Original Article

Differences between asthma and COPD in the elderly

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Summary. Asthma and chronic obstructive pulmonary disease (COPD) are both characterized by the presence of airflow obstruction. Both diseases are not rare in the elderly population. Distinguishing between these diseases is difficult and may be impossible in some older patients. The aim of the study was to investigate clinical and functional characteristics and the presence of atopic status in elderly subjects compared to COPD patients. Fifty-one patients over 60 years of age were selected for the study (27 patients with late-onset asthma, 24 patients with COPD). Atopy was defined by skin prick test and serum total IgE concentrations which were measured in all patients. Pulmonary function tests including airflow rates, lung volumes, airway resistance, diffusing capacity, and arterial blood gases analysis were performed in all patients. The rate of skin prick test positivity in asthmatics was significantly higher than that of the COPD patients. FEV1 was lower in COPD patients than in asthmatic patients. Bronchial reversibility in asthmatics became significantly higher than in COPD patients. While FRC and RV were increased in both groups showing same degree of pulmonary hyperinflation, patients with COPD demonstrated significantly decreased DLCO when compared to asthmatic patients. The level of both PO2 and PCO2 in patients with COPD significantly differed from asthmatics. In conclusion, a history of heavy smoking, decreased diffusing capacity for carbon monoxide, the presence of more prominent lung hyperinflation and chronic hypoxemia favour the diagnosis of COPD, whereas atopy and significant bronchodilator responsiveness favour the diagnosis of asthma.

Key words: Asthma, COPD, elderly, pulmonary function, atopy.

Resumen. El asma y la enfermedad pulmonar obstructiva crónica (EPOC) se caracterizan por la presencia de obstrucción del flujo de aire. Ambas enfermedades no son raras en la población de edad avanzada. Diferenciar estas dos enfermedades es difícil, y puede resultar imposible en algunos pacientes ancianos. El objetivo de este estudio fue investigar las características clínicas y funcionales y la presencia del estado atópico en sujetos ancianos, en comparación con pacientes con EPOC. Se seleccionaron para el estudio 51 pacientes de más de 60 años de edad (27 pacientes con asma de aparición tardía y 24 pacientes con EPOC). La atopia se definió mediante prick test y las concentraciones de IgE total sérica que se determinaron en todos los pacientes. Se realizaron a todos los pacientes pruebas de la función pulmonar, incluidas la frecuencia respiratoria, volumen pulmonar, resistencia al paso del aire, capacidad de difusión y gasometría arterial. La tasa de positividad del prick test en asmáticos fue significativamente superior a la de los pacientes con EPOC. El volumen espiratorio forzado (VEF_1) fue inferior en los pacientes con EPOC que en los asmáticos. La reversibilidad bronquial en asmáticos fue significativamente superior que en los pacientes con EPOC. Mientras que la capacidad residual funcional (CRF) y el volumen residual (VR) incrementaron en ambos grupos, mostrando el mismo grado de hiperinflación pulmonar, los pacientes con EPOC mostraron una menor capacidad de difusión del monóxido de carbono (CDCO) en comparación con los pacientes asmáticos. El nivel de PO_2 y PCO_2 en los pacientes con EPOC fue significativamente diferente del de los asmáticos. En conclusión, una historia de elevado consumo de tabaco, una menor capacidad de difusión del monóxido de carbono, la presencia de hiperinflación pulmonar más destacada e hipoxemia crónica favorecen el diagnóstico de EPOC, mientras que la atopia y una reactividad significativa al broncodilatador favorecen el diagnóstico de asma.

Palabras clave: Asma, EPOC, ancianos, función pulmonar, atopia.

