need for a breathing tube with mechanical ventilation. Any of these complications can be seen as a “failure” and are potentially distressing to staff and family. The best way to withdraw NCPAP once it has been started is unknown. Options include simply stopping, weaning the pressure, increasing the time off NCPAP each day or combinations of both. A recent study has suggested that stopping the NCPAP all together once compared to having periods of time off NCPAP decreases the incidence of chronic neonatal lung disease and the length of hospital stay.

We aimed to determine the benefits and risks of different strategies used for the withdrawal of NCPAP in preterm infants who are stable and may be ready to have NCPAP withdrawn. This review identified three studies but, due to differences in the studies and the limited data available, the results could not be combined.

Infants who have their NCPAP pressure weaned to a predefined level and then stop NCPAP completely have less total time on NCPAP and shorter durations of oxygen therapy and hospital stay compared with those that have NCPAP removed for a predetermined number of hours each day. Clear criteria need to be established for the definition of stability prior to attempting to withdraw NCPAP and for the definition of failure to withdraw.

Background

Description of the condition

Continuous positive airway pressure (CPAP) is a widely accepted method of respiratory support used in the care of preterm infants with a number of established risks and benefits (Davis 2003; Ho 2002a; Ho 2002b). While other investigators have attempted to determine the optimal technique of CPAP delivery (De Paoli 2002), the best strategy for the withdrawal of NCPAP remains unknown. At what point an infant is considered stable enough to attempt to start withdrawing their NCPAP is not clearly established. The criteria for a failed attempt at NCPAP withdrawal is also not clear. In a survey of Australian and New Zealand Neonatologists, 56% stated that CPAP weaning was “ad hoc” in their units (Jardine 2008). Reported criteria used for assessing the failure of coming off CPAP include an increased oxygen requirement, increased work of breathing, tachypnoea, increasing frequency and severity of apnoea, a PaCO$_2$ > 60 mmHg, pH < 7.2 and bradycardia (Jardine 2008).
**Description of the intervention**

Possible strategies for withdrawal of NCPAP include:

1. Stopping NCPAP completely, independent of the level of airway pressure, and remaining off NCPAP unless certain criteria are met that require the infant to go back onto NCPAP;
2. Decreasing NCPAP to predefined level of airway pressure, then stopping NCPAP completely;
3. Removing NCPAP for a predetermined number of hours each day (this can be a single time period: e.g., 4 hours off, 20 on; or a number of smaller time periods e.g., 1 hour off, 5 on) gradually increasing the amount of time off NCPAP each day until NCPAP is able to be stopped completely (graded time off);
4. Stopping NCPAP and starting low flow oxygen or humidified high flow air (and oxygen if required) via nasal cannula;
5. Combinations of the above strategies (e.g. decrease NCPAP to a defined level and then discontinuing NCPAP for a number of hours each day);
6. Combinations of the above strategies in addition to co-interventions (e.g. methylxanthines).

**How the intervention might work**

The possible benefits of different methods of NCPAP withdrawal are mostly anecdotal. Weaning the distending pressure may gradually increase respiratory muscle strength without the associated risk of atelectasis. Having periods of time off may have a similar effect of respiratory muscle training but for shorter more intense periods. Time off NCPAP may be more likely to cause "atelectrototrauma" (due to alveolar collapse when off NCPAP and re-recruitment once NCPAP recommences). Having periods of time off NCPAP may reduce the incidence of nasal trauma or possibly lead to increased nasal trauma secondary to the frequent re-application of the prongs.

**Why it is important to do this review**

While an infant is on NCPAP they have a risk of nasal trauma (Caliumi-Pelleg, 1974; Fischer 2010; Kattwinkel 1973) and pneumothorax (Ho 2002b; Morley 2007). Another reported risk of NCPAP may be an increased risk of intraventricular haemorrhage (Han 1987). Infants on NCPAP may also require more intensive nursing care and the use of extra equipment compared to those not on NCPAP. Therefore, minimising the amount of time that a patient requires NCPAP may be beneficial. Possible disadvantages of removing NCPAP too early include: increasing apnoea, increased oxygen requirement, increased work of breathing, the need to restart NCPAP, and intubation and mechanical ventilation. Any of these complications can be seen as a “failure” and are potentially distressing to baby, family and staff.

Despite the paucity of evidence, the practice of weaning NCPAP is widespread. In a survey of Australian Neonatologists, 70% of respondents reported using a graded time off NCPAP weaning strategy and 74% used a weaning strategy involving decreasing airway pressure prior to coming off NCPAP (Jardine 2008). The approach to withdrawing NCPAP may vary depending on the clinical situation. Different strategies may be used depending on birth weight, gestational age at birth, time already spent on respiratory support, presence of chronic lung disease and gestational age of the baby (Jardine 2008). The incidence of failure to come off NCPAP is unknown.

**OBJECTIVES**

To determine the benefits and harms of different strategies for the withdrawal of NCPAP in preterm infants who are stable and may be ready to have NCPAP withdrawn.

We planned subgroup analyses to attempt to determine whether results differed by:

1. gestational age at birth (e.g. < 29 weeks, ≥ 29 weeks);
2. birth weight (e.g. < 1000 grams, ≥ 1000 grams);
3. postnatal age (e.g. < 4 weeks of age, ≥ 4 weeks of age);
4. indication for NCPAP (e.g. respiratory distress, post extubation, apnoea, chronic lung disease);
5. delivery method of NCPAP (e.g. single prong versus binal prong, bubble bottles versus ventilator).

It is unclear for which patient groups (if any) these strategies would be most beneficial.

**METHODS**

**Criteria for considering studies for this review**

Types of studies

We considered randomised controlled trials of adequate quality and some non-randomised controlled trials (e.g. quasi-randomised trials) in which either individual newborn infants or clusters of infants (such as separate neonatal units) were randomised to different NCPAP withdrawal strategies (from the first time they come off NCPAP and any subsequent weaning and/or withdrawal attempt). We excluded trials that included varying nasal pressure waveforms (e.g. nasal intermittent positive pressure ventilation, bi-level NCPAP). We also excluded studies that did not include...
criteria for stability of participants prior to their first attempt at withdrawal.

