

Magnesium and Phosphate Ion Levels in Mechanically Ventilated Patients Treated at Persahabatan Hospital's Intensive Care Unit (ICU) and Respiratory Intensive Care Unit (RICU) in 2018

Filemon Suryawan Handjaja¹, Menaldi Rasmin¹, Prasenohadi¹, Ernita Akmal²

¹ Department of Pulmonology and Respiratory Medicine, Faculty of Medicine, Universitas Indonesia, Persahabatan Hospital, Jakarta, Indonesia

²Anesthesiology Functional Medical Staff, Intensive Care Installation - Persahabatan Hospital, Jakarta, Indonesia

Abstract

Background: History shows that respiratory system has a long and complicated arrangement so that many factors can affect a human's ability to breathe. Some electrolytes often considered as most important are sodium (Na⁺), potassium (K⁺), calcium (Ca²⁺) and chloride (Cl⁻). Other than that, magnesium (Mg²⁺) and phosphate (PO₄³⁻) are also important in all processes, especially at the neuromuscular junction and in muscle cells as adenosine triphosphate (ATP). Some researchers have found that PO₄³⁻ affected patients' clinical condition and ventilator weaning success, although Mg^{2+} gave inconsistent results. Until now, there have not been any studies or data about the significance of Mg^{2+} and PO_4^{3-} in ventilator weaning in Indonesia.

Methods: This was a cross sectional study with total sampling. A vein blood sample was taken after ICU/RICU admission at Persahabatan Hospital. Blood sample was taken consecutively until it reached a minimum of 30 subjects (pilot study). All patients found with mechanical ventilation were included, except for patients with complicated procedure (e.g. avian influenza, multidrug-resistant tuberculosis). Blood sample was analyzed for Mg²⁺, inorganic phosphate (Pi) and other additional tests. Failure in weaning was defined as reintubation within 48 hours after extubation or failure in the spontaneous breathing trial (SBT).

Results: Of the 31 subjects evaluated, there were 3 patients with weaning failure. The median Mg²⁺ value was 0.5 (0.5-2.6) in successfully weaned patients and 0.6 (0.6-2.7) in patients with weaning failure, lower than its normal value. The mean Pi value was 4.21±1.17 (normal value) in successfully weaned patients and 5.43±0.47 (high value) in patients with weaning failure. Further analysis found that no significant relation was found between weaning and patient's characteristics other than heart rate and Ca²⁺, although it was not clear if there were some biases which could affect these results. Low Mg²⁺ value was observed in 23 subjects, no low Pi value was seen in all subjects, high Mg²⁺ value was found in 1 subject, high Pi value was observed in 11 subjects, and the rest was in the normal range.

Conclusion: The median Mg^{2+} value in both weaning groups (successful and failed) were below the normal limit at 0.5 (0.5-2.6) and 0.6 (0.6-2.7). Mean Pi value in the successful weaning group was 4.21±1.17 (within normal range), and the value in failed weaning group was 5.43±0.47 (above normal range).

Keywords: magnesium, mechanical ventilation, phosphate, weaning

INTRODUCTION

The respiratory system is one of the important mechanisms that support human life. This system has many pathways that must be passed from the central nervous system to the respiratory muscles as effectors in carrying out their functions. All of these pathways can be grouped into the neuro-respiratory system. Galen was a doctor from Greece who realized that enslaved people or animals that had trauma to the vertebrae below the neck could still breathe spontaneously. In contrast, breathing Corresponding Author: Filemon Suryawan Handjaja | Department of Pulmonology and Respiratory Medicine, Faculty of Medicine, Universitas Indonesia, Persahabatan Hospital, Jakarta, Indonesia | drfilemonsh@gmail.com

Submitted: December 10th, 2020 Accepted: February 27th, 2023 Published: July 28th, 2023

J Respirol Indones. 2023 Vol. 43 No. 3: 167–76 https://doi.org/10.36497/jri.v43i3.456

Creative Commons

Attribution-

NonCommercial 4.0 International License

movements immediately disappeared in high-lying vertebral trauma (the neck area). Since then, the role of the central nervous system in controlling respiration has been understood.^{1–3}

• •

Control of the respiratory system by the central nervous system was first described by a neurologist named Whytt. He realized that breathing could be controlled at will, even though it was involuntary. Lorry, in 1760 postulated that areas of the brainstem control regular breathing. This was concluded from the persistence of respiratory movements in rabbits after the cerebrum and cerebellum of the rabbit were removed. A French scientist named Francois-Frank discovered the cortical (voluntary) breathing control center when he saw changes in breathing patterns in experimental animals that were given stimulation in their cortex.^{1,4}