Introduction

Asthma and in particular chronic obstructive pulmonary disease (COPD) are highly prevalent chronic diseases among the elderly, characterized by the presence of bronchial obstruction and chronic airway inflammation. Both diseases have a distinct pathogenesis and require unique treatment approaches. However, distinguishing between these diseases is difficult and may be impossible in some older patients. In fact, asthma is not rare in the elderly population, although it has been considered a disease of childhood and young adults. Asthmatic patients in the elderly mainly include subjects with long-standing disease. However, the first asthmatic symptoms may also occur in late adulthood or after 65 years of age. Despite affecting approximately 4 to 8% of this age group, clinical overlapping of COPD and late-onset asthma often lead to misdiagnosis in the elderly population [1-3]. In addition, inability to perform functional evaluation, together with older age and poor perception of symptoms such as shortness of breath, have been suggested as contributory factors for underestimation of asthma by both the patient and the physician. The fact is that both asthma and COPD appear to share some clinical similarities, although they are indeed different diseases. Therefore, it is essential to properly diagnose both diseases in order to provide appropriate treatment and improve outcome in this age group.

In general, the degree of reversibility to a bronchodilator has been used to determine whether a patient has COPD or asthma. On the other hand, the use of phenotypic features (e.g symptoms, allergy and bronchial hyperresponsiveness) may help to differentiate both obstructive airways diseases [4-7].

In this respect, we planned this study to investigate clinical and functional characteristics, the presence of atopic status in elderly subjects who had a history of late-onset asthma and to compare these findings with age-matched COPD patients.

Material and methods

Subjects

A total of 51 patients over 60 years of age were selected for the study. Twenty-seven (21 female, 6 male) were affected with asthma diagnosed according to the criteria as described by the Global Initiative for Asthma (GINA) [8]. The asthmatic patients exhibited a history of episodic dyspnea, cough and wheezing, a documented (recently or in the past) reversible airway obstruction (12≥ % increase in FEV1 from baseline after inhalation of salbutamol), and/or hyperresponsiveness to methacholine (PC20 of less than 8 mg/ml) in bronchial challenge test. Firm inclusion and exclusion criteria were used to recruite "pure asthma" patients. All asthmatic patients had late-onset asthma after 60 years of age, never-smokers or ex-smokers with very long duration.The mean age was 69.74±6.25 years (ranged between 60-83 years). Age of onset of asthma was determined on the basis of the year of the first onset of respiratory symptoms (dyspnea, etc.). We excluded subjects with an early onset of asthma symptoms before the age of 60 years. The cutoff point of 60 years was chosen because overt manifestations of COPD usually occur in late adulthood; therefore, asthmatic patients >60 years old were expected to be more frequently misrecognized as affected by COPD. Twenty-four patients (17 male, 7 female) with COPD were diagnosed according to the Global Obstructive Lung Disease (GOLD) 2003 update criteria [9]. The characteristic symptoms of all COPD patients are cough, sputum production and dyspnea with exertion over many years. There was smoking history of more than 10 pack-years. Best post-bronchodilator FEV1/FVC of less than 70% was the other entry criteria in COPD for the present study. The mean age was 68.83±4.82 years (ranged between 60-79 years). All patients were in a stable condition as assessed by clinical and laboratory findings and had been free of exacerbation or respiratory infection in the previous 4 weeks. Patients were excluded from the study if they had other pulmonary or uncontrolled systemic diseases or an inability to co-operate. Duration of disease was assessed by asking the patients when pulmonary complaints had started. Cigarette smoking habits were recorded as pack- years. The number of cigarette pack-years was calculated as the product of the period of tobacco use (in years) and the average number of cigarettes smoked per day.

Allergy evaluation

All patients meeting the inclusion criteria underwent skin testing. Skin prick tests were performed using a common panel of inhalant allergens including *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae* house dust mites, *Cladosporium* and *Alternaria* molds, cat and dog animal danders, grass, tree and weed pollens, and cockroach (Stallergenes, Pasteur, France). Negative and positive controls were histamine (10 mg/ml) and phenolated glycerol-saline, respectively. Reactions were measured after 15 minutes. A test was considered positive if it produced a wheal with a mean diameter (mean of maximum and 90^0 midpoint diameters) of > 3 mm greater than the saline control. Atopy was defined as the presence of history and positive skin test response to at least one inhalant allergen. Serum total IgE concentrations were measured by uni-CAP system (Pharmacia Diagnostics, Uppsala, Sweden). The normal limit of total IgE was 100 kU/L.

