Intensive Care Med (1997) 23: 463–468
© Springer-Verlag 1997

K. M. Smith
T. M. Wahlig
D. R. Bing
M. K. Georgieff
S. J. Boros †
M. C. Mammel

Lower respiratory rates without decreases in oxygen consumption during neonatal synchronized intermittent mandatory ventilation

Received: 9 April 1996
Accepted: 13 November 1996

This work was supported in part by grants from the Hugh J. Andersen Foundation, Ms. Sarah Andersen and family, Mr. William Holcomb, and the Research and Education Fund of Children's Hospital of St. Paul

This work was present in part at the annual meeting of the Society for Pediatric Research, May 1995, San Diego, California

K. M. Smith · T. M. Wahlig · D. R. Bing · M. K. Georgieff · S. J. Boros · M. C. Mammel[1] (✉)
Infant Diagnostic and Research Center, Children's Hospital of St. Paul, and the Department of Pediatrics, University of Minnesota, Minneapolis, Minnesota, USA

Mailing address:
[1] Department of Neonatal Medicine, Children's Hospital of St. Paul, 345 North Smith Avenue, Rm 2100, St. Paul, MN 55102, USA
FAX: +001 (612) 2207777
e-mail: mamme001@maroon.tc.umn.edu

Abstract *Objective:* We tested the hypothesis that synchronization to patient effort during intermittent mandatory ventilation (SIMV), when compared to conventional unsynchronized intermittent mandatory ventilation (IMV), will decrease energy expenditure, as reflected by decreased oxygen consumption (VO_2).
Design: We used a four-period crossover design. Each patient was studied over four 30-min continuous time intervals. Patients were randomized to receive initially IMV or SIMV, then crossed over such that each patient was treated twice with each modality. Data were analyzed using an analysis of variance technique.
Setting: Patients were receiving treatment in the newborn intensive care unit of Children's Hospital, St. Paul.
Patients: We studied 17 patients, who ranged from 23 to 37 weeks gestation, were $\leq$ 14 days old, and had study weights from 623 to 3015 g. All were mechanically ventilated for hyaline membrane disease.
Measurements and results: We measured and compared VO_2, carbon dioxide consumption (VCO_2), minute ventilation (V_E), total respiratory rate, heart rate, arterial blood pressure, and arterial oxygen saturation (SaO_2) values during IMV and SIMV. Total respiratory rate fell significantly during SIMV (73 ± 26 during IMV, 57 ± 17 during SIMV, $p < 0.01$) in spite of no significant change in VO_2 (0.6 ± 0.16 % fall in VO_2 during SIMV) or VCO_2 (4.2 ± 0.19 % increase in VCO_2 during SIMV) values. Moreover, there were no significant differences in heart rate, blood pressure, V_E, or SaO_2 values with either form of therapy.
Conclusions: Though total respiratory rate fell, these data do not support the hypothesis that SIMV significantly reduces respiratory rate by decreasing oxygen consumption and carbon dioxide production during infant mechanical ventilation. Rather, the marked fall in respiratory rate may be due to a more efficient respiratory pattern.

Key words Oxygen consumption · Mechanical ventilation · Synchronized ventilation · Respiratory distress syndrome

Introduction

Since the initial work of Kirby and Downs, which described the advantages of continuous flow intermittent mandatory ventilation (IMV) in newborns and adults, non-synchronized IMV has been the standard of care for the neonate with respiratory failure [1, 2]. This technique of delivering mechanically assisted breaths independent of patient effort has been associated with a number of serious clinical sequelae, including an increased risk of pulmonary air leak, alterations in cerebral blood flow, and intracranial hemorrhage [3–5]. Recently, infant ventilators have been introduced which have the ability to synchronize mechanical breaths to patient effort.

Most of the problems associated with IMV are at least in part related to spontaneous breathing efforts out of phase with mechanical breaths. Greenough et al. [3] described the phenomenon of "active expiration," which results from the patient attempting to exhale during mechanical inspiration. This respiratory pattern was associated with a 40% incidence of pneumothorax [3]. Perlman and Volpe described a pattern of fluctuating cerebral blood flow during IMV which was associated with a high incidence of severe intracranial hemorrhage. This pattern could be eliminated with the use of pancuronium bromide and was thought to result from out-of-phase respiratory efforts [5, 6]. Recently, Cleary and colleagues demonstrated elimination of asynchrony and small improvements in respiratory gas exchange during synchronized IMV (SIMV) when compared to IMV at the same rates [7]. They speculated that decreases in oxygen consumption might, in part, explain their findings [7].