This history shows that the respiratory system has a long and complicated arrangement. Many factors can affect human breathing ability. There have been no studies directly on human muscles in vitro to date, but many studies have been conducted on mammals that can be compared. Some important ions that are often considered are sodium (Na+), potassium (K⁺), calcium (Ca²⁺), and chloride (Cl-). Magnesium (Mg²⁺) and phosphate (PO4³⁻) are also important in all the processes, especially in the muscle-nerve junction and the muscle itself.^{5–8}

Several researchers, such as Dhingra et al, Fiaccadori et al, Moe, Aubier et al, Gravelyn et al, and Zhao et al, showed the importance of Mg^{2+} and PO_4^{3-} levels on respiratory muscle strength and successful weaning in patients treated in Intensive Care Unit (ICU).^{9–14} Dhingra et al and Fiaccadori et al gave conflicting results regarding the importance of Mg^{2+} levels to the clinical condition of patients.^{9,10}

Other researchers provided similar results regarding the importance of PO_4^{3-} levels to the clinical condition of patients and the success rate of weaning from invasive mechanical ventilation.^{11–14} Until now, no similar studies have been conducted in Indonesia with patient characteristics that differ from previous studies. This study aims to find basic data on Mg²⁺, PO₄³⁻ level profiles, physiological profiles, and other pathological profiles in patients with invasive mechanical ventilation.

This study aimed to determine the physiological and pathological profiles of ICU and RICU patients with invasive mechanical ventilation at Persahabatan General Hospital after the first weaning and after successful re-weaning.

METHODS

The study was conducted with a crosssectional design in patients treated in the ICU and RICU of Persahabatan General Hospital who used invasive mechanical ventilation. The study population was all ICU and RICU care patients at Persahabatan Hospital from January 1st, 2018, to December 31st, 2018.

The study sample was all ICU and RICU patients at Persahabatan Hospital who used invasive mechanical ventilation from January 1st, 2018, to October 30th, 2018, and underwent the weaning procedure at least once during the treatment period. The minimum number of samples in the pilot study, according to Johanson et al, was 30 subjects, but as many as possible were taken during the sampling period.¹⁵

All patients admitted to ICU and RICU were going to be examined according to the APACHE II score plus other tests as contained. All therapy and patient intake were recorded and included in the study status. Subsequent checks were carried out after the first weaning and subsequent weaning if the first weaning failed and the last weaning was successful. If the second weaning and so on were not successful, there was no need to examine the study, according to the status of the study.

All blood specimens were taken and put into blood tubes without heparin. The specimen was then centrifuged for 30 minutes so that the serum could be examined. Electrolyte levels, especially Mg²⁺, were checked using pHOx Ultra by flowing the serum through an isoelectric membrane. The value was then calculated based on the movement of ions across the membrane. Pi levels were checked using the phosphomolybdate method and then exposed to 340 nm light, and the turbidity was calculated to determine the Pi value.

The inclusion criteria in this study were all lung patients treated at the ICU and RICU at Persahabatan Hospital who used invasive mechanical ventilation and underwent a weaning procedure at least once during the treatment period. Exclusion criteria in this study were patients aged less than 12 years to equalize the normal value of vital signs, patients with infectious infections that complicated the procedure (e.g., avian influenza), and the patient's family refused to collect patient data.

RESULTS

The total subjects included in the study were 32 patients, but 1 patient was excluded from the analysis because there were no calcium, magnesium, or phosphorus examination results. A total of 28 subjects successfully underwent weaning from invasive mechanical ventilation, and the remaining 3 subjects failed to undergo weaning. The characteristics of the study subjects were divided based on sex, age, BMI, BMI classification, Mean Arterial Pressure (MAP), MAP classification, pulse frequency, respiratory rate, O₂ saturation (pulse oximetry), hemoglobin, hematocrit, platelets, leukocytes, urea, creatinine, sodium, potassium, chloride, calcium, magnesium, phosphorus, APACHE II score, and disease classification (Table 1).

