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Assessment of Impairment/Disability due to Occupational Asthma through a Multidimensional Approach

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Running head: impairment in occupational asthma

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Abstract

Background: Subjects with occupational asthma (OA) are often left with permanent sequelae after removal from exposure. Assessing impairment/disability should utilize various tools. Aims: Examine whether: 1) assessment of inflammation in induced sputum is relevant to impairment; and 2) use of questionnaires on quality of life and psychological factors can be useful to the evaluation of disability. Subjects and methods: 40 subjects were prospectively assessed for permanent impairment/disability due to OA two years after cessation of exposure. Impairment was assessed as follows: 1) need for asthma medication; 2) asthma severity; 3) airway calibre and responsiveness; and 4) degree of inflammation in induced sputum. Disability was assessed according to quality of life and psychological distress. Results: There was a significant improvement in airway responsiveness and inflammation from diagnosis to the present assessment. Sputum eosinophils ≥ 2% and neutrophils > 60% were present in 8 (20%) and 12 (30%) of subjects, one or the other feature being the only abnormalities in 15% of subjects. Quality of life was moderately affected and there was a prevalence close to 50% of depression and anxiety. Conclusion: In the assessment of subjects with OA, information on airway inflammation and psychological impacts are relevant to the assessment of impairment/disability although these findings need further investigation.

Key words: occupational asthma; impairment/disability; quality of life; psychological stress

INTRODUCTION

Once a diagnosis of occupational asthma (OA) is made, the ideal course of action is to remove the worker from the work environment that is causing the OA. The individual should be considered permanently unfit to work in this environment or similar work environments where he or she would be exposed to causative agents. This prevents deterioration of the worker's condition that occurs if the worker continues to be exposed (1) (2). Short-term compensation and rehabilitation should be offered to enable the worker to find another job or retrain for another profession. OA can leave permanent impairment in workers even after cessation of exposure to the causal agent (see (3) for a review). The majority of subjects with OA are left with respiratory symptoms, airway obstruction, hyperresponsiveness and inflammation even years after removal from exposure to the causal agent (4) and often still require anti-asthmatic medication. Bronchial hyperresponsiveness mainly improves in the first two years (5) and continues to improve thereafter, though at a slower pace (6).

Scales for assessing impairment have been proposed (3) (7) (8). Assessment should be made when asthma status is relatively stable. Clinical criteria proposed to assess impairment include the nature and doses of medication needed to control asthma (e.g. bronchodilator, inhaled steroids), and functional criteria include levels of bronchial obstruction and hyperresponsiveness. However, these scales do not take into account residual bronchial inflammation that can still be present after cessation of exposure. Increased levels of sputum eosinophils and neutrophils have indeed been observed in 15% and 20% of subjects with normal airway calibre and responsiveness assessed an average of ten years after diagnosis (4).

OA can also have significant psychological and quality of life impacts on affected workers. To our knowledge, no studies to date have evaluated the psychological impacts of OA after removal from the workplace, and few studies to date have evaluated quality of life in subjects

with OA after removal from exposure (9) (10).

Moreover, quality of life is an important dimension of the assessment of asthma and most clinical trials assess quality of life outcomes using standardized tools (11). Clinicians and Workers' Compensation Agencies are requested to assess both impairment that causes functional deficits and disability. Some elements of the latter can be assessed by examining quality of life (3). Moreover, the psychological impact of being diagnosed with OA also needs to be assessed using relevant and standardized questionnaires.

We believe that adding assessments of induced sputum as well as measures of quality of life and psychological distress to the evaluation of workers with OA after they are removed from exposure can significantly improve assessment of impairment and disability in these workers. This effort can lead to designing more complete scales to assess these workers. As such, the aims of the present study were twofold: 1) We first aimed to evaluate the usefulness of adding assessment of airway inflammation to the standard assessment of impairment (airway calibre and responsiveness; need for medication) in subjects with OA after removal from exposure; 2) Our second aim was to evaluate the psychological and quality of life impacts of OA on subjects after removal from exposure via administration of validated questionnaires.

