Original Article

New Insight in Weaning Failure: Saliva Aspiration

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Abstract

Background: The weaning failure has prevalence between 15 to forty percent depending of various factors. Level of consciousness, heart failure, advanced age, chronic obstructive pulmonary disease (COPD), glottic edema, cancer, neuromuscular diseases, metabolic disorders, local resources and many others factors contribute to this sometimes grim situation. In the last few years, efforts to reduce this figure were using non-invasive ventilation (NIV) or High Flow Nasal Cannula (HFNC) after extubation, cuff leak text to detect airway caliber reduction had some impact in improving the weaning failure but still we have significant failures rates. Aim: For a long time we have observed that many patients fail the weaning process due to lack of protect the airways. They aspirate saliva and fails nearly immediately after extubation. The evaluation of the ability to protect the airways in intubated patients is not an easy task. This was the reason to find a marker to diagnose oropharyngeal dysphagia in intubated patients before extubation. Methods: This prospective observational study evaluated 112 consecutive mechanically ventilated patients. Saliva and tracheobronchial secretions were collected, and the tracheal to salivary amylase's activities ratio were determined. We called this parameter as amylase index. Variables that could influence weaning failure and mortality were quantified and analyzed. We evaluated the presence heart failure, age, chronic obstructive pulmonary disease, glottic edema, cancer, neuromuscular diseases, and level of consciousness, as a cause of weaning failure. The Statistical Package for the Social Sciences (SPSS) version 20 for Windows (IBM Corporation, Armonk, NY, USA) was used for the statistical analysis. The Student t test was used for normally distributed continuous variables; a chi-square test, for categorical variables, binary logistic regression and descriptive statistics. All p values were two-tailed. Results: We found, in order of importance, that the level of consciousness, heart failure, and incomplete resolution of lung disease, saliva aspiration (amylase index), muscle weakness, and laryngeal edema were the causes of weaning failure. Further, the amylase index showed a strong correlation with mortality and weaning failure in patients who were mechanically ventilated. Conclusion: Amylase index is another factor to be considered during the weaning process.

Keywords: Alpha-amylases; Deglutition disorders; Aspiration; Mechanical ventilation; Weaning; Mortality

Introduction

Despite the divulgation of palliative care many patients are still admitted to the ICU with end-stage disease, such as advanced dementia, end stage renal disease and metastatic cancer.[1-3] Instead of efforts to maintain the patients in general wards and provide end-of-life care, the family members and some physicians prefer to transfer of these patients to the ICU, where the main focus is on cure. This approach is responsible for the high rate of treatment failure, suffering and futile use of money that could otherwise be used for other purposes (e.g., better education, security, sanitation).[4-6]

Weaning failure is, more frequently, defined as the necessity of reintubation beyond 48 hours after extubation.[7-9] The main causes of weaning failure include heart failure, incomplete resolution of the disease responsible for weaning failure (lung, central nervous system, metabolic disorders, endocrine diseases), chronic obstructive pulmonary disease, fluid overload, level of consciousness (Glasgow Coma Scale ≤9), muscle weakness (polyneuropathy, myopathy, etc.), electrolyte disorders (severe hypokalemia, hiphosporemia), glottic edema, advanced cancer, age, and inability to protect the airways (aspiration).[1,3,4,7,10-14] There are many researches in the literature on this issue, and the majority of the published work concludes that following a

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set protocol leads to better outcomes than using a traditional approach.[7,8,14-16]

The critically ill requires ventilator support for failure, impairment of the respiratory pump due to neuromuscular conditions, serious cardiac dysfunction, fluid overload, metabolic disorders or coma.[5,10-13,17-20]

Complications (e.g., critical care acquired weakness, catheter-related bloodstream infection, acute kidney injury, delirium, or ventilator-associated pneumonia) may unintentionally increase the duration of ventilation, of which approximately 40% is spent on weaning. These complications are associated with the lung disease, parameters chosen to ventilate the patients, age and duration of mechanical ventilation, including time spent in the weaning process.[4,7,14,20,21] Although rapid and safe discontinuation of mechanical ventilation should be the objective for the majority of patients, both premature and unreasonably delayed extubation occur, leading to adverse outcomes.[7,9,14]

The evaluation of the ability for airway protection is very subjective.[9,11,21] There is a driving need for an objective tool to evaluate airway protection.

