Intensive Care Med (2002) 28:1792–1796
DOI 10.1007/s00134-002-1527-8

Juan Casado-Flores
Amelia Martínez de Azagra
Maria Jesús Ruiz-López
Miguel Ruiz
Ana Serrano

Pediatric ARDS: effect of supine-prone postural changes on oxygenation

Received: 29 September 2001
Accepted: 16 September 2002
Published online: 30 October 2002

J. Casado-Flores (✉) · A.M. de Azagra
M.J. Ruiz-López · A. Serrano
Pediatric Intensive Care Unit,
Hospital Infantil Niño Jesús,
Universidad Autonoma de Madrid,
Avenida de Menéndez Pelayo 65,
28009 Madrid, Spain
e-mail: jcasadof@line-pro.es
Tel.: +34-91-5035900
Fax: +34+91+5035914

M. Ruiz
Department of Behavioral Sciences Methodology,
Universidad Autonoma de Madrid, Spain

Abstract *Objective:* To determine the effect of repeated prone positioning (supine-prone/prone-supine) on oxygenation in children suffering from ARDS. *Design:* Single-center prospective case series. *Setting:* University pediatric ICU. *Patients:* Consecutive pediatric patients with severe ARDS (PaO_2/FiO_2 <200, Murray score >2.5). *Interventions:* Patients were treated as soon as possible with supine-prone/prone-supine positioning every 8 h until clinical improvement or death occurred. *Measurements and results:* Twenty-three patients who had ARDS (0.5-months to 12.6-years-old), were placed in the prone position within 56±109 h after the diagnosis of ARDS. Prone-supine/supine-prone postural changes were repeated every 8 h for 9.7±5.5 days. Changes in PaO_2/FiO_2 ratio during supine-prone and prone-supine positioning were evaluated. A positive change was defined as an increase of 15% of baseline value. The patient was classified as a responder when the mean increase in the prone position was greater than 15%. There were 18 responders and five non-responders. The responders showed an increase in PaO_2/FiO_2 ratio of 22%, from 91±33 to 112±43 (P <0.001), when they were placed from the supine to the prone position. Their PaO_2/FiO_2 ratio dropped from 109± 37 to 94 ±36, P = 0.011, when changed from the prone to supine position. The overall mortality rate in this series was 48% (11 patients), which was higher in the non-responders (80%) than in the responders (39%), although this difference was not statistically significant (P = 0.95). *Conclusions:* The prone position improves oxygenation in a significant proportion of children with ARDS. Although no statistically significant difference was found for the mortality rate, it was higher for the non-responders (80%) vs the responders (39%).

Keywords ARDS · Children · Prone and supine · Body position

Introduction

Acute respiratory distress syndrome (ARDS) is a severe condition that carries a high mortality in both children and adults. Consequently, new therapeutic strategies aimed at reducing the mortality and morbidity in these patients are continually being developed. Over the last few years, permissive hypercapnia, I/E inversion, nitric oxide and, lately, prone positioning have been incorporated in the management of these patients.

Since 1974, when the effects of prone positioning on oxygenation were described, [1], several studies have reported its utility in adult patients with ARDS [2, 3, 4, 5, 6]. There is, however, less experience in children [7, 8, 9, 10], although the initial results appear to be favorable. Recently, Curley et al. [7] reported improvements in oxygenation in pediatric patients with acute lung injury/ARDS who were ventilated by prone positioning for 20 h daily. Similarly, Kornecki et al. [10] reported that oxygenation was significantly superior in the prone position than in the supine position.

The aim of our study was to evaluate the effects of repeated prone positioning (supine-prone/prone-supine) on oxygenation in children suffering from ARDS and its possible impact on mortality in these patients.

