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Research paper

Protocolized hyperventilation enhances electroconvulsive therapy

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ABSTRACT

Background: Hyperventilation is recommended in electroconvulsive therapy (ECT) to enhance seizures and to increase patients' safety. However, more evidence is needed regarding its effects and the optimum method of application.

Methods: This prospective study involving 21 subjects compared two procedures, protocolized hyperventilation (PHV) and hyperventilation as usual (HVau), applied to the same patient in two consecutive sessions. Transcutaneous partial pressure of carbon dioxide ($TcPCO_2$) was measured throughout all sessions. Ventilation parameters, hemodynamic measures, seizure characteristics, and side effects were also explored.

Results: PHV resulted in lower $TcPCO_2$ after hyperventilation ($p = .008$) and over the whole session ($p = .035$). The lowest $TcPCO_2$ was achieved after voluntary hyperventilation. Changes in $TcPCO_2$ from baseline showed differences between HVau and PHV at each session time-point (all $p < .05$). Between- and within-subjects factors were statistically significant in a general linear model. Seizure duration was greater in PHV sessions ($p = .028$), without differences in other seizure quality parameters or adverse effects. Correlations were found between hypocapnia induction and seizure quality indexes.

Limitations: Secondary outcomes could be underpowered.

Conclusions: PHV produces hypocapnia before the stimulus, modifies patients' $TcPCO_2$ values throughout the ECT session and lengthens seizure duration. Voluntary hyperventilation is the most important part of the PHV procedure with respect to achieving hypocapnia. A specific ventilation approach, CO_2 quantification and monitoring may be advisable in ECT. PHV is easy to apply in daily clinical practice and does not imply added costs. Ventilation management has promising effects in terms of optimizing ECT technique.

1. Introduction

Electroconvulsive therapy (ECT) has high efficacy in the treatment of affective disorders. However, augmentation strategies, such as the use of remifentanil, ketamine, xanthines or hyperventilation, are sometimes useful to optimize ECT in treatment-refractory patients and those with high seizure thresholds, or in order to achieve high efficacy with small side effects (Loo et al., 2010).

Adequate airway management and ventilation are therefore important (APA, 2001) in modern ECT, not only to ensure patients' safety under general anesthesia but also to optimize the ECT technique. Recent research has reported a 29% desaturation incidence (defined as oxygen saturation < 90%) during ECT (Surve et al., 2015). A number of ways of decreasing desaturation have been proposed, including ventilating during the seizure (Lew et al., 1986), application of positive pressure ventilations before the ECT stimulus (Swindells and Simpson, 1987), and high oxygen administration (Rasanen et al., 1988). A 20% increase in ventilation volume after the electrical stimulus is needed to compensate for the rise in carbon dioxide (CO_2) exhalation during ECT (Sakurazawa et al., 2006), the latter being due to seizure CO_2 production, apnea time, and muscle fasciculations. In addition, monitoring CO_2 values during ECT sessions can help to maintain lower CO_2 levels and to stabilize heart rate and blood pressure during the procedure (Saito et al., 2003).

It should also be noted that the hyperoxia and hypocapnia achieved through hyperventilation can optimize ECT stimulus efficiency by decreasing the required stimulus intensity (Buj-Alvarez et al., 2015; Nishikawa and Yamakage, 2015; Aksay et al., 2014; Haeck et al., 2011),

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extending seizure duration (Rasanen et al., 1988; Chater and Simpson, 1988; Bergsholm et al., 1984; Mayur et al., 2010; Haeck et al., 2011; Nishikawa and Yamakage, 2015; Sawayama et al., 2008; de Arriba-Arnau et al., 2016), and improving seizure quality (Aksay et al., 2014). Accordingly, current guidelines recommend preoxygenation (APA, 2001) and hyperventilation before the ECT stimulus (Guía de buena práctica clínica sobre la terapia electroconvulsiva, 2014 [Spanish Guidelines for Good Clinical Practice in Electroconvulsive Therapy]; The Royal College of Psychiatrists, 2013; Consenso Español sobre la TEC [Spanish Consensus Paper on Electroconvulsive Therapy], 1999), as well as attempting vigorous hyperventilation in the event of missed seizures (APA, 2001).

However, hyperventilation maneuvers have raised theoretical controversies linked to the physiological consequences of hypocapnia (Nishikawa and Yamakage, 2015; Reti et al., 2014). Hypocapnia induces transient alkalosis, resulting in vasoconstriction that diminishes cerebral perfusion (Reti et al., 2014; Szabo et al., 2011; Stocchetti et al., 2005). The relative ischemia that results could affect seizure length and, hypothetically, worsen cognitive side effects (APA, 2001; Nishikawa and Yamakage, 2015; Reti et al., 2014). It should be noted, however, that cerebral blood flow increases during the seizure (Saito et al., 1995), due to the hypertension that transiently overwhelms cerebral pressure autoregulation (Saito et al., 1996). Consequently, it has been speculated that hyperventilation may also be neuroprotective (Mayur et al., 2010).

