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J Intensive Care Med 2007; 22; 38

DOI: 10.1177/0885066606295221

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A Five-Year Experience With the Use of BiPAP in a Pediatric Intensive Care Unit Population

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The authors retrospectively reviewed their experience with bilevel positive airway pressure (BiPAP) to treat respiratory insufficiency in pediatric patients over a 5-year period. After excluding patients on chronic home BiPAP and those in whom BiPAP was used to facilitate tracheal extubation (because there were no pre-BiPAP values on which to judge its efficacy), the study cohort included 45 patients (1.5 to 22 years) in whom BiPAP was used for acute respiratory insufficiency. The primary indication for BiPAP was a primary pulmonary parenchymal process in 29 patients and postoperative atelectasis with respiratory insufficiency following cardiac or upper abdominal surgery in 16 patients. There were no differences in the pre-BiPAP values of oxygen requirement, P_{CO_2} , oxygen saturation, and respiratory rate between the 2 groups. With the application of BiPAP in patients with primary pulmonary parenchymal disease, there was a decreased oxygen requirement, P_{CO_2} , and respiratory rate. No change in oxygen saturation was noted. In patients with postoperative respiratory insufficiency, there was an improvement in all 4 parameters. There was no difference in post-BiPAP values of oxygen requirement, respiratory rate, or P_{CO_2} between the 2 groups. The post-BiPAP oxygen saturation was greater in patients with postoperative respiratory insufficiency ($96\% \pm 4\%$) than in patients with primary pulmonary parenchymal disease ($92\% \pm 6\%$, $P = .02$). Endotracheal intubation was required in 11 of 29 patients with primary pulmonary parenchymal pathology versus 1 of 16 patients with postoperative atelectasis and/or respiratory insufficiency ($P = .03$). The chances of requiring intubation were greater in patients ≤ 6 years of age (relative risk 1.9), if the oxygen requirement did not decrease to less than 60% within the first 24 hours of BiPAP use (relative risk 3.3) and if there were any P_{CO_2} values ≥ 55 mmHg during the first 24 hours of BiPAP use (relative risk 9.8). No severe complications to BiPAP were noted. BiPAP safely and effectively improves the respiratory status of and might decrease the need for endotracheal intubation in pediatric patients with acute respiratory insufficiency of various etiologies.

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Joshi G, Tobias JD. A five-year experience with the use of BiPAP in a pediatric intensive care unit population. *J Intensive Care Med*. 2007;22:38-43.

DOI: 10.1177/0885066606295221

Key words: *bilevel positive airway pressure, respiratory insufficiency, BiPAP, noninvasive ventilation, mechanical ventilation*

Noninvasive ventilation involves the administration of assisted ventilation without the presence of an endotracheal tube. The technique of noninvasive ventilation includes negative pressure ventilation (Drinker respiratory) as well as the technique that is used most commonly in today's intensive care unit setting, bilevel positive airway pressure, or BiPAP. Bilevel positive airway pressure involves the provision of expiratory positive airway pressure, which is physiologically and technically similar to continuous positive airway pressure (CPAP) combined with inspiratory assist with spontaneous ventilatory effort, support similar to that provided during mechanical ventilation by pressure support. Over the past 10 years, there has been an increased use of noninvasive ventilation or BiPAP for the treatment of acute and chronic respiratory failure [1,2]. Despite its increasing clinical use in the adult and pediatric populations, there are limited studies in pediatric-aged patients with a large cohort of patients to evaluate its efficacy and adverse profile. We present a retrospective review of our 5-year experience with BiPAP in a cohort of patients in a pediatric intensive care unit (PICU). Previous reports regarding the use of BiPAP in the pediatric population are reviewed.

