

Impact of minimizing asynchronies in mechanical ventilation on patient's outcome in pediatric intensive care unit

Abstract:

Background: Patients-ventilator asynchrony defined as a mismatch between the patient's respiratory effort and the ventilator delivered breaths and it is common in clinical practice. Patient ventilator interaction is a key element in optimizing MV. The change from inspiration to expiration is a crucial point in the mechanically ventilated breaths and is termed cycling, PVA may occur if the flow at which the ventilator cycles to exhalation does not coincide with the termination of neural inspiration. Ideally, the ventilator terminates inspiratory flow in synchrony with the patients neural timing, but frequently the ventilator terminates early or late.

Aims: The aim of this study was to detect the prevalence of asynchrony during assisted MV, IT and DT were the two main patterns of asynchrony.

Patients and Methods: This prospective study was carried out upon 60 patients from 2 to 180 months, 38 males and 22 females, with spontaneous triggering on MV, admitted to the PICU, Tanta University Hospital.

Results: There were non-significant difference in nearly all data regarding MV mode. Fortunately, ITI is increased with volume SIMV +PSV compared with pressure SIMV +PSV and PRVC. ITI is a highly significant diagnostic for synchronization. Pressure regulated volume control was better than pressure SIMV+PSV and both were better than volume SIMV +PSV proved by less ITI and increase mortality with $ITI \geq 10\%$.

Conclusion: Pressure regulated volume control was better than pressure SIMV+PSV and both were better than volume SIMV +PSV proved by less ITI and increase mortality with $ITI \geq 10\%$. The patient-ventilator synchrony is crucial in determining the patient comfort, MV duration, and survival ITI is diagnostic for synchronization. ITI, PIP/ITI on 1st day, and SpO₂ on 3rd day were significant predictors for synchronization.

Keywords: Asynchronies, Mechanical ventilation, Pediatric, ICU

Introduction:

In critically ill patients, mechanical ventilation (MV) aims to improve oxygenation and decrease the work of breathing and load on the respiratory muscles to support patients until their condition improves. ⁽¹⁾

Optimal patient-ventilator interaction can help avoid excessive sedation, anxiety, discomfort, episodes of fighting on the ventilator, diaphragmatic dysfunction and atrophy due to disuse, potential cognitive alterations, prolonged mechanical ventilation, and additional lung or respiratory muscle injury. ⁽²⁾

Research has shown that patients ventilated for 24 hours who can trigger the ventilator have a high incidence of asynchrony during assisted mechanical ventilation. ⁽³⁾

Asynchrony is common throughout MV, ⁽⁴⁾ occurs in all MV modes, and might be associated with a bad outcome, especially when they occur in clusters. ⁽⁵⁾

Patient-ventilator asynchrony (PVA) exists when the phases of breath delivered by the ventilator do not match those of the patient. ⁽⁶⁾ To meet the patient's demands, the ventilator's inspiratory time and gas delivery must match the patient's neural inspiratory time. ⁽⁷⁾

Asynchronies occur with minimal differences between day and night, and the most prevalent asynchrony overall and in every MV mode is ineffective inspiratory efforts, followed by double triggering.⁽⁸⁾

When the entire period of MV is taken into account, asynchronies are slightly more frequent in pressure support ventilation (PSV) than in volume control-continuous mandatory ventilation or pressure control-continuous mandatory ventilation.⁽⁹⁾

Nevertheless, within each mode, the settings for peak airflow, airway pressure, minute ventilation, rise time, and the criteria to terminate inspiration can strongly affect asynchrony generation.⁽¹⁰⁾

The efforts to minimize asynchrony are being observed and its beneficial outcome on patient morbidity is expected to have a fruitful end.

Patients and Methods:

This prospective study was carried out upon 60 patients from 2 to 180 months, 38 males and 22 females, with spontaneous triggering on MV, admitted to the PICU, Tanta University Hospital. This study was conducted between September 2020 and July 2022.