**Types of participants**

Infants who were born preterm (less than 37 weeks completed gestational age), who were currently receiving NCPAP, who had not been discharged from hospital and in whom the decision had been made to attempt withdrawal.

**Types of interventions**

Any strategy that involved the stopping or gradual withdrawal of NCPAP. Possible strategies for withdrawal of NCPAP included:

1. stopping NCPAP completely, independent of the level of airway pressure, and remaining off NCPAP unless certain criteria are met that require the infant to go back onto NCPAP;
2. decreasing NCPAP to predefined level of airway pressure, then stopping NCPAP completely;
3. removing NCPAP for a predetermined number of hours each day (this can be a single time period: e.g. four hours off, 20 on; or a number of smaller time periods e.g., one hour off, five on) gradually increasing the amount of time off NCPAP each day until NCPAP is able to be stopped completely (graded time off);
4. stopping NCPAP and starting high flow air (and oxygen if required) via nasal cannula;
5. combinations of the above strategies (e.g. decrease NCPAP to a defined level and then discontinuing NCPAP for a number of hours each day).
6. combinations of the above strategies in addition to co-interventions (e.g. methylxanthines).

**Types of outcome measures**

We planned intention-to-treat analysis based on the first assigned method of withdrawal.

**Primary outcomes**

- Time (from treatment group allocation) to successfully coming off NCPAP altogether (hours, days).
- Failure to stop or wean NCPAP (e.g. needing to restart NCPAP once it has stopped or needing to restart NCPAP during time off NCPAP or delaying any further weaning of NCPAP) however defined in individual studies.
- Endotracheal intubation and mechanical ventilation, excluding episodes required for elective procedures (e.g. surgery).
- Duration of hospital stay (days).
- Incidence of air leak (any and those requiring drainage) from time of treatment group allocation.
- Apnoea (defined as cessation of breathing > 20 seconds or > 10 seconds with desaturation) - however defined in individual studies.
- New intraventricular haemorrhage (grade 1 - 4), severe intraventricular haemorrhage (grade 3 - 4).
- Nasal trauma.
- Duration of oxygen therapy (days).
- Chronic lung disease (oxygen requirement at 36 weeks gestational age).
- Mortality (neonatal, at hospital discharge, or at one year).
- Neurodevelopmental outcome (cerebral palsy, sensorineural hearing loss, visual impairment and/or developmental delay - at one year, 18 months, two years, or five years).
- Any other clinically relevant outcomes identified in individual studies.

**Search methods for identification of studies**

See: Neonatal Group search strategy

**Electronic searches**

We used the standard search strategy for the Cochrane Neonatal Review Group. We searched the Cochrane Neonatal Review Group Specialised Register, MEDLINE from 1966 to June 2010, CINAHL from 1982 to June 2010, and the Cochrane Central Register of Controlled Trials (CENTRAL, The Cochrane Library 2010, Issue 2) using the following strategy:

MeSH search terms “Continuous Positive Airway Pressure”, “Respiration, Artificial”, “Positive-Pressure Respiration” OR the textwords “continuous distending pressure”, “CPAP”, “CDAP”, “distending pressure”, “continuous positive transpulmonary pressure”, “continuous transpulmonary pressure”, “continuous inflating pressure”, “positive pressure”, “positive expiratory pressure”, “positive end expiratory pressure”, “PEEP” AND

MeSH search term “Infant, Premature” OR the textwords “neonat$”, “infant”, “preterm”, “newborn”, “premature”.

AND


We did not restrict searches to publications in the English language.

**Searching other resources**
We searched previous reviews (including cross references). Searches were not restricted to publications in the English language or to published data. We searched ongoing trials at the following websites: clinicaltrials.gov and controlled-trials.com.

Data collection and analysis
We used the standard methods of The Cochrane Collaboration and its Neonatal Review Group. This review planned to analyse only studies that allocated subsequent withdrawal attempts to the policy originally allocated.

Selection of studies
Two of the authors worked independently to search for trials for inclusion.

Data extraction and management
Authors extracted data independently and resolved differences by discussion. We attempted to contact study investigators for additional information or data as required.

Assessment of risk of bias in included studies
Two of the authors worked independently to assess trials for methodological quality. We assessed studies using the following key criteria: allocation concealment (blinding of randomisation), blinding of intervention, completeness of follow up and blinding of outcome measurement assigning a rating of 'Yes', 'No' or 'Unknown' for each.

In addition, we evaluated the following issues and entered the findings into the Risk of Bias Table:
1. Sequence generation: Was the allocation sequence adequately generated?
2. Allocation concealment: Was allocation adequately concealed?
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?
4. Incomplete outcome data: Were incomplete outcome data adequately addressed?
5. Selective outcome reporting: Are reports of the study free of suggestion of selective outcome reporting?
6. Other sources of bias: Was the study apparently free of other problems that could put it at a high risk of bias?

Measures of treatment effect
Statistical analyses will be performed using Review Manager software. Categorical data will be analysed using relative risk (RR), risk difference (RD) and the number needed to treat (NNT).

Continuous data will be analysed using weighted mean difference (WMD). The 95% confidence interval (CI) will be reported on all estimates.

Assessment of heterogeneity
If sufficient included studies were identified, we planned to assess heterogeneity using two statistics (I^2 test) of heterogeneity, which are thought to be better at quantifying the heterogeneity than the Chi^2 test. If statistical heterogeneity had been found we planned to look for an explanation. Apart from the planned subgroup analyses detailed below, there were no other a priori specific potential causes of heterogeneity.

Data synthesis
For the meta-analysis we planned to report weighted mean differences (WMD) and 95% CI for continuous variables. For the categorical outcomes we planned to report the RR and 95% CI. For significant findings we planned to report the RD and NNT. We planned to use the fixed-effect model for meta-analysis.

Subgroup analysis and investigation of heterogeneity
We planned subgroup analyses to attempt to determine whether results differed by:
1. gestational age at birth (e.g. < 29 weeks, ≥ 29 weeks);
2. birth weight (e.g. < 1000 grams, ≥ 1000 grams);
3. postnatal age (e.g. < 4 weeks of age, ≥ 4 weeks of age);
4. indication for NCPAP (e.g. respiratory distress, post extubation, apnoea, chronic lung disease);
5. delivery method of NCPAP (e.g. single prong versus binausal prong, bubble bottles versus ventilator).

