Infant position in neonates receiving mechanical ventilation (Review)

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A B S T R A C T

Background
Several body positions other than standard supine position have been used in patients undergoing intensive care for reducing the incidence of pressure ulcers of the skin, contractures or ankylosis and for improving the patient's well being. In patients from different age groups undergoing mechanical ventilation (MV), it has been observed that particular positions, such as prone position, may improve some respiratory parameters. Benefits from these positions have not been clearly defined in critically ill newborns who may require mechanical ventilation for extended periods of time.

Objectives
To assess the effects of different positioning of newborn infants receiving MV on short term respiratory outcomes and complications of prematurity.

Search strategy
Databases searched (up to May 2006) were the Oxford Database of Perinatal Trials, CINAHL, MEDLINE, EMBASE and Cochrane Central Register of Controlled Trials (CENTRAL, The Cochrane Library, Issue 2, 2006). Hand searches of proceedings of the Society for Pediatric Research from 1990 to May 2006 were used to identify unpublished studies.

Selection criteria
Randomised or quasi randomised clinical trials comparing different positions in newborns receiving mechanical ventilation.

Data collection and analysis
Three independent and unblinded reviewers assessed the trials for inclusion in the review and extracted the data. Data were double-checked and entered into the Review Manager software.

Main results
Eleven trials involving 206 infants were included in this review. Several positions were compared: prone vs. supine, prone vs. lateral right, lateral right vs. supine, lateral left vs. supine, lateral right vs. lateral left and good lung dependent vs. good lung uppermost. Apart from one of the two studies that compared lateral right vs. lateral left positions, and one comparing prone vs. supine position, all the included studies had a crossover design. Comparing prone vs. supine position, an increase in arterial P02 in the prone position of between 2.75 and 9.72 mm Hg (95%CI) was observed (one trial). When % hemoglobin oxygen saturation was measured with pulse oximetry, improvement in the prone position was from 1.18 to 4.36% (typical effect based on four trials). In addition, there was a slight improvement in the number of episodes of desaturation. It was not possible to establish whether this effect remained once the intervention was stopped. Negative effects from the interventions were not described, although this issue was not studied in sufficient detail. Effects of position on other outcomes were not statistically significant; however, either positive nor negative effects cannot be excluded considering the small numbers that were studied.

Authors' conclusions

The prone position was found to slightly improve the oxygenation in neonates undergoing mechanical ventilation. However, we found no evidence concerning whether particular body positions during mechanical ventilation of the neonate are effective in producing sustained and clinically relevant improvements.

PLAIN LANGUAGE SUMMARY

We found no clear evidence that particular body positions in newborn babies who need assisted ventilation are effective in producing relevant and sustained improvement. However, putting infants on assisted ventilation in the face down position for short time slightly improves their oxygenation and infants in the prone position undergo fewer episodes of poor oxygenation.

BACKGROUND

Mechanical ventilation (MV) is often necessary when treating ill newborns, particularly when they are preterm. Although usually given for a short time, occasionally MV may be necessary for a long period. Mechanical ventilation has been related to short term complications and impaired long term respiratory and developmental outcomes (Fawer 1995; Singer 1997; Bancalari 2001), with longer duration of MV associated with an increased risk of complications.

Different methods of respiratory support have been developed with the aim of improving the effectiveness of assisted ventilation and minimising its adverse effects, i.e. high frequency ventilation , conventional ventilation (CV) with all its variants and continuous positive airway pressure (CPAP). (Bhuta 2001; Greenough 2001; Henderson-Smart 2001; Woodgate 2001).

It is uncertain whether the position of the infant while on MV has an impact on clinical outcome. The main positions that can be used are supine, prone or lateral decubitus. Although it is not known which is the best way to position the newborn, there is a trend towards keeping ventilated infants in a supine position, mainly for ease of observation and handling of the infant. These patients require frequent monitoring and interventions, and may have many catheters and tubes (including urinary, umbilical and other vascular catheters, and drainage tubes).

Studies performed on other types of patients suggest that the change from supine to other positions, specifically to prone, can have some advantages. For example, several studies in adults and children on MV, mainly for acute respiratory failure (ARF) and acute respiratory distress syndrome (ARDS), showed transitory benefits of the prone position on oxygenation (Piehl 1976; Douglas 1977; Fridrich 1996; Chatte 1997; Curley 2000; Gattinoni 2001). Other studies in newborn infants not needing assisted ventilation found some benefit of positions other than the traditional supine position, especially the prone position. Observed benefits were improvements in oxygenation (Schwartz 1975; Martin 1979; Kishan 1981) and in other functional respiratory parameters (Masterson 1987; Fox 1993; Wolfson 1992; Adams 1994; Martin 1995; Itakura 1998). It has been suggested that non-supine positions could have additional benefits regarding feeding, gastric emptying and suctioning (Yu 1975; Hewitt 1976; Mizuno 2000) and on some aspects of development during the first months of life (Jantz 1997; Davis 1998; Dewey 1998; Visscher 1998; Ratliff-Schaub 2001). In addition, postural changes could contribute to preventing motor abnormalities.

These interventions are easy to perform and have virtually no economic cost. In light of these results, it is of great interest to know whether placing infants in positions other than supine during MV could be of any clinical benefit.

OBJECTIVES

Primary objective:

- To assess the effects of different positioning of newborn infants receiving MV (supine vs lateral decubitus or prone) on improving short term respiratory outcomes

Secondary objectives

- To assess the effects of different positioning of newborn infants receiving MV on mortality, neuromotor and developmental outcomes in the long term and other complications of prematurity

Subgroup analyses are planned on the basis of:

- Gestational age (or birthweight): 37 or more completed weeks, and less than 37 weeks
- Birthweight: $\leq$ 1500 g, >1500 g
- Type of respiratory support: CV, synchronized intermittent mandatory ventilation (SIMV), high frequency oscillation (HFOV), high frequency jet ventilation (HFJV), and CPAP

CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

Types of studies

- Randomised or quasi-randomised trials

Types of participants

- Term or preterm neonates requiring any type of positive pressure MV including CPAP

Types of intervention

- Placing infants in a supine position compared with placing them in a prone or lateral decubitus position or undertaking a strategy of regular position change
- Studies that also evaluated concomitant therapeutic interventions will be excluded if the effect of the infant positioning cannot be assessed independently of the second intervention's effect

Types of outcome measures

Primary outcomes:
1. Oxygenation during MV; measured by arterial oxygen tension, transcutaneous method or hemoglobin oxygen saturation
2. Decrease in characteristics of ventilator: peak inspiratory pressure or mean airway pressure (cm H2O) and fraction of inspiratory oxygen
3. Short term pulmonary complications: pneumothorax or pulmonary interstitial emphysema (PIE)
4. Duration of ventilator support
5. Bronchopulmonary dysplasia (BPD) or chronic lung disease (CLD) either at 28 days after birth or 36 weeks' postmenstrual age, respectively
6. Changes in carbon dioxide tension (PCO2)
7. Changes on pulmonary mechanics
8. Short term complications (accidental extubation, dislodgement of central catheters, urinary or drainage tubes)

Secondary outcomes:
9. Peri or intraventricular haemorrhage
10. Gastrointestinal or feeding problems:
- Necrotizing enterocolitis (NEC) or
- intolerance of enteral feeding
11. Days of stay in NICU
12. Days of stay in hospital
13. Neonatal mortality (death during the first 28 days of life)
14. Infant mortality (death during the first year of life)
15. Long term neurodevelopmental outcomes at age two years: rates of cerebral palsy as assessed by physician, developmental delay (i.e. IQ < 2 standard deviations) on validated assessment tools (e.g. the Stanford-Binet Intelligence Scale or others) or sensory impairment
16. Cutaneous and joint problems, i.e. dependent oedema, pressure ulcers of the skin, joint contractures or ankylosis

SEARCH METHODS FOR IDENTIFICATION OF STUDIES

See: methods used in reviews.

