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Hypercapnia Correction in Chronic Obstructive Pulmonary Disease Patients with Sleep-Disordered Breathing

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This study was performed with the **aim** to evaluate the possibility of capnometry in efficacy and safety control of CPAP-therapy in chronic obstructive pulmonary disease (COPD) patients with sleep-disordered breathing and hypercapnia.

Materials and Methods: For 10 patients with COPD combined with obstructive sleep apnea or obesity hypoventilation syndrome, in whom hypercapnia was observed CPAP-therapy was performed under the control of capnometry.

Results: After treatment we observed a statistically significant reduction in CO_2 level in the exhaled air of the patients: $FECO_2$ decreased from (4.46 ± 0.13) % to (3.71 ± 0.15) %, $FETCO_2$ from (6.40 ± 0.21) % to (5.63 ± 0.24) %, $p < 0.01$, which means lower the degree of hypercapnia in patients.

Conclusion: Capnometry allow to control efficacy and safety of CPAP-therapy in patients with COPD and hypercapnia with the minimal clinically important difference for $FETCO_2$ is 0.31%.

Keyword: COPD, Gas Exchange Abnormalities, Hypercapnia, Capnometry.

1. Introduction

Global Initiative for Chronic Obstructive Lung Disease (GOLD) experts in 2011 identified: chronic obstructive pulmonary disease (COPD), a common preventable and treatable disease, is characterized by persistent airway limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases. Exacerbations and comorbidities contribute to the overall severity in individual patients [1]. Pathological changes in COPD occur in the four structures of lungs: the central airways, peripheral airways, lung parenchyma, blood vessels of the lungs, which in various forms present in each patient. These different pathogenesis mechanisms leading to pathophysiological disorders – hypersecretion of mucus, mucociliary dysfunction, airway obstruction, lung hyperinflation, gas exchange abnormalities, pulmonary hypertension and systemic effects [2].

Gas exchange abnormalities resulting in hypoxemia and hypercapnia are the part of the pathophysiology of COPD. Patients with hypercapnia often develop lung infections and

have an increased risk of death following pneumonia [3]. Hypercapnia can cause vasodilation with cerebral perfusion increasing. Even small increases in the partial pressure of CO_2 on the order of 5 to 6 mmHg are capable of generating appreciable changes on perfusion imaging. Patients with acute hypercapnia may present with increased intracranial pressures, altered mental status, slurred speech, confusion, headache, hallucination, stupor, or coma [4].

Compared with normocapnic COPD patients, hypercapnic subjects have low partial pressure of arterial oxygen (PaO_2), higher Hb concentration (secondary polycythaemia) and lower resting minute ventilation, with shallower and more rapid breathing. They are often edematous, and have been referred to as "blue bloaters" [5]. Once peripheral edema supervenes, the prognosis is poor with a 5 year mortality of 70–100% [6]. That's why it is very important to organize adequate medical care to such patients.

Due to hypercapnia is attributed to alveolar hypoventilation in COPD patients, the non-invasive ventilation (NIV) is an appropriate therapeutic option in hypercapnic patient. Many patients with COPD have worsening of hypoxaemia and hypercapnia in sleep, particularly in rapid eye movement (REM) sleep, due to a fall in central respiratory drive and increased upper airways resistance [7]. Especially it concerns for patients with concomitant obstructive sleep apnea (OSA). A number of studies have shown that NIV is feasible at home during sleep in patients with COPD, and that abnormal physiology can be corrected using NIV [6].

We study the possibility of non-invasive determination of gas exchange in patients with COPD with the use capnometry. For pulmonary practice in general, and in the management of patients with COPD in particular, the possibility of capnometry is not fully understood.

This study was performed with the aim to evaluate the possibility of capnometry in efficacy and safety control of CPAP-therapy in COPD patients with sleep-disordered breathing (SDB) and hypercapnia.

2. Materials and methods

This work was financed from the state budget of Ukraine. The study was coordinated with the local Medical Ethics Committee of the National institute of phthisiology and pulmonology named after F.G. Yanovsky National Academy of medical sciences of Ukraine, participants were familiarized with the study protocol and signed an informed consent form to participate in the study.

The study involved 100 COPD patients (74 men and 26 women) aged 38 to 84 years, mean age (61.0 ± 1.0) years.

For all participants capnometry was performed. Capnometry – a measurement and digital display of concentration or partial pressure of carbon dioxide (CO_2) in the air that the patient inhales or exhales during the respiratory cycle [8]. Capnometry was conducted on a set for the study of the cardiorespiratory system "Oxycon Pro", "Cardinal Health" (Germany), the following parameters were evaluated [9]:

- End-tidal CO_2 fraction, % ($FETCO_2$),
- Expired CO_2 fraction, % ($FECO_2$).