Table 1. Characteristics of study patient	Table 1.	Characteristics	of	study	/	patient
---	----------	-----------------	----	-------	---	---------

Characteristics	Value on weaning				
	Succeed	Fail			
Gender					
Men	16	1			
Women	12	2			
Age	45.07±16.42	46±14.11			
BMI	23.12±4.32	23.11±2.7			
BMI Classification					
Normal	14	3			
Abnormal	14	0			
MAP	99.89±21.51	77±18.66			
MAP Classification					
Low	1	1			
Normal	27	2			
Pulse frequency	95.9±27.85	133±31.77			
Breathing frequency	17.5 (12-31)	23±7			
O ₂ pulse saturation	100 (90-100)	100			
Hemoglobin	11.66±2.05	9.53±1.56			
Hematocrit	34.47±6.05	28.77±5.72			
Platelets (thousand)	233.5 (3-1.165)	408±236.32			
Leukocytes	15.935 (7.470-48.830)	24.240±9.530.11			
Urea	27 (13-244)	62.33±76.12			
Creatinine	0.75 (0.4-8.6)	1.47±1.51			
Sodium	135.96±4.27	136±8.19			
Potassium	3.85 (2.8-7.4)	5.06±1.27			
Chloride	103.51±5.96	104.67±8.02			
Calcium	1.23±0.07	1.33±0.1			
Magnesium	0.5 (0.5-2.6)	0.6 (0.6-2.7)			
Phosphor	4.21±1.17	5.43±0.47			
APACHE II score					
A score	8 (0-25)	4 (4-24)			
B score	2 (0-6)	1.67±1.53			
C score	0 (0-5)	0 (0-5)			
Total Score	11.5 (2-36)	14±11.36			
Disease Classification	11.0 (2.00)	11211.00			
Surgery					
Abdomen	11	1			
ENT	4	0			
Thorax	2	1			
Nerve	3	0			
Heart	3	0			
Bone	1	0			
	I	U			
Non-Surgical	<i>c</i>	4			
	5	1			
Abdominal malignancy	1	0			

A total of 16 of the 31 patients who were successfully weaned were male, and 12 \were female, while 1 male patient and 2 other female patients failed to wean. The mean age, BMI, sodium, and chloride in the successful weaning group were 45.07 ± 16.42 , 23.12 ± 4.32 , 135.96 ± 4.27 , and 103.51 ± 5.96 . These values were similar to those of the failed weaning group, namely 23.11 ± 2.7 , 23.11 ± 2.7 , 136 ± 8.19 , and 104.67 ± 8.02 . A total of 3 patients failed to wean and died (Table 1).

Value of MAP were normal in 2 patients and low (<65 mmHg) in 1 patient. The pulse rate was normal in 1 patient and increased (tachycardic) in 2 patients. Tachypnea was found in 1 patient, and normal respiratory rate was observed in 2 patients. A total of 2 of the 3 patients experienced hyponatremia and hypomagnesemia. K⁺ and Ca²⁺ values were normal in 2 of 3 patients. Hyperkalemia, hyperchloremia, hypercalcemia, and hypermagnesemia were present in 1 out of 3 patients who failed to wean. Hyperphosphatemia was found in all three patients. No hypophosphatemia was found in all patients who failed to wean.

The research subjects who underwent abdominal surgery were divided into several parameters. There were no low MAP values, hypopnea, hypochloremia, hypocalcemia, and hypophosphatemia in the 11 patients. Hyperkalemia was observed in 1 patient, hyperchloremia in 2 patients, and hyperphosphatemia in 4 study patients. Only 1 patient failed to wean in the surgical group.

Hypokalemia and hypocalcemia were not found in all ICU/RICU patients with pulmonary

infection indications. Hyponatremia was found in 3 patients, hypochloremia and hypomagnesemia in 2 patients, and hypophosphatemia in 1 patient. Hyperkalemia and hyperchloremia were obtained in 2 patients, hypercalcemia and hypermagnesemia in 1 patient, and hyperphosphatemia in 4 study patients. There was 1 patient who failed to wean in the pulmonary infection group.

The sexes of males and females did not show a significant difference in the two weaning groups, so there was no relationship between successful weaning and the sex of the research subjects. This relationship was analyzed using the Fisher's Exact test with an odds ratio (OR) of 2.67 (95% CI=0.22-0.33). There was no significant difference (unpaired t-test) between the mean ages of the successful weaning group and the failed weaning group, with a mean difference of 0.93 years (P=0.926).

The unpaired t-test showed no significant difference in the mean between the successful weaning group and the failed weaning group (P=0.997). BMI was combined into 2 groups, namely normal and abnormal. There was no significant correlation between BMI classification and invasive mechanical ventilation weaning (P=0.232) using the Fisher's Exact test. The OR value is also insignificant because it exceeds 1 (0.01-3.02) after the Haldane-Anscombe correction.¹⁶

Heart rate was significantly different between the successful and unsuccessful weaning groups with P=0.036 and a mean difference of ±37.5 mmHg. The failed weaning group had a higher pulse rate.