The standard search strategy of the Cochrane Neonatal Review Group, as outlined in The Cochrane Library, was used and combined with the following MeSH search terms: "Posture", "Prone Position", "Ventilators, Mechanical", "Respiration, Artificial", "Positive-Pressure Respiration", "Infant, Newborn". The following text words were also used: "infant positioning" (tw), "patient positioning" (tw), "body position" (tw), "prone" (tw), "lateral decubitus" (tw), "mechanical ventilation" (tw), "neonate" (tw) and "premature" (tw).

Searches in databases included the Oxford Database of Perinatal Trials, CINAHL (up to May 2006), the Cochrane Central Register of Controlled Trials (CENTRAL, The Cochrane Library, Issue 2, 2006), MEDLINE (up to May 2006) and EMBASE (up to May 2006). No language restrictions were set. References of included studies were also reviewed. Unpublished studies were identified by hand searching conference proceedings of the Society for Pediatric Research published from 1990 to May 2006.

METHODS OF THE REVIEW

Screening for eligibility
Three reviewers independently assessed the trials for inclusion in the review without prior consideration of their results. Disagreements on inclusion were resolved through discussion between the reviewers. Excluded studies are listed including the reasons for their exclusion.

Assessment of methodological quality
The standard methodology of the Cochrane Collaboration and its Neonatal Review Group was used to assess the methodological quality of studies. Each trial was allocated into the following categories based on the allocation concealment: A (adequate), B (unclear), C (clearly inadequate). Quality assessment of studies was based on
1) randomisation and allocation concealment
2) completeness of follow-up
3) blinding of outcome measurement
When necessary, additional information and clarification of published data were sought from authors of individual trials.

Data extraction
All reviewers extracted the data independently using prepared data extraction forms. Discrepancies were solved by discussion between all the reviewers. Authors were contacted for missing information. Data were extracted from graphs, if necessary (Bjornson 1992; Bozynski 1988).

Data analysis

Analysis of data was carried out using RevMan. Analysis of those studies with a crossover design was conducted using paired data according to the methodology outlined in Elbourne 2002. The statistical method took into account the correlation existing between repeated observations of the patients, and thus allowed the computation of adjusted standard deviations for the effect sizes (differences in means for continuous variables and odds ratios for dichotomous ones). A necessary imputation of the method was the degree of existing correlation between repeated measures.

For continuous variables, one of the studies (Fox 1990) provided individual data for PaO2, from what we derived a Pearson correlation coefficient, and assumed that the same degree of correlation existed on the other studies for all the variables. For the dichotomous variable, desaturation episodes, estimating the degree of correlation meant to estimate the number of patients presenting the outcome of interest under both treatments. Since only one crossover trial reported this outcome (Chang 2002), present in as few as five cases in one of the treatment groups, we compared the results assuming the lowest possible correlation between treatments (no patients desaturated under both treatments) and assuming the highest one (five patients desaturated under both treatments). Since the results didn't differ, it was irrelevant which assumption to take.

The adjusted effect sizes computed for cross-over trials, and the usual ones computed for parallel trials, were combined by means of the inverse-variance method, under a random-effects model. Presence of heterogeneity was assessed by means of the I^2 statistic. If clinically relevant and statistically significant heterogeneity was detected, causes of heterogeneity were have been sought a posteriori.

DESCRIPTION OF STUDIES

Sixteen trials were identified. Five of them failed to meet the inclusion criteria (Itakura 1998; McEvoy 1997; Schrod 1993; Baird 1991; Wagaman 1979). The reasons for exclusions are listed in the Table of Excluded Studies. Eleven trials were included (Antunes 2003; Bjornson 1992; Bozynski 1988; Chang 2002; Crane 1990; Fox 1990; Heaf 1983; Mendoza 1991; Mizuno 1995; Mizuno 1999; Schlessel 1993). Nine studies were randomised cross over controlled trials whereas Antunes 2003 and Schlessel 1993 were randomised parallel group controlled trial. One trial published in German (Schrod 1993) was translated.

Sample characteristics

Most trials included preterm infants with gestational age ranging from 23 to 36 weeks. One study did not report the gestational age at birth (Heaf 1983), but when the reported birth weight of study infants was inspected, it was considered that, on average, the included patients were born at term. Important variations in age of the neonate were found across the studies. In five studies, patients were less than a week of age (Chang 2002; Crane 1990; Fox 1990; Heaf 1983; Schlessel 1993), ranging between 22 hours and seven days. In the other six trials, neonates were between two and 138 days old.

All the studies enrolled preterm infants receiving mechanical ventilation. Infants were ventilated with intermittent mandatory ventilation (IMV) in nine trials (Antunes 2003 ; Chang 2002; Bozynski 1988; Crane 1990; Mizuno 1995; Mizuno 1999; Schlessel 1993; Mendoza 1991; Bjornson 1992). Two studies (Fox 1990; Heaf 1983) included patients on IMV and patients on CPAP. Infants were on mechanical ventilation due to RDS in six studies (Bjornson 1992; Chang 2002) in 20 out of 28 cases (Crane 1990; Fox 1990; Schlessel 1993; Mendoza 1991). In three studies patients were in stable condition and ventilated due to CLD (Bozynski 1988; Mizuno 1995; Mizuno 1999), and in one (Antunes 2003) patients were on IMV because of prematurity (presumably due to RDS) and entered in the study in the beginning of the weaning process. In one trial, ventilation was due to unilateral lung disease (three congenital diaphragmatic hernia and one with hypoplastic right lung) (Heaf 1983). No other associated conditions were defined in other trials, but Bjornson 1992 described two patients with sepsis and one with patent ductus arteriosus. Patient inclusion and/or exclusion criteria were not always well defined in the included studies. A variety of exclusion criteria were applied: presence of known congenital defects (Antunes 2003; Bjornson 1992; Chang 2002), infants treated with sedative or paralysing drugs (Fox 1990; Chang 2002) or infants with asymmetric lung disease (Bozynski 1988; Schlessel 1993).

In five trials, simultaneous treatments during the studies were not described (Crane 1990; Fox 1990; Mizuno 1995; Mizuno 1999; Schlessel 1993). In the study by Bjornson 1992, one infant received sedation, another corticosteroids and two patients received treatment for sepsis (one of them underwent a surgical ligation of a patent ductus arteriosus). Eighteen infants received surfactant in the study of Chang 2002. In the study by Bozynski 1988, twelve newborns received furosemide and seven infants spironolactone plus thiazide diuretics. Three infants were operated on for congenital diaphragmatic hernia in the study by Heaf 1983. In the trial by Mendoza 1991, all patients received theophylline.

Interventions

The age and the clinical status of those infants receiving MV with different positioning were different among the ten included trials. All the trials but one (Antunes 2003) tested positions for short periods of time, ranging from two minutes in Crane 1990 to two hours in Chang 2002. In the Antunes 2003 study, the position tested was the same from the start of MV weaning until extubation, except for 3 hours a day in the newborns allocated to the prone position. In the majority of papers it was specified (or the reviewers deduced) that patients were fasting. In only two studies (Mizuno 1995; Mizuno 1999) was it clear that enteral nutrition was used.

Several position changes were studied: Eight trials analysed short term respiratory outcomes placing infants in a supine position compared with placing them in a prone position (Antunes 2003; Bjornson 1992, Chang 2002, Crane 1990, Fox 1990, Mizuno 1995, Mizuno 1999, Mendoza 1991). Bjornson and Crane also analysed changes between prone and lateral right position and supine vs. lateral right position. Bozynski 1988 analyzed changes between supine vs. lateral right, supine vs. lateral left and lateral right vs. lateral left position. Schlessel 1993 analyzed lateral left vs. lateral right position in spite of using a sequence of positions including the supine, but this latter position was not randomised. Heaf 1983 analyzed impact of position in patients with unilateral lung disease, comparing the good lung dependent vs good lung uppermost.