Sensitivity analysis
We planned to perform a sensitivity analysis (data permitting) to see if results differed by quality of included studies - e.g., adequacy of randomisation: quasi-randomised versus randomised.

RESULTS

Description of studies
See: Characteristics of included studies; Characteristics of excluded studies.
Results of the search
The above search strategy identified four potential studies for inclusion (Abdel-Hady 1998; Singh 2006; Soe 2008; Todd 2010). After review, we excluded Abdel-Hady 1998 as the intervention involved a comparison of weaning pressure versus staying on NCPAP and no attempt to withdraw NCPAP was actually made. Soe 2008 has been partially published in a narrative review on the topic and results are also available as an abstract. The other included studies (Singh 2006; Todd 2010) have been published in abstract form only.

Included studies
Todd 2010 is an ongoing study of 154 infants and some outcome measures have been reported in abstract form only. Babies were eligible if they met all of the following criteria: less than 30 weeks gestation, requiring NCPAP for over 24 hours, no congenital abnormalities, no severe IVH (Grade IV) and being treated with primary NCPAP or secondary NCPAP following extubation. Once patients had reached stability criteria, they were randomised to one of three methods of NCPAP weaning. In method one, they were taken off NCPAP. In method two, they started having periods of time off NCPAP from a minimum of 30 minutes off at a time to complete withdrawal. When they were on NCPAP they were on for six hours before their next period of time off. The clinician gradually increased the duration of the periods off NCPAP until complete withdrawal. Method three also started having periods of time off NCPAP as in method two, but when the baby was having the time off they had supplemental air or oxygen via nasal cannula at 0.5 L/min. If certain failure criteria were met, the baby was recommenced on NCPAP for at least 48 hours, stability criteria had to be met before further attempts (in originally assigned method) were undertaken.

Singh 2006 was a study of 112 infants with birth weights less than 1500 grams who were requiring less than 0.3 FiO2 and were stable on NCPAP. Patients were then randomised to a strategy of gradual reduction of NCPAP pressure (actual methods are not described) or increasing duration of time off (actual methods are not described) NCPAP with nasal cannula and low flow oxygen. Participants were considered successfully weaned if they were off NCPAP for seven days.

Soe 2008 studied 98 preterm infants (23 to 31 weeks) who had required respiratory support for surfactant deficiency or immature lung disease. Infants were stratified according to gestational age (23 to 27 weeks or 28 to 31 weeks). Patients were then randomised into two groups. The controlled time weaning group were treated with the Infant Flow Driver NCPAP at 6 cm H2O. Each day was divided into three eight-hour time periods. On day one, each time period consisted of seven hours on NCPAP and one hour off. For the next five days, the time on NCPAP was decreased daily by one hour in each period and the time off NCPAP was correspondingly increased by one hour as long as stability criteria (satisfactory gases, incubator oxygen less than 0.3, no frequent bradycardia/apnoea) were met. The pressure weaning group were treated with Infant Flow Driver NCPAP at 6 cm H2O for two days, then 5 cm H2O for two days and 4 cm H2O for two days. In both groups the “Not to wean NCPAP criteria” were: pH less than 7.25, FiO2 more than 0.4, apnoea requiring IPPV, more than 1 apnoea requiring stimulation per hour, more than 5 self-limiting bradycardia/apnoea episodes per hour, or a decision by an on-call registrar/nurse. If any of these criteria were met the baby did not progress to the next stage or went back a step, whichever was deemed appropriate. Infants were considered successfully weaned if they were off NCPAP for six days.

Excluded studies
Abdel-Hady 1998

Risk of bias in included studies
Singh 2006:
• blinding of randomisation (allocation concealment) - unknown;
• blinding of intervention - no;
• completeness of follow-up - unknown;
• blinding of outcome measurement - unknown.

Soe 2008:
• blinding of randomisation (allocation concealment) - unknown;
• blinding of intervention - no;
• completeness of follow-up - unknown;
• blinding of outcome measurement - unknown.

Todd 2010:
• blinding of randomisation (allocation concealment) - yes;
• blinding of intervention - no;
• completeness of follow-up - unknown;
• blinding of outcome measurement - unknown.

Effects of interventions
Due to the lack of pre-specified outcome measures, abstract results only being available for two studies, and the possibility of significant heterogeneity in methods of weaning CPAP, there has been no attempt to pool results. Results of individual studies are described below. Only data available from Todd 2010 is suitable for possible meta-analysis and has been entered into RevMan.

Singh 2006

Primary outcome measures
The study stated that the median (range) number of days on NCPAP in the pressure group was 1.5 (0.9 to 50.5) days and in the time off group was 8.9 (9.0 to 33.3) days and this result was significant ($P < 0.001$).

- The study stated that 36 (65%) infants in the pressure group compared to 21 (37%) in the time off group successfully weaned and this result was significant ($P = 0.006$).

- No other predefined primary outcome measure was reported.

Secondary outcome measures

- This study stated that the median (range) total time spent on NCPAP in the pressure group was 6.0 (2.1 to 60.0) days and in the time off group was 13.2 (10.0 to 46.0) days and this result was significant ($P = 0.001$).

- No other predefined secondary outcome measure was reported.


Soe 2008

Primary outcome measures

- The study stated that “there was no difference in total CPAP days”. It is unclear if this was calculated from treatment group allocation or total time spent on NCPAP. In the 23 to 27 week subgroup, total NCPAP days for the pressure group were 10 days and the time arm 15 days. It is uncertain if this reported number is a total for all babies or a mean or median.

- The study stated that 45 (92%) infants in the pressure group compared to 38 (78%) in the controlled time weaning group weaned successfully and this result was significant ($P = 0.005$). In the 23 to 27 week subgroup, 18 (82%) infants in the pressure group compared to 12 (55%) in the controlled time weaning group weaned successfully and this result was significant ($P < 0.05$). In the 28 to 31 week subgroup, all infants except one weaned successfully and this result was significant ($P < 0.001$). In the 23 to 27 week subgroup, it stated that one (4%) infant in the pressure group compared to seven (26%) in the time arm developed chronic lung disease ($P = 0.001$). The study states that in the 23 to 27 week subgroup there was a “trend to less CLD” but actual results are not provided. In the 28 to 31 week subgroup, it stated that one (4%) infant in the pressure group compared to seven (26%) in the time arm developed CLD, the significance level was not provided for the subgroup.

