The effect of opioid use on pulmonary function test in advanced COPD patients

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Abstract

Background: Opium has previously been shown to increase exercise endurance and decrease breathlessness in patients with chronic obstructive pulmonary disease, but controversy in this issue persists, therefore the role of opium in the management of patients with advanced COPD remains undefined.

Method: In order to compare the effects of opium on pulmonary function, we studied two groups of patients with COPD who were attending the chest clinic of Labaffinejad hospital. Group A- consisted of COPD patients with history of smoking alone and group B- patients who consumed opium in addition to cigarette smoking. Patients were matched for their age, and packs/year cigarette smoking habit. Individuals with history of heart disease or occupational lung disease and those with severe COPD who needed hospitalization during 6 months prior to the study were excluded. A complete history and physical examination was done and patients' chest X-ray was taken. For each patient pulmonary function was evaluated by spirometry using Fukuda, Spirometric FVC, FEV 1, FEV 1 / FVC and predicted value for each parameter was recorded, and results were compared between the two groups of patients. Statistical analysis was done by using Kolmogorov - Smirnov test and student t-test.

Results: Results shows that there is significant difference (p = 0) between the two groups for FVC and FEVI. We concluded that opium may have a beneficial effect in improving lung function in patients with severe COPD.

Key words: opioid use, pulmonary function test, COPD patients

Introduction

In patients with severe chronic obstructive pulmonary disease (COPD) quality of life is usually declined due to breathlessness and they are usually limited in their daily activities (1), despite maximum treatment including bronchodilators, corticosteroid, rehabilitation programs and long term oxygen therapy (2).

In recent years, there have been significant advances in the understanding the nature of symptoms, but as far as breathlessness is concerned, it is not quite clear what makes patients to feel shortness of breaths during daily activities (2,3).

In order to alleviate this symptom, many therapeutic modalities have been tried including dihydrocodeine (4) and morphine with conflicting and inconclusive results.

Several reports emphasize the beneficial effects of oral opiate on breathlessness and exercise tolerance.

It is important to know the effects of opiate on pulmonary function of patients with severe COPD. Therefore we have studied the pulmonary function tests in two groups of COPD patients, with history of cigarette smoking habit alone and those with history of cigarette smoking plus opium addiction.

Material and Method

From October 2000 to February 2001 a total number of 4320 patients attended Labafinejad chest clinic. Among these patients: 1230 were diagnosed as COPD.

We performed this prospective study, sequential and case control, on COPD patients. The including criteria were as follows:

1- History of cough and expectoration for 3months in two consecutive years or HRCT finding compatible with diagnosis of emphysema.
2- Shortness of breath either in rest or activity.

Excluding criteria were as follows:
1- History of CHF or any other heart disease
2- History of exposure to noxious material.
3- History of exposure to war gases.
4- History of hospitalization from 6 months prior to study.
5- Severe COPD or complications such as hemoptysis or pneumonia which needed hospitalization.

After selection of patients, they were divided in to two groups. Group A with history of cigarette smoking habit and group B with history of opium addiction 2 years as well as cigarette smoking. Patients in these two groups were matched for age.

A questionnaire was filled for each patient. Chest X-rays were taken and spirometry done for each patient using Fukuda spirometer, (FEVI, FVC, FEVI/FVC) and percent of predicted value for each parameter recorded.

Statistical analysis:
For data analysis, we first transformed the research variables with natural logarithm for the variables to be in proportion. Then we tested hypothesis normality and homogeneity of variance in two groups with use of Kolmogorov - Smirnov and Levene's test. Then we Compared mean of variables in the two groups with use of t-test. We used SPSS relies 10.5 for data analysis.

Result

From October 2000 to February 2001, 60 patients with diagnosis of COPD included in our study, 30 patients for each group, (group A: only smoker and group B: opium addicts in addition to smoking.)

All patients were male and all were smokers with ranges of 15 to 180 packs/ year with a mean 48.00+/-25.31 packs/ year (49.2+/-29. 78 packs/ year for group A, and 46.80+/-20.35 packs/ year for group B.)

Group B patients were opium addicts for a minimum of 3 years and maximum of 40 years (mean 16.23+/-8.64 years). By Kolmogorov - Smirnov test we confirmed that our two groups are completely similar (95% confidence, and P> 0.5).