It seems logical to assume that the effort of asynchronous breathing during IMV should result in increased energy expenditure, while SIMV should help decrease this respiratory work. However, reduced work of breathing has not been demonstrated in adults with respiratory failure receiving synchronized ventilation. Marini and coworkers, in studies of adults using assist/control ventilation, where each patient inspiration results in ventilator assistance, and SIMV, where ventilator assistance only occurs during a preset number of breaths, were unable to demonstrate significant decreases in total force generated by the respiratory muscles [8]. Moreover, they showed that more work was required on a per breath basis during assisted breaths [8]. A recent paper by Imsand et al. did show reductions in work of breathing during SIMV, but the effect was less than predicted [9]. These studies estimated respiratory work mechanically, through traditional measures of respiratory pressures or electromyographically.

In this study, we tested the hypothesis that neonatal SIMV produces an acute decrease in energy expenditure, as reflected by changes in O_2 consumption, when compared to IMV at the same rate. Because of the concomitant decreases in CO_2 production, we expected total respiratory rate to show similar reductions. To test this hypothesis, we prospectively studied a group of newborns receiving IMV therapy for hyaline membrane disease.

Patients and methods

This study was approved by the hospital's institutional review board. Informed written consent was obtained from the parents of each infant included in the study.

Patients

Premature infants no more than 14 days old who required mechanical ventilation for hyaline membrane disease were eligible for study. All were receiving mechanical ventilation with IMV using pressure present, time-cycled neonatal ventilators capable of either IMV or SIMV. Patients were treated in the Newborn Intensive Care Unit of Children's Hospital of St. Paul. Exclusion criteria included lack of parental consent, culture-proven sepsis or meningitis, severe congenital anomalies, postoperative status, cardiovascular instability (determined by the attenting neonatologist), a fractional inspired oxygen of (FIO_2) > 0.6, IMV rate < 20, and air leaks around the endotracheal tube.

Study design

Infants were studied while recovering from respiratory failure induced by hyaline membrane disease. None had a clinically apparent patent ductus arteriosus at the time of study. All infants had either indwelling umbilical artery catheters or peripheral arterial catheters. All were studied in double-walled incubators. Skin temperature were maintained via servo control at 36–37 °C.

Infants were receiving mechanical ventilation using pressure present, time-cycled infant ventilators capable of both IMV and SIMV. Three different systems were used: the Dräger Babylog (Dräger, Chantilly, Va., USA), which uses a hot wire anemometer system to measure gas flow at the junction of the endotracheal tube adapter and the ventilator circuit; the Infant Star (Infrasonics, San Diego, Calif., USA), which detects inspiratory patient effort using a Graseby capsule attached to the patients' abdomen; and the VIP Bird (Bird Products, Palm Springs, Calif., USA), which uses a pneumotachograph interposed between the endotracheal tube adapter and the ventilator circuit. All have been previously tested and found to be effective in providing synchronized breaths in neonates [10]. Trigger sensitivity was adjusted for each patient to the minimum possible value which allowed synchronization without autocycling. Inspiratory times were adjusted by assessing gas flow waveforms such that inspiration ended when inspiratory gas flow returned to zero. This resulted in short inspiratory times, always less than 0.4 s. These different ventilators were all in clinical use at the time of this study and were selected by the individual attending physicians based on availability. No patient was treated with more than one ventilator system. We made no effort to compare each ventilator to the others.

Our study had a four-period crossover design; each infant was his or her own control. During each study period, we measured oxygen and carbon dioxide consumption (VO_2, VCO_2) in ml/kg per minute at standard temperature and pressure, and V_E in ml/kg per minute using an open circuit indirect calorimeter validated for neonatal use (MGM jr. Metabolic Cart, Life Energy Systems, Murray, Utah, USA) [11]. Prior to all studies, we evaluated gas flow pneumotachographically to assess for air leaks using a computer-assisted analyzer (PeDs Infant Pulmonary Cart, MAS, Hatfield, Penna., USA) [12]. Infants with air leaks noted on pressure-volume or flow-volume loops were not studied.