Methods

This retrospective review was approved by the Institutional Review Board of the University of Missouri. The computer database of the respiratory therapy department was searched and patients admitted to the PICU who had received BiPAP were identified. Patients receiving only CPAP were not included in the study cohort as this represented a different population of patients including neonates treated for apnea and bradycardia. The following demographic data were obtained from the hospital records of patients who had received BiPAP: age, weight, gender, and primary medical condition that

necessitated the use of BiPAP. Information regarding BiPAP included the initial settings, highest settings, duration of use, whether the BiPAP was discontinued abruptly or weaned by intermittent application, and adverse effects. The efficacy of BiPAP was judged primarily by whether the patient eventually required endotracheal intubation. As a secondary measure of efficacy, we evaluated changes in the patient's respiratory status as demonstrated by changes in respiratory rate, oxygenation (oxygen saturation on pulse oximetry and inspired oxygen concentration requirements), ventilation as measured by changes in carbon dioxide (either transcutaneous values or P_{CO_2} from venous, capillary, or arterial blood gas analyses), and improvements in atelectasis on chest radiographs. For these comparisons, parameters when available were obtained from the 1-2 hour period before the application of BiPAP and compared with the best values during the initial 24 hours after starting BiPAP. When considering P_{CO_2} values, data from arterial/venous blood gases or transcutaneous CO_2 monitoring were considered together as P_{CO_2} . Statistical analysis included a paired *t* test to compare respiratory rate, oxygenation, inspired oxygen concentration requirements, and P_{CO_2} values before and after the application of BiPAP. A nonpaired *t* test was used to compare the pre- and post-BiPAP values between patients who did not subsequently require endotracheal intubation and those for whom BiPAP failed and who required endotracheal intubation. The need for endotracheal intubation between patients with primary pulmonary parenchymal disease and those with postoperative respiratory insufficiency as well as predictive factors for BiPAP failure were analyzed using a contingency table and a Fisher's exact test. The data are presented as the mean \pm SD with *P* < .05 considered significant.

The bilevel positive airway device (BiPAP[®], Resironics, Murrysville, PA) used in these patients provides pressure-limited ventilation with EPAP (expired positive airway pressure) ranging from 2 to 20 cm H₂O and inspiratory positive airway pressure (IPAP) ranging from 2 to 25 cm H₂O. The device also allows selection of the cycle frequency between IPAP and EPAP (6 to 30 cycles per minute), the proportion of each cycle spent during IPAP (10% to 90%), and adjustment of the FiO₂ (0.21 to 1.0). The appropriate sized mask was chosen using the ComfortFull Sizing Gauge for the Resironics adult facemasks, which are available in small, medium, and large sizes. We found that the small adult face mask provided an appropriate fit even in younger pediatric patients. More information regarding the Resironics equipment and face masks is available

from their Web site at www.resironics.com. In all cases, the patients were breathing spontaneously, and the IPAP was set to augment spontaneous ventilation. Nonspontaneous, positive pressure breaths were not delivered.

Results

BiPAP was used in 77 instances for 62 patients over the 5-year study period. Twenty-seven of these applications were in 12 patients on chronic home BiPAP who were hospitalized for other reasons. In 5 other patients, BiPAP was used to transition from mechanical ventilation in patients who were thought to be high risk at failing extubation. After excluding patients on chronic home BiPAP and those in whom BiPAP was used to facilitate tracheal extubation (because there were no pre-BiPAP values on which to judge its efficacy), the study cohort included 45 patients in whom BiPAP was used for acute respiratory insufficiency. The patients ranged in age from 1.5 years to 22 years (11.2 ± 5.4 years, median 12 years) and in weight from 12.5 kg to 80 kg (40.1 ± 19.4). There were 25 boys and 20 girls. The primary indication for BiPAP was a primary pulmonary parenchymal process including pneumonia (bacterial, viral, or aspiration) or acute respiratory distress syndrome (ARDS) in 29 patients (median age, 13 years) and postoperative atelectasis with respiratory insufficiency following sternotomy for cardiac surgery, thoracotomy, or upper abdominal surgery in 16 patients (median age, 12 years).