Our main objective was to investigate the tracheal to salivary amylase's ratio greater than 0.1, what we called amylase's index, to diagnose micro aspiration and investigate the impact on weaning failure if the test was positive.

Material and Methods

Between April 2014 and June 2017, we prospectively studied a cohort of 112 patients undergoing mechanical ventilation, due to various etiologies, for more than 48 hours. This observational study was conducted at a 33-bed private general intensive care unit affiliated to the Monte Sinai Hospital, Juiz de Fora, Brazil. Data were retrieved in electronic hospital's medical records. Written informed consent was obtained from the legal guardians of the patients prior to their enrolment in this study. We evaluated:

- Clinical and demographic data: sex, age, race, mortality (ICU, in-hospital, 30-day, and 6-month mortality), stroke, tracheal stenosis, decannulation rate, dementia, Glasgow Coma Scale-GCS, metabolic coma;
- Laboratorial data: brain natriuretic peptide[BNP] , sodium, potassium, magnesium, acid–base balance, endocrine function (thyroid-stimulating hormone, free T4), tracheal to salivary amylase's ratios activities;
- Image and others: Echocardiography, chest x-ray, computerized tomography, vacumanometry, leak test (flow after cuff deflation).

We used a traditional weaning protocol that includes: 1. FiO2 of 40% with PO2 equal or greater than 200 mmHg; 2. PEEP 7 cm H_2O; 3. GCS equal or greater than 8; 4. Evidence of improvement of pulmonary function; 5. Hemodynamic stability (mean arterial pressure of 65 mmHg) without or with low-dose vasoactive drugs); 6. Normal metabolic profile (pH, base excess, sodium, potassium, magnesium, phosphorus); 7. Subjective evaluation of airway-protection ability (absence of drooling, mastication, strong cough reflex); 8. Negative leak test; 9. Absence of inadequately controlled withdrawal syndrome; 10. Vacumanometry greater than −20 cm H2O; and 11. No planned anesthesia administration on the same day as the SBT.

Saliva and tracheal secretions were collected using a tool used to collect tracheobronchial secretions.

Tracheal secretions were obtained by aspirating through the endotracheal tube. The cutoff values were based in a previous study conducted in patients without dysphagia.[23]

After collecting saliva and tracheobronchial secretions to dose amylase's activities the collected specimens were homogenized and sent to the hospital laboratory as a homogenized solution, composed of 0.2 ml of specimen and 0.8 ml to saline. This was necessary because of the high viscosity of salivary and tracheobronchial secretions, which prevents their use in their natural states. After the dosage was determined, the laboratory values were corrected by a factor of 5. Alpha-Amylase activities were determined using (2-chloro-4-nitrophenyl)-β-1, 4-galactopiranomaltoside as the substrate. Amylase index was defined as the ratio between the tracheobronchial and salivary amylase's activities. The total amylase activity was measured using commercially available kits.

The study was approved by the Committee on Ethical Research of the Faculdade de Ciências Médicas e da Saúde de Juiz de Fora with protocol number 697.187 June, 2012. The institutional ethics committee reviewed this study protocol and approved the study. This study was conducted in accordance with the principles of the Declaration of Helsinki and other guidelines on ethical research in human subjects.

Statistical analysis

The Statistical Package for the Social Sciences (SPSS) version 20 for Windows (IBM Corporation, Armonk, NY, USA) was used for the statistical analysis. The Student t test was used for normally distributed continuous variables; a chi-square test, for categorical variables; descriptives statistics were used to obtain frequences. All p values were two-tailed.

Results

We enrolled a total of 112 patients after reviewing their medical records.

Our study population was predominantly Caucasian, male, with a high prevalence of heart failure, neurogenic coma, dementia and elderly patients. Probably it explains the failure rate we found [Table 1].

