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Assessment of mechanically ventilated patients intoxicated with organophosphates by a novel surface electromyographic index

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ABSTRACT

Purpose: We present a new electromyographic index, named Engagement of Respiratory Muscle (ERM), for assessing the level of participation of respiratory muscles during spontaneous breathing test in patients poisoned with organophosphorus compound.
Methods: Diaphragm and sternocleidomastoid muscles activity was recorded by surface electromyography during spontaneous breathing test. A population of 23 patients poisoned with organophosphates and mechanically ventilated, and a control group of 28 healthy subjects were analyzed.
Results: All patients developed respiratory failure and 48% were diagnosed with intermediate syndrome by medical staff. The ERM index classified the patients in three clusters (p-value < 0.005): *Cluster I* presented more engagement of the sternocleidomastoid compared to diaphragm, *Cluster II* had low muscle engagement of both muscles and also muscle weakness, *Cluster III* were characterized for the diaphragm recovery associated with higher engagement. The control group showed a similar muscle engagement to *Cluster III*. The capacity of ERM index for classifying patients with (*sensitivity*) and without (*specificity*) muscle weakness were 90.91% and 100% respectively.
Conclusions: The ERM is a promising index to assess the level of participation of respiratory muscle on spontaneous breathing test in patients poisoned with organophosphorus compounds, which could improve the extubation prognosis for these patients.

1. Introduction

Organophosphorus compounds (OC) are used worldwide as agricultural pesticides and chemical weapons. Pesticide ingestion is among the most common methods of suicide globally and the 75% of them occurs in low and middle income countries [1]. Gunnell and collaborates estimated that 30% of suicides globally are pesticide self-poisoning [1]. The singularity of this poisoning is that toxic particles inhibit the degradation of the neurotransmitter acetylcholine (ACh), by stable bond with the enzyme acetylcholinesterase (AChE) [2,3]. This inhibition causes accumulation of the neurotransmitter, which results in a group of signs grouped as cholinergic crisis. In patients with acute poisoning, once apparently has passed the cholinergic crisis, appears a muscular paralysis. The neuromuscular block is attributed to the intense activation of nicotinic receptors in the neuromuscular junction. There are three types of paralysis caused by OC, the type II, originally described by Senanayake and Karalliedde [4] as an intermediate syndrome (IMS), is the cause of prolonging the period of ventilatory support [5]. This syndrome can occur after 24–96 h of the poisoning [4], it can affect the level of consciousness without cholinergic manifestations and is characterized by the presence of multiple cranial nerve palsies, cervical flexion weakened, proximal limbs and respiratory muscles weakness [4,6]. It is estimated that approximately 24% of patients intoxicated with OC suffer intermediate syndrome, hence patients require support with mechanical ventilation (MV) during the weakness of the respiratory muscles [7]. Studies have reported that in 76% of cases patients have a normal nerve

Abbreviations: ACh, acetylcholine; AChE, acetylcholinesterase; Dia, diaphragm; ERM, the engagement of respiratory muscle index; FiO_2, fraction of inspired oxygen; IMS, intermediate syndrome; MV, mechanical ventilation; OC, organophosphorus compounds; PaO_2, partial pressure arterial oxygen; P_{aw}, airway pressure; PEEP, positive end-expiratory pressure; P_{Imax}, the peak inspiratory pressure; PSV, pressure support; RASS, Richmond agitation sedation scale; RMS, root mean square; $RMS_{i/e}$, the ratio of inspiratory and expiratory RMS value; RR, respiratory rate; RSB, the rapid shallow breathing; sEMG, surface electromyography; SBT, spontaneous breathing test; Strn, sternocleidomastoid; $\dot{V}_E$, minute ventilation; WOB, work of breathing.

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conduction velocity [8]. Therefore, the diagnosis of the intermediate syndrome depends on the clinically evident muscle weakness.

In these kinds of patients, the ventilatory strategy has not been well reported in the literature; however it is clear the need to establish the risk factors that lead to a prolonged ventilatory support [9]. It is estimated that one third of all cases of poisoning require MV [10], having a high incidence in patients with IMS [9]. One of the main causes of failure in the withdrawal of invasive MV (weaning) is an imbalance between the capacity of respiratory muscles and demand of the respiratory control center [11]. However, there is no widespread use of information on the activity of the respiratory muscles, although its importance is undeniable in weaning procedures.

Identification of the weakness of respiratory muscles in the clinical practice is currently not trivial. Previous studies have evaluated the activity of some muscles involved in breathing through electromyography. Specifically, in these studies authors have compared breathing pattern with the electromyographic activity measured invasively during spontaneous breathing test (SBT) in mechanically ventilated patients [12,13]. Another study evaluated the interaction between patient and ventilator through surface electromyography (sEMG) of the inspiratory muscles [14]. However, there are no reports of respiratory muscle activity using sEMG in patients poisoned with OC.

In this article, we present a new electromyographic index, named Engagement of Respiratory Muscle (ERM), measured non-invasively and proposed for assessing the level of participation of respiratory muscles during SBT in patients poisoned with OC. The diaphragm as the main muscle and the sternocleidomastoid as accessory muscle during breathing were evaluated. The ERM index relates the energy of muscle contractions and its synchronism with mechanical ventilation. The objectives of our study were to assess the engagement of the respiratory muscles during SBT and to associate the level of engagement with the muscular weakness that is the IMS, in poisoned patients. This information based on sEMG can help to improve the extubation prognosis for critically ill patients because one of the main causes of failure of the extubation is the respiratory muscle weakness.