MATERIALS AND METHODS

Subjects and design

Subjects included in the study are OA claimants who applied to the Workers' Compensation Agency of Quebec (Commission de la santé et sécurité du travail du Québec, CSST) for assessment of impairment/disability after stopping exposure to the agent causing OA for at least two years. They were assessed by two of the four Quebec CSST medical committees (the Montreal committees) that evaluate claims for occupational respiratory diseases. All claimants assessed between October 2004 and March 2006 were requested to participate on a voluntary basis by adding induced sputum, psychological and quality of life questionnaires to their investigation. It was made clear to the participants that assessment of impairment/disability for current medico-legal purposes would be based only on the criteria currently used in Quebec (3), i.e. need for medication, airway calibre and responsiveness, and that the committee would not be informed of the results of the added tests, nor would these results be considered in the worker's assessment. All subjects gave written consent for their participation. The protocol was accepted by the ethics committees of both Sacré-Coeur Hospital and the Montreal Chest Institute, where the study took place.

Tests and measures

An open questionnaire was first used to ensure that the subject's asthma was clinically stable. Information about medication was obtained from a questionnaire administered to every subject by a trained research assistant.

Routine tests included: 1) spirometry before and after bronchodilator (12); and 2) assessment of bronchial responsiveness to methacholine using a standardized procedure with a Wright's nebulizer (output=0.14 ml/min) (13). The additional tests proposed to the participants were as follows: 1) induced sputum according to a standardized methodology (14); 2) completion

of an asthma-specific quality of life questionnaire (Asthma Quality of Life Questionnaire, AQLQ) (15); 3) completion of the St. George's Asthma Severity Questionnaire (16); and 4) completion of two psychological questionnaires, the Psychiatric Symptom Index (PSI) (17) and the Millon Clinical Multiaxial Inventory, 3rd Edition (MCMI-III)(18).

Reference values used for spirometry were Knudson et al. (19). Normal responsiveness was set at a provocative concentration of methacholine causing a 20% fall in FEV_1 (PC_{20}) greater than 16 mg/ml (20). Logarithmic transformation of PC_{20} was used for the statistical analysis. Changes in PC_{20} were considered significant when there was a 3.2-fold or greater difference from the value obtained at the time of diagnosis (21). Different levels of sputum eosinophils were considered and significant eosinophilic airway inflammation was defined when sputum eosinophils were equal to or greater than 2%. The percentage of neutrophils was also assessed and values above 60% were judged to be elevated.

To assess quality of life, all patients completed the Asthma Quality of Life Questionnaire (AQLQ) (15). The AQLQ includes 32 items and evaluates asthma quality of life across four life domains that may be negatively affected by asthma: asthma symptoms, emotional dysfunction, exposure to environmental stimuli and limitation of daily activities. Every field is scored from one (extremely severe) to seven (not limited at all) and the total score is the mean of the four scores. The St. George's Asthma Severity Questionnaire includes eight questions related to respiratory symptoms, and the total score (range: 0- 662.5) represents the sum of these elements (16). Psychological distress was assessed using the Psychiatric Symptom Index (PSI), which is a 29-item self-report questionnaire designed to assess the presence and intensity of psychological distress in the previous two weeks (22). Items are scored using a 4-point scale (0-3) from "never" to "very often." Total scores and subscale scores (depression, anxiety, anger and cognitive disturbance) are calculated as a percentage of the total possible score out of 100. Scores

exceeding 25 are considered “high.” Patients also completed the Millon Clinical Multiaxial Inventory-III (MCMI-III), which is a 175-item true-false inventory with 24 clinical scales designed to assess personality disturbances (e.g. avoidant personality) and psychiatric syndromes (e.g. anxiety disorders) (18). For the purposes of this study, only the results of the psychitric syndrome scales will be presented. Scores < 75 are considered within the normal range, scores between 75 and 85 identify those with a possible psychiatric syndrome, and scores ≥ 85 identify those with a high probability of a psychiatric syndrome.