Material and methods

A prospective study was conducted from September 1994 to January 1999 in the 14-bed polyvalent (medical-surgical) Pediatric Intensive Care Unit (PICU) of our hospital. All children with a diagnosis of ARDS according to the criteria established in the 1994 European-American Consensus were included in the study: 1) acute onset; 2) partial oxygen pressure (PaO_2)/fraction of inspired oxygen (FiO_2) ratio <200 mmHg without considering PEEP level; 3) bilateral lung infiltrates demonstrated radiologically; and 4) no clinical evidence of left atrial hypertension [11]. Children in whom postural change was difficult to accomplish were excluded from the study, i.e., patients who had undergone abdominal and thoracic surgery with midline incision, facial surgery or had severe multiple trauma, severe burns, intracranial hypertension or were on hemofiltration.

The Murray severity score [12] was utilized to assess all patients to quantify the severity of ARDS according to the extent of the infiltrates in the chest film, degree of hypoxemia, PEEP level utilized, and whether patient compliance was possible. Patients with a severity score of 2.5 were included in the study.

The patients were initially ventilated in the supine position, with hemodynamic monitoring (heart rate and arterial pressure) and oxygen saturation by pulse oximetry. After obtaining arterial blood gas, the patients were placed in the prone position. No change in the respiratory assistance was performed after changing the patient's position, except in FiO_2 if necessary. PaO_2/FiO_2 ratio was measured. The effect of the postural change was considered positive when the PaO_2/FiO_2 ratio increased over 15% of the baseline value. Patients with a mean increase in PaO_2/FiO_2 ratio greater than 15% were considered responders and those with a mean increase in PaO_2/FiO_2 ratio equal to or less than 15% were considered non-responders.

Due to the severity of the condition and the respiratory assistance required by the patients, all of these patients received midazolam and fentanyl or propofol for sedation, and relaxants when necessary. The level of sedation was increased according to each patient's requirements in order to avoid the disadaptation of the patient to the maneuver.

After 8 h, each patient was again placed in the supine position. The PaO_2/FiO_2 ratio before and after the postural change were recorded. Change in patient positioning was performed every 8 h and was discontinued temporarily or definitively if the patient presented: 1) hemodynamic instability; 2) pneumothorax; 3) worsening of oxygenation with vital compromise after the postural change or 4) improvement in ARDS that permitted weaning to be commenced.

The study was approved by the Ethical and Research Committee of the hospital and informed consent was obtained from the parents of the children included in the present study.

Statistical analysis

Statistical comparisons were carried out using *t*-tests for related measures to compare PaO_2/FiO_2 index before and after the postural change, and repeated measures ANOVA, with one within-factor for postural position (4 levels) and one between-factor for responder-nonresponder groups. Post hoc multiple comparisons were calculated with *t*-tests for related measures with Bonferroni adjustment. Mann Whitney U and Wilcoxon tests were also computed to prevent possible assumption violations, although results did not differ from those of parametric tests. All calculations were computed with SPSS for Windows 10.06.

Results

Twenty-three children (10 girls, 13 boys), with a mean age of 39.86±35.62 months (range 0.5–129) were included in the study (Table 1). Two other children undergoing venous-venous hemofiltration were excluded from the study due to the difficulty involved. All patients presented at the outset severe ARDS criteria with Murray score of 2.84±0.3. Eighteen patients (78%) presented previous pathology, basically cancer (ten patients) and neurological disease (four patients). The factor triggering ARDS was pulmonary infection in 19 of the 23 patients (82% of the cases).

At the time of commencing the changes, the patients were on regulated volume control ventilation (Siemens SERVO 300) or pressure control (Siemens SERVO 900C, BP 2000), with FiO_2 of 0.85±0.18 (range 0.5–1), PEEP 9.7±2.56 cmH_2O (range 6–14), peak inspiratory pressure 36.4±8.4 cmH_2O (range 23–55), and mean airway pressure 20.52±6.38 cmH_2O (range 13–34 cmH_2O). No patients were supported on high-frequency oscillatory ventilation (HFOV).

The postural changes were started at 56±109 h after the diagnosis of ARDS and were maintained for 9.7±5.5 days, accounting for 36% of total ventilator time (27±15 days). One hundred and sixty-four supine-to-prone (7.8±6 per patient) and 132 prone-to-supine postural changes (7.46±6 per patient) were analyzed.

