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ORIGINAL ARTICLE

Asthma is not a common cause of severe chronic respiratory failure in non-smokers: ALOT study

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ABSTRACT: ***Asthma is not a common cause of severe chronic respiratory failure in non-smokers: ALOT study. G. Caramori, M. Fabbri, D. Paioli, F. Falcone, C. Severino, G. Felisatti, O. Arar, I.M. Adcock, K. Fan Chung, P.J. Barnes, A. Ciaccia, A. Papi.***

Background. **Little is known about the long-term natural history of asthma and the long-term clinical and functional consequences in non-smoking patients. From a functional point of view, non-smoking asthmatic patients may have a significantly greater decline in forced expiratory volume in one second (FEV_1) compared with non-asthmatic subjects and may develop chronic irreversible (fixed) airflow limitation. This has been related to the physiological consequences of chronic airway inflammation causing airway remodeling. However these lesions are all potentially reversible and there is little radiological evidence indicating lung destruction (pulmonary emphysema), which is potentially irreversible, in non-smoking asthmatics. Severe chronic respiratory failure is the major cause of mortality in patients with severe chronic lung diseases. Domiciliary long-term oxygen therapy (LTOT) is an accepted treatment for patients with severe chronic respiratory failure. Our reasoning, therefore, was that if asthma is a cause of severe chronic respiratory failure in non-smokers we should be able to find non-smoking asthmatics within a large population of patients on LTOT.**

The aim of our study (Asthma and Long-term Oxygen Therapy, "ALOT") was to investigate the prevalence of non-smoking asthmatics in patients on LTOT in a multicentre, cross-sectional study.

Methods. **Between June and September 2003 we screened all subjects on long-term domiciliary oxygen therapy in three different hospitals in the North-East area of Italy (within the provinces of Ferrara and Bologna). Taken collectively, we have found one-hundred and eighty-four patients on LTOT. We have reviewed their clinical data (age, sex, smoking, history and physical examination, arterial blood gas analysis, pulmonary function).**

Results. **114 patients (all smokers) fulfilled the diagnostic criteria for COPD. Seventy patients (all smokers) had other diseases. We were unable to find any non-smokers in our screened population of subjects on long-term domiciliary oxygen therapy. Furthermore, there was no past history of asthma and/or acute wheezing episodes in either of the patient groups.**

Conclusions. **This data suggests that asthma is an uncommon cause of severe chronic respiratory failure necessitating long-term domiciliary oxygen therapy in non-smokers and supports the current consensus that asthma and COPD are different diseases with differing stages of severity and the concept that long-term avoidance of active smoking is fundamental for the prevention of severe chronic respiratory failure.**

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Keywords: Asthma, Long-Term Oxygen Therapy, Natural History, Chronic Respiratory Failure.

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Introduction

Asthma is one of the common chronic diseases worldwide resulting in a substantial and increasing social burden and cost to public and private health care systems [1]. Over the last 20 years the prevalence of asthma has increased considerably in many countries. Little is known about the long-term natural history of asthma and the long-term clinical and functional consequences in non-smoking patients [1]. From a functional point of view, non-smoking asthmatic patients may have a significantly greater decline in forced expiratory volume in one second (FEV_1) compared with non-asthmatic subjects [2] and may develop chronic irreversible (fixed) airflow limitation [3, 4]. This has been related to the physiological consequences of chronic airway inflammation causing airway re-

modeling, a collective term which includes large airway epithelial basement membrane thickening, airway wall oedema, airway smooth muscle hyperplasia and hypertrophy [5]. However these lesions are all potentially reversible and their long-term clinical consequences, particularly in non-smokers are unknown. There is little radiological evidence for lung destruction (pulmonary emphysema), which is potentially irreversible, in non-smoking asthmatics, including patients with severe persistent asthma [4, 6, 7]. A large longitudinal study suggests that FEV_1 does not decline more rapidly in asthmatics or in those with asthma and chronic obstructive pulmonary disease (COPD), compared with non-asthmatics [8]. Also, the life expectancy of asthmatic patients may not differ from the average population, when the socioeconomic status of the population and the availability of health services are taken into account [9]. Severe chronic respiratory failure is the major cause of mortality in patients with severe chronic lung diseases. Domiciliary long-term oxygen therapy (LTOT) is an accepted treatment for patients with severe chronic respiratory failure [10, 11]. Our reasoning, therefore, was that if asthma is a cause of severe chronic respiratory failure in non-smokers we should be able to find non-smoking asthmatics within a large population of patients on LTOT.

The aim of our study (Asthma and Long-term Oxygen Therapy, "ALOT") was therefore to investigate in a multicentre, cross-sectional study, the prevalence of non-smoking asthmatics between all the patients on domiciliary long-term oxygen therapy.

Methods

The study was approved by the Institutional Ethic Committee of the University of Ferrara and by the local Ethic Committee of the other participating hospitals.

Between June and September 2003 we screened all subjects on long-term domiciliary oxygen therapy in three different hospitals in the North-East area of Italy (within the provinces of Ferrara and Bologna).

Policlinico S. Orsola di Bologna is a large teaching hospital, Ospedale Bellaria di Bologna a large tertiary referral hospital and Ospedale Comunità di Copparo a small community based hospital.

All subjects referred to in each of the centre outpatient clinics were ambulatory. Taken collectively, we have found one-hundred and eighty-four patients on domiciliary LTOT.

We have reviewed their clinical data [age, sex, smoking, history and physical examination, arterial blood gas analysis, pulmonary function (including, at least, a flow-volume curve before and after 30 minutes the administration by inhalation of 400 μg of salbutamol through a metered dose inhaler connected to a large volume spacer, or ipratropium bromide in presence of any contraindication to use β_2 agonists)]. COPD diagnosis and severity have been defined according to International guidelines [12]. All former smokers had stopped smoking for more than one year.