Methods

We used a ventilatory support index (VSI) to assess the degree of respiratory illness at the time of study. VSI was defined as airway pressure (Paw) × FIO_2 × IMV rate. Patients with a VSI of > 20 were eligible for study. This number was selected to reflect a level of illness severe enough to require significant IVM support and thus possibly to show the hypothesized benefit from synchronization. Arterial blood gases were measured prior to study and ventilators adjusted, if necessary, to maintain pH values of 7.30–7.45, values for partial pressure of carbon dioxide in arterial blood of 30–50 torr, and values for arterial oxygen saturation (SsO_2) of 85–95%. Once these values were stable, ventilator settings (peak inspiratory and end-expiratory pressures, inspiratory and expiratory times, ventilator rate, FIO_2) remained constant throughout the study. All infants had received up to three doses of exogenous surfactant (Exosurf Neonatal, Burroughs-Wellcome, Research Triangle Park, N.C., USA) prior to study.

At study entry, patients were randomized to enter the study receiving either IMV or SIMV for a 30-min period, then crossed over to the alternate ventilatory mode for 30 min, back to the initial treatment for 30 min, and finally to the alternate treatment for a final 30-min study period. At the beginning of each study period, we allowed a 10–20-minute equilibration period while VO_2 and VCO_2 values stabilized (< 5% variation in VO_2 and VCO_2), then measurements were made continuously for 30 min. Patients were studied in a quiet resting state, with no extremity or head movement and a Brück score of 0 [13]. Those randomized to IMV continued to receive the IMV rate in use clinically prior to study. Those randomized to SIMV also received their previously determined rate, but using synchronization.

During the study, infants were not fed, suctioned, touched, or otherwise disturbed. During the sampling periods, three consecutive measurements of VO_2, VCO_2, and V_E were made online and averaged every 20 s using a pneumotachometer, a zirconium oxide oxygen sensor, and an infrared photometry carbon dioxide analyzer. The indirect calorimeter was connected to the ventilator circuit via a two-way non-rebreathing valve. This valve added less than 1 ml of dead space to the circuit. At the beginning of each study, the indirect calorimeter was calibrated and manually verified with known gas mixtures. Resolution was 0.5% for oxygen and 1.0% for carbon dioxide. We also measured and recorded at 2-min intervals continuous SaO_2 values using a standard pulse oximeter (Nellcor N-200, Nellcor, Hayward, Calif., USA). We measured arterial blood pressures through indwelling umbilical artery catheters attached to standard transducers and monitors (Spacelabs 521, Spacelabs, Redmond, Wash., USA). Total respiratory rate, defined as the sum of spontaneous breaths and ventilator-assisted breaths, was measured by the different ventilators' effort-sensing mechanisms and was recorded every 2 min.

Data analysis

Data were analyzed using an analysis of variance technique adapted for multiple period crossover designs. First, data were analyzed for the presence of significant carryover effects between treatment periods. Then, data were analyzed for statistical significance, with an alpha level of 0.05 [14, 15].

Results

We enrolled 17 mechanically ventilated neonates who met the study criteria. All were receiving IMV and demonstrated spontaneous breathing efforts during mechanical expiration. No patients were eliminated after study enrollment due to endotracheal tube leaks. Infants remained stable after enrollment and completed all four study periods. Eight were randomized to receive initial treatment with IMV and nine SIMV. Online evaluation of airflow recordings showed good synchrony during SIMV and frequent asynchronous breaths during IMV.

The infants we studied had study weights ranging from 623 to 3015 g and gestational ages from 23 to 37 weeks. Infants ranged from 1 to 14 days of age at the time of study and had VSI values from 24 to 302, with a mean of 88. No infants were treated with more than one ventilator system. Five infants were treated with the Dräger and Infant Star ventilators respectively; seven were treated with the VIP Bird. Patients were attended and observed throughout the study by one of the investigators; no patients had clinical evidence of autocycling at any time during the study. Individual patient information, including ventilator settings at the time of study, are shown in Table 1. There were no significant differences in ventilator settings or VSI values in patients randomized to IMV compared to SIMV.

