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BRIEF REPORT

Trends in Pediatric Patient-Ventilator Asynchrony During Invasive Mechanical Ventilation

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OBJECTIVES: To explore the level and time course of patient-ventilator asynchrony in mechanically ventilated children and the effects on duration of mechanical ventilation, PICU stay, and Comfort Behavior Score as indicator for patient comfort.

DESIGN: Secondary analysis of physiology data from mechanically ventilated children.

SETTING: Mixed medical-surgical tertiary PICU in a university hospital.

PATIENTS: Mechanically ventilated children 0–18 years old were eligible for inclusion. Excluded were patients who were unable to initiate and maintain spontaneous breathing from any cause.

MEASUREMENTS AND MAIN RESULTS: Twenty-nine patients were studied with a total duration of 109 days. Twenty-two study days (20%) were excluded because patients were on neuromuscular blockade or high-frequency oscillatory ventilation, yielding 87 days (80%) for analysis. Patient-ventilator asynchrony was detected through analysis of daily recorded ventilator airway pressure, flow, and volume versus time scalars. Approximately one of every three breaths was asynchronous. The percentage of asynchronous breaths significantly increased over time, with the highest prevalence on the day of extubation. There was no correlation with the Comfort Behavior score. The percentage of asynchronous breaths during the first 24 hours was inversely correlated with the duration of mechanical ventilation. Patients with severe patient-ventilator asynchrony (asynchrony index > 10% or > 75th percentile of the calculated asynchrony index) did not have a prolonged duration of ventilation.

CONCLUSIONS: The level of patient-ventilator asynchrony increased over time was not related to patient discomfort and inversely related to the duration of mechanical ventilation.

KEY WORDS: asynchrony; child; mechanical ventilation; patient-ventilator interaction

Mechanical ventilation (MV) is one of the most practiced interventions in the PICU (1). In the absence of severe lung injury, several advantages to targeting assisted rather than mandatory breathing during MV have been proposed (2). However, this requires optimal, synchronized interaction between patient demand and ventilator performance.

Patient-ventilator asynchrony (PVA) occurs when there is a mismatch between the patient demand and delivered ventilatory support at any moment during the respiratory cycle (3, 4). Previously, we and others reported high PVA occurrence in invasively ventilated children with almost one of every three breaths being asynchronous (5, 6). Occurrence of PVA changes over time and may negatively affect patient outcome in adults (7). An asynchrony index (AI) or ineffective triggering index greater than 10% in the first 24 hours of MV has been associated with increased ventilatory support and sedation, prolonged MV duration, and longer hospital stay (7–9).

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There are no data on the temporal distribution and clinical correlate of PVA in children. We sought to study the level and time course of PVA, and the association with patient comfort, duration of MV, and length of PICU stay through a secondary analysis of prospectively collected physiology data.

MATERIALS AND METHODS

We performed secondary analyses of prospectively collected data including ventilator scalars in mechanically ventilated children less than 18 years old who were able to initiate and maintain spontaneous breathing. The Institutional Review Board approved the study and waived the need for informed consent. Details on ventilator protocol and data acquisition can be found in **Supplemental Table 1** (http://links.lww.com/PCC/B816). Briefly, scalars were recorded for 10 minutes (Ventview 2; Dräger, Lubeck, Germany) and independently visually inspected offline for any type of asynchrony by the same two investigators as previously (interobserver reliability κ test 0.77; $p < 0.01$) (5).