- Mortality in hospital was a reported outcome measure however no information was available in the study except for the statement “there were no differences in the other outcome data.”

- Periventricular leukomalacia was a reported outcome measure but no information is available in the study except for the statement “there were no differences in the other outcome data”.

- Retinopathy of prematurity was a reported outcome measure but no information is available in the study except for the statement “there were no differences in the other outcome data”.

- No other predefined secondary outcome measure was reported.

Secondary outcome measures

- The study stated that “there was no difference in total CPAP days”. It is unclear if this was calculated from treatment group allocation or was the total time spent on NCPAP. In the 23 to 27 week subgroup, total NCPAP days for the pressure group was 10 and for the controlled time weaning group 15. It is uncertain if this reported number is a total for all babies or a mean or a median.

- Total duration of respiratory support (i.e. any form of mechanical ventilation or NCPAP) was not reported.

- The study stated that duration of hospital stay was a reported outcome measure but no information is available in the study except for the statement “there were no differences in the other outcome data”.

- The study stated that there were “no differences” in number of apnoea and bradycardia episodes between the two groups.

- The study stated that intraventricular haemorrhage was a reported outcome measure but no information is available in the study except for the statement “there were no differences in the other outcome data”.

- The study stated that three patients (6%) in the pressure arm and 13 (26%) in the time weaning arm developed chronic lung disease (not further defined), $P = 0.005$. The study states that in the 23 to 27 week subgroup there was a “trend to less CLD” but actual results are not provided. In the 28 to 31 week subgroup, it stated that one (4%) infant in the pressure group compared to seven (26%) in the time arm developed CLD, the significance level was not provided for the subgroup.

- No other predefined secondary outcome measure was reported.

Other outcome measures reported in study that were not pre-specified

- pH at 6 and 24 hours (it is unclear when these 6 and 24 hour measures were actually made, e.g. day 1 versus every day versus once off NCPAP) - authors reported “no differences” but no further details were provided in the study.

- pCO$_2$ at 6 and 24 hours (it is unclear when these 6 and 24 hour measures were actually made, e.g. day 1 versus every day versus once off NCPAP) - authors reported “no differences” but no further details were provided in the study.

- FiO$_2$ at 6 and 24 hours (it is unclear when these 6 and 24 hour measures were actually made, e.g. day 1 versus every day versus once off NCPAP) - authors reported “no differences” but no further details were provided in the study.
abdominal circumference at 6 and 24 hours (it is unclear when these 6 and 24 hour measures were actually made, e.g. day 1 versus every day versus once off NCPAP) - authors reported “no differences” but no further details were provided in the study.

• gastric air volume at 6 and 24 hours (it is unclear when these 6 and 24 hour measures were actually made, e.g. day 1 versus every day versus once off NCPAP) - authors reported “no differences” but no further details were provided in the study.

• gastric aspirate volume at 6 and 24 hours (it is unclear when these 6 and 24 hour measures were actually made, e.g. day 1 versus every day versus once off NCPAP) - authors reported “no differences” but no further details were provided in the study.

T odd 2010

Primary outcome measures

• Method one has significantly shorter duration of wean with a mean (SD) of 8.8 (0.8) days compared to method two with 14.2 (1.0) days and method three with 18.2 (1.3) days.

• No other predefined primary outcome measure has been reported to date, the study is ongoing.

Secondary outcome measures

• Method one significantly shortens the length of stay with a reported mean (SD) of 54.2 +/- 0.1 days, compared to method two with a mean (SD) of 58.6 +/- 0.1 days and method three with a mean (SD) of 66.8 +/- 0.2 days.

• Method one significantly shortens duration of oxygen with a reported mean (SD) of 20.3 (1.4) days, compared to method two with 35.9 (2.0) days and method three with 31.3 (1.9) days.

• No other predefined secondary outcome measure has been reported to date, the study is ongoing.

Other outcome measures reported in study that were not pre-specified

• Gestational age at discharge was also reported, this provides the same information as length of stay data.

Discussion

The studies included in this review have provided limited data about the best method of weaning NCPAP in preterm infants who are stable and may be ready to have NCPAP withdrawn.

Singh 2006 is particularly limited as it has been published only as an abstract and therefore the exact methods are not known and the available results are extremely limited. We could not tell which pressure generation device was used in this study and exactly how the withdrawal and weaning of NCPAP was done.

The pressure source used for NCPAP generation is known for only one of the studies (Soe 2008 used the Infant Flow Driver). This may be an independent confounder. The results of this study may not be generalisable to infants who are being treated with other types of NCPAP.

Soe 2008 provided stability criteria and “not to wean criteria” both of which are important when considering applying the results in practice and for future meta-analysis; no such criteria were available for Singh 2006. Stability criteria and failure criteria are clearly provided in the ongoing study as described by Todd 2010 and if adopted by future studies, would greatly help in any further meta-analysis.

In Todd 2010 all babies initially had their NCPAP pressure reduced before randomisation. Both Singh 2006 and Soe 2008 compared weaning the NCPAP pressure to increasing periods of time off NCPAP before any attempt was made to withdraw the NCPAP. It is not known if this approach is necessary or not and should be considered as part of the weaning strategy. Although both included studies seem to favour a “weaning pressure” approach, the description of trial methods and results makes it impossible to confirm the veracity of these findings.

Authors’ conclusions

Implications for practice

The currently available evidence suggests that infants who have their NCPAP pressure weaned to a predefined level and then stop NCPAP completely have less total time on NCPAP and shorter durations of oxygen therapy and hospital stay compared with those that have NCPAP removed for a predetermined number of hours each day.

Implications for research

Further research is required into the best methods for withdrawal on NCPAP and to which subgroups these apply. Any future trials of withdrawing NCPAP should compare proposed strategies with weaning NCPAP pressure to a predefined level and then stopping NCPAP completely. Clear criteria for the definition of stability prior to attempting to withdraw NCPAP have been defined by Todd 2010, whether or not these or other criteria are best, needs to be established.