Table 2 shows the results of physiologic measurements. Total respiratory rate fell by 21% during SIMV, from 72 ± 26 during IMV to 57 ± 17 during SIMV ($p < 0.01$). Changes in VO_2 and VCO_2 were not statistically significant. Likewise, there were no significant changes in heart rate, blood pressure, or SaO_2. Individual patient data for VO_2 and total respiratory rate following mode changes form IMV to SIMV and from SIMV to IMV are shown in Fig. 1. Of note, no patients were "in phase" with the ventilator – i.e., all had total respiratory rates in excess of the SIMV or IMV rate being used during the study.

Discussion

Previous study in neonates have attempted to define the potential benefits of synchronized ventilation, although the terminology utilized in these studies has been confusing. For example, "synchronization" in the adult literature refers to patient-triggered ventilator breaths, and the term SIMV is used similarly in the neonatal the adult intensive care unit. However, Morley, Greenough, and colleagues used the term to refer to a state of "in phase" breathing efforts by the newborn, achieved by "capturing" the patient's spontaneous respiratory rate with IMV [16–18]. They found that some,

Table 1 Patient characteristics ($n = 17$) and ventilator settings at study entry (P_{aw} airway pressure, FIO_2 fractional inspired oxygen, *VSI* ventilatory support index)

	Mean	Range
Study weight (g)	1257 ± 793	623–3015
Gestational age (weeks)	28.2 ± 4.1	23–37
Study age (days)	5.4 ± 4.9	1–14
Ventilator rate	30.1 ± 8.6	20–56
P_{aw} (cm H_2O)	6.8 ± 1.5	5.2–9.4
FIO_2	0.39 ± 0.11	0.21–0.60
VSI (cm H_2O)	88 ± 65	24–302

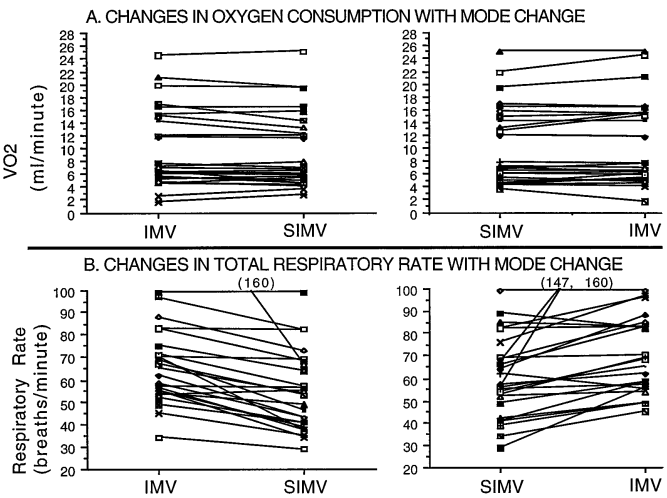

Fig. 1 Changes in oxygen consumption and total respiratory rate following mode changes from IMV to SIMV and from SIMV to IMV. All crossover data are shown as paired data points, where each data pair reflects one crossover in the direction indicated. Each patient underwent three crossovers, two in the direction of their initial randomization and one in the opposite direction. Thus, 25 paired datapoints are shown for the IMV–SIMV crossover and 26 for the SIMV–IMV crossover

but by no means all, infants could be "induced" to breath along with the ventilator and that oxygenation improved and pneumothorax rates decreased. Likewise, Amitay et al. were able to "synchronize" neonates using evaluation of their endogenous respiratory timing and adjusting IMV rates accordingly [19]. They found improved tidal volumes and minute ventilation with less variation in blood pressures [19]. Greenough and colleagues then described techniques of patient triggering, to allow true synchronization [20–22]. Using either esophageal pressure or changes in flow at the airway opening, they were able to demonstrate effective synchronization of patient and ventilator effort. In this study, we use the term "synchronization" as it is used in the adult literature.

Synchronization of mechanical ventilation in our study caused a marked fall in total respiratory rate. This change occurred in spite of the fact that oxygen consumption, carbon dioxide production, and minute ventilation were not changed by this intervention. One possible reason for this finding relates to the way in which breaths are counted during IMV and SIMV. During IMV, asynchronous breaths, IMV breaths, and spontaneous breaths unaffected by respirator cycling are all counted. During SIMV, ventilator-assisted breaths are initiated by a small patient effort. This effort is not counted as a separate breath; only the SIMV breaths and separate spontaneous breaths are counted. While this could alter the number of breaths we recorded, it would be inappropriate to include the patient effort which triggers an SIMV breath as a separate breath. This effort moves an insignificant amount of gas, and in fact is a part of the SIMV breath. In contrast, during IMV, asynchronous breaths may contribute in a positive or negative way to total minute ventilation, as well as have an impact on blood flow or air leak. For these reasons, such asynchronous breaths must be included in the total respiratory rate calculation.