Further we have identified a group of patients with COPD combined with OSA or obesity hypoventilation syndrome (OHS), in whom hypercapnia was observed and who needed NIV ventilation. According to the literature, the treatment of patients with SDB and simultaneous hypercapnia starts with continuous positive airway pressure (CPAP-therapy) under the control of the partial pressure of CO_2 in the blood. In the case of increase of CO_2 in the blood under the influence of CPAP-therapy bi-level positive airway pressure (BIPAP) should then be considered [10]. For our patients CPAP-therapy was prescribed and after its 10 sessions capnometry was repeated. We are tasked to analyze the dynamics of capnometry prior to and after 10 sessions of CPAP-therapy in order to monitor the effectiveness and safety of NIV in patients with hypercapnia.

Data collection and mathematical processing carried out by licensing software products included in the package Microsoft Office

Professional 2007 license Russian Academic OPEN No Level № 43437596. Statistical analysis was performed using mathematical and statistical features MS Excel. The parameters studied in this work were evaluated by determining the mean (M), the mean error (m), reliability (t), the level of significance (p) followed by comparison using t Student-test.

3. Results and discussion

The study involved 100 COPD patients (74 men and 26 women) aged 38 to 84 years, mean age (61.0 ± 1.0) years. Distribution of patients in groups by sex and age and also capnometry results are presented in Table 1.

Table 1: Gender and age distribution of patients, capnometry results

Indicators	Stage II COPD patients (n = 30)	Stage III COPD patients (n = 45)	Stage IV COPD patients (n = 25)
Mean age (years) (M±m)	57.5 ± 2.1	59.0 ± 1.8	65.6 ± 1.8*
Male (number)	23	30	21
Male (%) (M±m)	76.7 ± 7.7	66.7 ± 7.0	84.0 ± 7.3
Female (number)	7	15	4
Female (%) (M±m)	23.3 ± 7.7	33.3 ± 7.0	16.0 ± 7.3
$FETCO_2$ %	5.2 ± 0.1	4.8 ± 0.1	4.8 ± 0.2
$FECO_2$ %	3.6 ± 0.1	3.0 ± 0.1#	2.8 ± 0.1^

Note

***** – statistically significant difference between patients with stage IV COPD and patients with COPD stages II and III, $p < 0.05$;

– statistically significant difference between stage II and stage III COPD patients, $p < 0.05$;

^ – statistically significant difference between stage II and stage IV COPD patients, $p < 0.05$.

Data Table 1 shows that the groups were not equally distributed by age, with increasing severity of disease as patient's age increases. In all investigated groups the proportion of men is higher than women. Identified age and gender differences generally corresponds with the context that COPD is more common among males and persons older than 40 years [1]. At the same time the mean value $FETCO_2$ % didn't exceed the normal range for this parameter: 4.0-5.6 % [9]. After an individual analysis of the capnometry results, we found that 15 patients observed hypercapnia with $FETCO_2 > 5.6$ %. We separately analyzed the comorbidities of these 15 patients and found that 10 of them are suffering from concomitant SDB.

Accordingly, nine men and one woman (age (53.2 ± 2.6) years) were included to the observation group, five of whom had stage II, two – stage III, and one patient – stage IV COPD combined with OSA and two patients – with OHS and stage II COPD. Prior to treatment, we observed signs of hypercapnia in examined patients – $FETCO_2$ increase above 5.6 % (Table 2).

For these 10 patients appropriate drug therapy corresponding to severity of COPD was prescribed and additional treatment option – CPAP-therapy was initialized.

Table 2: Characteristics of the patients who had indications for CPAP-therapy

Characteristics of patients (n = 10)	
Male (n, %)	9 (90 %)
Female (n, %)	1 (10 %)
Diagnosis:	
COPD II + OSA (n, %)	5 (50 %)
COPD III + OSA (n, %)	2 (20 %)
COPD IV + OSA (n, %)	1 (10 %)
COPD II + OHS (n, %)	2 (20 %)
Age, years	53.2 ± 2.6

During 10 treatment nights patients received NIV by the use of autoCPAP-therapy when the device registers the signals from the sensors of the respiratory flow and snore and therefore modulates the level of therapeutic pressure in response to changes in airway resistance, which varies depending on the stage of sleep and posture patient. After treatment we observed a statistically significant reduction in CO_2 level in the exhaled air of the patients: $FECO_2$ decreased from (4.46 ± 0.13) % to (3.71 ± 0.15) %, $FETCO_2$ from (6.40 ± 0.21) % to (5.63 ± 0.24) %, $p < 0.01$, which means lower the degree of hypercapnia in patients (Fig. 1).