The initial BiPAP settings included an inspiratory pressure ranging from 4 to 20 cm H₂O (10 ± 3 cm H₂O) and an expiratory setting ranging from 2 to 10 cm H₂O (5 ± 2 cm H₂O). In 28 of the 45 applications of BiPAP, the settings were increased. The highest BiPAP settings included an inspiratory pressure ranging from 4 to 25 cm H₂O (15 ± 4) and an expiratory pressure ranging from 2 to 10 cm H₂O (7 ± 2). BiPAP was applied for 7 to 576 (123.8 ± 141.6) hours in patients with primary pulmonary parenchymal processes and for 12 to 168 (62 ± 44 ; *P* = NS) hours in the postoperative patients.

There were no differences in the pre-BiPAP values of oxygen requirement, P_{CO_2} , oxygen saturation, and respiratory rate between patients with primary pulmonary parenchymal disease and those with postoperative respiratory insufficiency and/or atelectasis (Tables 1 and 2). With the application of BiPAP in patients with primary pulmonary parenchymal disease, there was a statistically significant decrease in oxygen requirement, decreased P_{CO_2} , and decreased respiratory rate. No change in oxygen saturation was

noted (Table 1). In patients with postoperative respiratory insufficiency, there was a statistically significant improvement in all 4 parameters evaluated including a decreased oxygen requirement, decreased P_{CO_2} , increased oxygen saturation, and decreased respiratory rate (Table 2). There was no difference in post-BiPAP values of oxygen requirement, respiratory rate, or P_{CO_2} between the 2 groups of patients. The post-BiPAP oxygen saturation was greater in patients with postoperative respiratory insufficiency ($96\% \pm 4\%$) than in patients with primary pulmonary parenchymal disease ($92\% \pm 6\%$, $P = .02$). Endotracheal intubation was required in 11 of 29 patients with primary pulmonary parenchymal pathology versus 1 of 16 patients with postoperative atelectasis and/or respiratory insufficiency ($P = .03$). In patients with primary pulmonary parenchymal disease, the chances of requiring intubation were greater in patients ≤ 6 years of age (relative risk 1.9), if the oxygen requirement did not decrease to less than 60% within the first 24 hours of BiPAP use (relative risk 3.3), and if there were any P_{CO_2} values ≥ 55 mmHg during the first 24 hours of BiPAP use (relative risk 9.8).

BiPAP was initially used for 24 hours a day in all of the patients. Nineteen BiPAP applications were discontinued and the patient was placed on supplemental oxygen as needed, 11 patients were weaned off of BiPAP (see below), 12 patients required endotracheal intubation, 2 patients were transitioned to home BiPAP use, and 1 patient expired. The death occurred unrelated to, but during, BiPAP use in a patient with multiple medical problems for whom the parents had requested no further therapy escalation (endotracheal intubation). Of the 11 patients who were gradually weaned from BiPAP, the weaning time varied from 1 to 7 days. The methods by which these patients were weaned included decreasing the percentage of oxygen delivered, decreasing the IPAP and/or EPAP, applying BiPAP intermittently, or some combination thereof. Intermittent application most commonly initially consisted of alternating 2 hours of BiPAP and 2 hours without it, or applying BiPAP only during the night and daytime naps.

Adverse effects of BiPAP occurred in 10 of the patients and included skin breakdown or erythema, nausea or emesis, and abdominal pain or bloating (Table 3). One patient thought that BiPAP caused headaches. Ten patients experienced ≥ 1 adverse effect with the frequency described in Table 3. Patients who experienced adverse effects ranged in age from 7 to 19 years (12.8 ± 4.8 , $P = NS$) compared with patients who did not experience adverse effects.