Pulmonary function tests (PFT)

Pulmonary function tests including airflow rates, lung volumes, airway resistance and diffusing capacity were performed in all patients. Spirometric parameters (FEV_1, FVC, FEV_1/FVC%, PEFR, FEF_{25-75}) were measured at rest using Vmax 229 Pulmonary Function/ Cardio-

pulmonary Exercise Testing Instruments (SensorMedics, Bilthoven, The Netherlands). Lung volumes (TLC, FRC, RV, RV/TLC%), and airway resistance (Raw, sGaw) were measured by a body plethysmograph (SensorMedics 6200 Autobox, Bilthoven, The Netherlands). Single breath method was used in the assessment of CO Diffusing capacity (DLCO) (Vmax 229 Pulmonary Function/ Cardiopulmonary Exercise Testing Instruments (SensorMedics, Bilthoven, The Netherlands). All of the tests were performed in sitting position and the best of three attempts was evaluated. The tests were compatible with ATS criteria [10]. Predicted values were calculated using ECCS reference values [11].

To avoid any potential influence of medication on testing, treatment with all respiratory drugs was withheld for at least 12 h prior to evaluation.

Bronchodilator response was assessed by comparison of pre- and postbronchodilator FEV1 (ΔFEV1). The FEV1 increase greater than 200 ml and 12% of the baseline value was accepted as positive bronchodilator response. Reversibility of airflow limitation (ΔFEV1) was measured after administration of 200 μg salbutamol.

Arterial blood gas analysis (ABG)

ABG was performed at rest and in room air with a Rapidlab 348 pH/Blood Gas Analyser (Chiron Diagnostics Ltd., Essex, UK). pH, PaO_2, $PaCO_2$, and SaO_2 were measured while breathing room air.

Other tests

Alpha-1 antitrypsin (A1AT) levels were determined by nephelometric method (Beckman-Coulter, USA). The normal range was 88-174 mg/dl.

Statistics

Statistical analysis was done through SPSS (Statistical package for Social Sciences for Windows, SPSS, Inc., Chicago, IL, USA). Results are expressed as means±SD; $p<0.05$ was accepted as significant for all analysis. Student's t test was used to assess the differences between groups.

Table 1. Demographic and clinical features of patients.

	Asthma group	COPD group	p-value
Number of subjects (n)	27	24	
Gender (M/F)	6/21	17/7	
Age (years)*	69.74 ± 6.25 (60-83)	68.63 ± 4.82 (60-79)	NS
Duration of disease (years)*	9.74 ± 8.91	14.21 ± 9.29	NS
Smoking (pack-yrs)*	13.25 ± 21.28	44.67 ± 35.67	P< 0.05

* Values are mean ± SD NS: Not significant

Results

The two groups were similar in age and duration of disease. The characteristics of patients are shown in Table 1.

There was male dominance in COPD group, whereas the number of females was higher in the asthmatic group. All of the patients in the COPD group were heavy smokers. However, the majority of asthmatic patients did not have a smoking history. Six patients in the asthma group were ex-smokers. There was a statistically significant difference between two groups when pack-years were compared (44.67±35.67 vs 13.25±21.28, $p<0.05$) (Table 1). Total serum IgE levels were higher in asthmatic patients when compared to patients with COPD, but did not reach statistical significance (mean±SEM: 248.72±98.0 vs 130.71±34.8 kU/L). In addition, the rate

Table 2. The results of airflow rates and airway resistance.

Parameters	Asthma (n=27) Mean±SD	COPD (n=24) Mean±SD	p-value
FVC (L)	1.87 ± 0.68	1.88 ± 0.75	NS
FVC (%)	76.93 ± 17.57	59.54 ± 18.21	P< 0.01
FEV1 (L)	1.25 ± 0.48	1.07 ± 0.56	NS
FEV1 (%)	63.48 ± 15.76	43.79 ± 20.08	P< 0.01
ΔFEV1 (%)	26.00 ± 7.59	10.50 ± 2.21	P< 0.05
FEV1/FVC (%)	64.41 ± 11.25	56.08 ± 14.36	P< 0.05
FEF25-75 (L/sec)	0.86 ± 0.45	0.69 ± 0.44	NS
FEF25-75 (%)	33.00 ± 12.95	24.67 ± 14.36	P< 0.05
PEFR (L/sec)	2.79 ± 1.17	2.81 ± 1.21	NS
PEFR (%)	48.46 ± 15.30	41.52 ± 17.12	NS
Raw (cmH_2O/L/sec)	6.02 ± 2.02	5.59 ± 2.63	NS
sGaw (L/sec/cmH_2O/L	0.023 ± 0.07	0.052 ± 0.02	NS

Results are shown as mean ± SD NS: Not significant

Table 3. The results of lung volumes and diffusing capacity.