Acknowledgements

Dr Fiona Lawlor for work on the protocol and attempts to contact authors of studies included in review.
Editorial support of the Cochrane Neonatal Review Group has been funded with Federal funds from the Eunice Kennedy Shriver National Institute of Child Health and Human Development National Institutes of Health, Department of Health and Human Services, USA, under Contract No. HHSN267200603418C.

**REFERENCES**

**References to studies included in this review**

Singh 2006 *(published data only (unpublished sought but not used))*

Soe 2008 *(published data only (unpublished sought but not used))*

Todd 2010 *(published data only (unpublished sought but not used))*

**References to studies excluded from this review**

Abdel-Hady 1998 *(published data only)*

Additional references

*Caliumi-Pelleg. 1974

Davis 2003

*Indicates the major publication for the study*
# Characteristics of Studies

## Characteristics of included studies  
*ordered by study ID*

### Singh 2006

<table>
<thead>
<tr>
<th>Methods</th>
<th>Randomised controlled trial</th>
</tr>
</thead>
</table>
| Participants | Infants <1500 grams and stable in < 0.3 FiO2 on NCPAP. The study enrolled 112 infants with birth weights less than 1500 grams who were requiring less than 0.3 FiO2 and were stable on NCPAP. The median (range) birth weights and gestation were:  
- 'pressure' group, 940 g (614 - 1400 g) and 27 (24 - 32) weeks;  
- 'time off' group, 1080 g (520 - 1496 g) and 28 (24 - 31) weeks. Median PMA at randomisation 29 (28 - 31) weeks for both groups |
| Interventions | Patients were randomised to a strategy of gradual reduction of NCPAP pressure (actual methods are not described) or increasing duration of time off (actual methods are not described) NCPAP with nasal cannula and low flow oxygen. Participants were considered successfully weaned if they were off NCPAP for 7 days |
| Outcomes | **Primary outcome measures**  
- Number of days on NCPAP.  
- Successful weaning.  
- No other predefined primary outcome measure was reported.  
**Secondary outcome measures**  
- Total time spent on NCPAP.  
- No other predefined secondary outcome measure was reported. |
| Notes | Attempts to contact author for further information unsuccessful |

### Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment?</td>
<td>Unclear risk</td>
<td>Method not described</td>
</tr>
<tr>
<td>Blinding?</td>
<td>All outcomes</td>
<td>High risk</td>
</tr>
</tbody>
</table>

### Soe 2008

<table>
<thead>
<tr>
<th>Methods</th>
<th>Randomised controlled trial</th>
</tr>
</thead>
</table>
| Participants | Preterm infants (24 - 31 weeks) with respiratory distress or immature lungs  
In total 98 infants were randomised to pressure (n = 49) or time weaning (n = 49). The subgroups consisted of 44 infants 24 - 27 weeks gestation and 54 infants 28 - 31 weeks gestation |
| Interventions | Time weaning versus pressure weaning over 6 days.  
In the time weaning group, on day one, each time period consisted of seven hours on NCPAP and one... |
For the next five days, the time on NCPAP was decreased daily by one hour in each period and the time off NCPAP was correspondingly increased by one hour as long as stability criteria (satisfactory gases, incubator oxygen < 0.3, no frequent bradycardia/apnoea) were met. The pressure weaning group were treated with Infant Flow Driver CPAP at 6 cm H₂O for two days, then 5 cm H₂O for two days and 4 cm H₂O for two days.

In both groups the "Not to wean NCPAP criteria" were: pH < 7.25, FiO₂ > 0.4, apnoea requiring IPPV, > 1 apnoea requiring stimulation per hour, > 5 self limiting bradycardias/apnoeas per hour, or a decision by an on-call registrar/nurse. If any of these criteria were met the baby did not progress to the next stage or went back a step, whichever was deemed appropriate.

Infants were considered successfully weaned if they were off NCPAP for six days.

### Outcomes

#### Primary outcome measures
- Total NCPAP days. It is unclear if this was calculated from treatment group allocation or total time spent on NCPAP.
- Weaned successfully.
- No other predefined primary outcome measure was reported.

#### Secondary outcome measures
- Duration of hospital stay.
- Number of apnoea and bradycardia episodes.
- Intraventricular haemorrhage.
- Chronic lung disease (not further defined).
- Mortality in hospital.
- Periventricular leukomalacia.
- Retinopathy of prematurity.
- No other predefined secondary outcome measure was reported. Total duration of respiratory support (i.e., any form of mechanical ventilation or NCPAP) was not reported.

#### Other outcome measures reported in study that were not pre-specified
- pH at 6 and 24 hours. (it is unclear when these 6 and 24 hour measures were actually made, e.g., day 1 versus every day versus once off NCPAP).
- pCO₂ at 6 and 24 hours (it is unclear when these 6 and 24 hour measures were actually made, e.g., day 1 versus every day versus once off NCPAP).
- FiO₂ at 6 and 24 hours (it is unclear when these 6 and 24 hour measures were actually made, e.g., day 1 versus every day versus once off NCPAP).
- abdominal circumference at 6 and 24 hours (it is unclear when these 6 and 24 hour measures were actually made, e.g., day 1 versus every day versus once off NCPAP).
- gastric air volume at 6 and 24 hours (it is unclear when these 6 and 24 hour measures were actually made, e.g., day 1 versus every day versus once off NCPAP).
- gastric aspirate volume at 6 and 24 hours (it is unclear when these 6 and 24 hour measures were actually made, e.g., day 1 versus every day versus once off NCPAP).

### Notes

Study initially published in abstract form but also described in subsequent editorial by Soe. Attempts to contact author for further information unsuccessful.

### Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment?</td>
<td>Unclear risk</td>
<td>Method not described</td>
</tr>
</tbody>
</table>

Copyright © 2011 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.
Soe 2008  (Continued)

<table>
<thead>
<tr>
<th>Blinding?</th>
<th>High risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>All outcomes</td>
<td>High risk</td>
</tr>
</tbody>
</table>

**Todd 2010**

**Methods**

Multicentre randomised controlled trial. Randomisation via online web-based server.