2. Materials and methods

2.1. Populations and experimental design

2.1.1. Patients group

Twenty-three patients (14 men, 9 women; age 30.3 ± 10.0 years, weight 67.6 ± 12.0 kg, height 164.2 ± 9.4 cm) with organophosphorus poisoning were admitted and managed in the Hospital San Vicente Foundation (Medellin, Colombia). Patients were included in the study according to the following inclusion criteria: i) intoxication with OC, ii) requirement of mechanical ventilation, iii) absence of myopathy and thoracic trauma, iv) older than 16 and v) nonpregnant.

During the spontaneous breathing test the diagnosis of intermediate syndrome was performed whether the patient had at least one of the following symptoms: i) respiratory muscles weakness based on clinical observation, ii) weakness of proximal limb muscles and iii) cervical flexion weakened [4].

This study was conducted under the approval of the Ethical Review Committee (Acta 001, 2014) of the Hospital and written informed consent was obtained from the patient's family for publication of this study.

2.1.2. Control group

Twenty-eight healthy volunteers (21 men, 7 women; age 27.4 ± 6.5 years, weight 70.7 ± 12.2 kg, height 170.0 ± 7.5 cm) were included in the control group. Subjects were included in the study according to the following inclusion criteria: i) absence respiratory disease, ii) nonsmoker, iii) 48 h of not alcohol consumption, iv) older than 18 and v) nonpregnant. They were ventilated noninvasively for 15 min and were monitored by sEMG. The ventilatory and electromyographic signals were recorded, with support pressure of 7 cmH_2O and a PEEP level of 5 cmH_2O. All volunteers signed an informed consent, which was approved by the Bioethics Committee of the Sede de Investigación Universitaria in Medellin, Colombia (Acta 15-59-664).

2.1.3. Spontaneous breathing test

This time was defined by clinical expertise plus the results of the measurements of some ventilatory signals used as classical predictors (i.e., work of breathing - WOB), but always assessing the lack of any of the following previous conditions: (i) respiratory rate lower than 8 breaths/min or higher than 35 breaths/min for 5 min or longer; (ii) hypoxemia (oxygen saturation as measured by blood analysis lower than 88% for 5 min or longer); (iii) sudden changes in mental status; (iv) cardiac arrhythmia and (v) two or more symptoms of respiratory distress as bradycardia (lower than 60 beats/min), tachycardia (higher than 130 beats/min), paradoxical breathing, diaphoresis or dyspnea.

Signals were recorded once the patient: i) overcame security test in which the sedation was suspended, ii) overcame wake-up test during the next 4 h to the suspension of sedation and iii) there was no presence of delirium, evaluated by the RASS score [15].

2.2. Respiratory and surface electromyographic signals

Diaphragm and sternocleidomastoid muscles activity was recorded by sEMG (20–500 Hz) using an electromyography amplifier (Bagnoli EMG system, Delsys, Massachusetts, United States), coupled to an acquisition card (NI USB 6212) configured with a sampling frequency of 1024 Hz. A couple of electrodes (bipolar configuration) were located in following positions of each muscle of interest: (a) right activity of the diaphragm's serving sack, which lies in apposition with the ventrolateral portion of the rib cage, were recorded between the seventh and eighth intercostal space, on the line which is located in the middle of the mid axillary line and the external clavicular line [16,17]; (b) for the sternocleidomastoid muscle, electrodes were placed at 20% of the distance between the mastoid apophysis and the sternal notch and over the line that connects them [16].

In both populations, ventilatory and electromyographic signals were recorded during mechanical ventilation during 20 min. The ventilatory signals (tidal volume, air flow, airway pressure, esophageal pressure and respiratory rate) were recorded with HAMILTON-S1 (Hamilton Medical, Bonaduz, Switzerland).

2.3. Indexes

2.3.1. Respiratory variables

Respiratory pattern during the spontaneous breathing test was evaluated by the following variables: respiratory rate (*RR*, breath/min), the peak inspiratory pressure (P_{Imax}, cmH_2O), the ratio of partial pressure arterial oxygen and fraction of inspired oxygen (PaO_2/FiO_2, mm Hg), minute ventilation ($\dot{V}_E$, l/min), the rapid shallow breathing (*RSB*, breath/min/l) index and the work of breathing (*WOB*, J/l).

The WOB for each respiratory cycle was calculated according to the Campbell diagram [18]:

$$WOB(n) = \frac{1}{V_T}\left[\frac{1}{N}\sum_{i=1}^{N} P_{es}(i) * V_T(i)\right] \quad (1)$$

where N is the number of samples in the *n* respiratory cycle, the air flow signal was used to detect the beginning of the inspiration and expiration. P_{es} is esophageal pressure and V_T is the tidal volume. WOB was normalized by the tidal volume [Joules/liters].

2.3.2. Muscular variables

Contraction of diaphragm muscle allows the lungs expantion during inspiration. This contraction generates significant changes of energy in EMG signals, which is reflected by the root mean square (RMS). The