This finding of a lower total respiratory rate without a fall in VO_2 suggests that synchronization results in larger tidal volumes and a more efficient pattern of breathing. This is supported by data previously reported by Bernstein et al. [23] and is consistent with work performed in adults by Marini et al. [8]. They studied 12 adults with respiratory failure from a variety of causes. These patients were studied at different levels of synchronization, from 100 to 0%. They estimated the mechanical work needed for inspiration using traditional measures of tidal volume and esophageal pressures and found that patient work increased as mechanical support was decreased. They also saw decreasing total respiratory rates as machine support increased. However, this study did not directly compare synchronized versus unsynchronized IMV.

Table 2 Physiologic measurements during IMV and SIMV. Values represent means (SD) of all data from the different treatment modes

MODE	VO_2 (ml/min per kg)	VCO_2 (ml/min per kg)	V_E (ml/min per kg)	SaO_2 (%)	Heart rate (beats/min)	Blood pressure (mm Hg)	Respiratory rate (breaths/min)
IMV	8.1 ± 3.4	8.1 ± 3.9	449 ± 120	93.7 ± 3.4	145 ± 14	40.3 ± 5.4	72 ± 26
SIMV	7.8 ± 3.0	7.7 ± 2.5	447 ± 123	94.1 ± 3.0	147 ± 15	39.9 ± 5.4	52 ± 17*

* $p < 0.01$

Recent studies of neonatal synchronized ventilation have tended to compare traditional IMV against the assist/control technique, in which all patient efforts result in a ventilator-assisted breath. These studies have generally assessed respiratory outcomes. Viveshwara et al., in a retrospective review of 3 years' data, found a decreased duration of ventilation and oxygen therapy and fewer severe intraventricular hemorrhages [24]. Donn et al., in a randomized, prospective trial, saw shorter times to extubation and decreased costs [25]. However, the studied infants all had weights greater than 1100 g, and complication rates were similar between groups. More acute studies of this technique are also limited. Servant et al., in a study of 10 infants, found improved minute ventilation and oxygenation after 1 h of treatment [26]. Fox et al., in a similar study of 10 patients after 30 min of treatment, found decreased total respiratory rates after synchronization, as we did [27].

Cleary et al. recently evaluated 10 infants with the respiratory distress syndrome (RDS) in a randomized four-period crossover study of IMV and SIMV [7]. They were interested in the short-term effects of synchrony on gas exchange and found improvements in oxygenation and carbon dioxide elimination during SIMV. They wondered if reduced oxygen consumption produced the improvements they saw. Our data do not support this interpretation, though we did not assess gas exchange in the same way. They also speculated that these improvements could be due to improvements in tidal volumes and flow-volume relationships which they had shown previously [23]. We suspect this second explanation for changes they saw, and the improvements in respiratory rate we observed, is more likely correct. SIMV results in more uniform, larger tidal volumes and a more efficient respiratory pattern.

