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The effects of different weaning modes on the endocrine stress response

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Abstract

Introduction The aim of the present study was to investigate the effects of the stress response on plasma insulin, cortisol, glucose, and urinary vanilmandelic acid during weaning and after extubation, using pressure support (PS), continuous positive airway pressure (CPAP) and T-piece modes.

Methods Sixty patients were randomly divided into three groups ($n=20$). The PS group received $FiO_2 \leq 0.4$, PS ≤ 10 cmH_2O, and positive end expiratory pressure ≤ 5 cmH_2O for 2 hours. The CPAP group was given $FiO_2 \leq 0.4$ and CPAP ≤ 5 cmH_2O for 2 hours. The T-piece group (group T) received 4 l/min oxygen via a T-piece for 2 hours. After 1 hour and 2 hours in their respective weaning modes, blood and urine samples were taken for insulin, cortisol, glucose and vanilmandelic acid measurements. Forty-eight hours after extubation, blood and urine samples were again taken.

Results Plasma insulin was greater in group T than in the PS and CPAP groups ($P<0.01$ and $P<0.01$). The plasma cortisol concentration was greater in group T than in group PS during weaning ($P<0.05$) and after extubation ($P<0.05$). Blood glucose concentrations were greater in group T than in the other groups (both $P<0.01$) both during weaning and post extubation. Urine vanilmandelic acid was greater in group T than in the other groups during weaning and after extubation (both $P<0.001$).

Conclusion Weaning via the T-piece caused a greater stress response than the PS and CPAP modes.

Keywords cortisol, insulin, mechanical ventilation, stress response, ventilation modes, weaning

Introduction

Intubation and mechanical ventilation are safe and effective treatments for critically ill patients with respiratory failure [1]. However, while unnecessary prolongation of mechanical ventilation increases the risk of complications, including bronchopulmonary infections, barotrauma, and oxygen toxicity, its premature discontinuation may also increase morbidity and mortality. Intensive care can indeed be prolonged if reintubation is needed [2,3]. 'Weaning' is the withdrawal of mechanical ventilatory support, although the term 'liberation' may be more appropriate [4]. Selection of the most appropriate mode for weaning can be difficult [5].

The effect of weaning on the stress response in critically ill patients is uncertain, as are the effects of different weaning modes. The aim of the present study was to compare changes in plasma concentrations of insulin, cortisol and glucose, and in urine vanilmandelic acid (VMA) during weaning and after extubation, using the three different modes of pressure support (PS) ventilation, continuous positive airway pressure (CPAP) and T-piece, in intensive care patients.

CPAP = continuous positive airway pressure; FiO_2 = fractional inspired oxygen concentration; PaO_2 = partial arterial oxygen tension; PS = pressure support; VMA = vanilmandelic acid.

Materials and methods

The study was approved by the Human Studies Review Board of the Cerrahpasa Medical Faculty of Istanbul University, and informed consent was obtained from the patients' families. Sixty patients, mechanically ventilated for more than 48 hours, were studied. Their age, gender, and diagnosis at intensive care admission were recorded. Patients with endocrine or immune system disease, patients with malignant disorders, patients who were also receiving insulin, and patients who were on sympathomimetic agents or steroids were excluded from the study. Weaning was considered unsuccessful if reintubation was required within 48 hours, and these patients were excluded from the study.