Analysis of results

Functional variables such as spirometry and bronchial responsiveness and induced sputum results were compared at diagnosis and follow-up visits. Psychological and quality of life questionnaires were administered and examined only at the follow-up visit.

Continuous variables were expressed as means ± standard deviation. The other variables were expressed as median and interquartile range. Statistical analysis included unpaired t-test, ANOVA, Wilcoxon test and regression coefficients. They were performed by means of a statistical software package (SPSS for Windows, version 10). The level of statistical significance was set at a $p < 0.05$.

RESULTS

Selected characteristics of the participants are shown in Table 1. Only five of 45 potential subjects refused to participate (89% participation rate). The majority were male and atopic. Although these subjects were supposed to be re-assessed two years after diagnosis according to medicolegal procedures in Québec, the mean interval was more than three years. Low-molecular-weight agents were the principal agents causing OA, and isocyanates were the leading cause in 14 subjects (35% of all subjects included). Flour was the causal agent in five subjects, soldering and latex in four subjects each. In two subjects for whom monitoring was carried out at the workplace, the cause of OA was undetermined. A low proportion of subjects (17.5%) were unemployed or had been employed only on a part-time basis since removal from exposure.

Results of clinical, functional and inflammatory status at the time of diagnosis and in the present study are listed in Table 2. While 29 subjects required inhaled steroids alone or combined with long-acting beta adrenergic agents at the time of diagnosis, 22 used these medications at the time of follow-up. The daily dose of inhaled steroids showed a downward trend. Whereas FEV_1 and FEV_1/FVC values did not significantly change, the number of subjects with slightly increased values and the proportion of subjects with significant bronchial hyperresponsiveness ($PC_{20} \leq 16$ mg/ml) declined significantly. Nine of the 40 subjects (22.5%) showed at least 2-fold improvements in PC_{20}. Also, as shown in Table 2, there was a significant diminution in the % of sputum eosinophils and significantly fewer subjects had sputum eosinophils $\geq 2\%$ at the time of the current assessment. There was no significant change in sputum neutrophils. Spirometry and PC_{20} values at diagnosis did not differ in subjects with abnormal and normal levels of sputum eosinophils or neutrophils at follow-up.

As shown in Table 3, asthma severity could be judged, on average, to be moderate, with mild to moderate impairments in quality of life. With the exception of the anger subscale, mean

scores on all of PSI subscales (depression, anxiety, cognitive disturbance) as well as the total score, were ≥ 25, which is the cutoff denoting clinically significant levels of distress (22). Moreover, more than half of the subjects (52.5%) had scores ≥ 25 on the anxiety subscale, and nearly half of the subjects had scores ≥ 25 on the depression (47.5%) and cognitive disturbance (45%) scales, suggesting a significant level of psychological distress across multiple areas of psychological functioning. With regard to levels of psychiatric syndromes, the most common psychiatric disorder was anxiety disorders, with 35% (n=14) of subjects having a possible (n=5) or probable (n=9) anxiety disorder. Levels of dysthymia (a chronic form of depression) were also high, with 22.5% of subjects having possible (n=7) or probable (n=2) dysthymia. Levels of all other psychiatric disturbances were under 10%, and no subjects were alcohol dependent or psychotic. At follow-up, scores of all questionnaires used were not significantly different in those with and without airway hyperresponsiveness or airway inflammation. There were significant correlations ($p < 0.05$) between asthma severity on the one hand and some quality of life and psychological indices on the other hand as follows: 1) quality of life: total score (r= - 0.44), symptomatic score(r=-0.54), environmental score (r=- .40); 2) PSI: total score (r=0.36), anxiety (r=0.33), anger(r=0.33); psychiatric syndromes (MCM1-III): somatoform disorder (r=0.33). No psychological scores showed significant differences according to the various social outcomes listed in Table 1.