PVA was categorized into eight different groups based upon previously reported definitions, including ineffective triggering, double triggering, auto-triggering, trigger delay, flows asynchrony, delayed termination, premature termination, and expiratory asynchrony (i.e., air-trapping) (**Supplemental Fig. 1**, http://links.lww.com/PCC/B808; **Supplemental Fig. 2**, http://links.lww.com/PCC/B809; **Supplemental Fig. 3**, http://links.lww.com/PCC/B810; **Supplemental Fig. 4**, http://links.lww.com/PCC/B811; **Supplemental Fig. 5**, http://links.lww.com/PCC/B812; **Supplemental Fig. 6**, http://links.lww.com/PCC/B813; **Supplemental Fig. 7**, http://links.lww.com/PCC/B814; and **Supplemental Fig. 8**, http://links.lww.com/PCC/B815 [**legend**, http://links.lww.com/PCC/B817]) (5, 10–13). The AI was calculated by dividing the total number of asynchronies by the total number of breaths × 100. For analytical purposes, we defined severe AI as AI greater than 10% and by greater than 75th percentile of the calculated AI (AI_{p75}) (6, 8, 9). We also calculated the daily median AI (7).

The primary endpoint was the duration of MV; secondary endpoints were Comfort Behavior Score and length of PICU stay. Continuous data were analyzed using the Mann-Whitney *U* test or student *t* test. Generalized estimating equations (GEEs) analysis was used to study the level of PVA over time and the effect of different variables. Statistical analyses were performed using SPSS Version 26 (IBM, Armonk, NY). *p* values less than 0.05 were accepted as statistically significant.

RESULTS

Twenty-nine patients with median age 2.0 months (1.2–7.0 mo), weight 4.8 kg (3.9–7.3 kg), and duration of MV 3.5 days (1.9;–5.6 d) were consecutively studied for a total duration of 109 days. Twenty-two study days (20%) were excluded because patients were on neuromuscular blockade or high-frequency oscillatory ventilation, yielding 87 days (80%) with 44,665 breaths for analysis. Admission indications was acute respiratory failure in 18 patients (62%) and postcardiac surgery in seven patients (24%). Pressure assist/control (A/C) (92%) was the predominant ventilation mode. Fifty-five percent had cuffed endotracheal tubes. The median equipotent methadone dosage was 0.12 mg/kg/d (0.10–0.14 mg/kg/d) and for lorazepam 0.20 mg/kg/d (0.16–0.30 mg/kg/d) (14). Median Comfort Behavior Score was 12 (10–15). Ventilator settings and sedation were not changed during the recording.

During the entire study period, PVA was detected in 16.020 breaths (36%), with ineffective triggering being the predominant type of PVA (67%), followed by delayed termination (25%), trigger delay (2%), double triggering (2%), and premature termination (2%). Flow- and expiratory asynchrony was observed in less than 1%. Ineffective triggering and delayed termination being the most common type of PVA was also observed for each single study day. PVA increased significantly over time and peaked on the day of extubation (40% [26–53%]; $\beta = -0.08$, $p = 0.03$). Comfort Behavior Score ($\beta = -0.001$; $p = 0.955$), endotracheal tube leak ($\beta = 0.009$; $p = 0.491$), set breath rate ($\beta = 0.000$; $p = 0.978$), and PEEP ($\beta = 0.099$; $p = 0.105$) were not correlated. PVA was significantly associated with increasing age ($\beta = 0.008$; $p = 0.006$) and decreasing Pmean ($\beta = -0.162$; $p = 0.006$) (**Fig. 1**). Patients ventilated in a pressure A/C mode of ventilation experienced lower levels of PVA compared with those ventilated with pressure/synchronized intermittent mandatory ventilation or pressure-regulated volume control mode of ventilation ($p = 0.003$).

