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Original Research Article

A Prospective Observational Study to Determine the Association of Prolonged Assisted Mechanical Ventilation (AMV) with Fluid Balance and Pediatric Index of Mortality 2 (PIM2) Score

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Abstract

Aim: This study was conducted to determine the association of prolonged Assisted Mechanical Ventilation (AMV) with fluid balance and pediatric index of mortality 2 (PIM2) score.

Methods: This prospective observational study was conducted over a period of 12 months in the pediatric intensive care unit (PICU) at Nalanda Medical College and Hospital, Patna, Bihar, India after obtaining approval from the institutional ethics committee. The study enrolled all patients admitted in the PICU of age 29 days to 12 years, who fulfill the inclusion criteria during the 12-month period.

Results: This was a study of 50 participants of which infants (<1 year) were maximum (26, i.e., 52%). Males outnumbered females comprising 58% (29) of the study population. Maximum number of admissions (16) had central nervous system involvement followed by respiratory system involvement. Out of the 50 children admitted in PICU during the study period, 35 (70%) children had prolonged mechanical ventilation. 33 patients had positive fluid balance ≥ 15%. 30 patients who had ≥15% positive fluid balance required prolonged mechanical ventilation. Similarly, 30 patients who had PIM2 score ≥ 5 required prolonged mechanical ventilation. The Pearson chi-square test was applied to test the significance of association between positive fluid balance and prolonged mechanical ventilation. P value was 2:25 × 10−7 which is <0.05 suggesting rejection of null hypothesis and statistically significant association between two variants.

Conclusion: There was a significant association of prolonged AMV with positive fluid balance (>15%) and PIM2 score (>5). By strict maintenance of fluid balance with appropriate intervention, the length of AMV and PICU stay can be decreased.

Keywords: Fluid Balance, Mechanical Ventilation, Children, Pediatric Intensive Care Units.

Introduction

Fluid balance is one of the most challenging aspects of critically-ill children requiring pediatric intensive care. While early and aggressive fluid resuscitation is lifesaving and widely practiced, excess fluid may be detrimental. Mechanically ventilated children may be more prone to fluid overload as they have lesser evaporative losses due to warmed, humidified gases and thermocontrolled environment. [1] Presence of non-osmotic stimuli, in addition to osmotic stimuli, for anti-diuretic hormone (ADH) release may contribute to fluid retention. [2,3] In addition, overestimation of fluid requirement occurs if traditional methods designed primarily for healthy children are used. [4] The Fluids and Catheters Treatment Trial (FACTT) in adults concluded that, patients managed with fluid restriction had lesser duration of intensive care unit stay and mechanical ventilation than patients who received liberal fluids. [5] The observations from few retrospective studies in children suggest adverse effects of positive fluid balance on respiratory morbidity and mortality. [6]

Mechanical ventilation is a crucial component of intensive care unit (ICU) that helps in supporting and sustaining life of critically ill patients. Ventilator-associated lung injury (VALI) is an inevitable consequence of assisted mechanical ventilation (AMV) [7,8], and to curtail the same in acute respiratory distress syndrome (ARDS), lung protective ventilation strategies have been developed, which has led to significant reduction in death rates. [9-11] Assisted mechanical ventilation (AMV) is a frequently used life-supportsystem which, in spite of its benefit, might cause damage. Unwanted consequences arising from the use of AMV are generically known as ventilator-associated lung injury, [12] and were the reason for lung protective ventilation strategies which resulted in a significant mortality reduction among patients with acute respiratory distress syndrome. [13,14]

After gathering data corresponding to initial 48 hours of AMV, this study is trying to exhibit the association between fluid balance and prolonged mechanical ventilation if any and generalizing the same to wider population range and, similarly, to study the association of prolonged mechanical ventilation with other variables such as pediatric index of mortality 2 (PIM2) score, hypoxic respiratory failure, cardiovascular failure, age and gender. [15,16]

This study was conducted to determine the association of prolonged AMV with fluid balance and pediatric index of mortality 2 (PIM2) score.