The PaO_2/FiO_2 ratio increased from 92±35 (range 37±196) to 110 ±46 (range 36±262) (P <0.001) when the patients were placed in the prone position. However, it was found that not all patients behaved similarly. Eighteen patients (78%) were considered responders to the postural change; in these patients the oxygenation improved in the prone position, obtaining an increase in the PaO_2/FiO_2 ratio from 91±33 (range 37–196) to 112±43 (range 36–262) (P <0.001).

Five patients (24%) were considered non-responders and did not show a significant increase in the PaO_2/FiO_2 ratio (supine PaO_2/FiO_2 ratio 94±46; prone PaO_2/FiO_2 ratio 101±52).

No patients improved from prone to supine posture. Oxygenation became worse in the supine position and showed a decrease in the ratio from 104±36 (range 36–198) to 93 ±37 (range 37–211) for the overall group of patients. In the responders the decrease was from 109±37 to 94.±36. In the non-responders the PaO_2/FiO_2 ratio in the prone position had dropped up to 88±32 be-

Table 1 Characteristics of patients undergoing position changes. (*M* male, *F* female, *R* response, *NR* no response)

Patient	Age (months)	Sex	Cause of ARDS	Murray score	PaO_2/FiO_2 baseline	Response	Outcome
1	6	F	Pneumonia	2.5	72	R	Died
2	120	F	Pneumonia	3.0	105	NR	Died
3	39	M	Sepsis	2.6	73	NR	Died
4	7.5	F	Pneumonia	2.6	80	R	Survived
5	13	M	Pneumonia	2.6	91	R	Survived
6	0.5	F	Aspiration	2.5	154	NR	Survived
7	3	F	Pneumonia	2.6	113	R	Died
8	78	M	Pneumonia	2.6	40	R	Survived
9	20	M	Pneumonia	3.0	82	NR	Died
10	46	F	Pneumonia	2.7	48	R	Died
11	7	F	Pneumonia	3.0	58	R	Survived
12	74	M	Pneumonia	3.0	50	R	Survived
13	3	M	Pneumonia	3.0	108	R	Died
14	56	M	Pneumonia	2.6	60	R	Survived
15	60	M	Toxic shock	2.5	54	R	Survived
16	29	F	BAL hemorrhage	3.0	150	R	Survived
17	32	F	Pneumonia	2.8	65	NR	Died
18	52	M	Pneumonia	2.5	71	R	Survived
19	36	M	Toxic shock	3.3	79	R	Survived
20	63	M	Pneumonia	3.0	98	R	Died
21	129	F	Pneumonia	3.6	64	R	Died
22	18	M	Pneumonia	3.3	72	R	Died
23	25	M	Pneumonia	3.0	94	R	Survived

