İnönü Üniversitesi Tıp Fakültesi Dergisi
13(4) 231-236 (2006)

The Effect of Supplemental Oxygen on Hypoxemia and Hypercapnia in COPD Patients with Acute Respiratory Failure

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Background: Hypoxemia and hypercapnia are frequently encountered in chronic obstructive pulmonary disease (COPD) patients with acute attack.
Objectives: To investigate the effect of 2 L/min oxygen given with nasal cannula on hypoxemia and hypercapnia in COPD patients with respiratory failure.
Methods: Twenty-six type I (Group I) and 36 type II (Group II) respiratory failure patients were included in the study. The patients' initial clinical and laboratory findings were obtained. Spirometric examination and arterial blood gas (ABG) analysis were repeated after the administration of optimal medical therapy including 2 L/min oxygen given with nasal cannula. The patients whose $PaCO_2$ values increased more than 10 mmHg with the treatment were also grouped as Group III, and their comparison was made with the rest of the patients (Group IV).
Results: Among the initial laboratory parameters; PaO_2 was lower in Group II ($p<0.001$). Increases in PaO_2 values with the treatment in both groups were statistically significant ($p<0.001$). With the treatment PaO_2 value stayed under 60 mmHg in 23 patients (88.5%) and 26 patients (77.2%) in Group I and II, respectively ($p<0.05$).
Final $PaCO_2$ values were found higher in 21 patients (28.8%), and this was more than 10 mmHg in 7 (11.3%) patients (Group III). All but one of these patients belonged to Group II ($p>0.05$). In Group III, longer disease duration and higher rate of cor pulmonale were found to be statistically significant when compared with Group IV ($p<0.05$).
Conclusion: Two L/min oxygen given with nasal cannula is usually not sufficient to improve hypoxemia in COPD patients with acute attack, and oxygen therapy mentioned increases $PaCO_2$ further in 15-20% of hypercapneic patients.

Key Words: COPD, Supplemental oxygen therapy, Hypoxemia, Hypercapnia.

Akut Solunum Yetmezliği Olan KOAH Hastalarında İlave Oksijen Tedavisinin Hipoksi Ve Hiperkapniye Etkisi

Giriş: Kronik obstruktif akciğer hastalığı (KOAH) akut atağında; hipoksemi ve hiperkapniye sıklıkla rastlanılmaktadır.
Amaç: Solunum yetmezliği olan KOAH hastalarında, nazal kanül ile verilen 2 L/dk oksijenin, hipoksemi ve hiperkapniye etkisini araştırmaktır.
Gereç ve Yöntem: Yirmi altı tip I (Grup I) ve 36 tip II (Grup II) solunum yetmezlikli hasta çalışmaya alındı. Hastaların başvuru klinik ve laboratuar bulguları kaydedildi. Hastalar tam tıbbi tedavi yanısıra nazal kanülle 2 L/dk ilave oksijen aldıktan sonra, solunum fonksiyon testleri ve arter kan gazı (AKG) ölçümleri tekrar edildi. Tedavi ile $PaCO_2$ değerleri 10 mmHg'dan daha fazla yükselenler Grup III'ü oluşturdu ve geri kalan hastalarla (Grup 4) karşılaştırılmaları yapıldı.
Bulgular: Başlangıç laboratuvar parametrelerinden; PaO_2 Grup II'de daha düşüktü. Her iki grupta tedavi sonrası saptanan PaO_2 değerlerindeki artış istatistiksel olarak anlamlıydı ($p<0.001$). Tedavinin sonunda PaO_2 değerleri, Grup I ve II'de sırasıyla 23 hasta (%88.5) ve 26 hastada (%77.2) 60 mmHg'nın altında kaldı. Tedavi sonrası $PaCO_2$ değeri 21 hastada (%28.8) yüksek bulunurken, 7 hastada (%11.3) 10 mmHg'nin üzerinde artış saptandı (Grup III). Biri hariç bu hastaların tümü Grup II'ye aitti ($p>0.05$). Grup 3'de Grup 4'e göre hastalık süresinin daha uzun olması ve kor pulmonale'nin daha fazla olması istatistiksel olarak anlamlı saptandı ($p<0.05$).

