Clinical Profile of Patients Requiring Prolonged Mechanical Ventilation and their Outcome in a Tertiary Care Medical ICU

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Abstract

Introduction: An increasing number of patients require mechanical ventilation and there has been a proportional increase in patients needing prolonged mechanical ventilation (ventilated for ≥ 21 days, for at least 6 hours per day). It accounts for about 10% of all mechanically ventilated patients. Although these patients represent a smaller proportion of intensive care unit (ICU) patients, they consume substantial ICU resources. We studied etiology, metabolic and clinical profile, complications and outcome of these patients.

Methods: This was a prospective observational study in the medical ICUs of a tertiary hospital over 18 months. All patients above 12 years of age requiring prolonged invasive mechanical ventilation were recruited. Detailed clinical and laboratory records were noted. Sequential Organ Failure Assessment (SOFA) score was calculated on admission.

Results: Of a total 1150 patients who were admitted in ICU during study duration, 34.5% (n=397) needed mechanical ventilation and 3.91% (n=45) required prolonged mechanical ventilation. Most common patient subsets were: acute inflammatory demyelinating polyneuropathy (AIDP) 28.50% (n=13), cerebro-vascular accident (CVA): 17.30% (n=8), tetanus 8.60% (n=4) and acute respiratory distress syndrome (ARDS) 6.50% (n=3). The mean age of patients was 32 years. Electrolyte imbalances observed were hypocalcaemia (84.44%), hypomagnesaemia (40.9%), hypokalemia (31.11%) and hypophosphatemia (23.8%). Ventilator-associated pneumonia (VAP) (53.33%) was the most frequent complication, followed by decubitus ulcers (40%) and deep vein thrombosis (8.89%). Mean duration of ICU stay was 57.02 days ± 44.73 days. Twenty six out of 45 patients (57.75%) were successfully weaned off ventilator support and discharged from the hospital. The SOFA score of patients who survived (mean 2.15) was lesser than that of patients who expired (mean 2.89) (p= 0.36, ns).

Conclusions: The incidence of prolonged mechanical ventilation in our study was 3.91% of total 1150 ICU admissions and 11.3% of the 397 patients requiring invasive mechanical ventilation. AIDP, CVA, tetanus and ARDS were the most common diagnoses. Survival in the study population was 57.75%. VAP was the most common complication. High incidence of hypocalcaemia, hypomagnesaemia, hypokalemia and hypophosphatemia was noted in patients requiring prolonged mechanical ventilation.

Editorial Viewpoint

- Prolonged mechanical ventilation (PMV) is nowadays encountered more due to better healthcare facilities to manage basic illnesses.
- Young patients with AIDP and ARDS related to tropical infections are the most benefited ones with PMV in this study.
- To setup facilities for PMV is the need of the hour.

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per day. PMV accounts for about 10% of all mechanically ventilated patients.\textsuperscript{12} Although these patients represent a smaller proportion of intensive care unit (ICU) patients, they consume substantial ICU resources.\textsuperscript{3} Studies from referral centers have found poor long-term survival among PMV patients, with 1-year mortality of 56–71%.\textsuperscript{1,4,7}

Of those who are transferred to long term care hospitals, 52% die within the first year of follow-up.\textsuperscript{8} Considering the high morbidity, mortality, and cost of PMV,\textsuperscript{9,10} there is an increasing interest in identifying PMV patients. There is paucity of Indian data on PMV.

The purpose of this study was to determine the incidence, etiology, co-morbidities, complications and prognosis associated with PMV in a tertiary healthcare centre in India.

Severity scores and organ failure scores could be useful in predicting the outcome of patients requiring prolonged ventilator support and thus help the medical decision making.\textsuperscript{11} The Sequential Organ Failure Assessment (SOFA) scoring system is a practical predictor of outcome in ICU patients.\textsuperscript{12}

**Material and Methods**

**Study design:** This was a prospective observational study in the Medical ICUs- Medical and Neurological ICU (MNICU) and Emergency Medical Services ICU (EMS ICU) of a tertiary hospital.

**Study duration:** Eighteen months (May 2012 to October 2013)

**Patients:** All patients needing mechanical ventilation and admitted in Medical ICUs (MNICU and EMS ICU) during the study period were screened and those requiring prolonged mechanical ventilation were included in the study. All patients needing mechanical ventilation were offered routine physiotherapy services. In addition patients needing PMV were given intensive physiotherapy. Patients were progressed towards ‘Upright and Moving’ position with help of bed cycle exercises and tilt table standing. Relatives were educated about 2 hourly rotations of the patient in order to prevent bed sores and basal atelectasis. Their inspiratory pressures were measured using ‘MPM 100’. Accordingly, respiratory muscle strengthening exercises of adequate intensity were given with help of inspiratory muscle trainer (IMT). Neck flexor strengthening exercises and abdominal binder were also given to promote early weaning. Patients put on mechanical ventilation outside our hospital (due to lack of data) were not included in the study. The study was conducted in compliance with the protocol after approval by Institutional Ethics Committee. Detailed clinical and laboratory records were noted in the case record form.