To meet stability criteria babies must have had all of the following for the previous 12 hours:

1. NCPAP < 6 cm H2O
2. Oxygen requirement less than 26% and not increasing
3. RR less than 60
4. No significant chest recession
5. Less than 3 episodes of mild self reverting apnoea and/or bradycardias and/or desaturations in 1 hour for the previous 6 hours
6. Average saturation above 87% most of the time and/or transcutaneous (TcPO2)/arterial PaO2 > 50 mm Hg.
7. Tolerating nose rests well during nursing cares
8. Not treated for patent ductus arteriosus (PDA) or sepsis

Criteria for failed trial “OFF” were at least 2 of the following:

1. Increase work of breathing (Intercostal recession and accessory muscles contributing to respiration) with RR > 75 for > 1 hour
2. Increased apnoea and/or bradycardias and/or desaturations > 2 in previous 1 hour
3. Major apnoea or bradycardia requiring more sustained stimulation/resuscitation
4. Increased O2 requirement > 25% with average saturation < 85% and/or TcPO2/PaO2 < 45 mmHg.
5. pH of < 7.2 6. PaCO2 of > 65 mmHg.

The babies were put back on NCPAP if they failed trial “OFF” CPAP for 48 hours before the next attempt at weaning was made.

**Participants**

Eligibility criteria

1. Baby born < 30 weeks gestation
2. Baby requiring NCPAP for > 24 hours
3. No congenital abnormalities
4. No severe IVH (Grade IV)
5. Primary NCPAP of Secondary NCPAP following extubation

154 patients enrolled. 50 in method 1, 55 in method 2, 49 in method 3. No significant differences in reported demographics. Mean (SD) gestational age 27.2 +/- 1.4 weeks in method 1, 27.2 +/- 1.7 weeks in method 2 and 27.2 +/- 2.1 weeks in method 3. Mean (SD) birth weight 999 +/- 252 grams in method 1, 1030 +/- 236 grams in method 2 and 940 +/- 254 grams in method 3.

**Interventions**

This trial investigated 3 methods of weaning NCPAP.

Method 1. When the baby reached the stability criteria they were taken off NCPAP

Method 2. When the baby reached the stability criteria they were started having periods of time off NCPAP from a minimum of 30 minutes off at a time to completely off. When they were on NCPAP they were on for 6 hours before their next period of time off. The clinician gradually increased the duration of the periods off NCPAP until the baby was completely off

Method 3. When the baby reached the stability criteria they started having periods of time off NCPAP as in Method 2, but when the baby was having their time off they had supplemental air or oxygen via nasal cannula at 0.5 L/min.
Patients were considered successfully weaned if they spent 5 continuous days off NCPAP.

### Outcomes

**Primary outcome measures**
- Duration of wean.
- No other predefined primary outcome measure has been reported to date, the study is ongoing.

**Secondary outcome measures**
- Length of stay.
- Duration of oxygen.
- No other predefined secondary outcome measure has been reported to date, the study is ongoing.

**Other outcome measures reported in study that were not pre-specified**
- Gestational age at discharge was also reported, this provides the same information as length of stay data.

### Notes

Study is ongoing and results to date only published in two separate abstracts. Australian Clinical Trials Registry Number (ACTRN) ACTRN1260600015594

Reduction in time of respiratory support. For methods one and two this was defined as 24 hours "OFF" NCPAP and for those in method three, this was 24 hours "OFF" nasal cannula. So the time on NCPAP was calculated from the time commenced NCPAP to "OFF" support. This is recorded once off NCPAP for 5 days

Reduction in Chronic Lung Disease (CLD) rate defined as requiring oxygen at 36 weeks postconceptional age.

### Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adequate sequence generation?</td>
<td>Low risk</td>
<td>Web-based computer generated</td>
</tr>
<tr>
<td>Allocation concealment?</td>
<td>Low risk</td>
<td>Web-based computer generated</td>
</tr>
<tr>
<td>Blinding?</td>
<td>High risk</td>
<td>Blinding of intervention not possible</td>
</tr>
<tr>
<td>All outcomes</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Characteristics of excluded studies [ordered by study ID]

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdel-Hady 1998</td>
<td>Not a RCT of methods of weaning NCPAP. One group was weaned and the other group simply stayed on NCPAP</td>
</tr>
</tbody>
</table>
## Data and Analyses

### Comparison 1. Duration of hospital stay (days)

<table>
<thead>
<tr>
<th>Outcome or subgroup title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Off versus Periods off (no cannulae)</td>
<td>1</td>
<td>105</td>
<td>Mean Difference (IV, Fixed, 95% CI)</td>
<td>-4.40 [-4.44, -4.36]</td>
</tr>
<tr>
<td>2 Off versus Periods off (plus cannulae)</td>
<td>1</td>
<td>99</td>
<td>Mean Difference (IV, Fixed, 95% CI)</td>
<td>-12.60 [-12.66, -12.54]</td>
</tr>
<tr>
<td>3 Periods off - no cannulae versus cannulae</td>
<td>1</td>
<td>104</td>
<td>Mean Difference (IV, Fixed, 95% CI)</td>
<td>-8.20 [-8.26, -8.14]</td>
</tr>
</tbody>
</table>

### Comparison 2. Time (from treatment allocation) to successfully coming off NCPAP altogether

<table>
<thead>
<tr>
<th>Outcome or subgroup title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Off versus Periods off (no cannulae)</td>
<td>1</td>
<td>105</td>
<td>Mean Difference (IV, Fixed, 95% CI)</td>
<td>-5.40 [-5.74, -5.06]</td>
</tr>
<tr>
<td>2 Off versus Periods off (plus cannulae)</td>
<td>1</td>
<td>99</td>
<td>Mean Difference (IV, Fixed, 95% CI)</td>
<td>-9.40 [-9.83, -8.97]</td>
</tr>
<tr>
<td>3 Periods off - no cannulae versus cannulae</td>
<td>1</td>
<td>104</td>
<td>Mean Difference (IV, Fixed, 95% CI)</td>
<td>-4.0 [-4.45, -3.55]</td>
</tr>
</tbody>
</table>

