The Effect of Nasal Flow on Breathlessness in Patients with Chronic Obstructive Pulmonary Disease[1-3]

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SUMMARY Many patients with chronic obstructive pulmonary disease (COPD) receiving supplemental oxygen state that this treatment makes them less short of breath at rest. We postulated that this phenomenon may be related to improved arterial oxygenation, reduced ventilation, or stimulation of nasal receptors caused by the flow of gas. Eight patients who reported this phenomenon were studied in a quiet room. Each patient received zero flow, 2, or 4 L/min of air or oxygen through nasal cannula for 5 min at each level in random order in a single blind manner. At the end of each period, arterial blood gas composition was measured, and breathlessness was assessed with a visual analog scale. The scale was calibrated to read from zero (not at all breathless) to 100 (extremely short of breath). The entire protocol was repeated after application of topical lidocaine to the nasal passages. Results were assessed by analysis of variance. We found no significant effect of inspired oxygen concentration, gas flow, arterial oxygen tension, or arterial carbon dioxide tension on breathlessness. There was, however, a significant increase in breathlessness after nasal anesthesia from 44 ± 3 SEM to 52 ± 4 SEM ($p < 0.005$). We suggest that the reduction of breathlessness in these patients by nasal oxygen is a placebo effect caused by wearing the nasal cannulas and is unrelated to gas flow or the increased arterial oxygen tension.

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Introduction

Supplemental oxygen clearly prolongs the lives of hypoxemic patients with chronic obstructive pulmonary disease (COPD) (1, 2). Some patients with COPD who receive supplemental oxygen complain of breathlessness at rest, and they often report that their breathlessness is decreased by the use of supplemental oxygen. We postulated that the reduction in breathlessness in these circumstances results from the perception of flow through their noses or on their faces. This study was designed to test the hypothesis that the reduction of breathlessness in patients with COPD using supplemental oxygen is due to the effect of gas flow on nasal receptors rather than to an increased arterial oxygen tension or decreased alveolar ventilation.

Methods

Eight men with moderate to severe COPD were recruited from the Dayton Veterans Administration Medical Center. Six subjects were outpatients receiving chronic oxygen therapy, and 2 subjects were inpatients who received oxygen in the hospital. The majority of the subjects had a resting P_{O_2} below 60 mm Hg because this is a prerequisite to receive long-term supplemental oxygen. Pulmonary function data and room air blood gas measurements obtained prior to the study are shown in table 1. Selection criteria were (*1*) breathlessness at rest, (*2*) improvement of the breathlessness at rest with the use of supplemental oxygen, (*3*) an ability to sign informed consent, (*4*) no contraindications to an indwelling radial artery catheter, and (*5*) no allergy to lidocaine. This protocol was approved by the Human Studies Committee of Wright State University and the Dayton Veterans Administration Medical Center.

A factorial experimental design was used (3). All subjects were then given 5 different flows through the nasal cannula; zero flow, air at 2 and 4 L/min, and oxygen at 2 and 4 L/min. Flows were given in random order in a single blinded fashion. Gas flows were regulated by a series of stopcocks attached to continuously flowing air and oxygen behind the subject. The stopcocks were arranged so that any gas not flowing to the subject through the nasal cannula was expelled into the room. In this way, the subjects always heard gas flowing but were unaware as to which gas was flowing through the nasal cannula.

Each flow was given for 5 min. At the end of each interval a visual analog scale (VAS) 20 cm long was presented to the subject. The line was calibrated to read from zero (not short of breath) to 100 (extremely short of breath). The subject marked the point on the line that conveyed his degree of breathlessness. An arterial blood gas was drawn from an indwelling radial artery catheter at the end of each 5-min period, immediately placed on ice, and analyzed within 10 min.

The nasal mucosa was then anesthetized with lidocaine spray and jelly (Xylocaine; Astra Pharmaceutical Products Inc., Westboro, MA). The same gas flows were then administered to the subjects using a different random sequence. The VAS and blood gas data were collected as before.