Ethical considerations

- The study was accepted by the Research Ethics Committee of Faculty of Medicine Tanta University before starting the field work.
- An informed consent was signed by all the patients.
- Explanation of the study aim in a simple manner to be understood by the common people.
- The patient had the right to get a copy from the informed consent.
- No harmful maneuvers were performed or used.
- All data were considered confidential and did not used outside this study without patient's approval.
- All patients were notified with the results of imaging.
- Patients had the right to withdraw from the study at any time without giving any reason and were excluded from the study.
- The patient did not pay for any investigations in the research.

The studied patients were divided according to MV modes into three groups:

Group (I): Twenty patients on pressure SIMV+ PSV mode.

Group (II): Ten patients on volume SIMV+ PSV mode.

Group (III): Thirty patients on PRVC mode.

Inclusion criteria:

All patients aged from 2 months to 15 years, on invasive MV with spontaneous triggering for at least 7 days.

Exclusion criteria:

- Age more than 15 years old.
- Positive end-expiratory pressure > 9 cm H₂O.
- Ventilation through a tracheostomy.
- Inability to initiate breaths including that due to neuromuscular-blocking agents
- Patient with neuromuscular disorders.

Methods:

All studied patients were subjected to:

(1) Detailed history taking:

- Demographic data: name, age, sex, socio-economic status.
- Cause of PICU admission and MV.

- Length of PICU stay.
- Duration and mode of MV.
- (2) Thorough clinical examination:**
 - Anthropometric measurements.
 - Vital signs (blood pressure, heart rate, respiratory rate, temperature).
- (3) Neurological examination:**
 - Conscious level (all patients was on midazolam (Dormicum ®) sedative from 0.5-2 mic/kg/ hr intravenous infusion).
- (4) Routine investigation:**

Statistical analysis:

Statistical analysis was done by SPSS v27 (IBM©, Chicago, IL, USA). Shapiro-Wilks test and histograms were used to evaluate the normality of the distribution of data. Quantitative parametric data were presented as mean and standard deviation (SD) and were analysed by unpaired student t-test ^(11, 12)

Quantitative non-parametric data were presented as the median and interquartile range (IQR) and were analyzed by Mann Whitney-test ⁽¹³⁾.

Qualitative variables were presented as frequency and percentage (%) and were analyzed utilizing the Chi-square test or Fisher's exact test when appropriate ⁽¹⁴⁾. Repeated measures ANOVA was performed to compare the three measures within the same group ⁽¹⁵⁾.

two-tailed P value ≤ 0.05 was considered statistically significant.

Results:

Table (1): shows that regarding PIP: There was highly significant increase in group I compared with group II and III on the 1st, 2nd and 3rd days. Otherwise there was non-significant difference between studied groups.

Table (1): Comparison among the studied groups regarding peak inspiratory pressure (cm H₂O)

			Group I P-SIMV+PSV (n = 20)	Group II V-SIMV+PSV (n = 10)	Group III PRVC (n = 30)	Test	p		
PIP	1 st day	Mean±SD	16.65±3.17	13.8 ±3.61	14.25 ±2.59	F= 49.036	0.006*	p1	0.034*
		Range	11-22	10-21	10-18			p2	0.002*
					p3	0.876			
	2 nd day	Mean±SD	16.85 ±2.46	14 ±0.82	13.6 ±0.68	F = 15.454	<0.001*	p1	<0.001*
		Range	14-21	13-15	13-15			p2	<0.001*
					p3	0.184			
	3 rd day	Mean±SD	18.5 ±2.06	15.5 ±1.51	14.95 ±1.76	F = 16.630	<0.001*	p1	<0.001*
		Range	15-21	13-17	13-18			p2	<0.001*
					P 3	0.469			

Cm H₂O: centimeter water, PIP: Peak inspiratory pressure, PRVC: Pressure-regulated volume control, P-SIMV: Pressure-Synchronized intermittent mandatory ventilation, PSV: pressure support ventilation, V-SIMV: Volume-Synchronized intermittent mandatory ventilation.

* significant as p <0.05, P1: p between group I and group II, P2: p between group I and group III, P3: p between group II and group III, F: one-way ANOVA

Table (2): show that regarding PEEP: There was a highly significant increase in group II compared with group I on 1st day. There was significant increase in group II compared with group III on 1st day. Otherwise there was a non-significant difference between studied groups.