Sonuçlar: KOAH akut atak hastalarında nazal kanülle 2 L/dk oksijen verilmesinin hastaların önemli bir kısmında hipokseminin düzeltilmesinde yeterli olmayacağı ve hiperkapnik hastalarda söz konusu oksijen tedavisinin %15-20 olguda $PaCO_2$'yi daha fazla yükseltebileceği bulunmuştur.

Anahtar Kelimeler: KOAH, İlave oksijen tedavisi, Hipoksi, Hiperkapni.

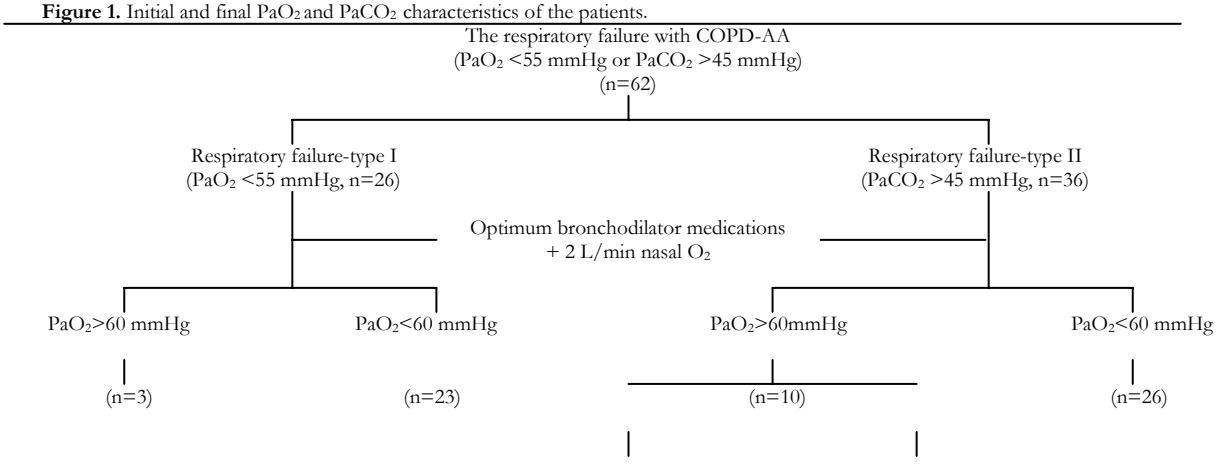
Hypoxemia and hypercapnia are frequently encountered in COPD patients with acute attack.[1] For these patients, optimal bronchodilator therapy consisting of nebulized ipratropium bromide, salbutamol, parenteral theophylline and prednisolone, and supplemental oxygen are the main stay of the treatment.[2] The rapid improvement of hypoxemia is essential for the prevention of cardiac arrhythmia and sudden deaths especially occurring at night.[3] Since the development of hypercapnia triggered by supplemental oxygen worsens respiratory failure, oxygen administration should be done with great care. In these patients, oxygen is generally administered with the aid of Venturi mask, nasal cannula or mechanical ventilation. Aim of the therapy is to raise the oxygen saturation to 90-92% and/or PaO_2 to 60-70 mmHg. It is generally recommended to begin the oxygen administration with minimum dose and to adjust the amount of oxygen according to following results of arterial blood gases (ABG) analysis. While doing so; it must be ensured that $PaCO_2$ does not rise more than 10 mmHg, or pH does not fall below 7.25.[4]

Sharing the same opinion that hypoxemia must certainly be improved, there is no consensus on how much supplemental oxygen should be given to which patient, and whether supplemental oxygen therapy causes serious CO_2 retention. This study was designed to investigate the effect of 2 L/min oxygen therapy with nasal cannula on hypoxemia and hypercapnia in COPD patients with respiratory failure.