Parameters	Asthma (n=27) Mean±SD	COPD (n=24) Mean±SD	p-value
VC (L)	2.15 ± 0.62	2.12 ± 0.83	NS
VC (%)	79.15 ± 9.68	65.33 ± 17.38	P< 0.05
TLC (L)	4.89 ± 1.47	5.76 ± 1.56	NS
TLC (%)	101.62 ± 22.17	103.86 ± 20.89	NS
FRC (L)	3.78 ± 1.36	4.62 ± 1.62	NS
FRC (%)	159.69 ± 51.59	184.46 ± 76.43	NS
RV (L)	2.99 ± 1.08	3.60 ± 1.39	NS
RV (%)	170.38 ± 55.51	192.36 ± 83.99	NS
RV/TLC (%)	56.00 ± 10.91	61.36 ± 10.39	NS
DLCO	15.58 ± 6.82	11.45 ± 5.13	P< 0.05
DLCO (%)	69.70 ± 25.43	49.16 ± 22.47	P< 0.05
DLCO/VA	4.97 ± 1.95	3.13 ± 0.90	P< 0.01
DLCO/VA (%)	103.10 ± 17.21	79.47 ± 24.65	P< 0.01

Results are shown as mean ± SD NS: Not significant

of skin prick test positivity in asthmatics was significantly higher than that of the COPD patients (37% versus 8.3%, respectively, p<0.05). A1AT levels did not show significant difference between COPD and asthma groups (160.13±10.3 vs 169.82 ± 7.9 mg/dl, respectively).

COPD patients had moderate or severe disease according to GOLD criteria (mean FEV1 (%): 43.79 ± 20.08). Asthmatic patients were also in the moderate or severe group (mean FEV1(%): 63.48 ± 15.76). Baseline FEV1 was lower in the COPD patients than in asthmatic patients (p<0.01). Bronchial reversibility (ΔFEV1%) in asthmatics was significantly higher than in COPD patients after administration of 200 µg salbutamol (p<0.05). The mean percentage increase in FEV1 after reversibility test was 26.00 ± 7.59 % in asthmatics versus 11.50 ± 2.21 % in COPD patients. Airflow rates, especially peripheral airflow rates, were significantly lower in COPD patients, whereas airflow resistance parameters were similar in both groups (Table 2).

Among lung volumes, FRC and RV were increased in both groups showing the same degree of pulmonary hyperinflation. Although the increase in lung volumes was higher in COPD patients, the difference was not statistically significant. On the other hand, patients with COPD demonstrated significantly decreased diffusing capacity for carbon monoxide when compared to asthmatic patients (DLCO %: 49.16 vs 69.70, p<0.05) (Table 3).

The level of both PO2 and PCO_2 in patients with COPD significantly differed from asthmatics (p<0.01) (Table 4). There was moderate hypoxemia in COPD patients whereas hypoxemia in asthmatics was mild. Some patients with COPD had mild hypercapnia, while the mean PCO2 value was 44.57 mmHg. On the contrary, no hypercapnia was observed in asthmatic patients.

Discussion

In recent years bronchial asthma in the elderly has received increasing attention because the prevalence of this disease is estimated at 3.8 % to 7.1% in patients older than 65 [12]. COPD is also a major cause of morbidity in old age, affecting approximately 16% of people over the age of 60-65 [1,13]. Asthma and COPD are both defined by the presence of chronic airflow obstruction, but they present distinguishing differences in terms of both risk factors and clinical phenotypes [3].

In our study, the COPD group was characterized by a higher number of male patients, heavy smokers or ex-smokers and a longer duration of disease. Asthmatics were characterized by higher atopy rate, predominance of female patients and lower rate of ex-smokers. Although both asthma and COPD groups had airflow obstruction, patients with COPD were associated with more decreased airflow rates than asthmatics. However asthmatic patients

Table 4. The results of arterial blood gas analysis.