Patients with cardiac disease or hypovolemia (Stocchetti et al., 2005) would be more exposed to myocardial ischemia risk under hyperventilation conditions (Nishikawa and Yamakage, 2015). Furthermore, hyperventilation is contraindicated in pregnant women (due to uterus vasoconstriction) and in patients with chronic obstructive pulmonary disease (COPD) (due to delayed awakening risk, respiratory drive alterations and complications) (Sundsted et al., 2014). Nevertheless, hyperventilation as applied in the ECT field is short-lasting and is generally considered safe (Loo et al., 2010). Prolonged seizures (Bergsholm et al., 1989; Choukalas et al., 2010; Haeck et al., 2011) are the main expected complications, but these can be stopped promptly with intravenous benzodiazepines. Moreover, hyperventilation may decrease certain side effects of ECT. For instance, hyperventilation lowers the intracranial pressure increase during ECT, which has been related to post-ECT headache (Gaines and Rees, 1992). A reduction in postictal delirious symptoms and an attenuated increase in heart rate have also been reported (Haeck et al., 2011). In addition, some studies have observed a decrease in postictal reorientation time that could be associated with reduced brain anesthetic, due to vasoconstriction caused by hyperventilation (Mayur et al., 2010), a factor that might also explain the improvement of seizure quality and decrease in seizure threshold.

Since higher ECT stimulus intensities are likely to be associated with increased cognitive side effects (Sackeim et al., 1993), hyperventilation could help to reduce these, owing to the smaller stimulus intensity required in treatments when hyperventilation is applied (Aksay et al., 2014; Haeck et al., 2011; Buj-Alvarez et al., 2015; Nishikawa and Yamakage, 2015).

In light of the above, a specific assisted ventilation approach and monitoring is required in ECT. However, there is little research on the optimum hyperventilation procedure, its repercussions in treatment sessions, or CO_2 measurement in ECT settings. With regard to the latter, monitoring the partial pressure of arterial blood gases is not practical, as it is too invasive and does not provide real-time feedback about changes in gas concentrations during treatment sessions. A non-invasive method for estimating CO_2 that is widely used in other short anesthetic procedures is the end-tidal CO_2 ($EtCO_2$). However, this measurement is limited when using a face mask for assisted ventilation, which is usually the case in ECT settings, where laryngeal masks or endotracheal intubation are not widely used in routine practice. One method that can overcome these limitations involves monitoring the transcutaneous partial pressure of carbon dioxide ($TcPCO_2$), which shows a good correlation with arterial blood gas values (Lermuzeaux et al., 2015) and offers a noninvasive, reliable, and continuous estimation of partial arterial CO_2 pressure ($PaCO_2$).

The present study compares the effects of protocolized hyperventilation (PHV) and hyperventilation as usual (HVau) on ventilation parameters, using $TcPCO_2$ monitoring. We hypothesized that PHV sessions would achieve a greater degree of hypocapnia than would control sessions (HVau), with clinical repercussions. We also explored the relationship between hyperventilation and hemodynamic parameters, seizure characteristics, and side effects.

2. Methods

2.1. Study design and participants

A prospective observational study was conducted over a 12-week period (April-June 2014) in the ECT Unit at the Psychiatry Department of Bellvitge University Hospital. All patients provided written informed consent and the study was approved by Bellvitge University Hospital Clinical Research Ethics Committee.

Two types of hyperventilation were compared in a single blind non-randomized crossover design. Consecutive subjects who had been referred for ECT in accordance with current guidelines were included (APA, 2001; The Royal College of Psychiatrists, 2013; Guía de buena práctica clínica sobre la terapia electroconvulsiva [Spanish Guidelines for Good Clinical Practice in Electroconvulsive Therapy], 2014; Consenso Español sobre la TEC [Spanish Consensus Paper on Electroconvulsive Therapy], 1999). Each patient was included only once. Inclusion criteria for the study were: being at least 18 years old; and having stabilized psychopharmacological treatment and ECT parameters (pulse width, energy stimulus intensity, frequency of ECT sessions, anesthesia, and muscle relaxant doses) during two consecutive sessions. Exclusion criteria were: pregnancy, COPD patients under specific treatment, language barrier or inability to cooperate, and major neurological deficits such as mental retardation or dementia. ECT sessions that required the use of vasoactive drugs or re-stimulations were excluded from the analysis. Patients and the recovery room nurses were blind to the type of hyperventilation applied.

2.2. Electroconvulsive therapy procedure

Electroconvulsive therapy was applied using a Thymatron System IV device (Somatics, LLC, Lake Bluff, III) and bitemporal electrode placement in all patients. Delivered stimulus parameters were in accordance with the device's brief pulse preset programs (.5–1 ms). ECT sessions were administered with a stimulus intensity that was 1.5–2.5 times above patient's seizure threshold and individually adjusted to patients' seizure quality and clinical evolution. Stimulus intensity remained unchanged during the two sessions prior to study inclusion and during the two consecutive sessions that were analyzed. Concomitant psychotropic medications were not withdrawn during the course of ECT. Benzodiazepines were maintained at the lowest dose that the patient could tolerate during the treatment course.

Patients scheduled for ECT were monitored with electrocardiogram (ECG), blood pressure, pulse oximetry (Datex Engstrom AS/3™ monitor), and $TcPCO_2$ (SenTec® Digital Monitoring System). Seizure duration and adequacy was determined by 2-channel electroencephalogram (EEG) with electrodes at the Fp1 and Fp2 sites of the International 10–20 system for EEG.

Anesthesia was performed by the same team of three anesthesiologists in all ECT sessions. Patients were preoxygenated with a face mask connected to a manual resuscitation device with high-flow oxygen administration (10 L/min) and were then told to take deep breaths (phase I). Anesthesia was induced intravenously with thiopental (1.5–2.5 mg/kg) and succinylcholine (.5 mg/kg). After anesthesia in-