Materials and Methods

This prospective observational study was conducted over a period of 12 months in the pediatric intensive care unit (PICU) at Nalanda Medical College and Hospital, Patna, Bihar, India after obtaining approval from the institutional ethics committee. The study enrolled all patients admitted in the PICU of age 29 days to 12 years, who fulfill the inclusion criteria during the 12-month period from the initiation of the study excluding those children previously admitted in the PICU of any other hospital and referred from those hospitals. Study participants were enrolled for a period of 7 days.

At the time of admission, the patients' clinical profile was recorded in a prefixed case record form consisting of age, sex, date of admission, provisional clinical diagnosis, PIM2 score, and organ system primarily involved. Information regarding

results of blood investigations like arterial blood gas parameters (PaO2, base excess, FiO2) was collected from the hospital records. Recordings of total fluid given and total fluid output in the first 48 hours of mechanical ventilation were documented. Fluid balance was calculated by the difference between the total amount of fluid administered and the sum of all the losses experienced during the first 48 hours of AMV by using the formula ðfluid input − fluid output/weight × 100. [17,18] PIM2 score was calculated by tabulating the following information such as (1) whether the admission was emergency/elective (in case of surgeries), (2) any underlying premorbid conditions (cardiac arrest out of hospital, severe combined immune deficiency, leukaemia/lymphoma after the first induction, spontaneous cerebral haemorrhage from aneurysm or AV malformation, cardiomyopathy, myocarditis, hypoplastic left heart syndrome, HIV infection, and neurodegenerative disorder), (3) response of pupils to light, (4) mechanical ventilation at any time during the first hour in PICU, (5) systolic blood pressure, (6) base excess, and (7) FiO2/PaO2 ratio. [19] The associated factors for mortality were scrutinized with SPSS 17. PIM2 score was used as a tool to distinguish death and survival at a 99.8 cutoff with 95% confidence interval (CI).

PaO2/FiO2 ratio was measured, and if found <200 in the absence of cyanotic heart disease or left ventricular dysfunction, diagnosis of hypoxic respiratory failure was made. [20] Individual patients were evaluated for the presence of cardiovascular failure which is defined as arterial hypotension (<5th percentile for the age) or the need to use vasoactive drugs (dopamine, epinephrine, and norepinephrine at any dose). [21,22] Duration of mechanical ventilation, duration of PICU stay, and outcome were recorded subsequently and analysed with precision.

Statistical Analysis

Qualitative data such as nominal data included sex, provisional clinical diagnosis, organ system involved, cardiovascular failure, and hypoxic respiratory failure were represented in the form of frequency and percentage. The association between qualitative variables was assessed by the chi-square test, with continuity correction for all 2 × 2 tables and by Fisher's exact test for all 2 × 2 tables where the chi-square test was not valid due to small counts. In the presence of small counts in tables with more than two columns, adjacent column data was pooled and the chi-square test reapplied. Continuity correction was applied for all 2 × 2 tables after pooling of data. Fisher's exact test was applied for all 2 × 2 tables where P value of continuity correction was not valid due to small counts, in spite of pooling of data (e.g., association between duration of mechanical ventilation ≥ 7 days and organ system involved). Among qualitative data, ordinal data included PIM2 score and was represented using mean ± SD and median and IQR (interquartile range). Comparison of PIM2 measured between cases with duration of mechanical ventilation ≥ 7 days and <7 days was done using the Mann–Whitney test.

Results

Table 1: Association among the cases between duration of mechanical ventilation ≥ 7 days and fluid balance (≥15%)

Duration of mechanical ventilation ≥7 days	Fluid balance (≥15%)		Total
	Yes	No	
Yes	30	5	35 (70)
No	3	12	15 (20)
Total	33	17	50 (100)

This was a study of 50 participants of which infants (<1 year) were maximum (26, i.e., 52%). Males outnumbered females comprising 58% (29) of the study population. Maximum number of admissions (16) had central nervous system involvement followed by respiratory system involvement. Out of the 50 children admitted in PICU during the study period, 35 (70%) children had prolonged mechanical ventilation. 33 patients had positive fluid balance ≥ 15%. 30 patients who had ≥15% positive fluid balance required prolonged mechanical ventilation.