The lack of an observable reduction in VO_2 may result from a variety of clinical and technical issues related to the use of indirect calorimetry or to our patient population. Our patients were often small and had differing severities of lung disease. However, Mayfield has previously suggested that this technique may be used with acceptable accuracy in patients whose VO_2 and VCO_2 are $\geq$ 4 ml/min, whose flow rate is $\leq$ 3000 ml/min, and whose FO_2 is ≤ 0.6 [11]. Our patients fit these criteria. We used relatively short measurement times of 30 min, which may not be long enough for a precise estimate of energy utilization. Still, Samiec et al. have used similar measurement times; the values they measured were similar to those we report here and to those we and others have previously reported in preterm infants [28–30]. We assumed that the work of breathing accounts for no more than 20% of total VO_2; therefore, the maximum potential change in VO_2 with SIMV would be 20% [31–33]. A change of this magnitude is detectable by current indirect calorimetry technology. On the other hand, if the improvement in oxygen consumption were in the range of $\leq 5\%$, we likely would not have been able to detect reliably such a small but still possibly significant change with this technique. If these infants were not significantly stressed, modest changes in respiratory effort might not be reflected in total VO_2 values. Greater changes in VO_2 might be expected in sicker infants who require > 60% inspired oxygen concentrations; yet, such infants cannot be assessed using this technique of VO_2 measurement, as resolution at such high oxygen concentrations is inaccurate. Nevertheless, given the VSI values of the patients we studied, clinically relevant improvements in respiratory work should have been detected had they occurred. We used three different ventilator systems capable of synchronized ventilation. These ventilators behave similarly, but not identically, when compared using a test lung at the same settings [34]. This potential problem, as well as the problem of a small sample size, is eliminated by our choice of a crossover design [14, 15]. This design allows greater power for assessment of treatment effects than does a two-group parallel study; also, since each patient serves as his or her own control, the ventilator used is compared to itself, not to another system. The impact of each change from synchronized to unsynchronized ventilation is then compared across the groups. Thus, while this study is not definitive, the conclusions can be considered reliable enough to suggest further study along these lines is warranted.

How can these findings best be applied in newborns? What fraction of breaths should be synchronized for maximum benefit? Dimitriou et al. recently compared SIMV to assist/control during weaning from mechanical ventilation [35]. They found no benefit to the combination of rate and pressure weaning, which SIMV allows, compared to pressure weaning alone, as during assist/control [35]. We need more information about these different techniques for the safest and most beneficial clinical use.

We conclude that SIMV, when compared to IMV at the same rate, results in lower total respiratory rates at similar levels of minute ventilation. This improvement seems likely due to a more efficient respiratory pattern, but not to reduced work of breathing, as we were unable to show reduced oxygen consumption during SIMV. Further work is needed to assess the role of SIMV and assist/control ventilation in the acutely ill newborn. Both show promise for continued reduction in acute and long-term complications of early respiratory treatment.