In the study, ventilator-associated pneumonia (VAP) was defined as, a new infiltrate on chest radiograph plus two or more of the following: fever >38.3°C, leucocytosis >12000/mm\(^3\), purulent trachea-bronchial secretions, reduction in gas exchange.\textsuperscript{13}

Sepsis was defined as Systemic Inflammatory Response Syndrome (SIRS) in response to an infectious process.\textsuperscript{14} [SIRS is the presence of two or more of: body temperature <36°C or >38°C, heart rate >90/min, respiratory rate >20/min or PaCO\(_2\)<32 mm Hg, WBC count <4000/mm\(^3\) or >12000/mm\(^3\) or 10% bands].

Severity of organ failure was quantified as per Sequential Organ Failure Assessment (SOFA) score.\textsuperscript{15}

**Outcome:** The primary end-point was either transfer out from ICU after successful weaning off ventilator support or death of the patient.

**Statistical Analysis**

Sample size calculation: Out of approx 900 patients admitted in Medical ICUs in a year (2011 statistics), approx 40% need mechanical ventilation. Out of those needing mechanical ventilation 5 to 13% require prolonged mechanical ventilation. Hence sample size was calculated as

\[900 \times 40/100 = 360 \text{ (approx. no. Of pts needing mechanical ventilation in 1 yr)}\]

\[360 \times 10/100 \times 1.5 = 54 \text{ (approx sample size for 18 months)}\]

Detailed analysis: Descriptive statistics were used. Continuous data was presented as mean ± S.D/ median [range]. Categorical data was presented as proportions. Normality of the data was checked using Kolmogorov-Smirnov test. Continuous data between two groups was analyzed using Mann-Whitney U test/ unpaired t test. Median survival was compared using Kaplan Meir survival curves and Cox regression was used to predict the hazard using different covariates. The analyses were done at 5% significance using SPSS 16.0 for Windows.

**Results**

**Demographics**

A total 1150 patients were admitted in the medical ICUs in the 18 months study duration. Of these, 397 required invasive ventilation and out of these 45 patients needed it for more than 21 days. Thus, 34.5% of total ICU admissions (397/1150) needed mechanical ventilator support and 3.91% of total ICU admissions (45/1150) needed PMV. Of the ventilated patients, 11.3% (45/397) needed PMV.

The mean duration of ICU stay of PMV patients was 57.02 days ± 44.73 days and the mean duration of mechanical ventilation in PMV patients was 47.84 days ± 40.79 days. There was a slight male predominance amongst patients needing PMV (26 males, 19 females). Thirty one patients (68.88%) were less than 40 years of age. Thirteen (28.88%) belonged to age group of 40 to 65 years and only one (2.22%) patient was above 65 years.

Table 1 gives the diagnoses of patients requiring PMV. Acute
Inflammatory Demyelinating Polyneuropathy (ADIP) (28.50%) and Cerebro-Vascular Accident (CVA) (17.30%) were the commonest diagnoses followed by tetanus (8.60%) and Acute Respiratory Distress Syndrome (ARDS) (6.50%).

Electrolyte imbalances observed were hypocalcaemia (84.44%), hypomagnesaeemia (40.9%), hyponatremia (33.33%), hypokalemia (31.11%) and hypophosphatemia (23.80%) (Table 2). Magnesium levels were tested only in 22 patients due to resource constraints. VAP (53.33%) and decubitus ulcers (40%) were the most frequent complications seen (Table 3).

Twenty six out of 45 patients (57.75%) were successfully weaned off ventilator support and discharged from the hospital. Eighteen patients (40%) expired and one patient was still on ventilator support at the end of study. This patient subsequently recovered.