Outcomes measures

Overall, there was a lack of consistency in the types of outcome measures reported by trialists, and a lack of consistency in the way data were reported. Oxygenation while on MV was measured by arterial oxygen tension (Schlessel 1993; Fox 1990), transcutaneous method (Bozynski 1988; Heaf 1983) or hemoglobin oxygen saturation using pulse oximetry (Antunes 2003; Bjornson 1992; Chang 2002; Mizuno 1995; Mizuno 1999). Mendoza 1991 measured oxygen saturation of hemoglobin by pulse oximetry, but the data was not useable due to deficiencies in data reporting (mean point estimate without measure of standard deviation). CO2 tension was measured by transcutaneous monitor (Bozynski 1988; Crane 1990; Heaf 1983; Mizuno 1995; Mizuno 1999) or by arterial samples (Schlessel 1993). Some papers measured different physiological pulmonary parameters. Tidal volume (spontaneous breath) in mL/kg and minute ventilation in mL/Kg/min were measured by Mizuno 1995, Mizuno 1999 and Mendoza 1991. Schlessel 1993 measured only tidal volume, but included other respiratory outcomes not used in this review (dynamic lung compliance, total pulmonary resistance, inspiratory pulmonary resistance and expiratory pulmonary resistance). Further characteristics of the trials are reported in the table Characteristics of Included Studies. As most of trials have a cross-over design we could not obtain data to assess the effects of different positioning of newborn infants receiving MV on mortality, neuromotor and developmental outcomes in the long term and other complications of prematurity. Long term follow up is not relevant for crossover trials: by the nature of their design crossover trials can only address short-term effects during treatment.

METHODOLOGICAL QUALITY

Details of the methodological quality of each trial are given in the table of included studies

Nine studies were randomised cross-over controlled trials, whereas Schlessel 1993 and Antunes 2003 were randomised parallel group controlled trial. The method of allocation was usually not stated, being described only by Chang 2002 (randomisation in blocks by a third person to ensure balanced combinations of positions and finally using an identification number in a sealed envelope) Fox 1990 (coin toss), and Antunes 2003 (drawing lots in the form of sealed envelopes). Only in these three studies could the allocation concealment be considered as adequate.

Due to the nature of the trials, blinding of intervention was not possible in any of the studies

Six studies had complete follow-up of enrolled infants (Bozynski 1988; Fox 1990; Heaf 1983; Mizuno 1995; Mizuno 1999; Schlessel 1993). In the study by Antunes 2003, one patient did not complete the protocol for unknown reasons. In the study by Bjornson 1992, two infants needed changes in the ventilatory parameters during the study and could not complete the nine sessions prescribed. In the study by Chang 2002, ten patients (four in prone, six in supine) did not complete the two hour protocol in the same position because of the need for interventions (airway suctioning, etc), in which case a time of equal duration was selected for comparison. Five infants were discarded in the study by Crane 1990 because of excessive tcPCO2/PaCO2 difference or inaccurate calibration. In the trial by Mendoza 1991, seven patients were excluded from analysis of some lung mechanics for not having good spontaneous breaths in one or both of the positions. The outcome measurements were not blinded in any of the studies.

RESULTS

COMPARISON 01: PRONE VS. SUPINE

Results for PaO2 and percent hemoglobin oxygen saturation (Sp02) show a small significant beneficial effect of the prone position. Only one study [Fox 1990] provided data for Pa02, showing a small but significant improvement in the prone position: mean difference (MD) of 6.24 mmHg (95%CI 2.93 to 9.55). Four studies provided data for Sp02, all showing small improvements in the prone position (0.8% to 4.4%), but with significant heterogeneity ($p < 0.001$). Three of the four trials found a statistically significant effect. The meta-analysis supported a significant increase in Sp02 in the prone position, MD 2.77% (95% CI 1.18 to 4.36).

In another study, on newborns in the weaning process (Antunes 2003), no differences were found in the SpO2 between Supine or Prone, but these results could not be considered because there was a simultaneous reduction in the ventilator parameters. In fact, patients in the prone position needed less aggressive ventilator parameters [inspiratory pressure (PIP)] on the second (14.4 ± 1.95 vs 13.0 ± 2.14, $P = 0.048$) and third (14.4 ± 1.95 vs 13.0 ± 2.14, $P = 0.048$) day of weaning.

Two studies (Antunes 2003, Chang 2002) quantified the number of desaturation episodes (DeSat). Both found a lower incidence of DeSat in the prone position. Both studies defined and quantified DeSat differently. Antunes 2003 defined DeSat as the detection of two episodes of Sp02 < 90% that require a temporary increase in FiO2. According to this definition, nine of the 21 patients experienced DeSat in the supine position and 1 in the prone position OR: 0.07(95% CI 0.01 to 0.59). Chang 2002 defined DeSat as SpO2<90% that lasted longer than 20 seconds, and he found that 14 of 28 patients experienced DeSat in the supine position and five in the prone position OR: 0.22 (95% CI 0.09 to 0.54). The meta-analysis of both studies shows no heterogeneity and the analysis with the random effects model shows a significant difference in favour of the prone position OR 0.18 (95% CI 0.08 to 0.42). Antunes also found that prematures who had been weaned in prone position subsequently had to be reintubated significantly less (seven out of 21) than those that had been weaned in supine (seven out of 21) p = 0.049

Three studies provided data for pCO2, without significant heterogeneity of effect (p = 0.83). The meta-analysis supported a small but significant decrease in the pCO2 in the prone position (MD - 3.77 mmHg, 95%CI -6.65 to -0.89).

Pulmonary mechanics were assessed by means of tidal volume and minute ventilation in three studies (Mendoza 1991; Mizuno 1995; Mizuno 1999). Results were heterogeneous for both outcomes (p = 0.009 and p = 0.044), and meta-analysis found no evidence of effect (MD for tidal volume 0.70 mL/kg, 95% CI -0.81 to 2.2); MD for minute ventilation 19.80 mL/kg/min, 95% CI -40.54 to 80.14).

The aforementioned study by Antunes 2003 found no differences in the duration of the process of weaning between the prone and supine position. However, once the patients had been extubated and placed in the supine position under CPAP, it was found that those who had been weaned in the supine position needed to be reintubated more often than those who had been weaned in the prone position during the first 48 hours (7 vs 1, p = 0.049).

COMPARISON 02: PRONE VS. LATERAL

Two studies provided data comparing the prone and the lateral positions. Crane 1990 assessed the effect on pCO2 and found no difference. Bjornson 1992 assessed the effect on hemoglobin oxygen saturation and found a slight improvement in the prone position (MD 2.13 mmHg, 95% CI 0.33 to 3.93).

COMPARISON 03: LATERAL VS. SUPINE

Three trials compared lateral position versus supine: Crane 1990 and Bjornson 1992 focused on right lateral position, Bozynski 1988 focused on both side positions. Neither lateral right position nor lateral left position showed significant differences compared with supine position for any of the outcomes (hemoglobin oxygen saturation, oxygen pressure, or carbon dioxide pressure). Two studies assessed effect on pCO2, with homogeneous data and non-significant result on meta-analysis (MD - 0.69 mmHg, 95%CI -4.15 to 2.78).

COMPARISON 04: LATERAL RIGHT VS. LATERAL LEFT

One parallel clinical trial (Schlessel 1993) and one cross-over trial (Bozynski 1988) provided data for this comparison. Neither showed significant effects on any outcome (oxygen pressure, carbon dioxide pressure or tidal volume). Meta-analysis results were also non-significant (MD for PaO2 - 0.05 mmHg, 95% CI -6.93 to 6.83; MD for pCO2 0.41 mmHg, 95% CI -2.01 to 2.82).

COMPARISON 05: GOOD LUNG DEPENDENT VS. GOOD LUNG UPPERMOST

One small cross-over trial (Heaf 1983) provided data for this comparison, and it found no significant differences in oxygen or carbon dioxide pressure.

For all position contrasts, effects of position on other outcomes defined a priori, including clinically important outcomes, could not be assessed because of lack of data. Planned subgroup analyses could not be performed because of lack of data.

DISCUSSION

There is no evidence from these studies that any specific body position is more effective than another in producing long-term clinically relevant benefits. However, neonates on MV who were habitually in the supine position improved their oxygenation when they changed to the prone position. It cannot be concluded from these studies whether the improvement in oxygenation was due to the fact that the prone position is better, or whether it is mainly due to the change in position. This improvement in oxygenation lasted only for the short time they were in prone position. A total of 10 trials studying different positions were included: prone vs. supine, prone vs. lateral right, lateral right vs. supine, lateral left vs. supine, lateral right vs. lateral left and good lung dependent vs. good lung uppermost. The most robust comparison was the effect of prone vs. supine on oxygenation outcomes, with a total of five studies providing useful data.