The most common complaint of our patients in both groups was cough and dyspnea as well as sputum production. One patient in group A also complained of weight loss. Patients with hemoptysis were excluded because most of them require hospitalization.

The most common chest examination finding in both groups was wheezing (68%), 60% in group A and 76% in group B (page 38). Early inspiratory crackle was the next common finding in both groups.

The most common chest X-ray finding in both groups was increased vascular marking and hyperinflation.

Spirometry was done in all patients after taking history and physical examination. And by Levenes' test we compared homogeneity FEV I, FVC, and FEV I/FVC in two group and with confidence 95% and P>0.5 we confirmed this homogeneity. FEV I/FVC ranges were from 35 to 91 with a mean 62.31+/- 13.24 in our patients.

In group A, FEV I/FVC ranged from 35 to91 with a mean of 58.31 +/-12.76, and in group B, ranged from 40 to85 with a mean 66.30+/- 12.68 (P = 0.19).FVC ranged from 16 to 83 % predicted with a mean of 46.37+/-17.20 in our patients, and in group A FVC ranged from 16 to 61% predicted with a mean 37.4+/-15.3 and in group B, ranged from 27 to 83% predicted with a mean of 55.3+/-14.2 (P=O). FEV I ranged from 2 to72% predicted in our patients with a mean of 44.67 +/-18.01. In group A, FEV I ranged from 2 to 72% predicted with a mean of 35.10+/- 15.6, and in group B, ranged from 22 to 72% predicted with a mean of 54.2 +/- 15.0 (P = 0). Therefore, according to above data, and similarity of our two groups that were confirmed by statistical analysis, and results of student t-test, mean value for FEV 1 and FVC in group B is significantly higher than group A.

Table 1: Group A patients

Age	Packs/year smoking	FEV1	FVC	FEV1/FVC
52	38	72%	61%	65
70	50	35%	24%	45
75	20	55%	27%	65
75	18	50%	39%	46
65	50	40%	56%	75
69	55	43%	19%	44
73	50	49%	53%	65
67	40	56%	46%	57
75	10	49%	55%	46
76	30	43%	42%	56
36	20	36%	58%	66
68	40	20%	16%	65
53	40	43%	52%	45
75	54	20%	23%	43
59	40	44%	53%	76
61	42	30%	19%	35
60	45	43%	48%	65
60	42	33%	27%	84
49	20	22%	27%	85
60	40	23%	24%	78
57	30	60%	61%	78
59	40	56%	50%	87
84	54	46%	52%	76
49	30	36%	16%	78
65	40	35%	32%	88
65	25	35%	32%	87
51	27	44%	33%	65
67	30	42%	62%	54

	t-test	sia	Lower limit	Upper limit
FVC	-4.705	0.0000	-25.56	-10.32
FEV1	-4.533	0.0000	-27.05	-4.20

Table 2: Group B patients

Age	Packs/year smoking	Opium Addiction/ years	FEV1	FVC	FEV1/FVC
58	80	10	1.57(54%	1.84(51%)	83
51	45	20	2.22(72%'	1.62(69%)	84
67	100	8	1.29(50%'	1.85(56%)	69
69	30	3	1.68(62%'	2.15(61%)	63
69	40	30	1.61(56%	2.52(68%)	66
62	30	20	1.12(43%'	1.58(48%)	63
70	50	10	2.43(71%"	2.85(80%)	85
47	20	10	2.08(62%'	2.54(67%)	81
63	15	10	1.07(37%'	1.86(34%)	56
69	40	10	0.98(41%'	1.38(45%)	58
72	100	20	1.12(40%'	1.33(36%)	84
64	30	20	0.79(25%'	1.73(46%)	46
80	60	40	1.10(55%'	1.31(48%)	83
54	30	20	2.22(70%'	3.09(83%)	72
63	40	10	34%	37%	55
65	45	15	65%	67%	70
78	50	10	71%	80%	50
57	30	10	50%	45%	56
58	30	10	29%	27%	43
54	30	20	42%	39%	73
64	503	36	72%	69%	53
50	70	34	54%	51%	62
52	40	10	72%	61%	77
72	60	20	22%	42%	40
74	50	20	57%	54%	64
58	55	30	64%	60%	70
49	54	20	68%	59%	66
53	50	20	55%	53%	70
47	30	20	64%	59%	77
60	50	30	70%	65%	70