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Table 4: Association of various predictors on outcome in PMV patients (N=44)

<table>
<thead>
<tr>
<th>predictor</th>
<th>P value</th>
<th>Hazard ratio</th>
<th>95% CI for hazard ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>.589</td>
<td>.692</td>
<td>.182 - 2.630</td>
</tr>
<tr>
<td>40-65 yrs age group</td>
<td>.620</td>
<td>2.71</td>
<td>.571 - 8.150</td>
</tr>
<tr>
<td>Hypocalcemia</td>
<td>.982</td>
<td>.976</td>
<td>.126 - 7.540</td>
</tr>
<tr>
<td>Hypophosphatemia</td>
<td>.953</td>
<td>1.047</td>
<td>.223 - 4.910</td>
</tr>
<tr>
<td>Hypokalemia</td>
<td>.530</td>
<td>.657</td>
<td>.177 - 2.437</td>
</tr>
<tr>
<td>Hyponatremia</td>
<td>.387</td>
<td>1.925</td>
<td>.436 - 8.497</td>
</tr>
<tr>
<td>SOFA Score</td>
<td>.357</td>
<td>1.152</td>
<td>.852 - 1.558</td>
</tr>
<tr>
<td>VAP</td>
<td>.230</td>
<td>2.229</td>
<td>.601 - 8.267</td>
</tr>
</tbody>
</table>

All values derived by multivariate analysis. SOFA: Sequential Organ Failure Assessment, VAP: Ventilator Associated Pneumonia.
ventilation is primarily determined by diagnosis at admission and degree of physiologic derangement as measured by APS.\textsuperscript{18}

In Table 5 we have compared the results of our study with 2 other studies on PMV. The incidence of mechanical ventilation is around 34\% in the study by Seneff et al as well as in our study while it is more than twice (70.7\%) in the U.K. based Lone et al study. This high incidence of mechanical ventilation in Lone et al study can probably be attributed to the strict ICU admission criteria in that region. Despite that, the need for PMV is approximately 4\%, both, in Lone et al and Our studies.

AIDP, stroke, SAH, tetanus and hypoxic encephalopathy were the commonest etiologies in our study (Table 1). Exact etiological comparison regarding PMV is not available in other Indian or international studies. We observed a very high incidence of electrolyte imbalances in PMV needing patients viz hypocalcaemia, hypomagnesaemia, hyponatremia, hypokalemia and hypophosphatemia (Table 2). These electrolyte abnormalities were studied for co-relation with outcome by Kaplan Meir survival curves and Cox regression analysis (Table 4). Hypocalcaemia had a hazard ratio of 0.982 with P value of 0.976 thus indicating no increase in risk. Serum phosphorus level abnormalities were associated with a slight higher risk of mortality. Hypophosphatemia had a hazard ratio of 1.047 with P value of 0.953. Hypokalemia did not contribute to increase in risk of mortality; (Hazard ratio 0.657). Lastly, hyponatremia had a hazard ratio of 1.38. 69\% of our patients were aged less than 40 years.

Seneff et al, in their study concluded that, for patients admitted to the ICU and ventilated on day 1, total duration of duration of the ventilator support in PMV patients was 47.84 ± 40.79 days. While the mean duration of ICU stay in this population was 57.02 ± 44.73 days. There was a slight male predominance in our cohort with a male to female ratio of 1.38. 69\% of our patients were aged less than 40 years.
Table 5: Prolonged mechanical ventilation: A comparison

<table>
<thead>
<tr>
<th>Study type</th>
<th>Benefit et al(^{a})</th>
<th>Lone et al(^{b})</th>
<th>Our Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study type</td>
<td>Prospective observational</td>
<td>Retrospective cohort study</td>
<td>Prospective observational</td>
</tr>
<tr>
<td>Study setting</td>
<td>Multicentric (42 ICUs) Medical and surgical</td>
<td>Multicentric (3 ICUs)</td>
<td>Single centre Medical ICU</td>
</tr>
<tr>
<td>Study duration</td>
<td>21 months (May 1988 to February 1990)</td>
<td>48 months (2002 to 2006)</td>
<td>18 months (May 2012 to October 2013)</td>
</tr>
<tr>
<td>Case definition</td>
<td>Patients needing mechanical ventilation</td>
<td>Patients needing PMV</td>
<td>Patients Needing PMV</td>
</tr>
</tbody>
</table>

Table 6: Ventilation duration and outcome in prolonged mechanical ventilation\(^{19}\)