Table 2 Laborator	v results and weani	ng from invasive m	echanical ventilation
Tuble E. Euserater	y roound and mounn	ng nom mudon o n	

Chanastanistics	The mean/media	n at weaning	Average difference (05% CI)		
Characteristics	Succeed	Fail	Average difference (95% CI)	Р	
Hemoglobin	11.66±2.05	9.53±1.56	2.12 (-0.38 – 4.63)	0.093	
Hematocrit	34.47±6.05	28.77±5.72	5.7 (-1.79 – 13.2)	0.13	
Platelets (thousand)	233.5 (3-1.165)	408±236.32		0.181	
Leukocytes	15.935 (7.470-48.830)	24.240±9.530.11		0.316	
Urea	27 (13-244)	62.33±76.12		0.826	
Creatinine	0.75 (0.4-8.6)	1.47±1.51		0.925	
Sodium	135.96±4.27	136±8.19	0.04 (-5.74 – 5.81)	0.99	
Potassium	3.85 (2.8-7.4)	5.06±1.27		0.077	
Chloride	103.51±5.96	104.67±8.02	1.16 (-6.45 – 8.77)	0.758	
Calcium	1.23±0.07	1.33±0.1	0.1 (0.01 – 0.19)	0.024	
Magnesium	0.5 (0.5-2.6)	0.6 (0.6-2.7)		0.181	
Phosphor	4.21±1.17	5.43±0.47	1.22 (-0.19 – 2.63)	0.087	

Other vital sign parameters such as MAP, respiratory rate, and O_2 saturation had no significant association with weaning success (*P*>0.05). MAP had a normal average value in both groups, although there was a mean difference of ±22.89 mmHg between the two groups. The distribution of respiratory rate and O_2 saturation data in the two weaning groups was not normal, so it was impossible to calculate the mean difference. The MAP classification (low and normal) with a cut-off value of 65 mmHg did not have a significant relationship (*P*=0.187) with successful weaning.

The successful weaning group had similar

proportions to the failed weaning group in sodium (P=0.281) and calcium (P=0.097). Even so, the OR value of calcium levels did not exceed one, namely 34.2 (1.08–1079.3). Potassium, chloride, and magnesium levels did not have a significant relationship with the success of invasive mechanical ventilation weaning (P>0.05). Phosphorus levels showed no significant relationship with successful weaning (P=0.38), and the OR value exceeded 0.38 (0.01–11.31). The calculation of the ORs for potassium and phosphorus was carried out after the Haldane-Anscombe correction (added 0.5 in all proportions) because there are zeros in table 2x2.¹⁶

Table 3. Classification of electrolytes and we	The mean/medi	— P	OR	
Characteristics	Succeed	Fail	— P	(95% CI)
Classification of sodium				
Hyponatremia	9 (32.1%)	2 (66.7%)	0.281	0.24
Normal	19 (67.9%)	1 (33.3%)		(0.02 – 2.97)
Classification of potassium				
Hypokalemia	9 (32.1%)	0 (0.0%)		
Normal	16 (57.1%)	2 (66.7%)		
Hyperkalemia	3 (10.7%)	1 (33.3%)		
New classification				
Hypokalemia	9 (32.1%)	0 (0.0%)		3.41
Normal	19 (67.9%)	3 (100.0%)	0.537	(0.16– 72.95)
Hyperkalemia	9 (32.1%)	0 (0.0%)		(0.10-72.00)
Chloride classification				
Hypochloremia	4 (14.3%)	1 (33.3%)		
Normal	18 (64.3%)	1 (33.3%)		
Hyperchloremia	6 (21.4%)	1 (33.3%)		
New classification				
Hypochloremia	4 (14.3%)	1 (33.3%)	0.422	0.33
Normal/Hyperchloremia	24 (85.7%)	2 (66.7%)	0.422	(0.024–4.6)
Calcium Classification				
Normal	28 (100.0%)	2 (66.7%)	0.097	34.2
Hypercalcemia	0 (0.0%)	1 (33.3%)	0.097	(1.08–1079.3)
Magnesium Classification				
Hypomagnesemia	21 (75)	2 (66.7%)		
Normal	7 (25%)	0 (0%)		
Hypermagnesemia	0 (0.0%)	1 (33.3%)		
New classification				
Hypomagnesemia	21 (75.0%)	2 (66.7%)	1.000	1.5
Normal/hypermagnesemia	7 (25.0%)	1 (33.3%)	1.000	(0.117–19.18)
Phosphorus classification				
Hypophosphatemia		0 (0.0%)		
Normal		0 (0.0%)		
Hyperphosphatemia		3 (100.0%)		
New classification				
Hypophosphatemia	0 (0.0%)	0 (0.0%)	1.000	0.38
Normal/hyperphosphatemia	27 (96.4%)	3 (100.0%)	1.000	(0.01–11.31)