Results were assessed by analysis of variance for multiple factors (3). This approach assessed the effects of using air or oxygen, nasal anesthesia, and gas flow rates on the VAS scores. The effects of blood gas composition on VAS scores were assessed by analysis of covariance (3). In all statistical analyses, significance was accepted at the 5% level.

Results

Blood gas data and VAS data are presented in tables 2 to 5. The mean P_{CO_2} for each flow was similar (range, 45 to 48 mm Hg), both before and after nasal anesthesia (table 2). There was a statistically significant, but clinically small, increase in the P_{CO_2} when the oxygen flows were delivered. Although ventilation was not measured, the subjects were clinically stable, and the flows were delivered for a short interval, so we interpreted the small changes in P_{CO_2} and pH to indicate that the alveolar ventilation was unchanged during the study period (tables 2 and 3).

As expected, there was a significant increase in the P_{O_2} when the subjects were receiving 2 L/min of oxygen instead of air. The P_{O_2} was significantly higher with 4 L/min of oxygen than with 2 L/min.

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TABLE 1

PATIENT DATA

Patient No.	Age (yr)	FVC (L)	FEV_1 (L)	FEV_1/FVC (%)	P_{O_2} (mm Hg)	P_{CO_2} (mm Hg)
1	66	1.82	0.74	41	55	43
2	60	2.30	0.73	32	53	41
3	58	2.50	1.46	58	65	43
4	73	2.14	0.89	42	60	43
5	66	1.92	0.97	51	56	45
6	65	2.55	0.89	35	43	62
7	54	1.88	0.65	35	50	50
8	66	1.55	0.51	33	45	54
Mean ± SD	64 ± 6	2.08 ± 0.35	0.86 ± 0.29	41 ± 9	53 ± 7	48 ± 7

TABLE 2

ARTERIAL P_{CO_2} BEFORE AND AFTER NASAL ANESTHESIA*

Subject No.	0†	A2	O2	A4	O4
Before					
	43	45	48	45	48
2	53	52	56	47	55
3	34	39	44	40	37
4	28	32	30	30	33
5	49	45	45	45	44
6	57	55	56	56	61
7	51	52	51	50	50
8	50	51	53	50	53
Mean ± SD	46 ± 10	46 ± 8	48 ± 8	45 ± 8	48 ± 9
After					
1	45	45	45	44	46
2	52	51	53	52	52
3	39	39	40	39	41
4	30	31	32	32	29
5	44	46	45	44	44
6	58	59	58	59	59
7	50	50	51	52	53
8	47	48	53	46	50
Mean ± SD	46 ± 9	46 ± 8	47 ± 8	46 ± 8	47 ± 9

* The data in the top half of the table were collected before nasal anesthesia and the data in the bottom half of the table were collected after nasal anesthesia. The flows were delivered in a different random order during each half of the study. Values are expressed as mm Hg.

† 0 = zero flow; A2 = 2 L/min of air; O2 = 2 L/min of oxygen; A4 = 4 L/min of air; O4 = 4 L/min of oxygen.

TABLE 3

PH DATA BEFORE AND AFTER NASAL ANESTHESIA*

Subject No.	0†	A2	O2	A4	O4
Before					
1	7.46	7.45	7.43	7.46	7.43
2	7.42	7.41	7.40	7.42	7.40
3	7.45	7.43	7.41	7.43	7.43
4	7.49	7.45	7.47	7.47	7.44
5	7.48	7.42	7.45	7.42	7.42
6	7.34	7.36	7.35	7.34	7.32
7	7.42	7.43	7.42	7.42	7.41
8	7.40	7.40	7.38	7.40	7.37
Mean ± SD	7.43 ± 0.05	7.42 ± 0.03	7.41 ± 0.04	7.42 ± 0.04	7.40 ± 0.04
After					
1	7.46	7.45	7.44	7.46	7.44
2	7.40	7.41	7.39	7.41	7.40
3	7.42	7.42	7.42	7.42	7.41
4	7.46	7.45	7.44	7.44	7.45
5	7.43	7.42	7.42	7.42	7.42
6	7.34	7.34	7.32	7.33	7.33
7	7.43	7.42	7.41	7.42	7.40
8	7.42	7.42	7.38	7.42	7.40
Mean ± SD	7.42 ± 0.04	7.42 ± 0.03	7.40 ± 0.04	7.42 ± 0.04	7.41 ± 0.04

For definitions, see footnotes to table 2.