Table 1. Changes in Respiratory Parameters Following the Application of BiPAP in Patients With Primary Pulmonary Parenchymal Disease

Parameter	Before	After	<i>P</i> Value
FiO ₂	0.78 ± 0.25	0.50 ± 0.22	< .001
P _{CO2}	56 ± 11	45 ± 7	< .001
O ₂ saturation	90 ± 12	92 ± 6	NS
RR	34 ± 10	22 ± 8	< .001

RR = respiratory rate.

Table 2. Changes in Respiratory Parameters Following the Application of BiPAP in Postoperative Patients (Mean ± SD)

Parameter	Before	After	<i>P</i> Value
FiO ₂	0.80 ± 0.24	0.45 ± 0.21	.001
P _{CO2}	53 ± 5	43 ± 6	< .001
O ₂ saturation	90 ± 6	96 ± 4	< .001
RR	31 ± 6	18 ± 10	< .001

RR = respiratory rate.

Table 3. Adverse Effects of BiPAP

Adverse Effect	Number of Patients
Skin breakdown/erythema/ blistering	7
Nausea/emesis	4
Abdominal pain/bloating	2

Discussion

Bilevel positive airway pressure ventilation allows the provision of positive pressure and ventilatory support to spontaneously breathing patients without placement of an endotracheal tube. For the purpose of this discussion, BiPAP and noninvasive positive pressure ventilation (NIPPV) will be used interchangeably. BiPAP can be delivered with a nasal or a full face mask. The initial reports of BiPAP were performed using standard, constant flow, pressure-targeted ventilators; however, there are now commercially available BiPAP machines such as the type used in our cohort of patients. Although initially used in patients with neuromuscular disorders, chronic lung diseases, central hypoventilation syndromes, and obstructive sleep apnea, BiPAP has emerged as a potentially useful tool in the management of pediatric patients with acute respiratory failure [1,2]. The obvious benefits include the avoidance in many patients of the need for endotracheal intubation and its antecedent risks. Although there are

several reports regarding the applications of this technique in pediatric patients, there are few that involve a large cohort of patients. Even with the exclusion of patients who were previous BiPAP users and those in whom no pre-BiPAP respiratory parameters were available (those extubated directly to BiPAP), our current series included 45 pediatric patients who were supported with BiPAP. To our knowledge, this is the largest series reported.

To evaluate the efficacy of BiPAP, we chose to separate the patients with acute respiratory insufficiency into 2 primary etiologic groups: patients with primary pulmonary parenchymal diseases and those with primary postoperative issues of atelectasis. The patients with primary pulmonary parenchymal disorders included a heterogeneous population of patients and primary etiologic factors for their respiratory insufficiency. These patients had disease processes that commonly lead to respiratory failure in the PICU setting including pneumonia and ARDS. The patients with atelectasis were all recovering from upper abdominal or thoracic surgery, most commonly surgery for congenital heart disease. Despite the relative diversity of these 2 groups, we noted no difference in their respiratory status based on P_{CO_2} values, oxygen requirement, oxygen saturation, or respiratory rate before the decision to use BiPAP. However, there appeared to be a more favorable response to BiPAP in patients with postoperative atelectasis, as we noted improvements in all 4 parameters following the application of BiPAP in these patients and in 3 of the 4 parameters in patients with primary pulmonary parenchymal disease. Most importantly, only 1 of 16 of the patients in the postoperative respiratory insufficiency group eventually required endotracheal intubation versus 11 of 29 in the primary pulmonary parenchymal disease group. Although ours is the first study in pediatric patients to demonstrate a difference in outcome based on the primary etiology of the respiratory failure, these findings are certainly not surprising because normal respiratory function should return immediately with resolution of atelectasis and be unlikely to progress, whereas treatment of primary pulmonary parenchymal diseases would take longer and be more likely to progress.