Parameters	Asthma (n=27) Mean±SD	COPD (n=24) Mean±SD	p
pH	7.44 ± 0.03	7.40 ± 0.03	P< 0.001
PO_2 (mmHg)	64.61 ± 6.53	54.66 ± 11.22	P< 0.01
PCO_2 (mmHg)	39.03 ± 5.57	44.57 ± 7.44	P< 0.01
SaO_2 (%)	92.93 ± 2.33	85.82 ± 8.30	P< 0.001

Data are shown as mean ± SD

had more reversible airflow obstruction compared to COPD patients.

It is less clear, however, that allergen exposure and sensitisation play the same role in the development of asthma in adults as they do in children. Although elderly asthmatic patients are indeed less atopic than younger ones, they have more evidence of atopy than age-matched controls without asthma. Previous studies have reported a 29% incidence of allergic history in asthmatics, starting at age 65 or over [14]. We found a significantly higher atopy rate in asthmatics when compared to COPD patients. Skin prick test positivity was 37% in asthmatics whereas it was 8.3% in COPD. Sitkauskiene et al did not find any difference in positive skin test response between asthma and COPD groups although the mean wheal size to common allergens was greater in asthmatics [15]. In another study, Huss et al showed skin test positivity in 74.6% of elderly asthmatics whereas a prevalence of positive skin tests in only 36.6% of a cohort of older patients has been described by a study by Burrows et al in accordance with our results [12,16].

Asthmatics also had higher serum total IgE levels than in COPD patients although the difference was not significant. In the study by Sitkauskiene et al, a significantly raised serum total IgE level was detected in the asthmatic patients as consistent with our findings [15].

Elderly patients with asthma also have elevated serum IgE levels as compared to age-matched patients without asthma [16]. Some authors have demonstrated a decline with age in serum total IgE values and slightly lower atopy incidence rates among those over 60 y. However, no change with age in sensitivity or severity of atopy was found in their study. According to data, they have suggested that atopic propensity remains into advanced age as well [17].

It was considered that skin test reactivity or high IgE levels are not useful for differential diagnosis between asthma and COPD in the elderly [18]. Despite some evidence of the progressive decline in IgE levels and skin reactivity with increasing age in the elderly, our findings support the importance of allergy evaluation in distinguishing asthma and COPD in the elderly.

The rate of decline in lung functions with age, as measured by FEV1, is greater than normal in patients with asthma and COPD. However, the rate of decline in lung function in patients with asthma was significantly less than observed in age-matched persons with diagnosis of COPD [1]. In our study, patients with asthma had mildly reduced FEV1 and FEV1/FVC, in concordance with various studies [19-23]. In the Cardiovascular Health Study, about 40% of the participants with definite elderly asthma had airway obstruction. The mean percent predicted FEV1 values were much lower in those who had definite asthma than those who did not have asthma [20]. Particularly in long-standing asthmatics a more striking decline in FEV1 and persistent airway obstruction was detected [3]. Several longitudinal studies have shown that the rate of decline in airflow rates with age is greater than normal in asthmatic patients. Peat et al found a medium loss of FEV1 of 50 ml/y in asthmatic patients [1,18,24]. COPD is defined as a chronic-non-specific pulmonary disease characterised by the presence of progressive bronchial obstruction and an accelerated loss of lung function with a doubling of the rate of annual FEV1 decline from approximately 30 ml/y to nearly 60 ml/y [7,14]. In our study, we observed significantly reduced FEV1 in our COPD patients compared with asthmatics and this finding was also consistent with other studies [19-22]. In fact, airflow rates were also reduced in elderly asthmatics, although this reduction was mild when compared with age-matched COPD patients.