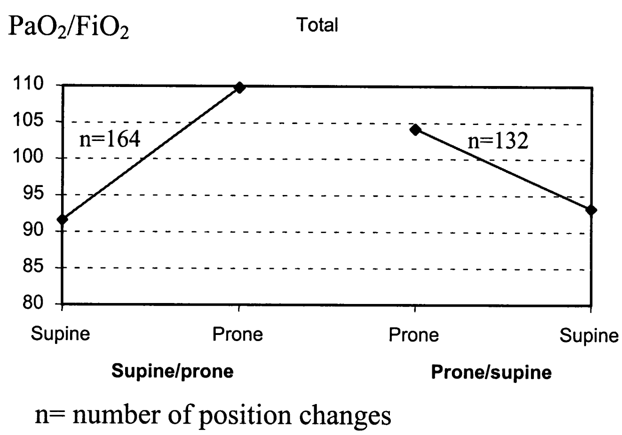

Fig. 1 PaO_2/FiO_2 index means in the four measures for the total sample

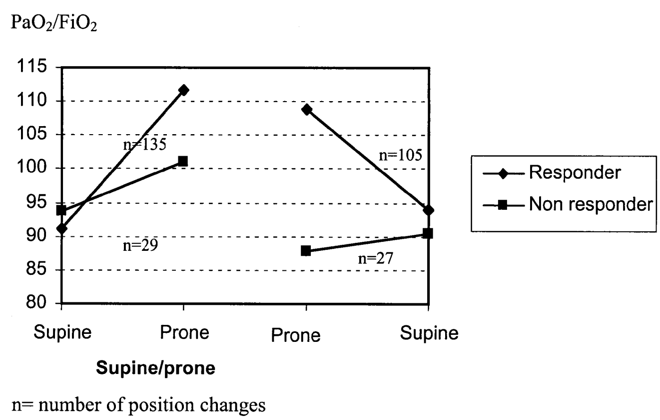

Fig. 2 PaO_2/FiO_2 index in the four measures for responder and non-responder groups in the supine-to-prone and prone-to-supine positioning

fore placement in the supine position and increased to 90±40 after placement in the supine position.

Comparison of the PaO_2/FiO_2 ratios of each patient in the supine-prone/prone-supine sequence for the overall group showed a significant increase in these values before and after the change from supine to prone (P <0.001), while the trend of these values to decrease before and after placement from prone to supine was not significant (P = 0.055). No differences were found between the levels of oxygenation in the first posture (prone-prone and supine-supine) (Fig. 1).

Analysis of the data, considering the responders and non-responders separately, showed a differential reaction to the postural changes. In the responder group the pattern was similar to that of the overall sample, but this time the decrease in oxygenation in the prone-supine postural change was found to be significant (P = 0.011). In six patients oxygenation became significantly worse in the supine position and they had to be placed in the prone position again.

In the group of non-responders, no significant differences were found; perhaps this might be ascribed to the small number of this group of patients (n = 5). The pattern suggests a relative loss of oxygenation while the patient is in the prone position, with partial recovery of oxygenation with a new postural change (Fig. 2).

Of the 18 responders, six patients (33%) did not show an increase in oxygenation after the first change to prone position, but the mean increase in the successive changes permitted including them within this first group. In the group of non-responders, only one patient improved with the first postural change, although the mean increase in the successive changes was not sufficient to include this patient in the responder group.

No significant differences were observed in the degree of severity of the condition or characteristics of the respiratory assistance between the responders and non-responders at the beginning of the postural changes.

Of the responders, two patients were kept in the prone position until weaning. In the remaining patients, the postural changes were discontinued due to improvement of ARDS and onset of weaning (six patients), pneumothorax (two patients), hemodynamic instability (one patient), and death (one patient).

Concerning the non-responders, in three patients the changes were discontinued temporarily due to pneumothorax and were reinitiated in two of these patients after resolution of the pneumothorax. In two cases the changes were definitively discontinued and the patients were left in the supine position due to non-improvement and compromise of oxygenation with minimal maneuvers.

All complications occurred during prone position. The most important were facial edema in patients who were on continuous ventilation in the prone position, and reduced saturation related with the maneuver who recovered in most cases after discontinuing the maneuver. Although pads and massage were applied to the pressure points, two of the children presented important scars in knees and one patient presented necrosis of the external ear (1/3 of helix) due to continuous prone positioning. One patient of the group of responders required discontinuation of the changes due to hemodynamic instability and required more inotropic support. No increments in sedative or analgesics were required in prone position.

The 28-day mortality rate was 48% (11 patients), which was higher for the nonresponders (4/5, 80%) than the responders (7/18, 39%), although these differences were not statistically significant ($P = 0.095$).

Discussion

In our study the prone decubitus position improved oxygenation in three out of every four children with ARDS. This improvement might have an impact on survival. Although the reponders to postural change had a lower mortality than the non-responders (39% vs 80%), the difference was not statistically significant due to the small size of the sample. However, in a recent multicenter study using prone positioning of 7 h, Gattinoni et al. [13] reported that placement of patients with ARDS in a prone position improves their oxygenation but does not improve survival.

Our results agree with those reported elsewhere in children [7, 8, 9,10] and adults [2, 3, 4, 5,6], although the protocols for application and the criteria used to define responders and non-responders in the different studies vary. Response rates to prone positioning in the adult population average 70% [13] and 80% in children [7], which is similar to our results.