We calculated the Acute Physiology and Chronic Health Evaluation II scores from clinical data available after the first 24 hours of intensive care. All patients received a nasojejunal tube, and feeding was commenced according to the Harris–Benedict formula. Entry criteria for the weaning trial were as follows: positive end expiratory pressure ≤ 5 cmH_2O, partial arterial oxygen tension (PaO_2)/fractional inspired oxygen concentration (FiO_2) ≥ 200, the resolution of (or significant improvement in) the underlying condition requiring mechanical ventilation, hemodynamic stability, an adequate neurological status, an absence of fever, a presence of cough reflex when on a passing suction catheter, an intact gag reflex, and an absence of vasopressor or sedative infusions drips. Dopamine < 5 μg/kg per min was allowed, as were intermittent doses of sedatives [6]. The criteria for tolerating weaning trials were $PaO_2 \geq 60$ mmHg or arterial oxygen saturation ≥ 90%, or $FiO_2 \leq 0.4$–0.5, $PaCO_2$ increase ≤ 10 mmHg or pH decrease < 0.1, systolic blood pressure ≥ 90 mmHg or ≤ 180 mmHg with any increase or decrease ≤ 20%, heart rate ≥ 50 beats/min or ≤ 140 beats/min with any increase or decrease ≤ 20%, respiratory rate ≤ 35 breaths/min, and no sign of excessive respiratory work (absence of thoracoabdominal paradox, respiratory alternans or accessory respiratory muscle action). No diaphoresis, agitation, depressed mental status, or distress were present [7].

Patients were ventilated by either the Siemens-Elema Servo 900 C or Servo 300 A ventilators (Siemens-Elema, Solna, Sweden). Patients were randomly divided into three groups (each $n = 20$). Two modes of partial ventilatory support during the weaning period were employed; group PS received $FiO_2 \leq 0.4$, PS ≤ 10 cmH_2O, and positive end expiratory pressure ≤ 5 cmH_2O for 2 hours. The CPAP group received $FiO_2 \leq 0.4$ and CPAP ≤ 5 cmH_2O for 2 hours. The T-piece group (group T) received 4 l/min oxygen via a T-piece for 2 hours. In group T, the mean respiratory rate was 20 breaths/min, the tidal volume was 550–600 ml and the T-piece reservoir volume was 60 ml, giving a mean FiO_2 of 0.35–0.4. Patients in group PS and in group CPAP were divided between the two ventilators. Eight patients in group PS thus received the Servo 900 C ventilator and 12 received the Servo 300 A ventilator. In the CPAP group, seven received the Servo 900 C ventilator and 13 received the Servo 300 A ventilator. An 8.0 mm inner diameter endotracheal tube was used for all patients.

At the beginning of the weaning trial, blood and urine samples were taken for insulin, cortisol, glucose, VMA and arterial blood gas measurements (PaO_2, $PaCO_2$, pH). The measurements were repeated at the end of the weaning trial, after 2 hours, when the patients were extubated. Weaning was considered successful if reintubation was not required within 48 hours. Samples were repeated 48 hours after successful extubation. Blood pressure was recorded every 2 hours.

The blood samples for measuring the endocrine stress response were taken between 07:00 and 09:00 am because of the circadian rhythm. No patient received any medication that could affect VMA measurement, such as insulin, reserpine, norepineprine, epineprine, morphine, or pentobarbital.

Plasma insulin levels were determined using a commercially available radioimmunoassay (Novo; Nordisk, Copenhagen, Denmark). Plasma cortisol measurements were measured by a competitive immunoassay with the use of an electrochemiluminescence immunoassay (ECLIA; Roche, Mannheim, Germany). VMA concentrations of spot urine samples (2-hour collection) were determined by chomatographic-spectrohotometric assay (FAR, Verona, Italy). Blood glucose levels were determined by Medisense Glucotrend (Behring, Mannheim, Germany).

Statistical analysis

Data are expressed as the mean ± standard deviation. Demographic and biochemical data were compared between groups using the Kruskall–Wallis test and, when appropriate, by multiple comparison tests (Dunn test). Within-group changes were analyzed using repeated analysis of variance. Differences between groups were considered significant at $P < 0.05$. Statistical analysis was performed by the Istanbul University Cerrahpasa Medical Faculty, Department of Biostatistics.