Table 2: Comparison among the studied groups regarding positive end-expiratory pressure (cm H₂O)

			Group I P_SIMV +PSV (n = 20)	Group II V-SIMV + PSV (n = 10)	Group III - PRVC (n = 30)	Test 5	P		
PEEP	1 st day	Mean ± SD	5.42 ± 0.51	7.5 ± 3.73	5.25 ± 1.1	F = 7.694	0.001*	p1	0.001*
		Range	5.00-7	4-9	4 -6			p2	0.971
						p3		0.031*	
	2 nd day	Mean ± SD	5.64 ± 1.43	6.89 ± 2.65	6.69 ± 3.45	F = 2.132	0.128		
		Range	4-8	4-7	4-7				
	3 rd day	Mean ± SD	5.62 ± 1.46	6.57 ± 2.83	7.03 ± 4.06	F = 1.690	0.194		
Range		4-9	5-9	5-10					

Cm H₂O: centimeter water, PEEP: Positive end-expiratory pressure, PRVC: Pressure-regulated volume control, P-SIMV: Pressure-Synchronized intermittent mandatory ventilation, PSV: pressure support ventilation, V-SIMV: Volume-Synchronized intermittent mandatory ventilation.

F: one-way ANOVA, * significant as p <0.05, P1: p between group I and group II, P2: p between group I and group III, P3: p between group II and group III.

Table (3): shows that regarding respiratory rate: There was a highly significant increase in group I compared with group II on 1st day. Otherwise there was non-significant difference among the studied groups.

Table 3: comparison among the studied groups regarding respiratory rate (Cycle/Minute)

			Group I pressure SIMV (n = 20)	Group II – SIMV+PSV (n = 10)	Group III – PRVC (n = 30)	Test of significance	P		
RR	1 st day	Mean ± SD	23.94 ± 6.16	18.11 ± 0.66	17.63 ± 0.44	F = 5.451	0.007*	P1	0.023*
		Range	15-35	17 -19	17-18			P2	0.090
						P3		0.992	
	2 nd day	Mean ± SD	21.16 ± 5.7	17.63 ± 0.4	17.81 ± 0.39	F = 2.149	0.126		
		Range	14- 30	17-18	17-18				
	3 rd day	Mean ± SD	20.15 ± 7.45	15.32 ± 2.99	16.5 ± 3.0	F = 2.034	0.140		
Range		10-30	12-18	12-18					

PRVC: Pressure-regulated volume control, P-SIMV: Pressure-Synchronized intermittent mandatory ventilation, PSV: pressure support ventilation, RR: respiratory rate, V-SIMV: Volume-Synchronized intermittent mandatory ventilation.

* significant as p <0.05, P1: p between group I and group II, P2: p between group I and group III, P3: p between group II and group III, F: one-way ANOVA.

ITI is a highly significant diagnostic for synchronization with P value <0.001 and 0.927 AUC (95% CI: 0.611 -0.765). Sensitivity was 88.89% (95% CI), specificity 98.04% (95% CI) (table 4).

Table 4: Validity of ITI for Diagnosis of Synchronization

Cut off	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	P	AUC
ITI >10	88.89% (51.8 - 99.7)	98.04% (89.6 - 100.0)	88.9% (53.1 - 98.3)	98.0% (88.7 - 99.7)	<0.001*	0.927

ITI: ineffective triggering index.

* Significant as p-value ≤0.05

In regression analysis, ITI, PIP/ITI on 1st day and SpO₂ on 3rd day were significant predictors for synchronization (Table 5).

Table 5: Logistic Regression of Different Variables for Prediction of Synchronization

	Coefficient	St. Error	P
Age (years)	0.004	0.008	0.573
Sex	-0.022	0.081	0.786
Duration of ventilation	-0.003	0.002	0.229
ITI	0.049	0.010	<0.001*
PIP	0.010	0.012	0.435
PIP/ITI at 1 st day	-0.034	0.015	0.035*
FiO ₂ at 1 st day	0.013	0.008	0.140
FiO ₂ at 2 nd day	-0.006	0.009	0.474
FiO ₂ /ITI at 1 st day	0.010	0.008	0.248
SpO ₂ at 3 rd day	-0.101	0.040	0.014*
PS at 3 rd day	-0.015	0.030	0.607
RR/ITI at 1 st day	-0.004	0.008	0.558

FiO₂: fraction of inspired O₂, ITI: ineffective triggering index, PIP: peak inspiratory pressure, PS: pressure support, RR: respiratory rate, SpO₂: oxygen saturation.