MATERIAL AND METHOD

Sixty-two consecutive COPD patients referred with acute attack to Turgut Özal Research Center, the Department of Pulmonary Medicine, were included in the study. All patients' diagnosis of COPD met the criteria set by American Thoracic Society.[5] Twenty-six patients had type I respiratory failure (PaO_2<55 mmHg, $PaCO_2$ < 45 mmHg, Group I) and 36 patients had type II respiratory failure ($PaCO_2$> 45 mmHg, Group II). Initially, the patients' pre-treatment demographic and clinical features, laboratory findings, and results of ABG samples (Nova-Biomedical,USA) drawn while breathing room air, spirometric studies (Flow sensitive SV max 20 C Series, Sensormedics,USA) and echocardiography examination (ATL HDI 5000, USA) were recorded. As described by ATS,[5] all patients received optimal acute attack treatment of COPD including nebulized ipratropium bromide-salbutamol (Combivent nebulizer–Boehringer Ingelheim), parenteral theophylline (Teobag-Eczacıbaşı-Baxter), methyl-prednisolone (Prednol tb-Mustafa Nevzat) and antibiotic treatment where necessary. With a nasal cannula, 2 L/min oxygen was administered to all patients. The patients who requiring non invasive mechanical ventilation was excluded. The patients whose $PaCO_2$ values increased more than 10 mmHg with the treatment were also grouped as Group III, and their comparison was made with the rest of the patients (Group IV). Patients' final ABG analysis and spirometric examination were performed 4.1±2.2 (2-12) hours later. The study protocol and its results can be viewed in Figure 1.

Figure 1. Initial and final PaO_2 and $PaCO_2$ characteristics of the patients.



$\Delta PaCO_2$>10mmHg (n=1)	$\Delta PaCO_2$>10mmHg (n=6)	$\Delta PaCO_2$<10mmHg (n=4)	$\Delta PaCO_2$<10mmHg (n=26)

*****$\Delta PaCO_2$: the minus from final value to initial value of $PaCO_2$

All mean values were presented with their standard deviations. Wilcoxon's test was utilized to compare the initial and final results within the groups, and Mann-Whitney U test, Fischer's exact test and independent-samples t test were utilized to compare the different groups. Correlation and regression tests also made to detect the relationships between parameters. P values less than 0.05 were assumed as statistically significant.

RESULTS

There were 25 male and one female patients in Group I and 33 male and 3 female patients in Group II. The demographic and clinical properties of patients in Group I and II are seen in Table 1. Results of ABG analysis and spirometric studies before and after the therapy are shown in Table 2.

The differences between means of the age and smoking habit (pack-years) in Group I and II were not statistically significant ($p>0.05$). Among the initial laboratory parameters; PaO_2 ($p<0.05$), pH ($p<0.001$) and FEV_1 ($p>0.05$) were lower in Group II. Serum HCO_3 concentration was higher in Group II than Group I ($p<0.05$). Although the increase in PaO_2 in Group I (from 48.8±4.8 mmHg to 55.4±7.5 mmHg) and Group II (from 39.6±12.1 mmHg to 56.6±19.1 mmHg) with optimal bronchodilator therapy and supplemental oxygen is highly significant ($p<0.001$), PaO_2 could be brought to the desired level of ≥ 60 mmHg in only 13 (21%) patients. Mean value of $PaCO_2$ in Group II decreased from 61.6±12.4 mmHg to 58.1±15.6 mmHg ($p>0.05$). Final $PaCO_2$ values were found higher in 21 patients (28.8%), and this was more than 10 mmHg in 7 (11.3%) patients (Group III). All but one of these patients belonged to Group II (Figure 2). Demographic, clinical and laboratory properties, and results of ABG analysis and spirometric tests of Group III (n=7) and Group IV (n=55) are presented in Table 3 and 4. While mean FEV_1 value was lower in Group III, mean PAP value, smoking habit (pack-years) and disease duration were found to be higher. Among these parameters, only the disease duration was statistically significant ($p<0.05$). Also higher rate of cor pulmonale in Group III, were found statistically significant when compared with Group IV ($p<0.05$).

There was a significant correlation between final $PaCO_2$ values and disease duration ($r=0.506$, $p<0.05$). When we used logistic regression analysis to determine the important factors associated with CO_2 retention, we found that FEV_1, smoking habit (pack-years), and PAP_S did not show a significant association with hypercapnia. But logistic regression analysis showed that longer disease duration were independent predictor of the CO_2 retention ($p<0.05$).