Results

There were no differences between the groups in age, weight, gender and Acute Physiology and Chronic Health Evaluation II scores (Table 1), and there were no differences over time in the heart rate or noninvasive blood pressure, arterial PaO_2, $PaCO_2$, or pH (data not shown). Four patients required reintubation within 48 hours in group T. Reintubation was not required within 48 hours in the CPAP and PS groups. There was no significant difference between groups according to patients receiving sedatives and according to sedative doses (data not shown).

Plasma insulin

Plasma insulin concentrations increased in group PS and in group T (both $P < 0.05$) during weaning, and in group T after extubation ($P < 0.01$) (Table 2). Plasma insulin was greater in

Table 1

Demographic data in all groups

	Group PS	Group CPAP	Group T
Age (years)	73 ± 13	71 ± 16	75 ± 12
Weight (kg)	61 ± 20	63 ± 21	66 ± 22
Gender (male/female)	9/11	11/9	8/12
Acute Physiology and Chronic Health Evaluation II	18 ± 8	17 ± 6	19 ± 6

PS, pressure support; CPAP, continuous positive airway pressure; T, T-piece.

Table 2

Plasma insulin levels (μU/ml)

Group	Initial	Weaning	48 hours extubation
Pressure support	25 ± 11.1	27.8 ± 8.4*	24.4 ± 11
CPAP	24 ± 9.3	23.5 ± 7.6	24.6 ± 6.5
T-piece	24.5 ± 7.6	27.9 ± 8.1*	30.4 ± 9.2**,†,‡

*$P < 0.05$, **$P < 0.01$ when compared with the initial level within the group. †$P < 0.01$, pressure support group compared with T-piece group. ‡$P < 0.01$, continuous positive airway pressure (CPAP) group compared with T-piece group.

group T than in the other groups after extubation ($P < 0.01$) (Table 2).

Plasma cortisol

Plasma cortisol was increased in group CPAP ($P < 0.01$) and in group T ($P < 0.001$) during weaning, and in group T after extubation ($P < 0.01$) (Table 3). Concentrations were greater in group T than in group PS during weaning and after extubation (both $P < 0.05$), and were greater in group T than in group CPAP ($P < 0.01$) post extubation (Table 3).

Blood glucose

Blood glucose increased during weaning in group PS ($P < 0.05$) and in group T ($P < 0.01$) (Table 4), increasing more in group T than in group PS and group CPAP (both $P < 0.01$). The blood glucose concentration was greatest in group T post extubation (group PS and group CPAP both $P < 0.05$) (Table 4).

Urine VMA

Urinary VMA increased in group PS ($P < 0.05$) and in group T ($P < 0.001$) during weaning, and increased in group CPAP ($P < 0.01$) and in group T ($P < 0.001$) post extubation (Table 5). Urinary VMA was greatest in group T during both weaning and post extubation ($P < 0.001$) (Table 5).

Discussion

Weaning fails in a significant proportion of mechanically ventilated patients. The pathophysiology of weaning failure is complex, multifactorial, and poorly understood [8,9]. We believe that the stress response may play an important role during weaning. We therefore measured blood insulin, blood cortisol and blood glucose, and urinary VMA during and after weaning in three modes: PS, CPAP and T-piece.

Brinkmann and colleagues found that catecholamine and stress hormone blood concentrations did not increase following withdrawal of sedation and cessation of mechanical ventilation after abdominal surgery [10]. Rathgeber and colleagues used biphasic positive airway pressure, controlled mandatory ventilation, or intermittent mandatory ventilation for weaning after cardiac surgery [11]. The hormonal response was not affected by the discomfort of breathing. Calzia and colleagues

Table 3

Plasma cortisol levels (μg/dl)

Group	Initial	Weaning	48 hours extubation
Pressure support	25.8 ± 14	27 ± 17	22.9 ± 11
CPAP	22.4 ± 13	28.5 ± 6.9*	20.1 ± 9.6
T-piece	24.8 ± 12	30 ± 11**,†	26.2 ± 6.7*,†,‡

*$P < 0.01$, **$P < 0.001$ when compared with the initial level within the group. †$P < 0.05$, pressure support group compared with T-piece group. ‡$P < 0.01$, continuous positive airway pressure (CPAP) group compared with T-piece group.