### Comparison 3. Duration of oxygen therapy (days)

<table>
<thead>
<tr>
<th>Outcome or subgroup title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Off versus Periods off (no cannulae)</td>
<td>1</td>
<td>105</td>
<td>Mean Difference (IV, Fixed, 95% CI)</td>
<td>-15.60 [-16.26, -14.94]</td>
</tr>
<tr>
<td>2 Off versus Periods off (plus cannulae)</td>
<td>1</td>
<td>99</td>
<td>Mean Difference (IV, Fixed, 95% CI)</td>
<td>-11.0 [-11.66, -10.34]</td>
</tr>
<tr>
<td>3 Periods off - no cannulae versus cannulae</td>
<td>1</td>
<td>104</td>
<td>Mean Difference (IV, Fixed, 95% CI)</td>
<td>4.60 [3.85, 5.35]</td>
</tr>
</tbody>
</table>
**Analysis 1.1. Comparison 1 Duration of hospital stay (days), Outcome 1 Off versus Periods off (no cannulae).**

*Review:* Strategies for the withdrawal of nasal continuous positive airway pressure (NCPAP) in preterm infants

*Comparison:* 1 Duration of hospital stay (days)

*Outcome:* 1 Off versus Periods off (no cannulae)

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Off</th>
<th>Periodes off (no cannulae)</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Todd 2010</td>
<td>50</td>
<td>54.2 (0.1)</td>
<td>55, 58.6 (0.1)</td>
<td>IV, Fixed, 95% CI</td>
<td>100.0 %, -4.40 [-4.44, -4.36]</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td>50</td>
<td>55</td>
<td></td>
<td>100.0 %</td>
<td>-4.40 [-4.44, -4.36]</td>
</tr>
</tbody>
</table>

Heterogeneity: not applicable

Test for overall effect: Z = 225.18 (P < 0.00001)

Test for subgroup differences: Not applicable

---

**Analysis 1.2. Comparison 1 Duration of hospital stay (days), Outcome 2 Off versus Periods off (plus cannulae).**

*Review:* Strategies for the withdrawal of nasal continuous positive airway pressure (NCPAP) in preterm infants

*Comparison:* 1 Duration of hospital stay (days)

*Outcome:* 2 Off versus Periods off (plus cannulae)

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Off</th>
<th>Periods off (cannulae)</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Todd 2010</td>
<td>50</td>
<td>54.2 (0.1)</td>
<td>49, 66.8 (0.2)</td>
<td>IV, Fixed, 95% CI</td>
<td>100.0 %, -12.60 [-12.66, -12.54]</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td>50</td>
<td>55</td>
<td></td>
<td>100.0 %</td>
<td>-12.60 [-12.66, -12.54]</td>
</tr>
</tbody>
</table>

Heterogeneity: not applicable

Test for overall effect: Z = 395.23 (P < 0.00001)

Test for subgroup differences: Not applicable

---

Strategies for the withdrawal of nasal continuous positive airway pressure (NCPAP) in preterm infants (Review)  
Copyright © 2011 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.
**Analysis 1.3.** Comparison 1 Duration of hospital stay (days), Outcome 3 Periods off - no cannulae versus cannulae.

Review: Strategies for the withdrawal of nasal continuous positive airway pressure (NCPAP) in preterm infants

Comparison: 1 Duration of hospital stay (days)

Outcome: 3 Periods off - no cannulae versus cannulae

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Periods off (no cannulae)</th>
<th>Periods off (cannulae)</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>IV/Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Mean(SD)</td>
<td>N</td>
<td>Mean(SD)</td>
<td>IV/Fixed, 95% CI</td>
</tr>
<tr>
<td>Todd 2010</td>
<td>55</td>
<td>58.6 (0.1)</td>
<td>49</td>
<td>66.8 (0.2)</td>
<td>100.0 %</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>55</td>
<td></td>
<td>49</td>
<td></td>
<td>100.0 %</td>
</tr>
</tbody>
</table>

Heterogeneity: not applicable

Test for overall effect: Z = 259.55 (P < 0.00001)

Test for subgroup differences: Not applicable

---

**Analysis 2.1.** Comparison 2 Time (from treatment allocation) to successfully coming off NCPAP altogether, Outcome 1 Off versus Periods off (no cannulae).

Review: Strategies for the withdrawal of nasal continuous positive airway pressure (NCPAP) in preterm infants

Comparison: 2 Time (from treatment allocation) to successfully coming off NCPAP altogether

Outcome: 1 Off versus Periods off (no cannulae)

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Off</th>
<th>Periods off (no cannulae)</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>IV/Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Mean(SD)</td>
<td>N</td>
<td>Mean(SD)</td>
<td>IV/Fixed, 95% CI</td>
</tr>
<tr>
<td>Todd 2010</td>
<td>50</td>
<td>8.8 (0.8)</td>
<td>55</td>
<td>14.2 (1)</td>
<td>100.0 %</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>50</td>
<td></td>
<td>55</td>
<td></td>
<td>100.0 %</td>
</tr>
</tbody>
</table>

Heterogeneity: not applicable

Test for overall effect: Z = 30.68 (P < 0.00001)

Test for subgroup differences: Not applicable

---

Strategies for the withdrawal of nasal continuous positive airway pressure (NCPAP) in preterm infants (Review)

Copyright © 2011 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.
### Analysis 2.2. Comparison 2 Time (from treatment allocation) to successfully coming off NCPAP altogether, Outcome 2 Off versus Periods off (plus cannulae).

**Review:** Strategies for the withdrawal of nasal continuous positive airway pressure (NCPAP) in preterm infants

**Comparison:** 2 Time (from treatment allocation) to successfully coming off NCPAP altogether

**Outcome:** 2 Off versus Periods off (plus cannulae)

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Off Periods off (cannulae)</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N  Mean(SD)</td>
<td>N  Mean(SD)</td>
<td>IV,Fixed,95% CI</td>
<td>IV,Fixed,95% CI</td>
</tr>
<tr>
<td>Todd 2010</td>
<td>50  8.8 (0.8)</td>
<td>49  18.2 (1.3)</td>
<td>100.0 %</td>
<td>-9.40 [-9.83, -8.97]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>50  8.8 (0.8)</td>
<td>49  18.2 (1.3)</td>
<td>100.0 %</td>
<td>-9.40 [-9.83, -8.97]</td>
</tr>
</tbody>
</table>

*Heterogeneity: not applicable*

*Test for overall effect: Z = 43.23 (P < 0.00001)*

*Test for subgroup differences: Not applicable*

### Analysis 2.3. Comparison 2 Time (from treatment allocation) to successfully coming off NCPAP altogether, Outcome 3 Periods off - no cannulae versus cannulae.