The increase in P_{O_2} was similar whether the nose was anesthetized or not (table 4).

The P_{O_2} values while breathing zero flow or air flows during the study were higher than the baseline P_{O_2} values (table 1). Baseline blood gases were drawn after the subjects had been breathing room air at least 30 to 60 min. During the study, our protocol resulted in blood gases being drawn after the subjects had not been receiving oxygen for 5 to 15 min. This may have prevented the P_{O_2} values from completely returning to their baseline values.

We found no significant effect of inspired oxygen concentration, gas flow rate, arterial oxygen tension, or arterial carbon dioxide tension on the degree of breathlessness. There was, however, an increase in breathlessness at each flow after nasal anesthesia (table 5). Overall, the mean VAS score significantly increased from 44 ± 3 SEM to 52 ± 4 SEM ($p < 0.005$).

Our study design allowed us to test the validity of our data. We used analysis of variance to determine whether or not the VAS scores were affected by the order in which the changes in flow rates of air or oxygen were made, both before and after nasal anesthesia. In neither case did order have any significant effect on the VAS score. This indicates that there was no deterioration of cooperation in the course of the study.

Discussion

Breathlessness is a subjective sensation of ventilatory effort that is perceived as inadequate or difficult. Although it is a common complaint in patients with COPD, its physiologic basis is multifactorial and involves input from mechanoreceptors and chemoreceptors, and output from the central nervous system respiratory center. Because it is a subjective sensation, evaluation of breathlessness is difficult. We chose to use a visual analog scale rather than a fixed interval scale. Visual analog scales have been used to assess other subjective sensations such as pain (4) or moods (5). They have been used to evaluate breathlessness in normal subjects who are exercising or exposed to increased levels of carbon dioxide (6-8). In these studies, it was found to be reproducible within a given patient and was useful in comparing various measurements from a single individual. For these reasons, we felt it was a valid method to assess breathlessness in our subjects and to determine how their degree of breathlessness changed with

TABLE 4

ARTERIAL P_{O_2} BEFORE AND AFTER NASAL ANESTHESIA*

Subject No.	0†	A2	O2	A4	O4
Before					
1	66	71	107	67	125
2	54	55	67	61	76
3	82	70	99	68	136
4	76	71	101	75	130
5	87	56	79	59	98
6	48	47	62	49	87
7	61	56	73	60	100
8	63	59	92	61	110
Mean ± SD	67 ± 14	59 ± 9	85 ± 17	63 ± 8	108 ± 21
After					
1	70	65	96	77	138
2	61	60	70	59	83
3	70	72	95	76	128
4	75	71	96	74	116
5	71	58	78	59	99
6	48	46	57	45	73
7	59	56	77	64	104
8	64	57	66	66	88
Mean ± SD	65 ± 9	61 ± 9	79 ± 15	65 ± 11	104 ± 23

TABLE 5

VISUAL ANALOG SCALE BEFORE AND AFTER NASAL ANESTHESIA*

Subject No.	0†	A2	O2	A4	O4
Before					
1	37‡	62	60	42	37
2	49	48	50	51	54
3	49	48	36	48	50
4	71	51	63	47	50
5	42	96	76	67	72
6	9	32	11	9	11
7	37	30	30	39	38
8	86	4	89	93	3
Mean ± SD	48 ± 23	46 ± 26	52 ± 26	50 ± 24	39 ± 23
After					
1	65	42	49	46	58
2	67	77	23	76	79
3	86	72	70	97	81
4	60	53	44	59	60
5	45	79	97	44	58
6	7	8	3	46	5
7	39	67	54	67	58
8	96	98	82	97	99
Mean ± SD	58 ± 28	62 ± 28	53 ± 31	67 ± 22	62 ± 28

* The data in the top half of the table were collected before nasal anesthesia and the data in the bottom half of the table were collected after nasal anesthesia. The flows were delivered in a different random order during each half of the study. Values are expressed as mm Hg.