In our study we included only the more severe patients (PaO_2/FiO_2 less than 200). Curley et al. [7] included acute lung injury (ALI) and ARDS with PaO_2/FiO_2 less than 300, 11 of which received conventional mechanical ventilation and the remaining 14 HFOV. The characteristics of the conventional mechanical ventilation in these 11 patients were less aggressive than those of our patients (FiO_2 0.65 vs 0.85; MAP 14 vs 20.5 cmH_2O, peak inspiratory pressure 30 vs 36.4, PEEP 9 vs 9.7). Furthermore, these patients were treated with postural changes for a shorter period (4 days vs 9.7 days) and were in the prone position longer than in the supine (20/24 h vs 12/24 h). A comparison of our study and that of Curley et al. shows that patients submitted to postural changes earlier for a shorter period and in the prone position 20/24 h were less severe (lower PaO_2/FiO_2, less mortality) and were ventilated less aggressively. We agree that postural change should be started earlier and the patient should be placed in the prone position for a longer period than in the supine position, and we are currently changing our protocol. Furthermore, changes were performed every 8 h if permitted by the hemodynamic situation. We have found that many of the responders did not maintain improvement when they were placed in the supine position, a finding that has been reported by other authors [6]. This indicates the need to develop protocols to permit a maximum time of ventilation in the prone position and take measures to prevent complications. In the extreme end of this group of patients are the so-called prone-dependent patients who do not tolerate ventilation in the supine position after they are changed to the prone position [15] and have to remain in this position for a prolonged period.

Kornecki et al. [10] found that improvement of oxygenation occurred early (within 2 h in nine of ten patients) and was sustained over 12 h of the study period. The position change was not found to affect static respiratory system compliance and resistance significantly. Like other authors [6,7], we have found that the response to the prone position is variable in time and that non-improvement at the first postural change does not imply that the patient will not respond subsequently. However, an initial response predicts subsequent positive responses. For this reason, postural changes should be continued in the initially non-responders and should be discontinued only if ventilation becomes worse in the prone position or if change-related complications develop. Papazian et al. [16] reported that a short-term trial of prone positioning does not appear to be a sufficient method for identifying patients who would benefit from the postural treatment. Seventy-three percent were responders at 1 h after the beginning of prone positioning, 27% were responders only at the end of the 6-h period of prone positioning. In all, 2/3 of the patients were considered persistent responders. The reasons why a certain positioning is efficient in some patients remain unclear, but several aspects distinguish responders from non-responders: higher levels of FiO_2, PEEP, and longer duration on mechanical ventilation after the diagnosis of ARDS in non-responders than in responders [5].

It is important to emphasize the need to start postural treatment as early as the patient's clinical condition permits. All but one of our patients that presented pneumothorax were started on postural changes within the first 3 days of the onset of ARDS. It has been reported that the maximum effect of prone ventilation on oxygenation is produced in the early stages of ARDS, i.e., during the stage of alveolar and interstitial edema. The effect of postural change is less later, perhaps due to the anatomopathological changes described in the phase of distress where pulmonary fibrosis is prevalent [17]. Perhaps this could be due to the fact that it is not possible to avoid the alveolar collapse that occurs at the end of expiration in the patient with ARDS despite the improvement in lung compliance that occurs in the prone position [18].

In spite of the possible complications described [19], there were none in this group of patients. Hemodynamic instability can become worse and we therefore consider that hemodynamic stability is necessary before we can perform postural changes. We also consider the need for pleural drainage due to pneumothorax an absolute contraindication to performing these maneuvers, since these may interfere with drainage or increase the pneumothorax. Concerning other complications, we observed facial edema or ulcers in the prone-dependent patients due to the prolonged period they were placed in this position. It is therefore necessary to take measures to prevent ulcers and re-establish postural changes as soon as possible. There was one patient who was in the prone position for 30 days, whose only complication directly related to the prone position was facial edema.