References

1. Kirby R, Robinson E, Schulz J, deLemos RA (1972) Continuous-flow as an alternative to assisted or controlled ventilation in infants. Anesth Analg 51: 871–875
2. Downs JB, Klein EF, Desautels D, Modell JH, Kirby RR (1973) Intermittent mandatory ventilation: a new approach to weaning patients from mechanical ventilators. Chest 64: 331–335
3. Greenough A, Morley CJ, Davis JA (1983) Interaction of spontaneous respiration with artificial ventilation in preterm babies. Pediatrics 103: 769–773
4. Rennie JM, South M, Morley CJ (1987) Cerebral blood flow velocity variability in infants receiving assisted ventilation. Arch Dis Child 62: 1247–1251
5. Perlman JM, McMenamin JB, Volpe JJ (1983) Fluctuating cerebral blood-flow velocity in respiratory distress syndrome: relation to the development of intraventricular hemorrhage. N Engl J Med 309: 204–209
6. Perlman JM, Goodman S, Kreusser KL, Volpe JJ (1985) Reduction in intraventricular hemorrhage by elimination of fluctuating cerebral blood flow velocity in preterm infants with respiratory distress syndrome. N Engl J Med 312: 1353–1357
7. Cleary JP, Bernstein G, Mannino FL, Heldt GP (1995) Improved oxygenation during synchronized intermittent mandatory ventilation in neonates with respiratory distress syndrome: a randomized, crossover study. J Pediatr 126: 407–411
8. Marini JJ, Smith TC, Lamb VJ (1988) External work output and force generation during synchronized intermittent mechanical ventilation. Am J Respir Crit Care Med 138: 1169–1179
9. Imsand C, Feihl F, Perret C, Fitting JW (1994) Regulation of inspiratory neuromuscular output during synchronized intermittent mechanical ventilation. Anesthesiology 80: 13–22
10. Bernstein G, Cleary JP, Heldt GP, Rosas JF, Scellenberg LD, Mannino FL (1993) The response time and reliability of three neonatal patient triggered ventilators. Am J Respir Crit Care Med 148: 358–364
11. Mayfield S (1991) Technical and clinical testing of a computerized indirect calorimeter for use in mechanically ventilated neonates. Am J Clin Nutr 54: 30–34
12. Bhutani VK, Sivieri EM, Abbasi S, Shaffer TH (1988) Evaluation of neonatal pulmonary mechanics and energetics: a two factor least mean squares analysis. Pediatr Pulmonol 4: 150–158
13. Freymond D, Schutz Y, Decombaz J, Micheli JL, Jequier E (1986) Energy balance, physical activity, and thermogenic effect of feeding in premature infants. Pediatr Res 20: 638–645
14. Cochran WG, Cox GM (1957) Experimental designs, 2nd edn. Wiley, New York, pp 133–138
15. Louis TA, Lavori PW, Bailar JC, Polansky M (1984) Crossover and self-controlled designs in clinical research. N Engl J Med 310: 24–31
16. South M, Morley CJ (1986) Synchronous mechanical ventilation of the neonate. Arch Dis Child 61: 1190–1195
17. Greenough A, Morley CJ, Pool J (1986) Fighting the ventilator – are fast rates an effective alternative to paralysis? Early Hum Dev 13: 189–194
18. Greenough A, Greenall F, Gamsu H (1987) Synchronous respiration: which ventilator rate is best? Acta Paediatr 76: 713–718
19. Amitay M, Etches PC, Finer NN, Maidens JM (1993) Synchronous mechanical ventilation of the neonate with respiratory disease. Crit Care Med 21: 118–124
20. Greenough A, Greenall F (1988) Patient triggered ventilation in premature neonates. Arch Dis Child 63: 77–78
21. Greenough A, Pool J (1988) Neonatal patient triggered ventilation. Arch Dis Child 63: 394–397
22. Hird MF, Grenough A (1990) Gestational age: an important influence on the success of patient triggered ventilation. Clin Phys Physiol Meas 11: 307–312
23. Bernstein G, Heldt GP, Mannino FM (1994) Increased and more consistent tidal volume during synchronized intermittent mandatory ventilation in newborn infants. Am J Respir Crit Care Med 150: 1444–1448
24. Visveshwara N, Freeman B, Peck M, Caliwag W, Shook S, Rajani KB (1991) Patient-triggered synchronized assisted ventilation of newborns: report of a preliminary study and three years' experience. J Perinatol 11: 347–354
25. Donn SM, Nicks J, Becker MA (1994) Flow-synchronized ventilation of preterm infants with respiratory distress syndrome. J Perinatol 14: 90–94
26. Servant GM, Nicks JJ, Donn SM, Bandy KP, Lathrop C, Dechert RE (1992) Feasibility of applying flow-synchronized ventilation to very low birthweight infants. Respir Care 37: 249–253
27. Fox WW, Bhutani VK, Abbasi S, Spitzer AR (1992) Assist control mechanical ventilation in preterm neonates recovering from respiratory disease. Pediatr Res 31: 307A
28. Samiec TD, Radmacher P, Hill T, Adamkin DH (1994) Measured energy expenditure in mechanically ventilated very low birth weight infants. Am J Med Sci 307: 184–192
29. Wahlig TM, Gatto CW, Boros SJ, Mammel MC, Mills MM, Georgieff MK (1994) Metabolic response of preterm infants to variable degrees of respiratory illness. J Pediatr 124: 283–288
30. Bell EF, Rios GR, Wilmoth PK (1986) Estimation of 24 hour energy expenditure from shorter measurement periods in premature infants. Pediatr Res 20: 646–649
31. Wilson RS, Sullivan SF, Malm JR, Bowman FO (1973) The oxygen cost of breathing following anesthesia and cardiac surgery. Anesthesiology 39: 387–393
32. Field S, Kelly SM, Macklem PT (1982) The oxygen cost of breathing in patients with cardiorespiratory disease. Am J Respir Crit Care Med 126: 9–13
33. Manthous CA, Hall JB, Kushner R, Schmidt GA, Russo G, Wood LDH (1995) The effect of mechanical ventilation on oxygen consumption in critically ill patients. Am J Respir Crit Care Med 151: 210–214
34. Mammel MC, Bing DR, Smith KM, Boros SJ (1995) Has infant ventilator performance improved in 10 years? Pediatr Res 37: 341A
35. Dimitriou G, Greenough A, Giffin F, Chan V (1995) Synchronous intermittent mandatory ventilation modes compared with patient triggered ventilation during weaning. Arch Dis Child 772: F188–F190