Discussion

Breathlessness and dyspnea are commonly experienced by patients with advanced lung disease. Some past studies have shown that the use of morphine increased exercise endurance and pulmonary function in this group of patients (7). Woodcock et al (4) demonstrated l 8% increase in treadmill walking distance and a 20% decrease in breathlessness at equivalent workload 45 minutes after administration of 15 mg of oral dihydrocodeine. Light et al (31) showed that the administration of 0.8 mg/kg morphine orally resulted in a 20% increase in the exercise tolerance of patients with COPD. However, the administration of opiates to patients has led to mental cloudiness in some studies (8). Another study reported that low doses of aerosolized morphine (<2mg) increased the endurance time by 35% in patients with lung disease. It is of interest that such a low dose of aerosolized morphine would lead to this degree of improvement since a higher dose of oral morphine (30mg) has not elicited significant improvement. This raises the possibility that aerosolized morphine acts directly on lung afferent nerves to reduce dyspnea. However, the mechanism responsible for the improved breathlessness and exercise tolerance is unknown. It has been suggested that the primary factor responsible for the increase tolerance is a decreased metabolic requirement at a given workload.

Our results also show that opium significantly improves spirometric value in patients with COPD, despite that our two groups had no significant difference in other parameters, such as occupation, other diseases that may adversely effects on lung function, and etc.

Our patients were selected randomly from those with a diagnosis of COPD visited in out¬patient clinic of Labafinejad hospital, and those needed admission into the hospital were excluded.

The pathophysiological basis of the sensation of breathlessness remain incompletely understood. Despite some advances in the knowledge of the perception and genesis of breathlessness, those have little impact on therapy (2). In clinical practice this often is a distressing symptom and demands relief. The treatment of breathlessness is most effective when the primary cause can be identified and modified, but in those conditions, in which treatment currently has little to offer, it is intuitively attractive to attempt to manipulate the symptom of breathlessness itself.

Over the years many attempts have been made in this regard and although there have been some claims of success, none have achieved more than an alteration of the underlying mechanical events which subserves the symptom of breathlessness, for example, ventilatory drive, the pattern of breathing, etc (6).

Opiates have long been popular treatment for the alleviation of breathlessness in patients with respiratory disease (2). However they have not achieved widespread usage largely because of potential side effects, such as respiratory depression and addiction. There are a number of possible mechanism by which morphine may alleviate the sensation of breathlessness in a short time after use. (2). Firstly morphine may reduce the degree of anxiety experienced by a particular subject and hence the degree of breathlessness. Secondly, perceptual responses to the incoming neural traffic or its central interpretation may be blunted and finally, morphine may alleviate the sensation of breathlessness for a short time after use by direct local action on peripheral neural receptors in the small airway and probably by this mechanism may improve spirometric values (2). If opiates work at the level of the bronchial mucosa, it is possible that lower doses administered via nebulization might be effective. Opiate-peptide like activity has been detected in bronchial mucosa, and thus morphine may be in a position to modify the perception of breathlessness in the same way as it alters the perception of pain.

Light et al, used oral morphine (0.8 mg/kg) in patients with severe COPD and showed that exercise capacity was increased and breathlessness, assessed by using a modified Borge scale, waas significantly decreased. The reduction in breathlessness in this study was achieved at the expense of an increase in Pa CO2, a reduction in ventilatory derive, and was thought by the authors to be due to a combination of lower ventilatory requirement for a given workload and also to altered perception. Dihydrocodeine administered orally before exercise has also been shown to reduce dyspnea by 20% (assessed using a visual analogue scale) in a similar group of patients. Minute ventilation and oxygen consumption were reduced in this study despite an increase in exercise capacity.
Also naloxan restored blunted ventilatory responses in patients with chronic airflow
obstruction.

Conclusion

Opium may be useful in improving pulmonary function and relieve of dyspnea in patients with COPD unresponsive to other medication. Because the risk of adverse effects such as respiratory depression is high, use of such drugs could be limited to advanced and end stage disease. Further studies for confirmation of result of this study should be done in a larger group of patients.

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