Although there is an increasing recognition of the potential benefits of BiPAP in children with acute respiratory failure, the initial reports in the literature centered around chronic respiratory failure including patients with cystic fibrosis and neuromuscular disorders. In patients with cystic fibrosis, BiPAP is frequently first instituted to treat an acute exacerbation that is superimposed upon the preexisting chronic lung disease [3]. In many patients,

when the acute episode has resolved, BiPAP is then continued primarily at night in an effort to retard the progression of chronic lung disease or to prolong survival (bridge) until lung transplantation is available [4-8]. Although there are no randomized trials in patients with cystic fibrosis, when comparing before and after respiratory variables, authors have reported improved oxygenation, decreased oxygen requirement, and decreased P_{CO_2} values following the application of BiPAP [4-7]. Additionally, BiPAP has been used to facilitate chest physiotherapy in patients with cystic fibrosis [8].

The second category of patients in whom BiPAP has seen significant use is children with respiratory failure related to neuromuscular diseases. In this setting, the acute and/or chronic use of BiPAP makes physiologic sense because in many cases respiratory failure is related to diaphragmatic failure and not to intrinsic lung disease [9-13]. Although several of these reports entail only 1 to 2 patients, there are larger series regarding the use of BiPAP for this specific indication. Padman et al reported their experience with the use of BiPAP in 15 patients ranging in age from 4 to 21 years with respiratory failure caused by neuromuscular disorders ($n = 11$) or cystic fibrosis ($n = 4$) [11]. The neuromuscular disorders included spinal muscular atrophy, Duchenne muscular dystrophy, spinal cord injury, or undiagnosed myopathy. The patients were followed for 1 to 21 months. In 14 of 15 patients, endotracheal intubation was avoided. Additionally, after the application of BiPAP, they noted a significant decrease in days hospitalized, respiratory rate, heart rate, serum bicarbonate, and arterial P_{CO_2} values. Improvement in quality of life issues were manifested as decreased dyspnea, increased activity tolerance, and improved quality of sleep.

Hertzog and Costarino reported their experience with BiPAP in 7 children with type II (hypercarbic, as opposed to type I or hypoxemic) respiratory failure [12]. BiPAP resulted in an improvement in pH, $PaCO_2$, and the PaO_2 - FiO_2 ratio. None of the 7 required endotracheal intubation; however, when compared with a cohort of 11 patients with similar respiratory issues who had undergone endotracheal intubation with positive pressure ventilation, no difference in length of PICU stay was noted. They noted 6 complications in 4 of the 7 patients, including skin breakdown over the bridge of the nose ($n = 4$), gastric distention ($n = 1$), and pneumothorax ($n = 1$).

Niranjan and Bach developed a protocol using NIPPV to treat neuromuscular respiratory failure and then prospectively evaluated its efficacy in 10 patients ranging in age from 13 to 21 years [13]. Four

of 10 patients who presented with acute respiratory failure were treated without endotracheal intubation. Six patients who were initially intubated underwent tracheal extubation to BiPAP when normal oxygenation could be maintained on room air. These 6 patients were successfully extubated despite their having no ventilator-free breathing.

There are also several reports in the literature on the use of BiPAP in infants and children in the treatment of acute respiratory insufficiency of various etiologies. As with other reports of BiPAP in the pediatric population, many of these are anecdotal isolated case reports or small case series [14-16]. However, other authors have reported experience from larger retrospective reviews [17-19]. Fortenberry et al reviewed their experience with BiPAP in a cohort of 28 patients with a median age of 8 years [17]. Following BiPAP application, they noted improvements in PaO₂, PaCO₂, oxygen saturation, respiratory rate, and pH. Only 3 of 28 patients eventually required endotracheal intubation. Similar success was reported by Padman et al in their retrospective review of their use of BiPAP in 34 patients ranging in age from 6 months to 20 years [18]. With the application of BiPAP, they noted a decrease in dyspnea scores, decreased heart rate, decreased respiratory rate, and increased room air oxygen saturation. Endotracheal intubation was required in 8% of their patients. In a more recent study, Padman and Henry reported the successful use of BiPAP in 25 episodes of acute chest syndrome in 9 pediatric patients with sickle cell disease [20]. With the application of BiPAP, there was a decreased oxygen requirement, increased oxygen saturation, decreased respiratory rate, and decreased heart rate. Only 1 patient required endotracheal intubation. Anecdotal success with BiPAP use has also been reported in the treatment of status asthmaticus, pulmonary hypertension associated with congenital heart disease, diaphragmatic paralysis, and upper airway obstruction following tonsillectomy [21-24].

