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The Characteristics and Duration of Mechanical Ventilator Use on Patient with Neuromuscular Paralysis Diseases in Intensive Care Unit (ICU) Prof. Dr. I.G.N.G. Ngoerah General Hospital Denpasar in December 2019 - December 2022

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ABSTRACT

Background: Amyotrophic Lateral Sclerosis (ALS), Guillain-Barre Syndrome (GBS), and Myasthenia Gravis (MG) are neuromuscular diseases which involved the dysfunction of peripheral nerves or muscles. Respiratory muscle weakness often happens in neuromuscular diseases, where it leads to the requirement of mechanical ventilation or even death from respiratory failure. This study aims to determine the characteristics and duration of mechanical ventilator usage in patients with neuromuscular paralysis diseases at Prof. Dr. I.G.N.G. Ngoerah General Hospital Denpasar.
Results: From December 2019 to December 2022, there were 5 GBS patients (20%), 19 MG crisis patients (76%), and 1 ALS patient (4%). The mean of age was 40.8 years and the majority was female. The average duration of ventilator use in GBS patients was 25.8 days, in MG crisis was 26.2 days, and in ALS was 30 days, therefore all of them were prolonged. The outcomes were 3 GBS patients (12%) lived and 2 GBS patients (8%) died; 14 MG crisis patients (56%) lived and 5 MG crisis patients (20%) died; and 1 ALS patient (4%) died. The ICU diagnosis which complicated the patients were electrolyte disturbances, hypoalbuminemia, and community or ventilator acquired pneumonia.
Conclusion: Neuromuscular disease mostly causes respiratory muscle weakness and results in increased mortality and morbidity requiring mechanical ventilation. Risk factors affecting the prolonged duration of ventilator use were electrolyte disturbances, hypoalbuminemia, and pneumonia.

Keywords: *length of ventilator usage, neuromuscular paralysis disease, amyotrophic lateral sclerosis, Guillain-Barre syndrome, myasthenia gravis, intensive care unit, Bali*

BACKGROUND

Neuromuscular disease is a group of disorders involving injury or dysfunction of peripheral nerves or muscles.[1] The incidence of neuromuscular disease ranges from 2.4 to 33.8 per 100,000 cases.[2] Neuromuscular disease is caused by any injury that can occur along the nerves. Some sites of injury are in the cell body such as Amyotrophic Lateral Sclerosis (ALS), in the Schwann cells such as Guillain-Barre Syndrome (GBS), and in the neuromuscular junction such as Myasthenia Gravis (MG).[1]
In neuromuscular disease, there is often respiratory muscle weakness that leads to death from respiratory failure.[3] There are four components that can contribute to the occurrence of respiratory failure and the need for mechanical ventilation. First, the upper airway response due to the weakness of facial, oropharyngeal, and laryngeal

muscles can interfere with swallowing and clearance of secretions, placing the patient at risk for aspiration. In addition, weakness of these muscles can result in mechanical obstruction of the upper airway, especially in the supine position. Second, weakness of the inspiratory muscles (diaphragmatic, intercostal, and accessory muscles) results in inadequate lung expansion, with microatelectasis, leading to ventilation or perfusion mismatch, and resulting hypoxemia. In this condition, the body will compensate with tachypnoea and small tidal volumes, however these conditions can exacerbate atelectasis which in turn increases the mechanical load on the already weakened respiratory muscles. Third, weakness of the expiratory muscles prevents adequate coughing and clearing of secretions, increasing the risk of aspiration and pneumonia. Finally, complications of acute illness, such as pneumonia or pulmonary embolism, can further increase the need for ventilation of an already failing respiratory system.[4]

The use of mechanical ventilation in neuromuscular disease has a different time span depending on the clinical condition and disease of the patient. Given the wide duration range, predictive factors for prolonged intubation will be helpful in guiding tracheostomy timing. One study identified three factors predictive of prolonged ventilation in patients with acute respiratory failure including pre-intubation HCO_3 >30 mEq/L ($p < 0.001$), peak vital capacity on the first to sixth days after intubation < 25 mL/kg ($p = 0.001$), and over 50 years of age ($p = 0.01$). From this study, patients would be intubated for more than 2 weeks if the patient had one, two, or three of the risk factors where each risk factor.[4]

Based on the description above, the use of mechanical ventilation in certain neuromuscular diseases is important in supporting the body's vital functions. Therefore, in this study aims to determine the characteristics and duration of mechanical ventilator usage in patients with neuromuscular paralysis diseases at Prof. Dr. I.G.N.G. Ngoerah General Hospital Denpasar.