STRENGTHS AND LIMITATIONS OF THE INCLUDED STUDIES

Considering that any change of position over the standard supine position may promote a more flexed position (similar to the fetal position) that could positively affect the outcomes, most included studies specified that both the standard position and the comparison position promoted flexion using soft cloth rolls, etc.

Nonetheless, the included studies in this review have several limitations. One limitation is related to the small sample sizes, which added up to only 164 infants for the review. Firm conclusions could not be drawn because this limitation, as well as variations in the interventions and outcomes assessed, resulting in multiple subgroups, each including small numbers of patients.

Furthermore, the use of a crossover design in all the studies except two (Antunes 2003; Schlessel 1993) removes the ability to measure effects on long-term outcomes. Because these two studies did not undertake a prolonged follow up, it was not possible to determine whether they might have important long-term effects.

PRONE POSITION VS. SUPINE

Compared to standard supine position, prone position was shown to be effective in improving oxygenation over short periods of time.

The magnitude of improvement in oxygenation could not be reliably established because the five eligible trials (Fox 1990; Bjornson 1992; Mizuno 1995; Mizuno 1999; Chang 2002) included a total of only 70 babies, and used two different measures of oxygenation. Oxygenation in the prone position was superior in the four studies that measured oxygenation by pulse oximetry. Although there was heterogeneity across studies in the magnitude of effect, an increase in haemoglobin oxygen saturation in the prone position was shown, with a 95% confidence interval from 1.18 to 4.36%. The only study that measured PO2 in arterial blood (the most precise measure of oxygenation) showed an increase of 6.24 mmHg (95%CI 2.93 to 9.55) (Fox 1990) in the prone position.

It is not possible to conclude whether the observed improvements in oxygenation in the prone position would be maintained over the long term. The time of exposure to the prone position in each patient was relatively short, varying from 15 minutes to two hours. It also cannot be concluded whether this benefit may be sustained after the intervention has been stopped.

It is possible that benefits of the prone position on oxygenation may have been underestimated considering that three out of five studies (Mizuno 1995; Mizuno 1999; Chang 2002) were conducted in relatively stable patients with respiratory insufficiency. Furthermore, one of the studies (Bjornson 1992) excluded some common conditions such as congenital defects and intraventricular haemorrhages.

One study (Chang 2002) assessed additional secondary outcomes such as motor activity, and the number, intensity and duration of episodes of desaturation. This study found that, compared to supine position, prone position produced fewer episodes of desaturation and lesser levels of activity. It also found that 74% of the episodes of desaturation were associated with vigorous motor activity and crying. The study concluded that prone position offered indirect benefits by achieving less agitation in the infants. Furthermore, this study found that improvement in oxygenation was higher in the subgroup of patients previously treated with surfactant. Another study undertaken on prematures on MV in the weaning phase (Antunes 2003) also found that the prone position was better than the supine position as far as desaturation episodes were concerned. The meta-analysis showed fewer patients experience desaturation episodes in the prone position. Antunes also found that prematures who had been weaned in prone position had to be reintubated less frequently than those that had been weaned in supine.

The two studies of Mizuno (Mizuno 1995; Mizuno 1999) raised questions about effects that enteral feeding may have on respiratory outcomes. Although both studies offered data that suggested that prone position may improve oxygenation during and after feeding, these data were not included in our review because all the other studies included were conducted during fasting periods (pre-feeding) of at least a few hours.

Only three studies including 27 patients provided data on the effect of prone position on pC02 (Crane 1990; Mizuno 1995; Mizuno 1999). The pooled result showed a slight decrease in pCO2, of doubtful clinical importance.

Several studies measured different pulmonary mechanics parameters. These outcomes were included in a meta-analysis only when studies using comparable measures were available. Only tidal volume and minute ventilation during spontaneous breathing could be analysed. Significant differences between prone and supine positions were not found. Nonetheless, considering the small numbers that were analysed, it cannot be excluded that small effects on these parameters may exist, or that effects on pulmonary mechanics due to changes in position might be better reflected by other parameters.

OTHER COMPARISONS

Only one study (Bjornson 1992) assessed the effect of prone position versus lateral on hemoglobin oxygen saturation and found a slightly improvement in the prone position (mean difference 2.13 mmHg, 95% CI 0.33 to 3.93).

One trial (Heaf 1983) compared blood gases in patients with asymmetric respiratory pathology who were positioned with their good lung dependent vs. good lung uppermost. There were no significant differences between the positions in p02 or pC02. It is not possible to draw reliable conclusions from this study considering the small number of patients eligible for this review (only four patients). Differences between other positions compared (prone vs. lateral right, lateral right or left vs. supine and lateral right vs. left) were not observed, although they cannot be disregarded considering the small number of patients that were included.

COMPLICATIONS ASSOCIATED WITH INTERVENTIONS

None of the trials reported complications or undesirable effects attributable to the change in positioning. Complications are referred to in a generic way, and in most of the trials complications were not explicitly mentioned in the objectives.

Immediate accidents such as accidental extubation, bleeding, airway loss, etc are manipulative problems that may be observed in general clinical practice even though they weren't observed in controlled settings of clinical trials with fairly stable patients.

AUTHORS' CONCLUSIONS

Implications for practice

Evidence from randomised controlled trials indicates that, compared to the supine position, the prone position improves oxygenation, including desaturation episodes, when used for short periods of time or when patients were stable and in the weaning process. We found no evidence about whether or not the prone position produces sustained benefits on pulmonary or other parameters.

Although adverse effects from the prone position were not observed in the studies reviewed, they cannot be disregarded with confidence. The effect of position has been generally tested under highly controlled circumstances in stable patients. Therefore, use of the prone position should be carefully monitored, particularly to avoid damage to the tracheal tube or central catheters during manipulation of the neonate.

Implications for research

Large controlled clinical trials comparing prone position against supine should be conducted. Controlled trials with a parallel design could assess not only short-term outcomes, but also long and medium-term outcomes such as mortality, duration of ventilator support and hospitalization, cutaneous and joint problems and neurodevelopment. The conduct of large studies among less selected patients (including those who are less stable) may help to verify whether the intervention benefits newborns with different diseases or disease severity and whether subgroups of responsive patients may be identified.

Questions concerning effects of lateral positions still need answers. Likewise, studies that assess lateral decubitus position with good lung dependent vs. good lung uppermost in patients with asymmetrical respiratory pathology should also be conducted.

POTENTIAL CONFLICT OF INTEREST

None

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TABLES

Characteristics of included studies

Study	Antunes 2003
Methods	Randomised Parallel Controlled Trial. Method of randomisation: drawing lots in the form of sealed envelopes defining the infant's position: supine or prone Blinding of intervention: no Complete follow up: no. One patient did not complete the protocol by not stated reason. Blinding of outcome measurement: no
Participants	Sample size 42. Gestational age at birth: 24-33 weeks; Supine (29.3 ± 2.57), Prone (29.6 ± 2.46). Age: Supine 2-50 days 4 (2; 10) quartiles (Q1;Q3); Prone: 2-37 days 11 (3; 25) quartiles (Q1;Q3) On mechanical ventilation due to a unspecified cause during the first week of life for a period > 48 hours. In stable condition when, weaning process was decided. Associated conditions: not stated. Exclusion: A) congenital defects or clinical or surgical conditions which make the randomised position impossible to maintain.