The indications for mechanical ventilation were respiratory failure (n=39; 38%), neurogenic coma (n=32; 29%), heart failure (n=26; 23%), metabolic coma (n=8; 7%), chronic obstructive pulmonary disease (COPD; n=4; 5%), shock (n=2; 2%) and others (n=5; 4.47%) [Table 2].

The rate of weaning failure was very high in our study sample: 72/112 patients (64%) experienced weaning failure in the first spontaneous breathing trial (SBT). After exclusion of the patients in coma (40/112; 36%), the net failure rate decreased to 28%.

The causes of weaning failure included heart failure (n=25; 22.3%), pulmonary disease (n=19; 17%), saliva aspiration (n=10; 9%), myasthenia (n=4; 3.6%), and laryngeal edema (n=4; 3.6%) and others conditions (n=10; 14%).

Saliva aspiration diagnosed through the amylase index was the third cause of weaning failure [Table 3].

Continuous variables that were associated with weaning failure in univariate analysis were tracheal amylase, tracheal to salivary amylase's ratios, C - reactive protein (CRP) and Brain Natriuretic Peptide (BNP) [Table 4].

We conducted a logistic binary regression for variables, including age 70 years or older, heart failure, metabolic disorders, and COPD. We found age greater than 70 years, heart failure; metabolic disorders and COPD obtained statistical significance as causes of weaning failure [Table 5 and Table 6].

Table 1: Demographic and clinical characteristics of the study population.

Characteristics	Frequency, n (%)
Caucasian	84% (94/112)
Male gender	47% (52/112)
30-day mortality	16% (18/112)
ICU mortality	28.6% (32/112)
In-hospital mortality	37.5% (42/112)
6-month mortality	32% (36/112)
Heart failure	56% (63/112)
Stroke	25% (28/112)
Neurogenic coma	31% (35/112)
Dementia	37.5% (42/112)
Metabolic coma	7% (8/112)
Tracheostomy	52% (58/112)
Critical illness	37.5% (42/112)
Decannulation	17% (19/112)
Tracheal stenosis	8% (9/112)

Table 2: Indications of mechanical ventilation.

Variables	Frequency's
Respiratory failure	34.8% (39/112)
Neurogenic coma	28.6% (32/112)
Heart failure	23.2% (26/112)
Metabolic coma	1.(8/112)
Chronic obstructive pulmonary disease	4.5% (5/112)
Shock	1.8% (2/112)

Table 3: Causes of weaning failure.

Causes	Frequency, n (%)
Heart failure	64% (72/112)
Pulmonary disease	17% (19/112)
Oropharyngeal dysphagia	9% (10/112)
Myasthenia	3.6% (4/112)
Laryngeal edema	3.6% (4/112)

Table 4: Continuous variables versus weaning failure.

Variables	Failure	Non-failure	p
Age (years)	70	67	0.18
Tracheal amylase (IU/L)	27,592	15,413l	0.02
Tracheal /salivary amylase's ratios	0.61	0.38	0.02
C-reactive protein	103	86	0.01
Brain natriuretic peptide (pg/mL)	812	544	0.08

Table 5: Logistic regression for age, heart failure, metabolic disturbances, and chronic obstructive pulmonary disease.

Variables	p
Age >70 years	0.02
Heart failure	0.04
Metabolic disturbances	0.06
COPD	0.01

COPD, chronic obstructive pulmonary disease

Table 6: Causes of death.

Causes	Frequency, n (%)
Chronic myocardial dysfunction	17.9% (20/112)
Sepsis	17.9% (20/112)
Respiratory failure	0.9% (1/112)
Others	1.8% (2/112)

Discussion

In this study, we studied the causes of weaning failure, and identified heart failure as the leading cause, followed by incomplete resolution of pulmonary disease and saliva aspiration diagnosed using tracheal to salivary amylase's ratios activities equal or greater than 0.1(amylase index). The amylase index was the third cause (9%) of weaning failure.