Table 2: Significance of association between positive fluid balance and prolonged mechanical ventilation and Significance of association between PIM2 score and prolonged ventilation

Significance of association between positive fluid balance and prolonged mechanical ventilation				
Chi-square test	Value	df	P value	Association
Pearson chi-square test	26.804	1	2:25 × 10−7	Significant
Continuity correction	22.953	1	1:66 × 10−6	Significant
Fisher's exact test			8:05 × 10−7	Significant
Significance of association between PIM2 score and prolonged ventilation				
Chi-square test	Value	df	P value	Association
Pearson chi-square test	19.177	1	1:19 × 10−5	Significant
Continuity correction	15.730	1	7:31 × 10−5	Significant
Fisher's exact test			5:15 × 10−5	Significant

Similarly, 30 patients who had PIM2 score ≥ 5 required prolonged mechanical ventilation. The Pearson chi-square test was applied to test the significance of association between positive fluid balance and prolonged mechanical ventilation. P value was 2:25 × 10−7 which is <0.05 suggesting rejection of null hypothesis and statistically significant association between two variants. Similarly, on applying the Pearson chi-square test to find out the association between PIM2 score and prolonged ventilation, observed P value was 1:19 × 10−5 (<0.05) suggesting statistically significant association. However, association of other variables with prolonged mechanical ventilation was not statistically significant. The mean duration of PICU stay was prolonged in patients who required prolonged mechanical ventilation.

Table 3: Correlation between duration of mechanical ventilation (days) and various other variables

Variables	Pearson	Duration of	Age	Duration	Fluid	PIM2

	correlation	mechanical ventilation	(yrs.)	of PICU stay (days)	balance (%)	score
Duration of mechanical ventilation (days)	Pearson's r	1.000	-0.224	0.925	0.297	0.034
	P value		0.165	0.01	0.063	0.833
Age (yrs.)	Pearson's r	-0.224	1.000	-0.175	-0.302	-0.031
	P value	0.165		0.280	0.059	0.852
Duration of PICU stay (days)	Pearson's r	0.925	-0.175	1.000	0.168	0.027
	P value	0.01	0.280		0.299	0.869
Fluid balance (%)	Pearson's r	0.297	-0.302	0.168	1.000	0.176
	P value	0.063	0.059	0.299		0.278
PIM2 score	Pearson's r	0.034	-0.031	0.027	0.176	1.000
	P value	0.833	0.852	0.869	0.278	

Correlation was found between duration of mechanical ventilation ≥ 7 days and fluid balance, PIM2 score ≥ 5, and duration of PICU stay with Pearson's r value 0.297, 0.034, and 0.925, respectively.

Discussion

Child admitted to PICU may require mechanical ventilation as a part of therapy for one or more reasons, for short or prolonged duration depending on indication for ventilation and multiple other factors which directly or indirectly contribute to the disease process. AMV is a frequently used life support system which, in spite of its benefit, might cause damage if appropriate principles are not followed. Multiple factors play important roles in determining duration of ventilation such as fluid balance, PELOD (pediatric logistic organ dysfunction) score, PIM2 score on admission, underlying comorbidities, and cardiovascular and respiratory failure on admission. [7,8]

The overall patients who had prolonged mechanical ventilation admitted to our PICU were 70.0% (35). Similar results were observed in the study done by Khwannimit and Koonrangsesomboon [23], which was 72.8% (763/1048), and the study was conducted in a tertiary referral university teaching hospital in southernThailand. In the study conducted by Vidal et al.[7], in a retrospective cohort of patients in the PICU of Hospital Italiano de Buenos Aires, 50.3% patients (82/163) had prolonged mechanical ventilation.