Nineteen of 22 patients (86%) had AI greater than 10% on day 1 of MV, and 27 (93%) during the MV course, but there was no difference in duration of MV or PICU stay (**Table 1**). Six patients (27%) had severe PVA

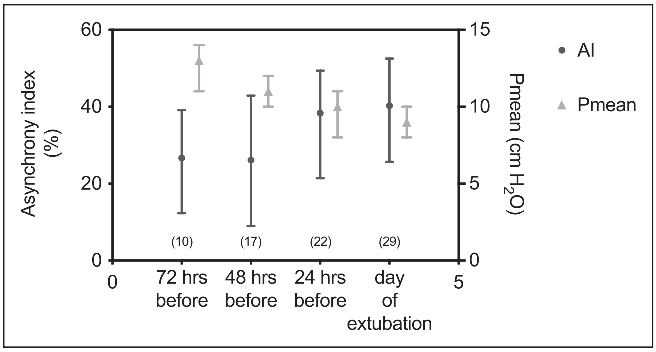

Figure 1. Patient-ventilator asynchrony during mechanical ventilation. Asynchrony index (%) and mean airway pressure (Pmean) score during mechanical ventilation. The level of asynchrony increases over time and peaks in the day of extubation, whereas Pmean decreased during the course of mechanical ventilation.

using the AI_{p75} definition on day 1 of admission, and seven (24%) during the MV course, corresponding to AI greater than 50%. Those patients were significantly older, less likely to have acute respiratory failure at admission, lower ventilatory support, and a shorter duration of MV (Table 1). Similar findings were made when the analysis was limited to ineffective triggering (Supplemental Table 1, http://links.lww.com/PCC/B816).

DISCUSSION

To our best knowledge, this is the first pediatric study reporting that the level of PVA increased over time and peaked on the day of extubation. The level of PVA during the first 24 hours was inversely correlated to the duration of MV. We could not identify an association with patient discomfort.

Our findings contract observations made in adults (9). In our study, patients with severe PVA needed lower ventilatory support and had a shorter duration of MV. Although our study design does not allow for identifying causality, several explanations may be proposed. First, we may have underestimated the actual prevalence of PVA since we did not have a continuous recording of the ventilator scalars (7). Despite that, we applied the same analytics as the adult studies (8, 9). On top of that, we applied the adult PVA definitions. Generalizability of these definitions to children has not been established. Remarkably, in our study patients, with severe PVA were ventilated less than 2 days, surmising that this period might be too short for any negative clinical impact of PVA in children.

Aside from methodological differences, there may also be actual pathophysiologic differences between children and adults. De Wit et al (9) reported high rates of PVA during the first 24 hours of MV associated with increased morbidity. These observations may be explained by excessive pleural pressure swings generated during an inspiratory effort made by the patient in the context of poor respiratory compliance early in the disease trajectory, leading to additional patient self-inflicted lung injury (15). The open question is if this also could occur in children. Especially in young children, the chest wall is very compliant possibly making that unlike older children and adults, they have to generate a smaller amount of energy to overcome the elastic properties of the chest wall (16).

We observed an inverse relationship between the level of ventilatory support and occurrence of PVA. It may be postulated that there is a link between the patient's respiratory drive, delivered ventilatory pressures, and the development of PVA. High levels of ventilatory support are likely to be given after initiating MV, especially when there is severe lung injury. These high ventilatory pressures may cause over assistance or reduce the patient's respiratory drive because of inhibitive reflexes leading to a reduced respiratory rate and increase in neural expiratory time caused by a mechanoreceptor reflex feedback (i.e., the Hering-Breuer reflex) (17). This reduced respiratory rate will also reduce the patient interaction with the ventilator and theoretically decreases the development of PVA. In fact, lower diaphragm activity during the acute phase of MV with higher ventilator pressures compared with the preextubation phase has been reported (18). Future studies are needed to explore this mechanism.