Characteristics of included studies (*Continued*)

	B) Failure to obtain the all information of research protocol. C) Inadvertent violation of research protocol or the newborn remaining in a position other than that prescribed by the study for more than an hour per day.
Interventions	Prone vs. Supine (From the start of weaning of VA until his/her extubation, except 3 hours a day in the newborns allocated to the prone position).
Outcomes	- During intervention: Oxygen saturation of haemoglobin by pulse oximetry (while changing ventilator parameters). Respiratory and cardiac rate. Number of desaturation episodes (SaO2 values of less than 90% requiring a temporary increase in FiO2). Ventilator parameters: FiO2, PIP and respiratory rate, (average values for each day). Atelectasis (based on the thorax radiography findings, performed for difficult to wean patients and during the first 12 hours post-extubation for all infants) Apnea (defined as an inspiration pause of more than 20 seconds duration or of lesser duration, but associated with bradycardia and/or cyanosis). Mechanical ventilation weaning duration. -Outcomes after intervention Weaning complication: Atelectasis. Need for reintubation (during 48 hours post-extubation).
Notes	
Allocation concealment	A – Adequate

Study	**Bjornson 1992**
Methods	Randomised Cross-over Controlled Trial. Method of randomisation: not stated. Blinding of intervention: no Complete follow up: no. Two newborns needed changes in the ventilatory parameters during the study and could not complete the 9 sessions prescribed (one newborn: 6 sessions, another one: 7). Blinding of outcome measurement: no
Participants	Sample size 4. Gestational age at birth: 24-30 weeks (26.50±2.08). Age: 9-24 days (10.75±2.50). On Conventional ventilation since birth due to RDS. Associated conditions: 2 sepsis, 1 patent ductus arteriosus. Exclusion: major congenital defects, cardiac anomalies (other than patent ductus arteriosus), major intraventricular haemorrhages, maternal substance abuse.
Interventions	Prone vs. Supine Prone vs. Lateral Right Supine vs. Lateral Right. Co-interventions (similar across comparison): 1 newborn received sedation, 1 corticoids, 2 treatment for sepsis (one of them underwent a surgical ligation of a patent ductus arteriosus)
Outcomes	Oxygen Saturation of haemoglobin by pulse oximetry (SpO2)
Notes	Results extracted from graph
Allocation concealment	B – Unclear

Study	**Bozynski 1988**
Methods	Randomised Cross-over Controlled Trial. Method of randomisation: not stated. Blinding of intervention: no Complete follow up: yes. Blinding of outcome measurement: no

Characteristics of included studies (*Continued*)

Participants	Sample size 18 Gestational age at birth: 24-30 weeks (27.5). Age > 14 days (31). On mechanical ventilation (IMV) due to CLD. In stable condition. Exclusion: asymmetric lung disease or any other major problem (including patent ductus arteriosus)
Interventions	Lateral Right vs. Supine Lateral Left vs. Supine Lateral Left vs. Lateral Right Co-interventions (similar across comparison): Furosemide in 12 newborns, Spironolactone + Thiazide in seven.
Outcomes	Transcutaneous PO2 (tcPO2) and Transcutaneous PCO2 (tcPCO2): only means and range (the reviewers extracted the results from a graph). Other outcomes not used in this review: sleep state
Notes	Results extracted from graph
Allocation concealment	B – Unclear

Study	**Chang 2002**
Methods	Randomised Cross-over Controlled Trial. Randomisation method: randomisation in blocks by a third person to ensure balanced combinations of positions and finally using an identification number in a sealed envelope. Blinding of intervention: no Complete follow up: no. 10 patients (4 in prone, 6 in supine) did not complete the 2-hour protocol in the same position because of the need for interventions (airway suctioning, etc), then equal duration of a selected similarly distributed length of time was used for analysis. Blinding of outcome measurement: no
Participants	Sample size 28. Gestational age at birth: 25-36 weeks (29.5± 3.5). Age < 7 days (38 ± 31). On mechanical ventilation (IMV) due to RDS in 20 cases, the remaining 8 due a unspecified cause. In relatively stable condition (no need for frequent change in ventilator settings) Associated conditions: not stated. Exclusion: known congenital defects or newborns treated with sedatives.
Interventions	Prone vs. Supine. Co-interventions were similar across comparison: Surfactant in 18 newborns
Outcomes	Oxygen saturation of haemoglobin by pulse oximetry (SpO2) as continuous variable, number of desaturation episodes and their duration. Motor Activity.
Notes	
Allocation concealment	A – Adequate

Study	**Crane 1990**
Methods	Randomised Cross-over Controlled Trial. Method of randomisation: not stated. Blinding of intervention: no Complete follow up: no. Only 14 patients were included finally in the study (data from 5 were not used because excessive tcPCO2/PaCO2 difference or inaccurate calibration) Blinding of outcome measurement: no.
Participants	Sample size: 14 (from a study of 19, data from 5 were discarded by the authors of this study because excessive tcPCO2/PaCO2 difference or inaccurate calibration) Gestational age at birth: 24-36 weeks (31±3). Age: 20-72 hr. On mechanical ventilation (IMV) due to RDS. Associated conditions: the only information is that none had evidence of persistent pulmonary hypertension or systemic arterial hypotension.

Characteristics of included studies (*Continued*)

	Exclusion: not stated.
Interventions	Prone vs. Supine Prone vs. Lateral Right Supine vs. Lateral Right. Co-interventions: not stated.
Outcomes	Transcutaneous PCO2 (tcPCO2).
Notes	
Allocation concealment	B – Unclear

Study	**Fox 1990**
Methods	Randomised Cross-over Controlled Trial. Method of randomisation: coin toss. Blinding of intervention: no Complete follow up: yes. Blinding of outcome measurement: no.
Participants	Sample size 25 Gestational age at birth: 26-35 weeks (30.68±2.41). Age: 22 hr-5 days (55.4 ± 32.17). On respiratory support (IMV. or CPAP) due to RDS. Associated conditions: not stated. Exclusion: newborns treated with paralysing drugs.
Interventions	Prone vs. Supine Co-interventions: not stated.
Outcomes	Arterial PO2 (umbilical catheter attached to a monitor)
Notes	
Allocation concealment	A – Adequate

Study	**Heaf 1983**
Methods	Randomised Cross-over Controlled Trial Method of randomisation: not stated. Only randomised lateral position (left-right), no supine position. Blinding of intervention: no Complete follow up: yes Blinding of outcome measurement: no.
Participants	Sample size: 4 (from a study of 10, only 4 were eligible for this review because of age and need of respiratory support) Gestational age at birth: not stated (probably term newborns -deduced by the weight-). Age: 2-5 days (2.75±1.5). On respiratory support (IPPV or CPAP) due to unilateral (asymmetrical) lung disease. Associated conditions: 3 congenital diaphragmatic hernia, 1 hypoplastic right lung. Exclusion: not stated.
Interventions	Good lung dependent vs. Good lung uppermost. Co-interventions (similar across comparison): in 3 newborns surgery for congenital diaphragmatic hernia.
Outcomes	Transcutaneous PO2 (tcPO2) and Transcutaneous PCO2 (tcPCO2).
Notes	
Allocation concealment	B – Unclear

Study	**Mendoza 1991**
Methods	Randomised Cross-over Controlled Trial Method of randomisation: not stated. Blinding of intervention: no

	Complete follow up: 7 patients were excluded from analysis of some lung mechanics for having good spontaneous breaths in neither or only one of the positions. Blinding of outcome measurement: no
Participants	Sample size: 26 (from a study of 33, data from 7 were excluded from analysis by the authors because those 7 patients did not have good spontaneous breaths in each of the positions studied) Gestational age at birth: 23-33 weeks (mean: 27). Age: 15-138 days (mean:28). On mechanical ventilation (IMV) due to RDS needing MV for more than 2 weeks. Exclusion: not stated.
Interventions	Prone vs. Supine Co-interventions (similar across comparison): theophylline.
Outcomes	Tidal Volume (TV) in mL/kg (spontaneous breath), Minute ventilation (MV) in mL/kg/min, Other outcomes not used in this review: Oxygen Saturation of haemoglobin by pulse oximetry (SpO2): unusable data due to deficiencies in data reporting (mean point estimate without measure of standard deviation). Other outcomes not used in this review: Dynamic Lung Compliance, Resistance (expiratory and inspiratory), Total Work of Breathing and Heart Rate.
Notes	
Allocation concealment	B – Unclear

Study	**Mizuno 1995**
Methods	Randomised Cross-over Controlled Trial Method of randomisation: not stated. Blinding of intervention: no Complete follow up: yes Blinding of outcome measurement: no
Participants	Sample size: 6 Gestational age at birth: 23.9 - 26 weeks (24.8± 0.9). Age: > = 21days (47.5 ± 25.9). On mechanical ventilation (IMV) due to CLD in stable condition and receiving more than 100 ml/kg/day of feeding volume. Associated conditions: not stated. Exclusion: not stated.
Interventions	Prone vs. Supine (Before and After feeding) Co-interventions: not stated.
Outcomes	SpO2, tcPCO2, Tidal Volume (TV) in mL/kg (spontaneous breath), Minute ventilation (MV) in mL/kg/min. Other outcomes not used in this review: the aforementioned measured after feeding; and Spontaneous respiratory rate and Heart Rate measured before and after feeding.
Notes	
Allocation concealment	B – Unclear

Study	**Mizuno 1999**
Methods	Randomised Cross-over Controlled Trial Method of randomisation: not stated. Blinding of intervention: no Complete follow up: yes Blinding of outcome measurement: no
Participants	Sample size: 7 Gestational age at birth: 25.7-27.7 weeks (26.5±0.9). Age: >= 28 days (57.4±25.9). On mechanical ventilation (IMV) due to CLD in stable condition and receiving more than 100 ml/kg/day of feeding volume. Associated conditions: not stated.