As with any type of therapy, complications may occur with BiPAP. In a retrospective review such as ours, it is likely that minor complications are underreported, thereby making any definitive comment on the incidence of complications such as skin irritation somewhat difficult. However, we noted relatively few complications, the most common being skin irritation and blistering from the pressure during mask application. Fauroux et al reported skin complications in 48% of their 44 patients during BiPAP use, with transient erythema in 18%, prolonged erythema in 23%, and skin necrosis in 3 patients (7%) [25]. Because of the high incidence of

such problems, we routinely place a protective self-adhesive barrier on the patient's face before mask application. An additional concern with the use of positive pressure ventilation without airway protection is gastric insufflation and the potential for vomiting with aspiration [26]. We currently consider altered mental status or inability to protect the airway a relative contraindication to the use of BiPAP. Although we noted occasional bouts of emesis in a limited number of our patients, no episodes of aspiration occurred. When reviewing the literature, more serious complications of BiPAP have included barotraumas and cerebral air embolism [12, 27, 28].

There remain an ongoing interest and an increased use of BiPAP to treat respiratory failure of various etiologies in pediatric patients with or without a history of previous lung disease or neuromuscular problems. The obvious limitation of our current review is its retrospective nature. As there was no randomization and no comparable group that did not receive BiPAP, we cannot comment on whether BiPAP hastened recovery, decreased ICU and hospital stays, limited morbidity and mortality, or was more effective than non-BiPAP support. Additionally, although failure of BiPAP was defined as the need for endotracheal intubation, it is feasible that we missed patients in whom BiPAP was discontinued early on because of failure to tolerate the mask. This would occur only if the experience was so brief that no respiratory therapy charge was generated. We likewise feel that this scenario is unlikely.

In the current cohort, we used BiPAP in 3 clinical scenarios: to facilitate extubation in patients who we thought might be at high risk for failure [29], in patients who were already home BiPAP users (predominantly patients with chronic lung disease caused by cystic fibrosis), and in the treatment of acute respiratory insufficiency. In the last group, we noted 2 basic populations of patients, those with respiratory insufficiency during the postoperative course and those with primary pulmonary parenchymal disease. We noted that BiPAP was more effective in preventing the need for endotracheal intubation in patients with postoperative respiratory issues predominantly related to atelectasis. Given the move toward fast-tracking of cardiac patients even in the pediatric population, we have found great utility of BiPAP in facilitating early tracheal extubation and improving respiratory function when atelectasis occurs in this population. In addition to suggesting that primary pulmonary parenchymal lung disease is a risk factor for BiPAP failure, we also noted other factors that might influence outcome, including age \leq 6 years, an oxygen

requirement that does not decrease to less than 60% within the first 24 hours of BiPAP use, and any P_{CO_2} value ≥ 55 mmHg during the first 24 hours of BiPAP use. We are aware of only one other study in children that identified criteria which were predictive of the need for eventual endotracheal intubation. Bernet et al in a prospective study of 42 pediatric patients treated with BiPAP or CPAP reported that $FiO_2 > 80\%$ after 1 hour was predictive of nonresponse to therapy and the need for endotracheal intubation (sensitivity 56%, specificity 83%) [30]. BiPAP safely and effectively improves the respiratory status of and might decrease the need for endotracheal intubation in pediatric patients with acute respiratory insufficiency of various etiologies. To date, the majority of the information in the literature remains anecdotal with no randomized, controlled studies.

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