<table>
<thead>
<tr>
<th>Study</th>
<th>Type of unit</th>
<th>Sample size</th>
<th>Mean age</th>
<th>Gender % female</th>
<th>Diagnoses</th>
<th>ICU days on ventilator</th>
<th>% Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indiher (1991)</td>
<td>NRCU(^{a})</td>
<td>171</td>
<td>NA</td>
<td>54</td>
<td>COPD</td>
<td>55</td>
<td>60</td>
</tr>
<tr>
<td>Potrat (1996)</td>
<td>RWC(^{a})</td>
<td>388</td>
<td>72</td>
<td>53</td>
<td>Med &gt; Surg</td>
<td>42</td>
<td>66</td>
</tr>
<tr>
<td>Clark (1997)</td>
<td>RWC</td>
<td>113</td>
<td>65</td>
<td>56</td>
<td>Med &gt; Surg</td>
<td>NA</td>
<td>61</td>
</tr>
<tr>
<td>Scheinorn (1997)(^{b})</td>
<td>RWC</td>
<td>1,123</td>
<td>69</td>
<td>57</td>
<td>Med &gt; Surg</td>
<td>44</td>
<td>71</td>
</tr>
<tr>
<td>Carson(^{b}) (1999)</td>
<td>RWC</td>
<td>133</td>
<td>71</td>
<td>52</td>
<td>Med &gt; Surg</td>
<td>25</td>
<td>50</td>
</tr>
<tr>
<td>Our study (2012-2013)</td>
<td>MNICU</td>
<td>45</td>
<td>32</td>
<td>42</td>
<td>Medical; N&gt; R</td>
<td>47.84</td>
<td>57.75</td>
</tr>
</tbody>
</table>

\(^{a}\) Noninvasive Respiratory Care Unit, \(^{b}\) Regional Weaning Center, a: mean, COPD: Chronic Obstructive Pulmonary Disease, Med: Medical, Surg: Surgical, N: Neurological, R: Respiratory

could not be established in view of a small sample size. Decubitus ulcer development was yet another frequent complication in our study patients. It was an observation that relatives who were compliant with patient care contributed better in preventing bed sores.

The outcome was studied in terms of mortality. 57.75% of our patients survived and were discharged home after successful weaning from PMV. A comparative data of patient profile, predominant diagnosis, ICU days on ventilator and percentage survival of 10 studies is given in Table 6. The mean age of patients in all other studies was >65 years. In our study the mean age was 32 years. In the West it is the elderly who predominantly require PMV. Our study brings out the vulnerability and need of a much younger population, both for ventilation and PMV. In most of other studies, there was a slight female predominance, whereas in our study, there was a slight male predominance. Most of the western studies were in mixed ICUs having medical as well as surgical patients. Our ICUs catered to medical and neurological patients. The mean duration of ventilation varied from 23 to 55 days. In our study it was 47.84 days. The mean survival of PMV patients is around 50% to 60% (57.75% in our study). Only in the studies by Dasgupta et al and Gracey et al do we have a higher survival of 82% and 94% respectively. The higher survival in these studies can be attributed to the study setting being in Noninvasive Respiratory Care Units (NRCU). Our study involved a sample size of 45 PMV patients over 18 months study duration at a single centre. The sample size is much higher in other studies which were multi-centric and involved Regional Weaning Centers (RWC).

Amongst all the variables studied, age of the patient was found to be an important outcome determining factor (Table 4). We divided the study population in three groups based on age. The young population (less than 40 year age) had the most favorable outcome while the elderly population (more than 65 year age) had the worst outcome. As compared to the young age group, Hazard ratio of 2.71 was associated with the middle age group. Here again the statistical significance could not be proven in view of a small sample size. No such strong corelation was seen between male or female gender and the outcome.

The APS (Acute Physiology Score) is calculated using the most abnormal value for each of 17 different clinical and physiologic variables over a 24-hr period. SOFA score is calculated using six variables, namely, PaO\(_2\)/FiO\(_2\) ratio, platelet count, total bilirubin levels, blood pressure and need for vasopressors, Glasgow Coma Score and serum creatinine levels. Thus SOFA score is a more feasible scoring system with less chance of personal/calculation errors. Hence we opted to use SOFA score in our study to predict the outcome of PMV needing patients. There was no statistically significant difference in the SOFA Score of patients who survived (SOFA Score: 2.15) and patients who expired (SOFA score: 2.89); P value being 0.357.

As majority of our patients were having primary neurological involvement with little affection of other system SOFA score was not very high in both survivors and nonsurvivors. Other limitation of our study was that calcium was not corrected for the albumin levels.

Although the utility and accuracy
of sophisticated predictors of mortality in the ICU, such as the APACHE scores, have been repeatedly validated, there are no such universally accepted scientific evidence-based predictors of PMV. Thus there is a need to develop a scoring system to predict the need and outcome in PMV patients. This scoring system will probably include primary diagnosis, age of the patient and electrolyte abnormalities along with other respiratory parameters as variables for determining the score.

There is also a need to study the number of PMV patients region-wise and establish Regional Weaning Centers (RWC) in India.

References