Calcium is significantly associated with invasive mechanical ventilation weaning (P=0.024). Calcium values in the successful group were ±0.1 mmol/L lower compared to the failed weaning group. Other laboratory results parameters did not significantly correlate with weaning success (Table 2). Platelets had guite a large difference in values (mean and mean) in the two weaning groups, although not statistically significant (P=0.181). The electrolyte results were divided into several groups and analyzed using crosstabs (Table 3). Several parameters, such as potassium, chloride, magnesium, and phosphorus, were divided into two groups (normal and abnormal) because they did not meet the chi-square requirements for the 3x2 table. If there are still zeros (0) after redistribution, then the Haldane-Anscombe correction is used to calculate OR.16

 Table 4. The relationship between magnesium and sodium, potassium and chloride

Laboratory	Magnesium	P	
Laboratory	Low	Normal/High	P
Sodium			
Hyponatremia	7 (30.4%)	4 (50.0%)	0.405
Normal	16 (69.6%)	4 (50.0%)	0.405
Potassium			
Hypokalemia	8 (34.8%)	1 (12.5%)	0.379
Normal/hyperkalemia	15 (65.2%)	7 (87.5%)	0.379
Chloride			
Hypochloremia	2 (8.7%)	3 (37.5%)	0 002
Normal/hyperchloremic	21 (91.3%)	5 (62.5%)	0.093

The APACHE II scores calculated within 24 hours after the study subjects were admitted to the ICU/RICU were divided into 3 scores, namely physiological scores (A), age (B), and chronic disease scores (C). Score A has an abnormal distribution of data in both groups and has no significant relationship (P=0.975) with successful weaning, as does score B (P=0.875), score C (P=0.925), and the total score (P=0.826). The C score had a median value of zero and similar minimum and maximum limits in the two groups. The A and B scores tended to be higher in the group that successfully weaned, while the total score tended to be higher in the group that failed to wean, although not significantly different (P>0.05). The Fisher's Exact test, carried out on sodium, potassium, and chloride levels on magnesium levels, did not give significant results (Table 4) with value of *P* are 0.405, 0.379, and 0.093.

Table 5.	The	relationship	betwee	en	phosphorus	and	sodium,
	potas	ssium and chl	oride				

Laboratory/	Phospho	Р		
Laboratory	Low	Normal	High	Ρ
Sodium				
Hyponatremia	1	4	6	
	(100.0%)	(21.1%)	(54.5%)	0.565
Normal	0	15	5	0.505
	(0.0%)	(78.9%)	(45.5%)	
Potassium				
Hypokalemia	0	7	2	
	(0.0%)	(36.8%)	(18.2%)	0.979
Normal/hyperkalemia	1	12	9	0.373
	(100.0%)	(63.2%)	(81.8%)	
Chloride				
Hypochloremia	0	2	3	
	(0.0%)	(10.5%)	(27.3%)	0.866
Normal/hyperchloremic	1	17	8	0.000
	(100.0%)	(89.5%)	(72.7%)	

None of the study subjects experienced hypernatremia. The potassium and chloride groups were divided into 2 groups, namely, low and normal/high levels because they did not meet the chi-square requirements for the 3x2 table. Sodium, potassium, and chloride levels did not significantly correlate with the blood's phosphorus levels (Table 5).



Figure 1. Scatter plot between magnesium and phosphate with other electrolytes

The value of P for the three electrolytes were 0.565, 0.979, and 0.866, respectively. The Kolmogorov-Smirnov test was used because it did not meet the chi-square requirements for a 2x3 table. The scatter plots between magnesium and phosphate with sodium, potassium, and chloride provide a picture consistent with the statistical test (Figure 1).