In conclusion, the prone decubitus positioning is a simple, relatively harmless, and well-tolerated procedure that improves oxygenation in most children with ARDS, with the greatest response in the first postural changes. Although it could not be demonstrated that postural changes reduced mortality, randomized controlled studies in larger series might show whether this procedure improves survival in children with ARDS or not.

References

1. Bryan AC (1974) Comments of a devil's advocate. Am Rev Respir Dis 110 [suppl]:143–144
2. Piehl MA, Brown RS (1976) Use of extreme position changes in acute respiratory failure. Crit Care Med 4:13–14
3. Douglas WW, Rehder K, Beynen FM, Sessler AD, Narsh HM (1997) Improved oxygenation in patients with acute respiratory failure: the prone position. Am Rev Resp Dis 115:559–566
4. Stocker R, Neff T, Stein S, Ecknauer E, Trentz O, Rusi E (1997) Prone positioning and low-volume pressure-limited ventilation improve survival in patients with severe ARDS. Chest 111:1008–1017
5. Chatte Sap JM, Dubois JM, Sirodot Mgaussorgues P, Robert D (1997) Prone position in mechanically ventilated patients with severe acute respiratory failure. Am J Respir Crit Care Med 155:473–478
6. Jolliet P, Bulpa P, Chevrolet JC (1998) Effects of the prone position on gas exchange and hemodynamics in severe acute respiratory distress stndrome. Crit Care Med 1977–1985
7. Curley MAQ, Thompson JE, Arnold H (2000) The effects of early and repeated prone positioning in pediatric patients with acute lung injury. Chest 118:156–163
8. Drew HN, Hammer J, Newth CJL (1997) Effect of prone and supine position on functional residual capacity, oxygenation and respiratory mechanics in ventilated infants and children. Am J Respir Crit Care Med 156:1185–1189
9. Murdoch IA, Storman MO (1994) Improved arterial oxygenation in children with the adult respiratory distress syndrome: the prone position. Acta Paediatr 83:1043–1046
10. Kornecki A, Frndova H, Coates AL, Shenie AD (2001) Randomized trial of prolonged prone positioning in children with acute respiratory failure. Chest 119:211–218
11. Bernard GR, Artigas A, Brigham KL, Carlet J, Falke L, Hudson L, Lamy M, LeGall JR, Morris A, Spragg R (1994) The Consensus Committee. Intensive Care Med 20:225–232
12. Murray JF, Matthay MA, Luce JM, Flick MR (1988) An expanded definition of the adult respiratory distress syndrome. Am Rev Respir Dis 138:720–733
13. Gattinoni L, Tognoni G, Pesenti A, Tacione P, Mascheroni D, Labarta V, Malacrida R, Di Giulio P, Fumagalli R, Pelosi P, Brazzi L, Latini R (2001) Effect of prone positioning on the survival of patients with acute respiratory failure. N Engl J Med 345:568–573
14. Curley MAQ (1999) Prone positioning in patients with acute hypoxemic respiratory failure: a systematic review. Am J Crit Care 8:397–405
15. Marik PE, Iglesias J (1997) A "prone dependent" patient with severe adult respiratory distress syndrome. Crit Care Med 25:1085–1087
16. Papazian L, Paladine MH, Bregeon F, Huiart L, Thirian X, Saux P, Jammes Y, Auffay JP (2001) Is a short trial of prone positioning sufficient to predict improvement in oxygenation in patients with acute respiratory distress syndrome? Intensive Care Med 27:1044–1049
17. Gattinoni L, Bombino M, Pelosi P, Lissoni A, Pesenti A, Fumagalli R, Taglione M. (1994) Lung structure and function in different stages of severe adult respiratory distress syndrome. JAMA 271:1772–1779
18. Blanch L, Mancebo J, Pérez M, Martinez M, Mas A, Betbese AS, Joseph D, Ballus J, Lucangelo V, Bak E (1997) Short-term effects of prone position in critically ill patients with acute respiratory distress syndrome. Int Care Med 23:1033–1039
19. Willems MCM, Voets AJ, Welten RJTJ (1998) Two unusual complications of prone-dependency in severe ARDS. Intensive Care Med 24:276–277