Results

114 patients (all smokers) fulfilled the diagnostic criteria for COPD (table 1). Seventy patients (all smokers; summarised in table 2) had other diseases. The last group of patients includes twenty-one subjects where bronchodilator reversibility testing was not been performed (one patient refused to perform bronchodilator reversibility testing), seven subjects in whom both bronchodilator reversibility testing and arterial blood gas analysis in room air were not performed, seven subjects with mixed restrictive and obstructive syndrome (one patient had a vital capacity of 62% of the predicted and a total lung capacity of 82% of the predicted), six subjects with bronchiectasis (diagnosis confirmed by high-resolution computed tomography of the chest), six subjects with severe chronic respiratory failure post-surgical resection of lung carcinoma, two subjects with normal lung function and primary pulmonary arterial hypertension, three subjects with chronic pulmonary arterial hypertension secondary to pulmonary thromboembolism, three subjects with severe kyphosis, four subjects with pneumoconiosis, three subjects with fibrosis secondary to healed pulmonary tubercolosis, one subject with idiopathic pulmonary fibrosis, one subject with thoracoplasty sequelae, six subjects with absence of lung function tests. Most patients (n=174) were former smokers, only ten were current smokers. We were unable to find any non-smokers in our screened population of subjects on long-term domiciliary oxygen therapy. Furthermore, there was no a past history of asthma and/or acute wheezing episodes in either of the patient groups.

Discussion

Despite all the limitations inherent in a cross-sectional study we believe that our screened population is fully representative of the spectrum of patients with severe chronic respiratory failure on long-term oxygen therapy in Italy. This data shows the complete absence of non-smokers and asthmatic patients in a large unselected population of patients with severe chronic respiratory failure on LTOT in Italy demonstrating that asthma is an uncommon cause of severe chronic respiratory failure necessitating long-term domiciliary oxygen therapy in non-smokers. We cannot exclude with certainty that some of our smokers with COPD or chronic airflow obstruction are also asthmatics. However, a previous study has clearly demonstrated that in patients with chronic airflow obstruction the presence of a history of asthma is very important to distinguish the asthmatics from the COPD patients [4]. For this reason the absence of a history of asthma in all our patients strongly suggests that most of the smokers with COPD or chronic airflow obstruction are not asthmatics. The same study has also shown that chronic airway inflam-

Table 1. - Patients on long-term oxygen therapy with severe chronic respiratory failure and chronic obstructive pulmonary disease (n=114)

Age (years)	Pack-years	FEV_1 (mL) before*	FEV_1 (mL) after*	FVC (mL) before*	FVC (mL) after *	FEV_1/ FVC%°	PaO_2 (kPa)	$PaCO_2$ (kPa)
71 ± 8	51 ± 24	894 ± 380	978 ± 400	1,949 ± 754.4	2,124 ± 743	46 ± 13.3	7.0 ± 0.7	6.5 ± 1.1

Values are expressed as mean ± SD (standard deviation). All patients were smokers. Abbreviations: FEV_1 = forced expiratory volume in one second; FVC = forced vital capacity.
*before and after bronchodilator.°post-bronchodilator.

Table 2. - Patients on long-term oxygen therapy with severe chronic respiratory failure and other lung diseases (n=70)

	Age (years)	Pack-years	FEV_1 (mL)	FEV_1/ FVC%	TLC %	PaO_2 (kPa)	$PaCO_2$ (kPa)
Bronchodilator reversibility testing not performed (n=21)	75 ± 8	48 ± 26	901 ± 535	50 ± 14	//	8.1 ± 1.7	6.1 ± 1.2
Bronchodilator reversibility testing and arterial blood gas analysis in room air not performed (n=7)	65 ± 19	41 ± 24	771 ± 307	41 ± 5	//	//	//
Mixed restrictive and obstructive syndrome (n=7)	74 ± 9	51 ± 22	1559 ± 256	70 ± 5	68 ± 11	6.9 ± 0.1	6.1 ± 1.4
Bronchiectasis (n=6)	71 ± 6	80 ± 40	1448 ± 544	66 ± 4	//	7.2 ± 0.2	6.9 ± 0.8
Lung carcinoma (n=6)	75 ± 1	52 ± 8	703 ± 229	50 ± 2	//	6.9 ± 0.7	5.7 ± 1.4
Normal lung function (n=2)	70 ± 1	40 ± 0	855 ± 785	86 ± 13	//	8.1 ± 0.8	6.4 ± 1.1
Others (n=15) ¶	70 ± 14	34 ± 18	1196 ± 468	60 ± 14	//	7.9 ± 1.9	6.4 ± 1.4
Absence of lung function tests (n=6)	80 ± 9	32 ± 20	//	//	//	7 ± 1.2	6.7 ± 0.6

Values are expressed as mean±SD (standard deviation). All patients, in all subgroups, were smokers. Abbreviations: FEV_1 = forced expiratory volume in one second; FVC = forced vital capacity; TLC = total lung capacity; PaO_2 = partial oxygen pressure; $PaCO_2$ = partial carbon-dioxide pressure.
¶Chronic pulmonary arterial hypertension secondary to pulmonary thromboembolism (3), severe kyphosis (3), pneumoconiosis (4), fibrosis secondary to healed pulmonary tuberculosis (3), idiopathic pulmonary fibrosis (1), thoracoplasty sequelae (1).

mation is always different in asthma and COPD even when asthmatic patients develop a fixed airflow obstruction [4]. Our results also support the current consensus that asthma and COPD are different diseases along all their stages of severity [1, 12] and the concept that avoidance of active smoking is fundamental for the prevention of severe chronic respiratory failure necessitating LTOT.

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