DISCUSSION

Due to limited funds and the feasibility of sampling, the total number of research subjects that could be analyzed was 31. Repeat laboratory examinations during weaning were not carried out because most patients were weaned before 24 hours of treatment in the ICU on RICU, especially postsurgery patients. Laboratory tests were also difficult to perform in non-surgical patients because the investigators were not always present during weaning. Characteristics of sex, age, BMI, BMI classification, MAP, MAP classification, respiratory frequency, O₂ saturation, blood laboratory results except for calcium levels, APACHE II A, B, C scores, and total were not significantly different between the two invasive mechanical ventilation weaning groups. The two groups had almost similar data.

Funk et al conducted a cohort study that included 257 patients with invasive mechanical ventilation during their stay in the ICU.¹⁷ The main outcomes were divided into 3 weaning groups: simple, difficult, and prolonged weaning. Age and gender were not significantly different in the three weaning groups, with P=0.58. Another study by Vallverdu et al, conducted on 217 patients, showed that age characteristics were not significantly different in the two weaning groups (successful and failed), which were divided into 3 disease groups (acute respiratory failure, COPD, and neurologic disease).¹⁸

The gender characteristics of this study did not differ significantly between the 2 weaning outcome groups, similar to the study of Vallverdu et al, Funk et al, O'Brien et al, and Anzueto et al also had similar study subject characteristics.^{17–20} These results indicated that age and type of gender were not confounding factor, although the number of subjects who failed to wean was only three.

BMI values and classifications did not differ significantly between the two invasive weaning groups. The average BMI value was only ± 0.01 kg/m² with a *P* value of 0.997. The proportion of BMI classification after being divided into normal and abnormal did not differ significantly, with *P*=0.232 (95% Cl=0.01–3.02). O'Brien et al conducted a prospective cohort study on 580 research subjects who were treated in the ICU using invasive mechanical ventilation and assessed the success of their first extubation based on their BMI group.²⁰

With successful weaning, Anzueto et al found that BMI did not have a significant correlation with the duration of invasive mechanical ventilation, length of stay, or mortality.¹⁹ However, a higher BMI increased complications during invasive mechanical ventilation, such as acute respiratory distress syndrome (ARDS) and kidney failure. In this case, BMI could be ruled out as a confounding factor.

The mean value of MAP in the successful weaning group was 99.89 \pm 21.51, higher than the failed weaning group (77 \pm 18.66), although not significantly different (*P*=0.088). Similarly, the MAP classification was not significantly different between the two weaning groups, and weaning success had no relationship with MAP score and classification. Khamiees et al studied 91 patients admitted to the ICU due to respiratory failure and obtained that pulse rate, respiratory rate, and MAP did not have a significant relationship with the successful weaning of these patients (Value of *P* are 0.81, 0.86, and 0.4, respectively).²¹

This study showed similar results except for pulse frequency. Both respiratory rate and MAP had P>0.05, while pulse frequency had P=0.036 when compared between the two weaning groups, with a mean difference of 37.55 (2.55–72.46). The mean pulse rate in the successful weaning group was within normal limits (95.9 beats/minute), while the failed weaning group tended to have tachycardia (133 beats/minute).

All laboratory parameters included in the study had no significant relationship (P>0.05) with weaning success except for blood calcium levels (P=0.024). The difference in mean blood calcium values in the two groups was 0.0 (0.01-0.19), with the successful weaning group having a lower value than the failed weaning group. Khamiees et al performed hemoglobin checks on all ICU patients who met the inclusion criteria and obtained a significant association with weaning success (P=0.01).²¹

However, the mean difference in hemoglobin was only ±1 mg/dL, so it was not clinically significant. In contrast to Table 2, hemoglobin levels did not have a significant relationship (P=0.093) with weaning success. Chang et al studied 175 subjects and compared the outcomes of successfully weaned patients and those who failed to wean (The outcome group had P=0.857 for white blood cells 10x10³/µl, 0.076 for BUN, mg/dL, and 0.706 for Creatinine, mg/dL).²² Table 2 shows that the above parameters have no significant relationship with weaning success, in contrast to the results of Chang's study.²²

Of the 31 study subjects found, 11 patients (35.5%) had hyponatremia, 9 patients had hypokalemia (29%), 5 patients (16.1%) had hypochloremia, no patients had hypocalcemia, 23 patients (74.2%) had hypomagnesemia, no patients had hypophosphatemia, 4 patients (12.9%) had hyperkalemia, (22.6%) 7 patients had hyperchloremia, 1 (0.03%) had patient 1 hypercalcemia, patient (0.03%)had hypermagnesemia, and 11 patients (35.5%) hyperphosphatemia. Fiaccadori et al observed a 20% incidence of hypomagnesemia in ICU patients.¹⁰ Another study by Fiaccadori et al in 1994 pointed out that serum phosphorus levels in patients with COPD were lower than the control group (P<0.001).¹¹