When airflow obstruction is detected in elderly patients, attempts to demonstrate reversibility can uncover an asthmatic component for the disease. In our study, asthmatics showed an important degree of reversible airflow obstruction when compared to COPD patients. We found a significantly higher improvement in FEV1 after a bronchodilator in patients with asthma. On the other hand, the bronchodilator response in COPD patients is generally very limited. However, Calverley et al stated that bronchodilator responsiveness may be found in up to 23% to 42% of patients with COPD [25]. Moreover, Sitkauskiene found that more than one-third of patients with stable COPD had partial reversible airway obstruction [14]. In our study, 15% of patients with COPD had reversible airflow obstruction but mean improvement in FEV1 in patients with COPD was still lower than asthmatics. In our patients with late-onset asthma, the rate of reversibility was 67%. Only 33% of our elderly patients with late-onset asthma represented irreversible airflow obstruction, in whom there was a smoking history in the past. In the literature, it is reported that 53% of patients with late-onset asthma showed completely reversible airway obstruction [18]. There is also some evidence about the possibility of development of fixed airflow obstruction in asthmatics. The overlap between COPD and asthma is more marked in elderly patients, because older asthmatics may develop irreversible airway obstruction and some patients with COPD have a degree of reversibility [2,3].

The distinction between asthma and COPD based simply on spirometric parameters is difficult, therefore there is a need for more discriminatory tests such as lung volumes and DLCO measurements in terms of lung function. In this study, both COPD and asthmatic patients showed increase in lung volumes, especially FRC, RV, RV/TLC ratio were elevated. However, the increase in lung volumes in COPD patients was greater although statistical significance was not established. Fabbri et al found significant differences in RV between COPD and asthma groups (131.8% vs 106.6%, respectively) [26]. The higher RV in patients with airflow obstruction due to COPD suggest that paranchymal destruction is present in COPD. Detailed morphologic evaluations have revealed that 79% of patients with COPD had evidence of parenchymal emphysema. Hyperinflation which results in increased lung volumes is manifested by an increase in the functional residual capacity [6,7]. Another physiologic abnormality seen in our patients with COPD included moderately reduced diffusing capacity (50%). On

the other hand, some asthmatics also had mildly decreased DLCO (70%). There was a significant difference in DLCO values between patients with COPD and asthma. The decreased DLCO may be directly related to the loss of alveolar-capillary surface area that is associated with emphysema [6]. There are some data about the presence of emphysema in elderly asthmatic patients. Mitsunobu et al showed that the %RV value was significantly increased and %DLCO was significantly decreased in elderly asthmatics with a smoking history compared to lifetime non-smokers (RV: 170.1% vs 131.0% respectively, DLCO:70.1% vs 88.4%, respectively) [27]. In our study, only 6 patients in the asthma group had a history of smoking and all of them were ex-smokers. Because of the low number of smokers we were unable to perform a statistical analysis. However, when we examined mean values of these parameters in both non-smoker and ex-smoker asthmatics, we observed that RV and FRC were higher and DLCO was lower in ex-smokers. This finding might be explained by the inflammatory effect of cigarette smoke on airways and lung parenchyma.

In some articles it has been reported that DLCO was significantly lower and lung volumes (RV, FRC) were significantly higher in COPD patients compared to asthma even if they had similar FEV1 levels [3,6,28-29]. Similarly, we observed significantly greater RV, FRC and airflow limitation in COPD patients compared to asthmatics. Moreover, we found significant differences in DLCO between both groups.

The degree of hypoxemia in COPD patients was significantly different from asthmatics. Some patients with COPD had hypercapnia, whereas no hypercapnia was observed in asthmatics. Fabbri et al also reported higher oxygen tension in arterial blood in asthmatics compared to COPD patients [26].

In conclusion, it is true that the differential diagnosis of obstructive airway diseases is obviously overlooked in older patients. Although the diagnosis of asthma may be more difficult in this age group, a less intensive diagnostic approach is responsible for a lower rate of asthma diagnosis in older people. Considering the data presented; on the basis of a detailed clinical history, especially smoking status, pulmonary function examination including DLCO, lung volumes and arterial blood gas measurement, it may be possible to differentiate asthma from COPD. In other words, common diagnostic tools are still helpful in elderly patients for discrimination between these two obstructive diseases. We also have to keep in mind the distinct possibility of an allergic basis in elderly asthmatics. We believe that greater physician awareness of the differences between asthma and COPD will also contribute to improved diagnosis and treatment outcomes in the older population.

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