We identified as high risk of weaning failure the presence of heart failure (60%);age greater than 70 years old (66%), tracheal to salivary ratio equal or greater than 0.1 (60%) and obstructive pulmonary disease . Using binary logistic regression, we found that heart failure, age over 70 years, metabolic disorders, and COPD were statistically significant markers of weaning failure.[4,19,20,24,25] Even excluding coma we had a high failure rate which is explained by very older patients included in this study and consequently the presence of cardiac disfunction and dementia, a population in whom is frequent the lack of reflex to protect the airways. On exclusion of the patients in coma (40/112; 36%), the net weaning failure rate decreased to 28%. This result is in agreement with reports in the literature.[2,12,15]

We observed high rates of ICU, 30-day, 6-month, and in-hospital mortality rate that was different according to the etiology, age, comorbidities.[1-3,24]

Moreover, age, stroke, dementia, neurogenic coma were the main characteristics associated with mortality. Myocardial dysfunction and sepsis were the main causes of mortality, although respiratory failure was directly responsible for only one patient's death.

Weaning failure have a wide variation from 13 to forty percent depending on the cause of failure and the phase of the beginning process; if it is after discontinuing sedation or after putting the

patients to breath according to a weaning protocol.[1-3,9-11,15] We have to emphasize that the prognosis , complications and mortality are associated with the duration of the whole process. If the extubation is premature resulting on reintubation the mortality rate is 4 to 9 times than usual and if the duration is greater than necessary the number of ventilation associated complications is amplified.[9] To reduce the wasting time in weaning due this factors some strategies were adopted by researchers in this field:

- Creating protocol called protocolized weaning
- Using Noninvasive ventilation or high flow nasal cannula after extubation
- Optimizing cardiac function, airway resistance, muscle function

Even doing so we still have at least 14% (14/100) of weaning failure.[2]

Saliva aspiration could be a cause of weaning failure that is very difficult to evaluate in intubated patients.[26,27] The usual method to make this diagnose in this specific population is through scintigraphic methods, but this is cumbersome and caries a risk because one's have to transport the patient do radiology department.[27]

Very few researchers have used amylase to diagnose saliva aspiration. Pecora pioneered the use of tracheal amylase and salivary activity to predict a worsening of infection when these parameters were high.[28] Weiss used a cutoff point of 191 IU/L to predict the development of pneumonia in patients on mechanical ventilation.[29] Filloux found that 1832 IU/L was the better cutoff value for tracheal amylase based on a study in twelve volunteers [26] Dewavrin used pepsin activity greater than 220 pg/mL as a comparative parameter to diagnose saliva aspiration.[27] However, the drawback of this study was that pepsin is a marker of gastric to lung aspiration.[31]

In 1995, Nandapalan used a value of tracheal amylase of 1.125I U/L as a reference and dose amylase on days 1, 2 and 3 after a tracheostomy, and he found that patients in whom amylase's activities increase from 1 to the third day had a poor prognosis. [31]

Clark found that high amylase levels were associated with lung infection and worse prognosis.[32]

It is very important to recognize the inability to protect the airways before extubation to taken measures with the objective to reduce weaning failure. We could use medications (anticholinergic drugs), a protocolized physiotherapy including chest wall mobilization, secretion removal, cough function training, early mobility, manual hyperinflation and inspiratory muscle training and even performing tracheostomy in high risk patients.[9,18]

To the best of our knowledge, there is no published work on the use of the amylase index as a marker of weaning failure. We hope that others researchers try to replicate our work to confirm or refuse ours data.

Conclusion

The amylase index had a strong correlation with mortality and weaning failure in patients who were on mechanical ventilation.

Limitations

This study has a few limitations. Our single-center study had a small study sample. Moreover, the absence of any comparative groups detracts from the validity and generalizability of the findings of this study. Future research is necessary to validate these findings through a comparative approach that evaluate weaning success on the basis of the traditional protocol, measures to reduces salivary secretion, and tracheostomy to justify the inclusion of the amylase index in a weaning protocol to reduce weaning failures.

Competing Interests

The authors declare that they have no competing interests.

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