* Significant as P value ≤ 0.05.

Discussion:

The present study showed that there was a significant increase of PIP with ITI \geq 10% compared with ITI $<$ 10% on the 1st and 2nd days. There was a highly significant increase in PIP in P-SIMV group compared with V-SIMV group and PRVC on the 1st, 2nd and 3rd days.

In accordance to the present study, Thrill et al.,⁽¹⁾ found that patients with high incidence of DT, ITI had higher values of PIP, this may be due to the associated increased severity of lung injury.

However, De wit et al.,⁽¹⁶⁾ found that no correlation between PIP and asynchrony. This may be explained by the small sample size (pilot study).

The present study showed that there was highly significant increase of PEEP with ITI \geq 10% compared with ITI $<$ 10% on 2nd and 3rd day and There was significant increase in V-SIMV+PSV group compared with P-SIMV+PSV group and PRVC group on 1st day.

In accordance to the present study, Nava et al.,⁽¹⁷⁾ found that lower level PEEP in patients with COPD and high levels of intrinsic PEEP reduce the frequency of asynchrony.

This may be explained by that lower PEEP improve synchrony by reducing dynamic hyperinflation and improve the quality of sleep in chronically ventilated patients.⁽¹⁷⁾

However, Chao et al.,⁽²⁾ and Varon et al.,⁽¹⁸⁾ found that applying 5 cm H₂O of external PEEP had no influence on ITI.

This may be explained by their patient's diagnosis (intrinsic PEEP in COPD).⁽¹⁹⁾

The present study showed that there was significant increase of RR with ITI \geq 10% compared with ITI $<$ 10% in 1st and 2nd day and There was a highly significant increase in T_I with ITI \geq 10% compared to ITI $<$ 10% on 2nd and 3rd day.

In accordance to the present study, Purro et al.,⁽²⁰⁾ found that high RR occur with increased IT.

This may be explained by that the increase in frequency was proportional to the decrease in ventilator inspiratory time, IT occurs when the patient's demand is high, and T_I on the ventilator is too short.⁽²⁰⁾

However, Tassaux et al.,⁽²¹⁾ found that ITI was less frequent with high RR in patients with COPD.

This may be explained by the high flow often used for lowering intrinsic PEEP by achieving a shorter T_I and thus allowing more time for exhalation. In patients with COPD changing the

cycle criteria to a higher percentage of peak inspiratory flow (high frequency) decreased ITI and improve PVI.⁽²¹⁾

The present study showed that there was a significant increase in MV duration with ITI \geq 10% compared with ITI $<$ 10%.

In accordance with the present study, Chao et al.,⁽²⁾ Thille et al.,⁽¹⁾ and De wit et al.,⁽¹⁶⁾ found that patients with an asynchrony index \geq 10% had a longer duration of MV.

This may be explained by those patients with an ITI \geq 10% were more likely to require more than a week of MV due to inappropriate ventilator setting or greater disease severity.⁽²²⁾

However, Nava et al.,⁽²³⁾ found that no correlation between high-level asynchrony and the duration of MV. This may be explained by their usage of ventilator settings leading to a reduced frequency of wasted efforts.

Reference:

1. Pettenuzzo T, Fan E.; mechanical ventilation. *Respir Care* 2017;62(5):29-35.
2. Mauri T, Yoshida T, Bellani G, Goligher EC, Carteaux G, Rittayamai N, et al.; Pleural pressure working Group (PLUG—Acute Respiratory Failure section of the European Society of Intensive Care Medicine). Esophageal and transpulmonary pressure in the clinical setting: meaning, usefulness and perspectives. *Intensive Care Med* 2016; 42(9):1360-60.
3. Thille AW, Rodriguez P, Cabello B, Lellouche F, Brochard L.; Patient-ventilator asynchrony during assisted mechanical ventilation. *Intensive Care Med* 2006;32(10):1515-22.
4. Blanch L, Villagra A, Sales B, Montanya J, Lucangelo U, Luján M, et al.; Asynchronies during mechanical ventilation are associated with mortality. *Intensive Care Med* 2015;41(4):633-41.
5. Vaporidi K, Babalis D, Chytas A, Lilitsis E, Kondili E, Amargianitakis V, et al.; Clusters of ineffective efforts during mechanical ventilation: impact on outcome. *Intensive Care Med* 2017;43(2): 84-91.
6. Gilstrap D, MacIntyre N.; Patient-ventilator interactions. Implications for clinical management. *Am J Respir Crit Care Med* 2013; 150(4):896-903.
7. Murias G, Villagra A, Blanch L.; Patient-ventilator desynchrony during assisted invasive mechanical ventilation. *Minerva Anesthesiol* 2013;79(4):34-44.
8. Kallet RH.; Patient-ventilator interaction during acute lung injury, and the role of spontaneous breathing: part 1: respiratory muscle function during critical illness. *Respir Care* 2011;56(2):81-89.
9. Sassoon CS.; Triggering of the ventilator in patient-ventilator interactions. *Respir Care* 2011;56(1):39-51.
10. Georgopoulos D, Prinianakis G, Kondili E.; Bedside waveforms interpretation as a tool to identify patient-ventilator asynchronies. *Intensive Care Med* 2006;32(1):34-47.
11. Mishra P, Pandey CM, Singh U, Gupta A, Sahu C and Keshri A. Descriptive statistics and normality tests for statistical data. *Ann Card Anaesth.* 2019;22(1):67-72.
12. Mishra P, Singh U, Pandey CM, Mishra P and Pandey G. Application of student's t-test, analysis of variance, and covariance. *Ann Card Anaesth.* 2019;22(4):407-11.
13. Vermeulen K, Thas O and Vansteelandt S. Increasing the power of the Mann-Whitney test in randomized experiments through flexible covariate adjustment. *Stat Med.* 2015;34(6):1012-30.
14. Pandis N. The chi-square test. *Am J Orthod Dentofacial Orthop.* 2016;150(5):898-9.
15. Shen J and He X. Generalized F test and generalized deviance test in two-way ANOVA models for randomized trials. *J Biopharm Stat.* 2014;24(3):523-34.

16. Vignaux L, Vargas F, Roeseler J, Tassaux D, Thille AW, Kossowsky MP, et al. Patient-ventilator asynchrony during non-invasive ventilation for acute respiratory failure: a multicenter study. *Intensive Care Med* 2009; 35(5):840-6.
17. Ostermann ME, Keenan SP, Seiferling RA, Sibbald WJ. Sedation in the intensive care unit: a systematic review. *JAMA*.2000;283: 1451-9.
18. Fabry B, Guttman J, Eberhard L, Bauer T, Haberthur C, Wolff G, et al. An analysis of dyssynchronization between the spontaneously breathing patient and ventilator during inspiratory pressure support. *Chest* 1995; 107(5):1387-94.
19. Vitacca M, Bianchi L, Zanotti E, Vianello A, Barbano L, Porta R, et al. Assessment of physiologic variables and subjective comfort under different levels of pressure support ventilation. *Chest* 2004; 126:851-9.
20. Purro A, Appedini L, Degateono A. Appedini L, A physiological determinants of ventilator dependence in long term mechanically ventilated patients. *Am J Respir Crit Care Med* 2000; 161(4 pt1): 1115-23.
21. Tassaux D, Gainnier M, Battisti A, Jolliet P. Impact of expiratory trigger setting on delayed cycling and inspiratory muscle workload. *Am J Respir Crit Care Med* 2005; 172(10): 1283-9.
22. Thille AW, Cabello B, Galia F, Lyazidi A, Brochard L. Reduction of patient- ventilator asynchrony by reducing tidal volume during pressure support ventilation. *Intensive Care Med* 2005;172(10):1283-9.
23. Pohlman MC, Mc Callister KE, Schweickert WD, Pohlman AS, Nigos CP, Krishman JA, et al. Excessive tidal volume from breath stacking during lung protective ventilation for acute lung injury. *Crit. Care Med* 2008; 36 (11): 3019-23.