Table 4 summarizes the findings in terms of specific alterations. Five subjects (12.5%) could be considered to be cured as all indices were within normal limits. Persistence of bronchial hyperresponsiveness was the most common abnormality, this being the only abnormality at follow-up in 22.5% of subjects and in combination with other features in 57.5% of subjects. The most common combination of abnormalities was the presence of airway obstruction and hyperresponsiveness (15%). Six subjects (15%) showed isolated sputum eosinophilia or/and

neutrophilia, and in 20 (50%) this abnormality was combined with other alterations. Six of the eight subjects who had sputum eosinophilia were on inhaled steroids at the time of assessment. Four of the 12 subjects (33%) with sputum neutrophilia at the time of follow-up had isocyanate-induced OA, by comparison with 8/22 (36%) subjects with OA caused by other agents.

Asthma severity and daily doses of inhaled steroids correlated significantly with various functional and inflammatory indices such as FEV_1, PC_{20} and sputum eosinophilia (Table 5). There was no significant correlation between the levels of sputum eosinophilia or neutrophilia on the one hand and PC_{20} on the other hand.

DISCUSSION

Our study confirms that subjects with OA are often not only left with airway hyperresponsiveness, as found in most follow-up studies of OA (23), but also airway inflammation as shown by abnormal levels of eosinophils or neutrophils in induced sputum (4). Fifty percent of subjects had such abnormalities and, in 10% of subjects, this was the only abnormal finding observed at follow-up. The proportion of subjects with evidence of airway inflammation is higher than in a previous study (4) in which increased eosinophils and neutrophils were documented in only 15% and 20% of subjects respectively. This difference can be explained by the fact that our subjects were assessed two years after cessation of exposure, whereas the average cessation of exposure was nearly ten years in the cited study (4).

Recent studies have examined the prognostic impact of inflammation on asthmatic flare-ups (24) (25). The presence of increased levels of eosinophils has been consistently found to increase the risk of asthmatic flare-ups. The fact that subjects with OA have persistent increased eosinophils in induced sputum, even without airway obstruction and hyperresponsiveness (this represented 10% of our subjects), should be considered when determining levels of impairment in these subjects because they are at high risk of asthma exacerbation. Moreover, airway caliber and hyperresponsiveness was not related to the level of eosinophils in induced sputum (Table 5). Currently, airway calibre and responsiveness, as well as need for medication, are the only three criteria used to determine levels of impairment in scales that are proposed to assess impairment (8). Results of our study therefore point to the relevance of adding information about the status of airway inflammation. Although our results should be confirmed in other studies, we would therefore propose that this information obtained from induced sputum be used to quantify the degree of impairment. First some subjects (7 of 40 or 17.5% had isolated increased sputum eosinophils (n=1) or neutrophils (n=4) or both eosinophils and neutrophils (n=2) (see Table 4).

Moreover, thirteen of the 20 subjects with airway inflammation had other abnormalities, all of this combined possibly making them even more at risk of asthmatic exacerbations. Neutrophilic inflammation is a well documented phenomenon in chronic asthma, although it is not known whether this represents a prognostic factor in asthma flare-ups, though this has been shown to be the case with eosinophils (26). Anees et al. have shown that subjects with OA due to low molecular weight agents may show two patterns of changes in sputum while at work, either eosinophilic or non-eosinophilic inflammation, with subjects with eosinophilic inflammation showing lower FEV_1 and more pronounced airway responsiveness (27). Although our subjects were studied on average more than three years after cessation of exposure, some clinical and functional parameters were significantly correlated with the levels of eosinophils and neutrophils (Table 5); for instance, levels of neutrophils were inversely correlated with baseline FEV_1. We have also shown that subjects with OA due to isocyanates may show neutrophilic inflammation at the time of specific inhalation challenge(28) although, in the current study, the proportion of subjects with sputum neutrophilia was not higher in the case of OA due to isocyanates. Sputum cells may therefore differ at the time of exposure and after cessation, though levels of eosinophils or neutrophils correlate with some clinical and functional parameters in one or other of these situations.