METHODS

This research is a cross-sectional descriptive study on all patients with neuromuscular paralysis treated by the Neurology Department in the ICU room of Prof. Ngoerah Denpasar for the period December 2019 to December 2022. Data was obtained from the patient's medical records. Data collected included age, gender, duration of ventilator use, outcome, and admission and discharge diagnoses. The collected data was then processed using IBM SPSS (Statistical Package for Social Sciences) software version 21.

RESULTS

Of the 24 patients with neuromuscular paralysis who were treated in the Intensive Care Unit (ICU) at Prof. Dr. I.G.N.G. Ngoerah General Hospital Denpasar for the period of December 2019 to December 2022 found 5 GBS patients (20%), 19 MG crisis patients (76%), and 1 ALS patient (4%).

Table 1. Distribution of Neuromuscular Paralysis Diseases in Prof. Dr. I.G.N.G. Ngoerah General Hospital Period December 2019 – December 2022

Neuromuscular Paralysis Disease	Frequency (n)	Percentage (%)
Guillain-Barre Syndrome	5	20%
Myasthenia Gravis Crisis	19	76%
Amyotrophic Lateral Sclerosis	1	4%
Total	25	100%

From patients with GBS, MG crisis, and ALS, data were obtained such as age, sex, duration of ventilator use, and outcome. The youngest patient was 25 years old and the oldest was 61 years old, with a mean age of 40.8 years. Majority of the samples, 14 subjects (56%), were female and there were 11 male (44%). The duration of ventilator

use in GBS patients was 2 days to 2 months with an average of 25.8 days, in MG crisis patients was 1 day to 10 months with an average of 26.2 days, and in ALS patient was 1 month or 30 days. Outcome of GBS patients were 3 patients (12%) lived and 2 patients (8%) died, in MG crisis 14 patients (56%) lived and 5 patients (20%) died, and 1 patients (4 %) died with diagnosis of ALS from a total of 25 patients.

Table 2. Patients Characteristics of Neuromuscular Paralysis Diseases in Prof. Dr. I.G.N.G. Ngoerah General Hospital Period December 2019 – December 2022

Characteristic	Frequency (n)	Percentage (%)	Mean
Age			
1. Youngest	25 years	-	
2. Oldest	61 years	-	40.8 years
Gender			
1. Male	11	44%	-
2. Female	14	56%	-
Duration of Ventilator Use			
1. GBS	2 days – 2 months	-	25.8 days
2. MG Crisis	1 day – 10 months	-	26.2 days
3. ALS	1 month	-	30 days
Outcome			
1. GBS			
a. Live/Observation	3	12%	-
b. Death	2	8%	-
2. MG Crisis			
a. Live/Observation	14	56%	-
b. Death	5	20%	-
3. ALS			
a. Live/Observation	-		-
b. Death	1	4%	-

From the data of five subjects diagnosed with GBS, 2 subjects (40%) experienced complications of electrolyte and/or hypoalbuminemia who lived and being observed, 1 subject (20%) experienced Community Acquired Pneumonia (CAP) complications, 1 subject (20%) experienced Ventilator Acquired Pneumonia (VAP) complications and died, and 1 subject (20%) experienced VAP complications and electrolyte and hypoalbuminemia disturbances and died.

Table 3. Diagnosis of ICU Discharge in Patients Admitted to ICU with GBS

	Electrolyte Disturbance and/or Hypoalbuminemia	**CAP**	**VAP**	**Without Other Complications**
GBS	2 (40%) (live/observation)	1 (20%) (live/observation)	1 (20%) (died)	-
Electrolyte Disturbance and/or Hypoalbuminemia	-	-	1 (20%) (died)	-
CAP	-	-	-	-
VAP	-	-	-	-

CAP: Community Acquired Pneumonia; VAP: Ventilator Acquired Pneumonia.

From the data of 19 subjects diagnosed with MG crisis, 5 subjects (26%) experienced CAP complications who lived and being observed while 1 subject (20%) died, 4 subjects (21%) experienced VAP complications who lived and being observed, whereas 2 subjects (10%) died, 3 subjects (15%) experienced complications of CAP and electrolyte and hypoalbuminemia who lived and being observed, 1 subject (5%) experienced complications of VAP and electrolyte and hypoalbuminemia who lived and being observed, 1 subject (5%) had no complications and 2 subjects (10%) died.

Table 4. Diagnosis of ICU Discharge in Patients Admitted to ICU with MG Crisis

	Electrolyte Disturbance and/or Hypoalbuminemia	**CAP**	**VAP**	**Without Other Complications**
MG Crisis	-	5 (26%) (live/observation) 1 (5%) (died)	4 (21%) (live/observation) 2 (10%) (died)	1 (5%) (live/observation) 2 (10%) (died)
Electrolyte Disturbance and/or Hypoalbuminemia	-	3 (15%) (live/observation)	1 (5%) (live/observation)	-
CAP	-	-	-	-
VAP	-	-	-	-

CAP: Community Acquired Pneumonia; VAP: Ventilator Acquired Pneumonia

From the data of subjects diagnosed with ALS, there was 1 subject (100%) experiencing VAP complications and electrolyte and/or hypoalbuminemia who died as the outcome.