Because of clinical deterioration despite the treatment mentioned, 6 patients were connected to mechanical ventilation (one patient from Group I, 5 patients from Group II).

Table 1. The demographic and clinical features of patients in Group I and II.

	Group I	Group II	p value
Number of patients	26	36	-
Mean age (years)	64.7±6.6	64.8±9.7	NS*
Disease duration (years)	15.9±1.6	17.8±4.7	<0.05
Smoking habit (pack-years)	36.4±13.5	38.8±12.3	NS
Pulmonary artery pressure (mmHg)	47.2±16.8	60.0±15.6	NS
Presence of cor pulmonale (n)	14	25	NS
Leukocyte count (10^3/µL)	9.0±2.3	10.3±3.4	NS
Hemoglobin (gr/dL)	14.7±1.1	16.2±2.3	<0.05
Hematocrit (%)	45.0±3.6	51.2±7.4	<0.05

*NS. Statistically non-significant.

Table 2. The initial and final results of arterial blood gas and spirometric measurements in Group I and II.

	Group I		Group II	
	Initial	**Final**	**Initial**	**Final**
PH	7.45±0.05‡	7.45±0.03‡	7.39±0.06‡	7.40±0.07‡
$PaCO_2$ (mmHg)	37.7±4.9‡	38.9±5.2‡	61.6±12.4‡	58.1±15.6‡
PaO_2 (mmHg)	48.8±4.8+ ‡	55.4±7.5+	39.6±12.1+ ‡	56.6±19.1+
HCO_3- (mmol/L)	27.1±3.1‡	28.5±3.4‡	36.7±5.1‡	35.9±5.7‡
SpO_2 (%)*	85.9±6.1+ ‡	89.8±5.5+ ‡	70.4±13.1+ ‡	85.0±9.1+ ‡
FVC (%predicted)	73.3±22.3+	81.5±23.9+	62.3±26.5	70.2±24.1
FEV_1 (%predicted)	41.2±15.9+	48.4±19.5+	36.5±15.2	39.3±14.2
FEV_1/FVC	44.9±13.6	46.6±12.4	44.2±20.5	43.0±15.7
FEF_{25-75}	18.4±7.3+	23.7±13.1+	19.4±14.9	21.6±14.1

*SpO_2. Oxygen saturation

+. The statistically significant parameters comparison values of pre-treatment and post-treatment in groups ($p<0.05$).

‡. The statistically significant parameters comparison values between the groups ($p<0.05$).

Table 3. The demographic and clinical characteristics of the patients in Group III and IV.

	Group III	Group IV	p value
Number of patients	7	55	
Mean age (years)	64.7±9.5	64.2±8.2	NS*
Disease duration (years)	24.3±7.3	16.1±1.6	<0.05
Smoking habit (pack-years)	38.4±13.7	37.6±12.8	NS
Pulmonary artery pressure (mmHg)	68.5±12.0	53.2±17.1	NS
Presence of cor pulmonale (n)	7	32	<0.05
Leukocyte count (10^3/µL)	9.8±2.7	9.7±3.1	NS
Hemoglobin (gr/dL)	14.3±2.2	15.7±1.9	NS
Hematocrit (%)	46.5±8.7	48.9±6.6	NS