The APACHE II score did not have a significant correlation with weaning success in this study, including the A, B, and C scores which were the basic components. Study by Khamiees et al discovered that the APACHE II score was not significantly different in the two weaning groups with a P value of 0.46.²¹ Likewise, a study by Chang et al in 175 subjects obtained a P value of 0.664 when comparing the APACHE II scores in the successful versus failed weaning group.²² Keim-Malpass et al studied 1202 subjects and found that the difference in median APACHE II scores in patients living (14 [8-21]) and dying (19 [12-24]) during an ICU stay was significant, with a score difference of $\pm 5.^{23}$

Gholyaf et al, Ryzen et al, and Sabatier et al stated that low magnesium levels did not affect sodium (P=0.405), potassium (P=0.379), and chloride (P=0.093) levels.^{24–26} In contrast to the literature review by Huang et al in 2007, magnesium affected the potassium levels.²⁷ Hypomagnesemia is associated with hypokalemia by wasting potassium and increasing the effects of hypokalemia on target organs. No studies have assessed the relationship between phosphorus levels and levels of other electrolytes in the blood.

LIMITATION

Some of the limitations during the study were the number of research subjects, time to take blood samples for laboratory tests, and costs. The minimum number of subjects was 30, according to the rules for the number of pilot study samples. It was planned to collect more data, but the number of subjects was limited due to blood calcium, magnesium, and phosphorus examinations, which were not covered by state health insurance. The number of subjects who failed to undergo the weaning process was only a few (3 subjects) compared to the total study subjects (31 subjects), so confounding factors could not be removed. Many patients who can be taken as studv subiects use postoperative invasive mechanical ventilation, so patients with respiratory failure or distress due to other diseases were less representative of the analysis results. This research was still descriptive, and confounding factors could not be analyzed.

CONCLUSION

The median value of magnesium levels in both invasive mechanical ventilation weaning groups (success and failure) was below the normal range. The mean value of phosphorus levels in the successful weaning group was within normal limits, while in the failed weaning group was above normal values. Hypomagnesemia was found in both weaning groups, whereas hypophosphatemia was not found in both group. Pulse frequency and calcium levels had significantly lower values in the successful weaning group compared to the failed weaning group. The mean or median APACHE II A, B, C and total scores were not significantly different between the successful weaning groups and the failed weaning group.

Further research can be performed with a more balanced number of subjects between successful weaning and failed to wean, and also assisted by applying laboratory tests as service standards, especially magnesium and phosphorus. Subjects need to be more balanced so that the analysis can be more accurate. The application of magnesium and phosphorus examination as a service standard in the ICU/RICU can help pick up study subjects, especially outside working hours and holidays, and obtain data on subjects who are weaned other than working hours.

ACKNOWLEDGMENTS

None.

CONFLICT OF INTEREST

None.

FUNDING

None.

REFFERENCES

- Benditt JO. The neuromuscular respiratory system: physiology, pathophysiology, and a respiratory care approach to patients. Respir Care. 2006;51(8):829–37.
- Barrett KE, Barman SM, Boitano S, Ganong WF, Brooks HL. Cellular and molecular basis for medical physiology. In: Kim E. Barrett, Barman SM, Boitano S, editors. Ganong's Review of

Medical Physiology. 25th ed. New York: McGraw Hill Education; 2016. p. 1–156.

- Barrett KE, Barman SM, Boitano S, Ganong WF, Brooks HL. Central and peripheral neurophysiology. In: Ganong's Review of Medical Physiology. 25th ed. New York: McGraw Hill Education; 2016. p. 1–156.
- Haymaker W, Baer KA. Neurophysiologists. In: Haymaker W, Baer KA, editors. The founders of neurology: one hundred and thirty-three biographical sketches. Springfield IL: Charles C Thomas Publisher; 1953. p. 105–62.
- Fawcett WJ, Haxby EJ, Male DA. Magnesium: physiology and pharmacology. Br J Anaesth. 1999;83(2):302–20.
- Kawai M, Halvorson HR. Role of MgATP and MgADP in the cross-bridge kinetics in chemically skinned rabbit psoas fibers. Study of a fast exponential process (C). Biophys J. 1989;55(4):595–603.
- Ko YH, Hong S, Pedersen PL. Chemical mechanism of ATP synthase. Magnesium plays a pivotal role in formation of the transition state where ATP is synthesized from ADP and inorganic phosphate. J Biol Chem. 1999;274(41):28853–6.
- Moe SM. Disorders involving calcium, phosphorus, and magnesium. Prim Care. 2008;35(2):215.
- Dhingra S, Solven F, Wilson A, McCarthy DS. Hypomagnesemia and respiratory muscle power. Am Rev Respir Dis. 1984;129(3):497–8.
- Fiaccadori E, Del Canale S, Coffrini E, Melej R, Vitali P, Guariglia A, et al. Muscle and serum magnesium in pulmonary intensive care unit patients. Crit Care Med. 1988;16(8):751–60.
- Fiaccadori E, Coffrini E, Fracchia C, Rampulla C, Montagna T, Borghetti A. Hypophosphatemia and phosphorus depletion in respiratory and peripheral muscles of patients with respiratory failure due to COPD. Chest. 1994;105(5):1392– 8.
- Aubier M, Murciano D, Lecocguic Y, Viires N, Jacquens Y, Squara P, et al. Effect of hypophosphatemia on diaphragmatic