Table 4

Blood glucose levels (mg/dl)

Group	Initial	Weaning	48 hours extubation
Pressure support	145 ± 61	152 ± 85*	148 ± 71
CPAP	148 ± 37	151 ± 57	139 ± 41
T-piece	140 ± 51	187 ± 60**,††,‡‡	155 ± 41†,‡

*$P < 0.05$, **$P < 0.01$ when compared with the initial level within the group. †$P < 0.05$, ††$P < 0.01$, pressure support group compared with T-piece group. ‡$P < 0.05$, ‡‡$P < 0.01$, continuous positive airway pressure (CPAP) group compared with T-piece group.

Table 5

Urinary vanilmandelic acid concentrations (μg/mg)

Group	Initial	Weaning	48 hours extubation
Pressure support	16 ± 8	14.6 ± 9.7*	17.3 ± 6.9
CPAP	14.6 ± 7.3	14 ± 7.6	19 ± 11**
T-piece	15 ± 8	35.5 ± 12.4***,†,‡	28 ± 10.6***,†,‡

*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$, when compared with the initial level within the group. †$P < 0.001$, pressure support group compared with T-piece group. ‡$P < 0.001$, continuous positive airway pressure (CPAP) group compared with T-piece group.

and Quinn and colleagues compared the effects of synchronized intermittent mandatory ventilation and biphasic positive airway pressure on the stress response, also during weaning after cardiac surgery [12,13]. Neither mode affected postoperative plasma cortisol, epinephrine, or norepinephrine concentrations. In patients who underwent cardiac surgery, Brinkmann and colleagues and Calzia and colleagues found no significant differences in plasma ephineprine and norephineprine levels during weaning [10,12].

Soop and colleagues studied enterally fed patients scheduled for elective surgery [14]. Insulin and blood glucose concentrations were increased 12–18 hours postoperatively (i.e. there was insulin resistance). In a study of trauma patients, Ljungqvist and colleagues found increased insulin and glucose levels as a response to the stress of trauma [15].

We have not found any study in the literature investigating stress responses during weaning in intensive care patients ventilated for more than 48 hours. In our study, plasma insulin and glucose increased in group PS and in group T during weaning. At 48 hours post extubation, the glucose and insulin levels were returning to their initial levels in group PS. The reason for the significant increase of glucose and insulin levels in the PS group is not clear. The greatest changes in measured variables during the 2 hours of weaning occurred in group T. The increase in blood glucose in group T during weaning was accompanied by an increase in blood insulin, which remained elevated after extubation, while the blood glucose decreased. There were signs of insulin resistance, and patients in group T showed the greatest increase in glucose. The plasma cortisol level was greatest in group T during both weaning and after extubation. Cortisol increased significantly during weaning in the CPAP group but not in the PS group. Cortisol, glucose and VMA were greater in the T group than in the CPAP group.

The increased stress response in group T has not been reported by other authors, for which there are two possible reasons. Previous reports were observations in surgical patients, ventilated for less than 48 hours. Second, different weaning modes were used. In our study, because it was not possible to measure plasma catecholamine levels, we measured urinary VMA, the end product of catecholamine metabolism [16]. VMA was greatest in group T, both during weaning and post extubation, but in spite of this there were no hemodynamic differences between groups, possibly because our patients were well hydrated and not in cardiac failure. The reasons for the higher endocrine stress response in group T may be explained by the T-piece not having ventilatory support.

Conclusion

In our study of patients weaned after more than 48 hours of ventilation, using the T-piece was associated with a greater stress response than using the PS or CPAP modes.

Key messages

- Weaning process increases endocrine stress response
- Weaning via T-piece caused a greater stress response that the PS and CPAP modes
- The use of PS and CPAP modes may be more appropriate during weaning process

Competing interests

None declared.

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