	Exclusion: not stated.
Interventions	Prone vs. Supine (Before, During and After feeding) Co-interventions: not stated
Outcomes	SpO2, tcPCO2, Tidal Volume (TV) in mL/kg (spontaneous breath), Minute ventilation (MV) in mL/kg/min, Other outcomes not used in this review: the aforementioned measured During and After feeding; and the following measured Before, During and After (Total Minute ventilation, Pulmonary Resistance, Static Compliance, Work of Breathing for spontaneous breath, Spontaneous respiratory rate)
Notes	
Allocation concealment	B – Unclear

Study	**Schlessel 1993**
Methods	Randomised Controlled Trial (No cross-over) Method of randomisation: not stated. Blinding of intervention: no Complete follow up: yes Blinding of outcome measurement: no
Participants	Sample size: 16 Gestational age at birth: <= 36 weeks (33.4±1.5). Age: 5±2 days. On mechanical ventilation (IMV) recovering from RDS in stable condition. Exclusion: patent ductus arteriosus, asymmetric lung disease, pneumothorax, pulmonary interstitial emphysema.
Interventions	Lateral Left vs. Lateral Right (in spite of using a sequence of positions including the supine, that position was not randomised) Co-interventions: not stated.
Outcomes	Arterial PO2, Arterial PCO2, Tidal Volume (spontaneous breath). Other outcomes not used in this review: Dynamic Lung Compliance, Total Pulmonary Resistance, Inspiratory Pulmonary Resistance, Expiratory Pulmonary Resistance
Notes	
Allocation concealment	B – Unclear

Characteristics of excluded studies

Study	**Reason for exclusion**
Baird 1991	Not randomised. In this study mechanically ventilated patients were mixed with non ventilated.
Itakura 1998	Not randomised. This study didn't supply oxygenation data but measured different pulmonary mechanics parameters.
McEvoy 1997	Not randomised. Study of 55 infants from which only 17 were being mechanically ventilated.
Schrod 1993	Not randomised.
Wagaman 1979	Not randomised.

ANALYSES

Comparison 01. Prone vs Supine

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 pO2 (mmHg)	1	50	mean difference (Random) 95% CI	6.24 [2.93, 9.55]
02 Hb O2Sat (%)	4	90	mean difference (Random) 95% CI	2.77 [1.18, 4.36]
03 pCO2 (mmHg)	3	54	mean difference (Random) 95% CI	-3.77 [-6.65, -0.89]
04 tidal volume (mL/Kg)	3	78	mean difference (Random) 95% CI	0.70 [-0.81, 2.20]
05 Minute ventilation (mL/Kg/min)	3	78	mean difference (Random) 95% CI	19.80 [-40.54, 80.14]
06 Patients desaturating	2	98	OR Becker-Balagtas (Random) 95% CI	0.18 [0.08, 0.42]

Comparison 02. Prone vs Lateral

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Hb O2 Sat (%)	1	8	mean difference (Random) 95% CI	2.13 [0.33, 3.93]
02 pCO2 (mmHg)	1	28	mean diff (Random) 95% CI	0.00 [-6.67, 6.67]

Comparison 03. Lateral vs Supine

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 pO2 (mmHg)			mean difference (Random) 95% CI	Subtotals only
02 Hb O2 Sat (%)			mean difference (Random) 95% CI	Subtotals only
03 pCO2 (mmHg)			mean diff (Random) 95% CI	Subtotals only

Comparison 04. Lateral Right vs Lateral Left

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 pO2 (mmHg)	2	68	mean difference (Random) 95% CI	-0.05 [-6.93, 6.83]
02 pCO2 (mmHg)	2	68	mean difference (Random) 95% CI	0.41 [-2.01, 2.82]
03 tidal volume (mL/Kg)	1	32	mean difference (Random) 95% CI	-0.80 [-1.87, 0.27]

Comparison 05. Good lung dependant

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 pO2 (mmHg)	1	8	mean difference (Random) 95% CI	-7.75 [-31.19, 15.69]
02 pCO2 (mmHg)	1	8	mean diff (Random) 95% CI	0.75 [-4.16, 5.66]

INDEX TERMS

Medical Subject Headings (MeSH)

Infant, Newborn; *Posture; Randomized Controlled Trials; Respiration, Artificial [*methods]

MeSH check words

Humans

C O V E R   S H E E T

Title	Infant position in neonates receiving mechanical ventilation
Authors	Balaguer A, Escribano J, Roqué M
Contribution of author(s)	Information not supplied by author
Issue protocol first published	2002/2
Review first published	2003/2
Date of most recent amendment	23 August 2006
Date of most recent SUBSTANTIVE amendment	16 June 2006
What's New	This is an update of the review "Infant position in neonates receiving mechanical ventilation" published in The Cochrane Library, Issue 2, 2003 (Balaguer 2003). The search was updated in May 2006. One new trial (Antunes 2003) was identified and is now included in this review update. The addition of this study did not change the conclusions reported in the previous version.
Date new studies sought but none found	Information not supplied by author
Date new studies found but not yet included/excluded	Information not supplied by author
Date new studies found and included/excluded	Information not supplied by author
Date authors' conclusions section amended	Information not supplied by author
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DOI	10.1002/14651858.CD003668.pub2
Cochrane Library number	CD003668
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GRAPHS AND OTHER TABLES

Analysis 01.01. Comparison 01 Prone vs Supine, Outcome 01 pO2 (mmHg)

Review: Infant position in neonates receiving mechanical ventilation

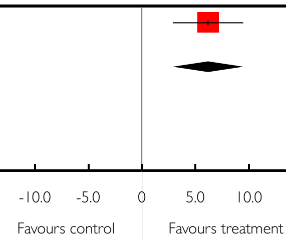
Comparison: 01 Prone vs Supine

Outcome: 01 pO2 (mmHg)

Study	Control N	Treatment N	mean difference (SE)	mean difference (Random) 95% CI	Weight (%)	mean difference (Random) 95% CI
Fox 1990	25	25	6.24 (1.69)		100.0	6.24 [2.93, 9.55]
Total (95% CI)					100.0	6.24 [2.93, 9.55]

Test for heterogeneity: not applicable

Test for overall effect z=3.70 p=0.0002



Analysis 01.02. Comparison 01 Prone vs Supine, Outcome 02 Hb O2Sat (%)

Review: Infant position in neonates receiving mechanical ventilation

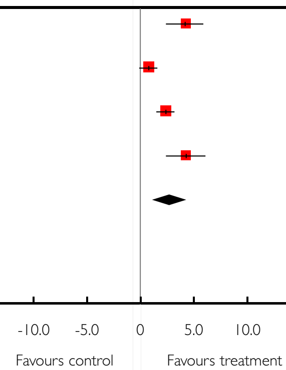
Comparison: 01 Prone vs Supine

Outcome: 02 Hb O2Sat (%)