contractility in patients with acute respiratory failure. N Engl J Med. 1985;313(7):420–4.

- Gravelyn TR, Brophy N, Siegert C, Peters-Golden M. Hypophosphatemia-associated respiratory muscle weakness in a general inpatient population. Am J Med. 1988;84(5):870– 6.
- Zhao Y, Li Z, Shi Y, Cao G, Meng F, Zhu W, et al. Effect of hypophosphatemia on the withdrawal of mechanical ventilation in patients with acute exacerbations of chronic obstructive pulmonary disease. Biomed Rep. 2016;4(4):413–6.
- Johanson GA, Brooks GP. Initial scale development: Sample size for pilot studies. Educ Psychol Meas. 2009;70(3):394–400.
- Fagerland MW, Lydersen S, Laake P. Recommended confidence intervals for two independent binomial proportions. Stat Methods Med Res. 2015;24(2):224–54.
- Funk GC, Anders S, Breyer MK, Burghuber OC, Edelmann G, Heindl W, et al. Incidence and outcome of weaning from mechanical ventilation according to new categories. Eur Respir J. 2010;35(1):88–94.
- Vallverdú I, Calaf N, Subirana M, Net A, Benito S, Mancebo J. Clinical characteristics, respiratory functional parameters, and outcome of a twohour T-piece trial in patients weaning from mechanical ventilation. Am J Respir Crit Care Med. 1998;158(6):1855–62.
- Anzueto A, Frutos-Vivar F, Esteban A, Bensalami N, Marks D, Raymondos K, et al. Influence of body mass index on outcome of the mechanically ventilated patients. Thorax. 2011;66(1):66–73.
- O'Brien JM, Philips GS, Ali NA, Aberegg SK, Marsh CB, Lemeshow S. The association between body mass index, processes of care, and outcomes from mechanical ventilation: a prospective cohort study. Crit Care Med. 2012;40(5):1456–63.
- Khamiees M, Raju P, DeGirolamo A, Amoateng-Adjepong Y, Manthous CA. Predictors of extubation outcome in patients who have

successfully completed a spontaneous breathing trial. Chest. 2001;120(4):1262–70.

- 22. Chang YC, Huang KT, Chen YM, Wang CC, Wang YH, Tseng CC, et al. Ventilator dependence risk score for the prediction of prolonged mechanical ventilation in patients who survive sepsis/septic shock with respiratory failure. Sci Rep. 2018;8(1):5650.
- Keim-Malpass J, Enfield KB, Calland JF, Lake DE, Clark MT. Dynamic data monitoring improves predictive analytics for failed extubation in the ICU. Physiol Meas. 2018;39(7):075005.
- Gholyaf M, Basiri Z, Taghizadeh T, Nemati E, Taghipour M, Motalebi M. Magnesium level changes and its possible effects on the outcome of patients admitted to intensive care unit. Nephrourol Mon. 2017;9(4):e14007.
- 25. Ryzen E, Wagers PW, Singer FR, Rude RK. Magnesium deficiency in a medical ICU population. Crit Care Med. 1985;13(1):19–21.
- Sabatier M, Pont F, Arnaud MJ, Turnlund JR. A compartmental model of magnesium metabolism in healthy men based on two stable isotope tracers. Am J Physiol Regul Integr Comp Physiol. 2003;285(3):R656-63.
- Huang CL, Kuo E. Mechanism of hypokalemia in magnesium deficiency. J Am Soc Nephrol. 2007;18(10):2649–52.