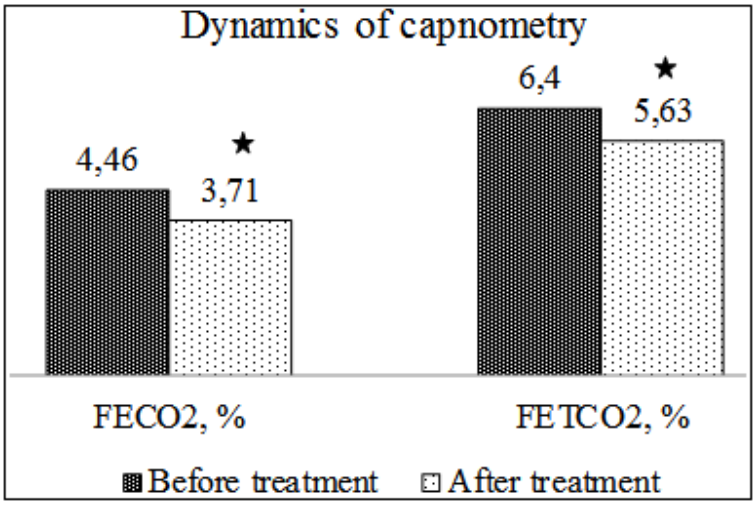

Fig 1: Dynamics of capnometry in patients treated with CPAP-therapy
Note: * – statistically significant differences before and after treatment ($p < 0.01$).

At the same time, capnometry allowed us to control that $FETCO_2$ values didn't increase during the treatment process, which means that autoCPAP-therapy was sufficiently safe, without the CO_2 accumulation and the need to switch patients to the BiPAP-therapy.

Is indicated after the treatment changes of clinically importance? This especially applies to the $FETCO_2$, which is the basis for the diagnosis of hypercapnia. The minimal clinically important difference (MCID) is the smallest difference in a measure that may be perceived to be important, either beneficial or harmful, and that would lead a clinician to consider a change in a patient's therapy [11]. MCID is a clinically important concept, because it may assist with the interpretation of observed changes in a measure and may influence the perceived success of an intervention [12].

Perhaps the earliest criterion for identifying important change was devised by Cohen, who expressed differences as an effect size – the average change divided by the baseline standard deviation. He stated that in the context of comparing group averages, a small effect size was 0.2, a medium was 0.5, and a large effect size was 0.8. Another approach is the provision, that a moderate effect size of half a standard deviation was typically important [13]. One-third of the estimated standard deviation has also been suggested as an approximation of minimal clinically important difference [11].

The standard error of measurement (SEM) is calculated by multiplying the estimated standard deviation at baseline by the square root of one minus the estimated reliability coefficient. One SEM is defined to be the minimal clinically important difference [12]. SEM = baseline SD x √(1-r), where r is the test–retest reliability coefficient (interclass correlation coefficient) [14].
Therefore, we calculate influenced CPAP-therapy clinical significance of changes $FETCO_2$, which before treatment was (6.40 ± 0.21) % (standard deviation – 0.62) and after treatment – (5.63 ± 0.24) %, change rate is 0.78%. Cohen's effect size for these data is 1.26, that is greater than 0.8. Thus, effect size is significant. Change rate (0.78%) is more than half a standard deviation (0.31) and, moreover, his third (0.207), so the difference is clinically significant.
Counted us the test–retest reliability coefficient (interclass correlation coefficient) for $FETCO_2$ is 0.75. The standard error of measurement equal to 0.62 x √ (1-0.75) = 0.31.

Thus, the minimal clinically important difference for $FETCO_2$ after the standard error of measurement calculation is 0.31%, which incidentally coincides with the concept that half the standard deviation is a measure of clinically important change.
Effectiveness of autoCPAP-therapy in patients with SDB and hypercapnia confirmed by capnometry results. $FETCO_2$ reduction has not only statistically but also clinically significance.

4. Conclusions

Under the influence of autoCPAP-therapy lower the degree of hypercapnia in patients with COPD and hypercapnia occur; capnometry allow to control efficacy and safety of CPAP-therapy in patients with COPD and hypercapnia; the minimal clinically important difference for $FETCO_2$ to apply capnometry to control efficacy and safety of CPAP-therapy is 0.31%.

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