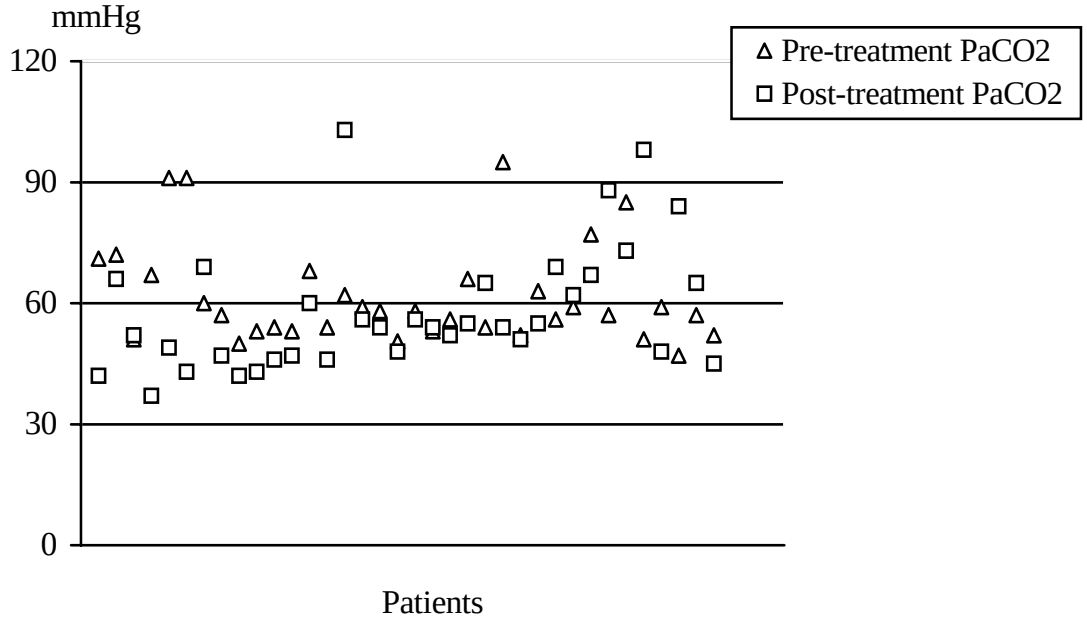
*NS. Statistically non-significant.

Table 4. The initial and final results of arterial blood gas and spirometric measurements in Group III and IV.

	Group III		Group IV	
	Pre-treatment	**Post-treatment**	**Pre-treatment**	**Post-treatment**
PH	7.39±0.07	7.34±0.1‡	7.42±0.06	7.43±0.04‡
$PaCO_2$ (mmHg)	64.0±21.3+	80.1±18.7+‡	52.7±7.7+	50.0±14.1+‡
PaO_2 (mmHg)	53.7±19.8+	82.9±29.7+‡	42.1±8.4+	52.7±7.7+‡
HCO_3^- (mmol/L)	33.3±6.5	39.7±7.5	32.2±6.5	32.0±5.7
SpO_2 (%)*	83.2±12.7	87.2±15.9	77.3±12.8+	87.3±6.6+
FVC (% predicted)	64.5±24.6	66.0±21.5	68.4±25.0+	77.9±24.6+
FEV_1 (% predicted)	28.5±5.2	30.8±6.2	40.0±15.9+	46.1±18.2+
FEV_1/FVC	39.3±8.8	37.3±9.4	45.0±17.6	45.9±14.1
FEF_{25-75}	13.3±2.9	13.3±3.7	19.4±11.7+	23.8±13.6+

*SpO_2. Oxygen saturation
+. The statistically significant parameters comparison values of pre-treatment and post-treatment in groups ($p<0.05$).
‡. The statistically significant parameters comparison values between the groups ($p<0.05$).

Figure 2. The initial and final $PaCO_2$ levels in Group II.



DISCUSSION

This study has demonstrated that 2 L/min nasal oxygen given complementary to optimal bronchodilator therapy is not sufficient to correct hypoxemia in majority of COPD patients with respiratory failure. Besides, this level of supplemental

oxygen can worsen the hypercapnia in some patients with type II respiratory failure.

Hypoxemia with or without hypercapnia is almost the rule in COPD patients with acute attack. Although the improvement of hypoxemia is vitally important in the treatment of acute attacks, unless $PaCO_2$ is already very high with low pH values or there is a sharp rise in $PaCO_2$, it may not be of emergency importance.[6] Supplemental oxygen prevents pulmonary vasoconstriction and myocardial ischemia, decreases right ventricular loading pressure, and it supplies adequate oxygen distribution to the central nervous system and other critical organs by regulating cardiac output, and it improves pulmonary defense and mucociliary transport.[4,7] For the accurate estimation of the concentration of supplemental oxygen, Venturi masks are ideal. However nasal cannula are also used in many cases. FiO_2 changes according to rate of oxygen delivery (1-6 L/min) and minute volume. Nasal cannulas differ from facial masks in not allowing re-breathing exhaled air and in allowing patients' speaking or eating.[4,8,9] It is clear from our study that 2 L/min oxygen therapy given with nasal cannula is not sufficient to raise the PaO_2 value (20.9%) to the desired level.

