Australian Critical Care 28 (2015) 116–121

Contents lists available at ScienceDirect

Australian Critical Care

journal homepage: www.elsevier.com/locate/aucc

Research paper

Brain natriuretic peptide as a predictor of weaning from mechanical ventilation in patients with respiratory illness

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ARTICLE INFORMATION

Article history:
Received 3 September 2014
Received in revised form
14 December 2014
Accepted 18 December 2014

Keywords:
Weaning
Spontaneous breathing trial
BNP
Mechanical ventilation

ABSTRACT

Background: Cardiovascular dysfunction has been reported as an important mechanism of weaning failure. Brain natriuretic peptide (BNP) is a sensitive and specific marker for cardiovascular dysfunction.
Objective: To determine the value of BNP levels measured at initiation and end of a 2 h spontaneous breathing trial (SBT) as a predictor of successful weaning of mechanical ventilation in patients with respiratory illness.
Patients and methods: Thirty consecutive patients ready for weaning were prospectively enrolled in this cross-sectional analytic study over a 6-month period. All patients had been on spontaneous mode of weaning for at least 2 h. Tidal volume, respiratory rate, rapid shallow breathing index (RSBI), minute ventilation and PaO_2/FiO_2 were observed at initiation of SBT. BNP was measured at the initiation (BNP1) and at the end of SBT (BNP2). Weaning failure is defined as either the failure of SBT or the need for reintubation within 48 h following extubation.
Results: Out of the 30 included patients, 14 (46.6%) patients had failed weaning. $PaCO_2$ and BNP2 were significantly higher in the patients with failed weaning as compared to those with successful weaning ($P = 0.025$, $P = 0.031$ respectively). However, BNP1 levels were not statistically significant between the 2 groups ($P = 0.722$). On multiple regression analysis, BNP% (percent change in the BNP level during the 2-h SBT) was the only predictor of weaning success. As compared to other weaning parameters, BNP% $\leq$ 14.9 had the best sensitivity, specificity, positive and negative predictive value.
Conclusion: Measuring the percentage change in the BNP level during a SBT may be a good predictor of weaning success from mechanical ventilation in respiratory patients.

1. Introduction

Weaning critically ill patients from mechanical ventilation (MV) is a gradual and challenging process. Accurate weaning time is critically important in the general and respiratory intensive care unit (ICU). Any delay in ventilation removal may lead to ventilator acquired pneumonia and other possible side effects.[1] Premature removal may increase the rate of reintubation, the length of ICU stay or result in patient's death.[2] Many different weaning predictors have been proposed.[3] These indices have different specificities and sensitivities.[4] The 2 h spontaneous breathing trial (SBT) is currently the most accurate index for predicting weaning outcome, but the extubation failure rate is still high (15–20%) in patients who have passed SBTs.[5]

There are multiple mechanisms of weaning failure. Cardiovascular dysfunction has been reported as an important one of these mechanisms.[6] During the weaning process, spontaneous inspiratory efforts decrease intrathoracic pressure (ITP) which

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http://dx.doi.org/10.1016/j.aucc.2014.12.002

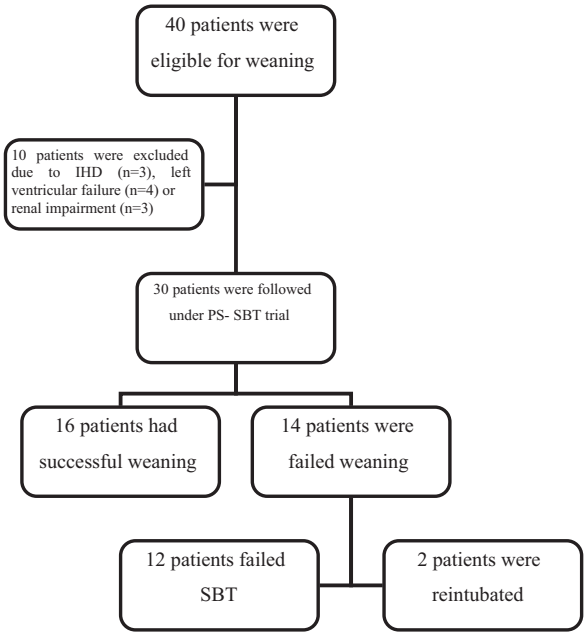

Fig. 1. A flow chart showing patient selection and follow up through out the study.

will augment venous return and thus increase intrathoracic blood volume.[7] Furthermore, the greater the decrease in ITP, the greater the increase in LV afterload for a constant arterial pressure, and right ventricle stroke output increases. This leads to possible decompensated heart failure or pulmonary oedema.[8]

However, in critically ill patients, it is difficult to detect cardiovascular dysfunction during weaning using the traditional methods, such as echocardiography, cardiac scintiscan and pulmonary artery catheterisation as these methods are either operator-dependent, lacking sensitivity, unavailable at the bedside, or invasive.[9]

B-type natriuretic peptide (BNP) is a plasma neurohormone secreted by ventricular myocytes in response to myocardial stretch or volume overload.[10] Plasma BNP levels are elevated in patients with left ventricular dysfunction,[11] right ventricular dysfunction,[12] and acute congestive heart failure.[13] It has been shown to be a sensitive and specific serum marker for cardiovascular dysfunction.[14]

2. Aim of the study

The aim of this study was to determine whether BNP levels at initiation and end of a 2 h SBT may predict successful weaning from mechanical ventilation in patients with respiratory illness as compared to other traditional weaning parameters.