† 0 = zero flow; A2 = 2 L/min of air; O2 = 2 L/min of oxygen; A4 = 4 L/min of air; O4 = 4 L/min of oxygen.

‡ Numbers reflect the visual analog scale rating of breathlessness with a scale from zero (not short of breath) to 100 (extremely short of breath).

supplemental oxygen and/or nasal anesthesia.

Effect of Arterial Blood Gas Composition on Breathlessness

Hypoxemia and hypercapnia can cause breathlessness, although the exact mechanism for this effect is not known. Some evidence suggests that abnormal partial pressures of oxygen and carbon dioxide directly contribute to breathlessness (7, 9, 10). If our subjects' breathlessness was caused by hypoxemia per se, then improving P_{O_2} should have relieved their breathlessness. In fact, the increased P_{O_2} was not associated with any decrease in breathlessness as measured by the VAS in either the presence or absence of nasal anesthesia. The baseline level of hypoxemia in our patients was mild; the mean P_{O_2} while they breathed room air was 53 mm Hg. Perhaps with more severe hypoxemia, supplemental oxygen would have had an effect on breathlessness.

An alternate explanation is that arterial hypoxemia or hypercapnia may contribute to breathlessness by increasing ventilation (11, 12). If this were true, then we would expect our subjects' breathlessness to increase or decrease as their ventilation changed. However, the changes in breathlessness seen in our subjects occurred after nasal anesthesia and were not associated with any changes in their alveolar ventilation.

Effect of Nasal Anesthesia on Breathlessness

Nasal receptors sensitive to air flow are involved in modulating ventilation while awake and asleep. Loss of these receptors by obstruction or anesthesia results in sleep-disordered breathing, decreased ventilation, and blood gas abnormalities (13–17). Perhaps our subjects' increased breathlessness with nasal anesthesia resulted from the loss of perception of flow by blockade of these receptors. Another possibility is that lidocaine caused swelling of the nasal mucosa, which could have increased resistance through the nose and led to the increased breathlessness noted.

Clinical Implications

Our original hypothesis was that supplemental oxygen decreased breathlessness at rest in patients with COPD because of an effect of gas flow on nasal receptors and not as a result of changing the arterial oxygen tension or alveolar ventilation. According to this hypothesis, we would have expected supplemental air to relieve their breathlessness as well as supplemental oxygen and that a higher flow of air or oxygen would make the subjects less breathless than either a lower or no flow of either gas. This hypothesis appears to be wrong since low flows through the nose did not decrease breathlessness at all. We believe that the relief of breathlessness with supplemental oxygen reported by our subjects was due to a placebo effect of the nasal cannulas rather than relief of hypoxemia, decreased alveolar ventilation, or stimulation of nasal receptors.

Other investigators have also studied the effect of gas flow on the face and nose. Burgess and Whitelaw (18) demonstrated a reduced ventilatory response to carbon dioxide when nasally breathing a cold gas mixture (−4° to 10° C) compared with the same gas mixture at a war-

mer temperature (23° to 30° C). A reduced ventilatory response to carbon dioxide results in a lower minute ventilation for any end-tidal CO_2, which could reduce breathlessness in patients with COPD. More recently, Schwartzstein and coworkers (19) demonstrated that cold air blown onto the face reduced breathlessness during CO_2 rebreathing. However, the gas flows delivered to our subjects through their nasal cannulas were too low and too warm to produce an effect on alveolar ventilation or breathlessness similar to that in these studies. This is consistent with our conclusion that the relief of breathlessness our subjects got from supplemental oxygen has nothing to do with the flow of gas through the nose.

Unfortunately, breathlessness can be severe in patients with COPD. Various modalities that have been used to decrease breathlessness in these patients include drugs (20–22), surgery (23), pulmonary rehabilitation (24), and changes in posture (25). Oxygen has been used successfully to reduce exercise-related breathlessness (26). For patients with COPD, we found no evidence that supplemental oxygen per se relieves breathlessness at rest.

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