Table 5. Diagnosis of ICU Discharge in Patients Admitted to ICU with ALS

ALS	**Electrolyte Disturbance and/or Hypoalbuminemia**	**CAP**	**VAP**	**Without Other Complications**
	-	-	-	-
Electrolyte Disturbance and/or Hypoalbuminemia	-	-	1 (100%) (died)	-
CAP	-	-	-	-
VAP	-	-	-	-

CAP: Community Acquired Pneumonia; VAP: Ventilator Acquired Pneumonia.

DISCUSSIONS

Neuromuscular diseases are conditions that affect the skeletal muscles, motor nerves or the neuromuscular junction. Most of these diseases are characterized by progressive destruction of muscle fibers with reduced muscle strength, disability, and quality of life associated with poor health of the patient.[5] Neuromuscular disorders encompass a large group of genetic conditions that affect approximately 1 in 1000 individuals worldwide.[1]

Based on the results, the age distribution of neuromuscular disease varies widely. Deenen et al. stated that neuromuscular disorders are more prevalent in childhood because most patients with neuromuscular diseases have symptoms early in life or even at birth.[6] Another study by Deenen et al. also mentioned the age distribution of the neuromuscular disease showed a diverse distribution. Friedreich ataxia, Duchenne muscular dystrophy and congenital muscular dystrophy occur early in life, whereas ALS, post-polio syndrome, Lambert-Eaton myasthenic syndrome and inclusion body myositis are discovered later in life.[2]

Gender of neuromuscular diseases are evenly distributed among men and women. Several neuromuscular diseases are predominantly male, including ALS, chronic inflammatory demyelinating polyneuropathy, Guillain-Barre syndrome, Lambert-Eaton myasthenic syndrome, Duchenne and Becker muscular dystrophies, and facioscapulohumeral dystrophy. Meanwhile Myasthenia gravis, non-dystrophic myotonia, polymyositis and dermatomyositis occur twice as often in women.[2] The results of this study are in accordance with the data above where the distribution of neuromuscular diseases was found to vary in both men and women where the number of male and female patients was almost the same.

Age and gender can affect the duration of ventilator use. However, in a study belonging to Khalil et al., there was no significant relationship between the age and gender and the duration of mechanical ventilation ($p > 0.05$).[9] This study was also in accordance with the study of Richard et

al. where there were 95 patients with acute respiratory failure aged 69.6 ± 9.3, 52.6% were males and 47.3% were females. They found no statistically significant relationship between age, gender, and mechanical ventilation results.[10]

In neuromuscular disease, the most alarming symptom is respiratory muscle weakness which can result in death. Respiratory muscle weakness initially causes hypoventilation and difficulty speaking and swallowing. This is then exacerbated by repeated aspiration. Normally, there is a cough mechanism to clear the airway. However, an effective cough mechanism requires good inspiratory, expiratory, and bulbar muscle function. Therefore, this mechanism cannot be carried out in neuromuscular patients with respiratory muscle weakness. Weak respiratory muscles often require mechanical ventilation. The duration of mechanical ventilation can be related to whether the underlying disorder is reversible such as GBS and MG, or rapidly progressive such as ALS. In addition, accompanying diseases or complications also affect the duration of ventilation use.[3]

Prolonged Mechanical Ventilation (PMV) and failure to wean are factors associated with prolonged hospital stay and increased morbidity and mortality.[7] The National Association for Medical Directions of Respiratory Care (NAMDRC) conference defines PMV as at least 21 days of continuous mechanical ventilation (MV) for six or more hours per day. The weaning process was first described at the International Consensus Conference (ICC) which, in 2005, defined three categories of weaning: easy weaning (ICC group 1), difficult weaning (ICC group 2), and prolonged weaning (ICC group 3). According to these criteria, prolonged weaning was defined as the weaning process in a patient who has failed at least three attempts at weaning or who requires more than 7 days of weaning after the first spontaneous breathing attempt. In 2016, the Weaning According to a New Definition (WIND) study group revised this weaning category and suggested adding an additional "no weaning" category consisting of patients who had never attempted weaning. In addition, WIND recommends that ICC group 3 be divided into group 3a (prolonged weaning with successful weaning of seven days or more after the first attempt) and group 3b (prolonged weaning without success). The current German "Prolonged weaning" guidelines further divide patients with failed weaning into Group 3b, who are discharged with persistently invasive MV and Group 3c patients who died in hospital.[8]