3. Methods

We conducted analytic, cross sectional prospective study of 30 critically ill patients being considered for weaning from MV. This study was conducted in the ICU of Chest Department, Assiut University Hospital from October 2013 to March 2014 and we had received ethical approval. Consent to participate in the study was obtained from the patient's relatives. We prospectively enrolled patients ready for weaning from MV. This includes patients meeting the following criteria: (1) improvement or resolution of the underlying causes of acute respiratory failure; (2) PaO_2 > 60 mmHg at FIO_2 < 0.40 and positive end-expiratory pressure (PEEP) < 5 cm H_2O; Glasgow Coma Scale score > 13; core temperature < 38.0 °C; mean blood pressure (BP) > 65 mmHg without the use of vasoactive agents in the previous 24 h.[15,16] Patients with left ventricular failure and ischaemic heart disease were excluded from the study as both conditions are associated with elevated BNP levels. Also patients with renal impairment were also excluded.

3.1. Protocol of weaning

All patients who fulfilled the criteria for weaning had been put on spontaneous mode of weaning with low pressure support (8 cm H_2O) and zero PEEP with the same FIO_2 (<40%) for at least 2 h using Puritan Bennett™ 840 ventilator. Bedside mechanics including tidal volume (Vt), respiratory rate (RR), rapid shallow breathing index (RSBI), minute ventilation and PaO_2/FiO_2 were observed at initiation of SBT. Arterial blood gas (ABG) was also obtained. All patients were intubated with an oral endotracheal tube. Patients were considered to have failed SBT if they developed any of the following signs during the 2-h SBT[15]: RR > 35 breaths per minute, arterial oxygen saturation < 90%, heart rate > 140 beats per minute or a sustained increase or decrease in heart rate > 20%, systolic blood pressure > 180 mmHg or <90 mmHg, thoracoabdominal desynchrony, agitation, diaphoresis, or anxiety. Patients who had none of these features at the end of the SBT were subsequently extubated. After extubation, the patients received controlled oxygen therapy on venturi mask (31–40%) and were closely monitored for 48 h. The patient would be reintubated if one or more of the following developed: hypoxaemia with SaO_2 < 90% or PaO_2 < 60 mmHg at FIO_2 > 50%, respiratory acidosis with pH < 7.30 and PCO_2 > 50 mmHg or one or more of the clinical signs of respiratory distress as thoraco-abdominal desynchrony, retraction of intercostal spaces, use of the accessory muscles, agitation, increasing of the respiratory rate > 35 bpm and sustained increase in heart rate > 20%.

Weaning failure was defined as either the failure of SBT or the need for reintubation within 48 h following extubation.[15,17]

Of note, we could not assess cardiac function using echocardiography or pulmonary wedge pressure at time of weaning as these were not available in our ICU centre. We are a respiratory ICU and not a general ICU.

BNP measurement: To measure plasma BNP levels, venous blood samples were drawn into serum separator tube (SST) and allowed samples to clot for 10–20 min at room temperature before centrifugation for 20 min at the speed of 2000–3000 r.p.m. Samples were then stored at −20 °C. Centrifugation of samples was then done again after thawing before assay. We used Human Brain Natriuretic Peptide ELISA Kit (a commercially available kit supplied by Wkea Med supplies CORP kit), purified human BNP antibody to coat microtiter plate wells, and make solid-phase antibody, and then we add samples containing BNP to wells. Combined BNP antibody which with enzyme labelled, became antibody – antigen – enzyme–antibody complex. After washing completely, we added the substrate. The substrate became blue colour at HRP enzyme-catalysis, then the reaction was terminated by the addition of a sulphuric acid solution and the colour change was measured spectrophotometrically at a wavelength of 450 nm. The concentration of BNP in the samples was then determined by comparing the optical density of the samples to the standard curve. Each sample was measured in duplicate. This assay has high sensitivity (can detect as low as 12.5 pg/ml) and excellent specificity for detection of human BNP. The coefficient variance for detection of BNP within an assay is <10% and between assay is <12%. It took about one hour for the sample to come back for routine use.

3.2. Statistical analysis

Statistical Package for the Social Sciences (SPSS) version 16 (SPSS Inc., Chicago, IL, USA) was used for analysis of results. Results in this study were presented in mean ± standard deviation or number and