**Review:** Strategies for the withdrawal of nasal continuous positive airway pressure (NCPAP) in preterm infants

**Comparison:** 2 Time (from treatment allocation) to successfully coming off NCPAP altogether

**Outcome:** 3 Periods off - no cannulae versus cannulae

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Periods off (no cannulae)</th>
<th>Periods off (cannulae)</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N  Mean(SD)</td>
<td>N  Mean(SD)</td>
<td>IV,Fixed,95% CI</td>
<td>IV,Fixed,95% CI</td>
<td></td>
</tr>
<tr>
<td>Todd 2010</td>
<td>55  14.2 (1)</td>
<td>49  18.2 (1.3)</td>
<td>100.0 %</td>
<td>-4.00 [-4.45, -3.55]</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>55  14.2 (1)</td>
<td>49  18.2 (1.3)</td>
<td>100.0 %</td>
<td>-4.00 [-4.45, -3.55]</td>
<td></td>
</tr>
</tbody>
</table>

*Heterogeneity: not applicable*

*Test for overall effect: Z = 17.43 (P < 0.00001)*

*Test for subgroup differences: Not applicable*
Analysis 3.1. Comparison 3 Duration of oxygen therapy (days), Outcome 1 Off versus Periods off (no cannulae).

Review: Strategies for the withdrawal of nasal continuous positive airway pressure (NCPAP) in preterm infants

Comparison: 3 Duration of oxygen therapy (days)
Outcome: 1 Off versus Periods off (no cannulae)

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Off CPAP</th>
<th>Periods Off</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Todd 2010</td>
<td>50</td>
<td>20.3 (1.4)</td>
<td>55</td>
<td>35.9 (2)</td>
<td>IV,FIXED,95% CI</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>100.0 %</td>
<td>-15.60 [-16.26, -14.94 ]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>50</td>
<td>20.3 (1.4)</td>
<td>55</td>
<td>35.9 (2)</td>
<td>IV,FIXED,95% CI</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>100.0 %</td>
<td>-15.60 [-16.26, -14.94 ]</td>
</tr>
</tbody>
</table>

Heterogeneity: not applicable
Test for overall effect: Z = 46.63 (P < 0.00001)
Test for subgroup differences: Not applicable

Favours experimental Favours control

Analysis 3.2. Comparison 3 Duration of oxygen therapy (days), Outcome 2 Off versus Periods off (plus cannulae).

Review: Strategies for the withdrawal of nasal continuous positive airway pressure (NCPAP) in preterm infants

Comparison: 3 Duration of oxygen therapy (days)
Outcome: 2 Off versus Periods off (Plus cannulae)

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Off CPAP</th>
<th>Periods Off</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Todd 2010</td>
<td>50</td>
<td>20.3 (1.4)</td>
<td>49</td>
<td>31.3 (1.9)</td>
<td>IV,FIXED,95% CI</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>100.0 %</td>
<td>-11.00 [-11.66, -10.34 ]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>50</td>
<td>20.3 (1.4)</td>
<td>49</td>
<td>31.3 (1.9)</td>
<td>IV,FIXED,95% CI</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>100.0 %</td>
<td>-11.00 [-11.66, -10.34 ]</td>
</tr>
</tbody>
</table>

Heterogeneity: not applicable
Test for overall effect: Z = 32.74 (P < 0.00001)
Test for subgroup differences: Not applicable

Favours experimental Favours control
Analysis 3.3. Comparison 3 Duration of oxygen therapy (days), Outcome 3 Periods off - no cannulae versus cannulae.

Review: Strategies for the withdrawal of nasal continuous positive airway pressure (NCPAP) in preterm infants

Comparison: 3 Duration of oxygen therapy (days)

Outcome: 3 Periods off - no cannulae versus cannulae

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Periods off (no cannulae)</th>
<th>Periods off (cannulae)</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Todd 2010</td>
<td>N: 55, Mean(SD): 35.9 (2)</td>
<td>N: 49, Mean(SD): 31.3 (1.9)</td>
<td>IV/Fixed, 95% CI</td>
<td>100.0%</td>
<td>4.60 [3.85, 5.35]</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td>55</td>
<td>49</td>
<td>100.0%</td>
<td>4.60</td>
<td>3.85, 5.35</td>
</tr>
</tbody>
</table>

Heterogeneity: not applicable

Test for overall effect: Z = 12.02 (P < 0.00001)

Test for subgroup differences: Not applicable

---

**HISTORY**

Protocol first published: Issue 1, 2008

Review first published: Issue 2, 2011

<table>
<thead>
<tr>
<th>Date</th>
<th>Event</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>27 October 2008</td>
<td>Amended</td>
<td>Converted to new review format.</td>
</tr>
</tbody>
</table>

**CONTRIBUTIONS OF AUTHORS**

LAJ and MWD performed the searches.

LAJ wrote the review.

MWD and GDI revised the review.
DECLARATIONS OF INTEREST

Dr Jardine is a co-investigator in Todd 2010.

SOURCES OF SUPPORT

Internal sources

• Department of Neonatology, Mater Mother’s Hospital, South Brisbane, Australia.
• Grantley Stable Neonatal Unit, Royal Brisbane and Women’s Hospital, Brisbane, Australia.
• Department of Paediatrics and Child Health, The University of Queensland, Royal Children’s Hospital, Brisbane, Australia.

External sources

• No sources of support supplied

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

The background has been substantially amended. The following sections were also completed: abstract, plain language summary, results, discussion, authors’ conclusions, acknowledgements, contributions of authors, differences between protocol and review, characteristics of studies table, and references to studies.

INDEX TERMS

Medical Subject Headings (MeSH)

∗Continuous Positive Airway Pressure; ∗Infant, Premature; Length of Stay; Oxygen Inhalation Therapy; Randomized Controlled Trials as Topic; Ventilator Weaning [∗methods; standards]

MeSH check words

Humans; Infant, Newborn