Study	Control N	Treatment N	mean difference (SE)	mean difference (Random) 95% CI	Weight (%)	mean difference (Random) 95% CI
Bjornson 1992	4	4	4.24 (0.90)		22.3	4.24 [2.48, 6.00]
Chang 2002	28	28	0.80 (0.44)		28.2	0.80 [-0.06, 1.66]
Mizuno 1995	6	6	2.40 (0.46)		28.0	2.40 [1.50, 3.30]
Mizuno 1999	7	7	4.30 (0.96)		21.5	4.30 [2.43, 6.17]
Total (95% CI)					100.0	2.77 [1.18, 4.36]

Test for heterogeneity chi-square=20.19 df=3 p=0.0002 I^2 =85.1%

Test for overall effect z=3.41 p=0.0006



Analysis 01.03. Comparison 01 Prone vs Supine, Outcome 03 pCO2 (mmHg)

Review: Infant position in neonates receiving mechanical ventilation

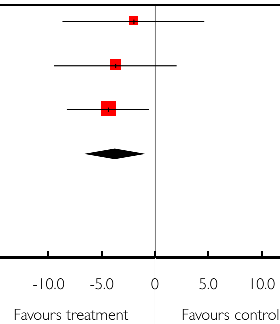
Comparison: 01 Prone vs Supine

Outcome: 03 pCO2 (mmHg)

Study	Treatment N	Control N	mean difference (SE)	mean difference (Random) 95% CI	Weight (%)	mean difference (Random) 95% CI
Crane 1990	14	14	-2.00 (3.40)		18.7	-2.00 [-8.67, 4.67]
Mizuno 1995	6	6	-3.70 (2.91)		25.5	-3.70 [-9.40, 2.00]
Mizuno 1999	7	7	-4.40 (1.97)		55.8	-4.40 [-8.26, -0.54]
Total (95% CI)					100.0	-3.77 [-6.65, -0.89]

Test for heterogeneity chi-square=0.37 df=2 p=0.83 I² =0.0%

Test for overall effect z=2.57 p=0.01



Analysis 01.04. Comparison 01 Prone vs Supine, Outcome 04 tidal volume (mL/Kg)

Review: Infant position in neonates receiving mechanical ventilation

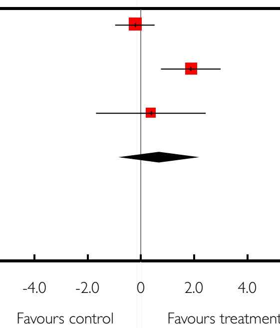
Comparison: 01 Prone vs Supine

Outcome: 04 tidal volume (mL/Kg)

Study	Control N	Treatment N	mean difference (SE)	mean difference (Random) 95% CI	Weight (%)	mean difference (Random) 95% CI
Mendoza 1991	26	26	-0.20 (0.38)		40.0	-0.20 [-0.95, 0.55]
Mizuno 1995	6	6	1.90 (0.57)		35.8	1.90 [0.79, 3.01]
Mizuno 1999	7	7	0.40 (1.05)		24.3	0.40 [-1.66, 2.46]
Total (95% CI)					100.0	0.70 [-0.81, 2.20]

Test for heterogeneity chi-square=9.43 df=2 p=0.009 I² =78.8%

Test for overall effect z=0.91 p=0.4



Analysis 01.05. Comparison 01 Prone vs Supine, Outcome 05 Minute ventilation (mL/Kg/min)

Review: Infant position in neonates receiving mechanical ventilation

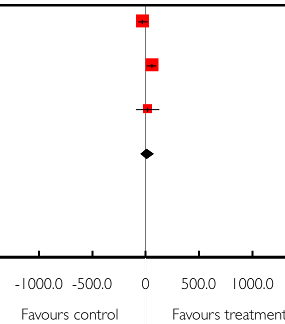
Comparison: 01 Prone vs Supine

Outcome: 05 Minute ventilation (mL/Kg/min)

Study	Control N	Treatment N	mean difference (SE)	mean difference (Random) 95% CI	Weight (%)	mean difference (Random) 95% CI
Mendoza 1991	26	26	-21.70 (22.67)		40.5	-21.70 [-66.12, 22.72]
Mizuno 1995	6	6	60.00 (23.61)		39.8	60.00 [13.72, 106.28]
Mizuno 1999	7	7	24.00 (54.74)		19.7	24.00 [-83.28, 131.28]
Total (95% CI)					100.0	19.80 [-40.54, 80.14]

Test for heterogeneity chi-square=6.24 df=2 p=0.04 I^2 =68.0%

Test for overall effect z=0.64 p=0.5



Analysis 01.06. Comparison 01 Prone vs Supine, Outcome 06 Patients desaturating

Review: Infant position in neonates receiving mechanical ventilation

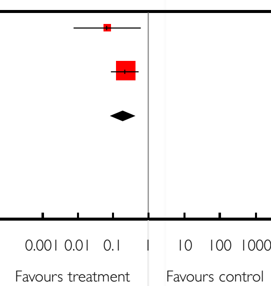
Comparison: 01 Prone vs Supine

Outcome: 06 Patients desaturating

Study	Treatment N	Control N	log [OR Becker-Balagtas] (SE)	OR Becker-Balagtas (Random) 95% CI	Weight (%)	OR Becker-Balagtas (Random) 95% CI
Antunes 2003	21	21	-2.71 (1.12)		14.6	0.07 [0.01, 0.59]
Chang 2002	28	28	-1.53 (0.46)		85.4	0.22 [0.09, 0.54]
Total (95% CI)					100.0	0.18 [0.08, 0.42]

Test for heterogeneity chi-square=0.96 df=1 p=0.33 I^2 =0.0%

Test for overall effect z=3.99 p=0.00007



Analysis 02.01. Comparison 02 Prone vs Lateral, Outcome 01 Hb O2 Sat (%)

Review: Infant position in neonates receiving mechanical ventilation

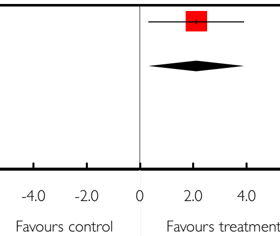
Comparison: 02 Prone vs Lateral

Outcome: 01 Hb O2 Sat (%)

Study	Control N	Treatment N	mean difference (SE)	mean difference (Random) 95% CI	Weight (%)	mean difference (Random) 95% CI
Bjornson 1992	4	4	2.13 (0.92)		100.0	2.13 [0.33, 3.93]
Total (95% CI)					100.0	2.13 [0.33, 3.93]

Test for heterogeneity: not applicable

Test for overall effect z=2.33 p=0.02



Analysis 02.02. Comparison 02 Prone vs Lateral, Outcome 02 pCO2 (mmHg)

Review: Infant position in neonates receiving mechanical ventilation

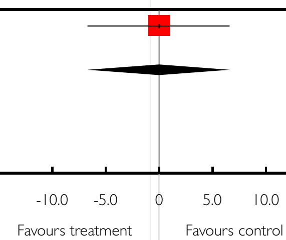
Comparison: 02 Prone vs Lateral

Outcome: 02 pCO2 (mmHg)

Study	Treatment N	Control N	mean diff (SE)	mean diff (Random) 95% CI	Weight (%)	mean diff (Random) 95% CI
Crane 1990	14	14	0.00 (3.40)		100.0	0.00 [-6.67, 6.67]
Total (95% CI)					100.0	0.00 [-6.67, 6.67]

Test for heterogeneity: not applicable

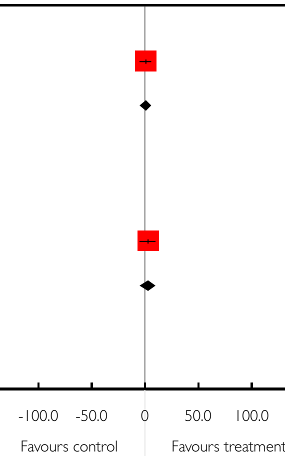
Test for overall effect z=0.00 p=1



Analysis 03.01. Comparison 03 Lateral vs Supine, Outcome 01 pO2 (mmHg)

Review: Infant position in neonates receiving mechanical ventilation
Comparison: 03 Lateral vs Supine
Outcome: 01 pO2 (mmHg)