There are some limitations to our study. First, our data represent a single-center study, limiting generalizability to other centers although our PICU is similar to many units across the globe. Second, we studied the prevalence of PVA through visual inspection of the ventilator scalars since they are readily available. Obviously, this is a cumbersome method and may underestimate the true prevalence of PVA because it lacks confirmation of patient effort by means of esophageal pressure manometry or electrical activity of the diaphragm (10, 19, 20). Reassuringly, the prevalence of PVA in our study was

TABLE 1.
Asynchrony Index in First 24 Hours and During the Course of Mechanical Ventilation

Asynchrony in First 24 hr	AI < 10% (*n* = 3)	AI > 10% (*n* = 19)	*p*	AI < 50% (*n* = 16)	AI > 50% (*n* = 6)	*p*
Age (mo)	2.0 (1.2–3.4)	2.2 (1.2–15.6)	0.667	2.0 (1.1–4.0)	15.7 (2.1–63.4)	0.021
Duration of MV (d)	3.0 (1.9–3.8)	2.9 (1.2–5.5)	0.962	3.8 (2.2–5.6)	1.1 (0.9–2.3)	0.002
PICU stay (d)	4.4 (3.7–4.7)	5.6 (3.5–8.0)	0.363	5.2 (3.9–7.5)	4.3 (3.1–10.9)	0.641
Respiratory	3 (100)	11 (56)	0.226	12 (75)	1 (20)	0.036
Postsurgical	–	6 (32)		4 (25)	2 (40)	
Other	–	2 (11)		–	2 (40)	
Pressure assist/control	3 (100)	15 (79)	0.680	15 (94)	3 (50)	0.049
Pressure synchronized intermittent mandatory ventilation	–	3 (16)		1 (6)	2 (33)	
Continuous positive airway pressure/pressure support	–	1 (5)		–	1 (17)	
Measured peak inspiratory pressure (cm H_2O)	13 (12–14)	16 (13–16)	0.291	23 (20–26)	18 (14–20)	0.032
Measured positive end-expiratory pressure (cm H_2O)	6 (5–6)	6 (5–6)	0.571	6 (5–7)	5 (5–6)	0.266
Mean airway pressure (cm H_2O)	13 (13–13)	10 (10–11)	0.032	12 (10–13)	7 (7–9)	0.007
Set breath rate (/min)	25 (20–30)	25 (20–30)	0.605	35 (30–40)	25 (20–30)	0.007
Comfort Behavior Score	12 (8–12)	12 (10–15)	0.277	12 (11–14)	13 (10–17)	0.603
Equipotent dose methadone (mg/kg/d)	0.13 (0.12–0.14)	0.12 (0.12–0.14)	0.550	0.12 (0.12–0.14)	0.13 (0.09–0.24)	0.673
Equipotent dose lorazepam (mg/kg/d)	0.22 (0.16–0.32)	0.20 (0.20–0.22)	0.682	0.20 (0.20–0.22)	0.20 (0.17–0.40)	0.937
Asynchrony During Course of MV	**AI < 10% (*n* = 2)**	**AI > 10% (*n* = 27)**	***p***	**AI < 50% (*n* = 22)**	**AI > 50% (*n* = 7)**	***p***
Duration of MV (d)	2.8 (1.9–2.8)	3.5 (1.9–5.6)	0.636	3.9 (2.8–5.7)	1.1 (0.9–2.5)	0.011
Length of PICU stay (d)	4.2 (3.7–4.2)	5.6 (4.1–10.5)	0.389	5.1 (4.2–7.7)	6.5 (3.5–11.8)	0.878

AI = asynchrony index, MV = mechanical ventilation.Data are presented as median (interquartile range) or percentage (%) of total.

comparable with other reports (5, 21, 22). Third, our study population was younger than 12 months of age, making it unclear if and how our findings can be extrapolated across the pediatric range. Fourth, the most predominant mode of ventilation used was pressure A/C. To date, it is not clear if the ventilation mode used can increase or reduce the level of PVA in mechanically ventilated children. Last, the median duration of MV was short, especially in patients with severe PVA. These limitations underscore the need for a continuous, long-term PVA monitoring to gain better understanding of the actual possible negative effects of PVA.

CONCLUSIONS

The level of PVA increased over time was not related to patient discomfort and inversely related to the duration of MV. Future studies are needed making use of continuous PVA monitoring to further explore the relation with patient outcome.

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