One study has shown that the quality of life of OA subjects two years after removal from the workplace is worse than non-occupational asthmatics with comparable asthma severity (9). In a recent study that examines quality of life using the same questionnaire (11) as used in the previous (9) and current studies by our group, Al-Otaibi et al. found a minimal impact in ten asthmatic subjects with latex allergy who were assessed on average two years after cessation of exposure (10). Compared to scores reported in this previous study, quality of life scores were worse in subjects in the present study. The reason for this is not known. It is unlikely to be due to

changes in compensation in the interval of 15 years between the two studies, as the cost of compensation has increased significantly, from an average of $50,000 to $75,000 CAN, over this period in Quebec. The lower quality of life scores observed in the present study could be due to relatively high levels of psychological distress reported by patients, which may have affected quality of life levels. Previous studies have shown that asthma patients with depressive and anxiety disorders have worse asthma-related quality of life compared to patients with these disorders, independent of age, sex, asthma duration and severity (29)(30).

In the current study, we assessed levels of psychological distress using a general symptom index (PSI), an inventory that assesses levels of psychiatric syndromes (MCMI-III). Levels of psychological distress observed in the present study were quite elevated according to scores on the PSI. Levels of anxiety, depression and cognitive disturbance were all in the clinical range (>25), suggesting that the psychological consequences of OA are not only significant but affect a range of psychological factors. Moreover, the fact that psychological distress was measured at least two years after OA was diagnosed and two years after subjects had been removed from the workplace suggests that psychological distress persists beyond the shock of the initial diagnosis and withdrawal from the workplace. With respect to psychiatric syndromes, which reflect more severe psychopathology, anxiety disorders and dysthymia were relatively common in this study, with 35% and 22.5% of patients having a possible or probable anxiety disorder or dysthymia respectively. This suggests that patients with OA are anxious and some are chronically depressed, a finding that is consistent with previous studies with non-occupational asthmatics (29). However, rates of anxiety disorders and dysthymia in this study were much higher than those observed in Lavoie et al.'s study on tertiary care asthmatics, which reported rates of anxiety disorders at 25% and rates of dysthymia at only 4% (29). However, the study by Lavoie et al. as well as most studies in the literature used a psychiatric interview to assess psychiatric disorders,

which may provide a more conservative estimate of rates of psychiatric disorder than self-report questionnaires like the ones used in our study (31).

Disability is defined by the American Thoracic Society as the "total effect of an impairment on a patient's life" (7). Our study confirms that disability is not generally associated to the extent of impairment. The use of answers to quality of life questionnaires has been advocated in examining disability due to OA (23). We believe that the use of other standardized psychological tools, such as those used in the current study, should also be advocated to provide extra information that can be used in assessing disability. These questionnaires should be used both at the time of diagnosis and follow-up so as to compare the same worker in both situations, which is a limitation of our study in which these tools were used at the follow-up only. Although our study was carried out in the context of assessing permanent impairment for medico-legal purposes in subjects with OA, we do not believe that this could have significantly affected answers to questions. Indeed, our subjects were clearly informed that the extra information obtained from these questionnaires would not be used for the assessment of impairment/disability since this was a research project.

Disability is related to the social impact of OA. In Quebec, rehabilitation programs that are run in the two first years following removal from exposure have satisfactory efficiency, as a minority of workers are left unemployed or only hold part-time jobs (32). In the current study, this proportion was 17.5% compared to 8% in a previous study (32). Therefore, other studies addressing the question of disability in situations of less satisfactory socioeconomic outcomes should be carried out. OA and work-related asthma have indeed significant socioeconomic impact. Unemployment affects from 20 to 38% of workers after diagnosis as documented in studies carried in UK, France, Belgium and British Columbia, Canada (33).