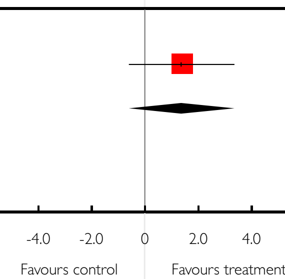
Study	Control N	Treatment N	mean difference (SE)	mean difference (Random) 95% CI	Weight (%)	mean difference (Random) 95% CI
01 Lateral Right						
Bozynski 1988	18	18	1.10 (3.00)		100.0	1.10 [-4.78, 6.98]
Subtotal (95% CI)					100.0	1.10 [-4.78, 6.98]
Test for heterogeneity: not applicable						
Test for overall effect z=0.37 p=0.7						
02 Lateral Left						
Bozynski 1988	18	18	3.20 (3.91)		100.0	3.20 [-4.46, 10.86]
Subtotal (95% CI)					100.0	3.20 [-4.46, 10.86]
Test for heterogeneity: not applicable						
Test for overall effect z=0.82 p=0.4						



Analysis 03.02. Comparison 03 Lateral vs Supine, Outcome 02 Hb O2 Sat (%)

Review: Infant position in neonates receiving mechanical ventilation
Comparison: 03 Lateral vs Supine
Outcome: 02 Hb O2 Sat (%)

Study	Control N	Treatment N	mean difference (SE)	mean difference (Random) 95% CI	Weight (%)	mean difference (Random) 95% CI
01 Lateral Right						
Bjornson 1992	4	4	1.39 (1.02)		100.0	1.39 [-0.60, 3.38]
Subtotal (95% CI)					100.0	1.39 [-0.60, 3.38]
Test for heterogeneity: not applicable						
Test for overall effect z=1.37 p=0.2						



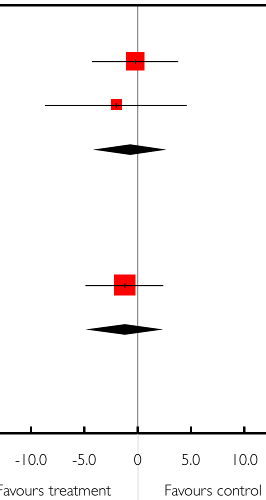
Analysis 03.03. Comparison 03 Lateral vs Supine, Outcome 03 pCO2 (mmHg)

Review: Infant position in neonates receiving mechanical ventilation

Comparison: 03 Lateral vs Supine

Outcome: 03 pCO2 (mmHg)

Study	Treatment N	Control N	mean diff (SE)	mean diff (Random) 95% CI	Weight (%)	mean diff (Random) 95% CI
01 Lateral Right						
Bozynski 1988	18	18	-0.20 (2.07)		73.0	-0.20 [-4.25, 3.85]
Crane 1990	14	14	-2.00 (3.40)		27.0	-2.00 [-8.67, 4.67]
Subtotal (95% CI)					100.0	-0.69 [-4.15, 2.78]
Test for heterogeneity chi-square=0.20 df=1 p=0.65 I² =0.0%						
Test for overall effect z=0.39 p=0.7						
02 Lateral Left						
Bozynski 1988	18	18	-1.20 (1.87)		100.0	-1.20 [-4.86, 2.46]
Subtotal (95% CI)					100.0	-1.20 [-4.86, 2.46]
Test for heterogeneity: not applicable						
Test for overall effect z=0.64 p=0.5						



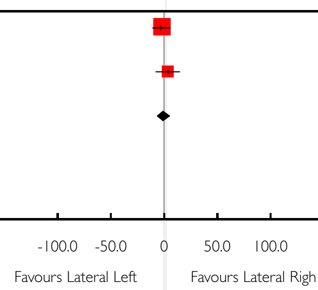
Analysis 04.01. Comparison 04 Lateral Right vs Lateral Left, Outcome 01 pO2 (mmHg)

Review: Infant position in neonates receiving mechanical ventilation

Comparison: 04 Lateral Right vs Lateral Left

Outcome: 01 pO2 (mmHg)

Study	Lateral left N	Lateral right N	mean difference (SE)	mean difference (Random) 95% CI	Weight (%)	mean difference (Random) 95% CI
Bozynski 1988	18	18	-2.10 (4.31)		66.4	-2.10 [-10.54, 6.34]
Schlessel 1993	16	16	4.00 (6.05)		33.6	4.00 [-7.86, 15.86]
Total (95% CI)					100.0	-0.05 [-6.93, 6.83]
Test for heterogeneity chi-square=0.67 df=1 p=0.41 I² =0.0%						
Test for overall effect z=0.01 p=1						



Analysis 04.02. Comparison 04 Lateral Right vs Lateral Left, Outcome 02 pCO2 (mmHg)

Review: Infant position in neonates receiving mechanical ventilation

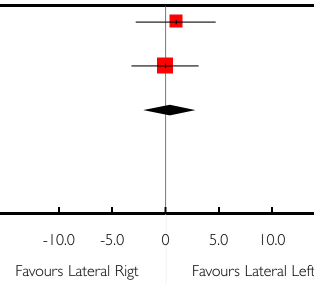
Comparison: 04 Lateral Right vs Lateral Left

Outcome: 02 pCO2 (mmHg)

Study	Lateral Righ N	Lateral Left N	mean difference (SE)	mean difference (Random) 95% CI	Weight (%)	mean difference (Random) 95% CI
Bozynski 1988	18	18	1.00 (1.93)		40.7	1.00 [-2.78, 4.78]
Schlessel 1993	16	16	0.00 (1.60)		59.3	0.00 [-3.14, 3.14]
Total (95% CI)					100.0	0.41 [-2.01, 2.82]

Test for heterogeneity chi-square=0.16 df=1 p=0.69 I² =0.0%

Test for overall effect z=0.33 p=0.7



Analysis 04.03. Comparison 04 Lateral Right vs Lateral Left, Outcome 03 tidal volume (mL/Kg)

Review: Infant position in neonates receiving mechanical ventilation

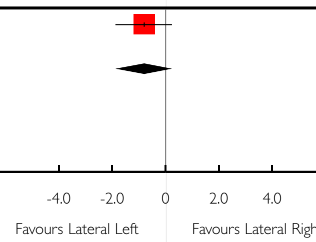
Comparison: 04 Lateral Right vs Lateral Left

Outcome: 03 tidal volume (mL/Kg)

Study	Lateral Left N	Lateral Righ N	mean difference (SE)	mean difference (Random) 95% CI	Weight (%)	mean difference (Random) 95% CI
Schlessel 1993	16	16	-0.80 (0.55)		100.0	-0.80 [-1.87, 0.27]
Total (95% CI)					100.0	-0.80 [-1.87, 0.27]

Test for heterogeneity: not applicable

Test for overall effect z=1.46 p=0.1



Analysis 05.01. Comparison 05 Good lung dependant, Outcome 01 pO2 (mmHg)

Review: Infant position in neonates receiving mechanical ventilation

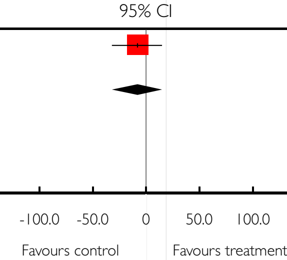
Comparison: 05 Good lung dependant

Outcome: 01 pO2 (mmHg)

Study	Control N	Treatment N	mean difference (SE)	mean difference (Random) 95% CI	Weight (%)	mean difference (Random) 95% CI
Heaf 1983	4	4	-7.75 (11.96)		100.0	-7.75 [-31.19, 15.69]
Total (95% CI)					100.0	-7.75 [-31.19, 15.69]

Test for heterogeneity: not applicable

Test for overall effect z=0.65 p=0.5



Analysis 05.02. Comparison 05 Good lung dependant, Outcome 02 pCO2 (mmHg)

Review: Infant position in neonates receiving mechanical ventilation

Comparison: 05 Good lung dependant

Outcome: 02 pCO2 (mmHg)

Study	Treatment N	Control N	mean diff (SE)	mean diff (Random) 95% CI	Weight (%)	mean diff (Random) 95% CI
Heaf 1983	4	4	0.75 (2.50)		100.0	0.75 [-4.16, 5.66]
Total (95% CI)					100.0	0.75 [-4.16, 5.66]

Test for heterogeneity: not applicable

Test for overall effect z=0.30 p=0.8