33 patients in this study had positive fluid balance of ≥15% and 35 patients (70%) had prolonged mechanical ventilation. 33 patients who had ≥15% positive fluid balance required prolonged mechanical ventilation. The Pearson chi-square test was applied to test the significance of association between positive fluid balance and prolonged mechanical ventilation. P value was $2{:}25 \times 10{-}7$ (<0.05) suggesting rejection of null hypothesis and statistical significance. In a study by Vidal et al.[7] on fluid balance and length of mechanical ventilation in children admitted to a single PICU, during the study period, 1655 patients were admitted; 249 remained on AMV for over 48 hours and 163 were included in the study. The univariate analysis showed that the age younger than 4 years old (OR 3.21, 95% CI: 1.38-7.48), respiratory disease (OR 4.94, 95% CI: 1.51-16.10), septic shock (OR 4.66, 95% CI: 1.10-19.65), PELOD > 10 (OR 2.44, 95% CI: 1.23-4.85), and positive balance > 13% of the body weight (OR 4.02, 95% CI: 1.08-15.02) were associated with prolonged mechanical ventilation.

In a study from a South African PICU by Ketharanathan et al. [24], one hundred consecutive PICU admissions were included; before PICU admission, 59 children received a median 8.0 (4.0–15.0) ml/kg of fluid bolus. During PICU admission, 40 patients received a median fluid bolus amount of 10.0 (3.0–27.5) ml/kg. A total of three patients had a fluid overload ðFOÞ% ≥ 10, even after correction for convalescent weight. The median minimum and maximum amount of maintenance fluid during PICU admission was 60 (46.0– 80.0) ml/kg/day and 100.0 (60.0–120.0)ml/kg/day, respectively. The PICU mortality was 8%, and 28-day mortality was 10%.

In a study by van Mourik et al. [25], 600 ARDS patients were studied to know the predictability of fluid balance with 28-day and 90-day mortality along with length of ICU stay. 156 patients (26%) died within 28 days. Patients with a higher cumulative fluid balance on day 7 had a longer length of ICU stay and fewer ventilator-free days on day 28. Similar results were found for 90-day mortality. A more positive fluid balance predicted mortality, and a negative fluid balance showed a trend towards survival. Confounding factors that alter fluid balance such as hemodialysis and diuretic use have been considered separately. However, in our study, none of the patient required hemodialysis or diuretics. [26]

Our study emphasises the significant association of prolonged mechanical ventilation (duration ≥ 7 days) with positive fluid balance ≥ 15% and PIM2 score ≥ 5 in children admitted to PICU. Strict fluid input and output monitoring and adjusting fluid intake accordingly in the first 48 hrs significantly affect duration of AMV and outcome. Appropriate fluid management plays a crucial role in PICU especially in ventilated patients by limiting the lung injury thereby oxygenation and final outcome. PIM2 score assessment helps in predicting the duration of ventilation and final outcome. However, there are other scoring systems such as PELOD which more precisely indicates the duration of ventilation. We would like to emphasise on the strict fluid input and output charting on admission and for whole duration of PICU stay, monitoring vitals and maintenance of normal oxygenation, because early recognition of excessive positive fluid balance, hypoxic respiratory failure, and cardiovascular failure and treating accordingly may alter the duration of mechanical ventilation and outcome of patients.

Conclusion

The study has demonstrated significant associations of fluid balance ≥ 15% and PIM2 score ≥ 5 with prolonged duration of mechanical ventilation. Patients who had positive fluid balance ≥ 15% had more chances of prolonged mechanical ventilation in comparison to those who had PIM2 score ≥ 5, indicating more significant association of positive fluid balance with duration of mechanical ventilation. We found less significant association with hepatobiliary and renal involvement; however, because of small sample size it cannot be applied to the general population. To establish a clear-cut association with organ system involvement and to strengthen the significance of association, further prospective studies are required with a large sample size.

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