Based on the definition, the duration of ventilator use was mostly prolonged use. Although some patients were only on a ventilator for 1 or 2 days, most patients were on a ventilator for more than 7 days. This is related to the data that the average duration of ventilator use in patients with GBS was 25.8 days, MG crisis was 26.2 days, and ALS was 30 days. In specialized weaning centers, successful weaning is possible in about 60% of cases. Therefore, it is important to assess the risk of prolonged weaning in a patient in order to take specific steps for high-risk patients or to plan timely transfer to a dedicated weaning facility if needed.[8]

Some of the risks that affect the long duration of ventilation use are electrolyte disturbances, hypoalbuminemia, and pneumonia. Regarding electrolyte disturbances, hypophosphatemia, hypomagnesemia, and hypocalcemia are considered important factors for myopathy and neuropathy. Regarding serum albumin and its association with neuromuscular dysfunction such as GBS, a study by Khalil et al. suggested a significant relationship between hypoalbuminemia and respiratory muscle weakness ($p = 0.037$).[9]

In this study, most subjects had pneumonia, both CAP and VAP. Pneumonia may result from repeated aspiration and ineffective bulbar system. In GBS, respiratory muscle weakness may progress rapidly and bulbar function is frequently impaired.

Consequently, invasive ventilation is usually more appropriate than NIV.[3] Clinical features on admission inform the risk of early respiratory failure. Risk of respiratory insufficiency within 7 days of Guillain-Barre Syndrome using the Erasmus GBS Respiratory Insufficiency Score.[10,11]

In the study of Orlikowski et al., pneumonia occurred in 53-83% of patients who received MV for GBS. In that study, longer time in ICU since admission to intubation, and repeated aspiration were factors associated with early-onset pneumonia.[12] VAP is usually caused by Gram-negative bacteria, either single or polymicrobial infection or also by Gram-positive bacteria. The American Thoracic Society suggests that the bacteria that cause late onset VAP are S. aureus (29%), Gram negative rods (15%), S. pneumoniae (9%) and Pseudomonas sp. (4%). Multiple Drug Resistant Organism (MDRO) pathogens are mostly found in patients with late-onset VAP or those who are immunocompromised.[13]

This cross-sectional study confirmed the association between prolonged MV and higher residual disability in these patients after 11 years of follow-up. This study also suggests that after prolonged MV, patients may show slow but continuous recovery over many years and most will even regain the ability to walk unaided and attain a state of independence. Meanwhile, in MG crisis, the factors that predict failure of extubation are a history of having had a previous MG crisis, atelectasis, and pneumonia. This is consistent with research by Seneviratne et al. which identified atelectasis as the strongest predictor of reintubation.[15]

Thymectomy in Thymoma Associated with Myasthenia Gravis (TAMG) patients has a better outcome or prognosis compared to patients without thymectomy. This can happen because thymectomy reduces the effects of respiratory muscle weakness due to reduced effects of respiratory muscle paralysis due to MG crisis. These results are also supported by other factors such as younger age so that the prognosis in post-thymectomy TAMG patients will be better.[16]

In ALS, bulbar function can be assessed using the revised ALS Functional Rating Scale (ALSFR) scores. ALSFRS assesses speech rate, impaired swallowing, and abnormalities of salivation. Each question has a five-point scale from 0 = not able to, to 4 = normal ability.[17] Most ALS require a long ventilation duration of more than 14 days with a poor ALSFR score. This is influenced by the clinical condition of the patient at admission and accompanying diseases such as pneumonia.[3]

CONCLUSION

Neuromuscular paralysis assessed were GBS, MG crisis, and ALS. Neuromuscular disease mostly causes respiratory muscle weakness and results in increased mortality and morbidity requiring mechanical ventilation. Risk factors that can affect the long duration of ventilation use such as electrolyte disturbances, hypoalbuminemia, and pneumonia.

List of Abbreviations

ALS : Amyotrophic Lateral Sclerosis
ALSFR: Amyotrophic Lateral Sclerosis Functional Rating Scale
CAP : Community Acquired Pneumonia
GBS : Guillain-Barre Syndrome
ICC : International Consensus Conference
ICU : Intensive Care Unit
MDRO: Multiple Drug Resistant Organism
MG : Myasthenia Gravis
NAMDRC: National Association for Medical Directions of Respiratory Care
NIV : Non-invasive Ventilator
PMV : Prolonged Mechanical Ventilation
SPSS : Statistical Package for Social Sciences
TAMG: Thymoma Associated with Myasthenia Gravis
VAP : Ventilator Acquired Pneumonia
WIND : Weaning According to a New Definition

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