In clinical practice, the consequence that supplemental oxygen given during COPD acute attacks may cause CO_2 retention has limited the liberal use of supplemental oxygen for many years.[10] Generally this is thought to be related with decrease in minute ventilation from raised PaO_2 value.[11,12] Sassoon et al. stated that disorder in gas exchange rather than the ventilation depression due to CO_2 narcosis from hyperoxia is the cause, and it was concluded that high FiO_2 causes a small but significant transcutaneous CO_2 rise in COPD patients with acute attack.[13] In our study also, in 7 of 13 cases whose PaO_2 had increased to or over 60 mmHg, $PaCO_2$ had also increased more than 10 mmHg. Six of those 7 patients (85%) already had high $PaCO_2$. For this reason, we also agree with the former investigators that correction of hypoxemia in patients with type II respiratory failure may cause CO_2 retention in majority of patients.

In a study which 23 COPD patients with respiratory failure took part, it has been stated that 28% oxygen caused an average of 4 mm Hg rise (-2,11 mmHg) in $PaCO_2$, but did not cause a serious CO_2 retention.[14] Where as in our study mean $PaCO_2$ value decreased with 2 L/min supplemental oxygen therapy. In another study which included 50 patients who were supplied with 24% and/or 28% oxygen when necessary, hypercapnia developed in 13 (26%) patients, and resulted with the need for mechanical ventilation afterwards. The age, basal spirometric values and response to initial therapy were not found different from the rest.[15] In our study $PaCO_2$ had increased with oxygen therapy in 21 (28.8%) patients. We also could not establish any correlation between CO_2 retention and age, smoking load, initial PAP and laboratory findings and spirometric parameters except disease duration. Disease duration was longer in patients with CO_2 retention ($p<0,05$). Five patients whose $PaCO_2$ had increased more than 10 mmHg in Group II and one patient whose hypoxemia did not improve in Group I were connected to mechanical ventilation ($p>0.05$).

In their study, Batemen and Leach have stressed that, "The inefficiency of improving hypoxemia due to the fear that it will cause hypoventilation or CO_2 retention is unacceptable in clinical practice".[4] Although, the total rate of hypercapnia in our patients is 11.2%, this rate was 3.8% in patients with type-I respiratory failure and 16.6% in patients with type-II respiratory failure. Similar to our findings, Moloney et al. have also found that hypercapnia was not an expected consequence in normocapnic COPD patients referred with acute attack to emergency department, but CO_2 retention occurred in one third of hypercapnic patients. The investigators have neither been able to find a relationship between the initial $PaCO_2$ level and inspired oxygen concentration, nor the increase in PaO_2 and $PaCO_2$.[16]

Serum HCO_3 concentration is an important ABG parameters which usually rise in chronic hypercapnic patients. During the initial period of respiratory acidosis, renal compensation takes about three to five days, during which time there is enhanced reabsorption of proximal tubular bicarbonate, enhanced secretion of H, and increased ammonia production. This process will lead to an increase of the serum HCO_3 concentration and a rise in the systemic pH toward normal. In our study, all HCO_3 concentrations were higher than normal values. Also serum mean HCO_3 concentration was higher in Group II than Group I. This increment was found statistically significant. In other hand, some patients might administered oxygen therapy in ambulance or other hospital before admitted to our hospital, this might be affect some ABG samples. We could not record this condition; this is one of lack of our study.

In conclusion, 2 L/min nasal O_2 given complementary to optimal bronchodilator therapy does not increase PaO_2 to the desired level in majority of patients, however may cause serious CO_2 retention in 15-20% of patients with type II respiratory failure. Longer disease duration is the predictor of severe CO_2 retention due to 2 L/min supplemental nasal oxygen administration.

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