Results of this study may contribute to the development of a scale that can more accurately

assess permanent impairment due to OA, a scale based not only on physiological parameters but also on information obtained from assessment of inflammation. The current scale proposed in 1993 by the American Thoracic Society (7), which retained previously published criteria (34) has not been revised for nearly 15 years, although its implementation is recent (8). In addition, this study included psychological and quality of life measures that provide information on psychosocial disability due to OA. Although physicians are often requested to provide advice not only on impairment but also on disability, they are generally hesitant and reluctant to commit to a judgment on the latter, probably because they are less familiar with the validated tools used to measure quality of life and psychological variables. Nonetheless, these tools are widely available and may provide valuable information with which to assess the psychosocial impacts of OA.

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Table 1. Selected baseline characteristics of participants

N	40
Age (years)	46.2 ± 11.4
Gender (M/F)	32/8
Time lapse between diagnosis and assessment (months)	43.6 ± 33.6
Atopy (%) *	29 (72.5%)
Smoking habit (NS/exS/S)**	14/18/8
Duration of exposure to the causal agent (years)	14.9 ± 12.2
Duration of respiratory symptoms before leaving work (years)	7.0 ± 8.7
Nature of causal agent	
High-molecular-weight agents (%)	14 (35%)
Low-molecular-weight agents (%)	24 (60%)
Undetermined	2 (5%)
Social outcome at time of assessment ***	
Work for same employer without exposure to causal agent	8 (20%)
Work for different employer	13 (32.5%)
Training for different occupation	5 (12.5%)
Early retirement	7 (17.5%)
Part-time job or unemployed	7 (17.5%)

Legend: *atopy: defined by at least one immediate skin reaction to a battery of 15 ubiquitous aeroallergens; ** NS= non-smoker; exS=ex-smoker; S=smoker; *** financial compensation is offered if needed to salary level at time of cessation of exposure to causal agent; part-time job workers were no longer exposed to the agent.

Table 2. Clinical, functional and inflammatory status at time of diagnosis and current assessment

	Diagnosis	Current assessment	test (p value)
Need for medication			
No medication	2 (5%)	8 (20%)	
Short-acting bronchodilator only	9 (22.5%)	10 (25%)	
Inhaled corticosteroid	15 (37.5%)	7 (17.5%)	
Inhaled corticosteroid and long-acting bronchodilator	14 (35%)	15 (37.5%)	NS *
Daily dose of inhaled corticosteroid (micrograms)	609 ±704	449 ± 507	0.06
FEV_1 (% predicted)	81.5 ± 18.6	82.7 ± 20.6	NS
FEV_1/FVC (% predicted)	96.7 ± 15.4	97 ± 15.1	NS
Significant bronchial hyperresponsiveness	39 (97.5%)	22 (55%)	0.01
PC_{20} (mg/ml)			
> 16; 2-16; 0.25-<2; <0.25	1/11/16/12	10/13/9/0	-
Changes in PC_{20} (-fold variation)			
<2; 2-<3.2; ≥ 3.2	-	24/5/4	-
Induced sputum			
Total cell count	1.68 (3.39)	2.36 (5.07)	NS
Eosinophils (%)	3.5 (6.2)	0.5 (2.0)	0.005
Eosinophils			
<1%; 1-< 2%; ≥ 2-<5%; ≥5%	9/3/9/10	18/8/2/6	0.01 **
Neutrophils (%)	42.1 (51.0)	46.5 (47.1)	NS
Neutrophils > 60%	10 (32%)	12 (35%)	NS

Legend: * by comparing the number of subjects taking no medication vs others and those taking no medication + BDT only vs others; ** by comparing those with eosinophils ≥ 2% vs others. Four of eight subjects who did not undergo methacholine tests had positive bronchodilator tests (increase >12% in FEV_1 after inhalation of short-acting bronchodilator). Slightly more subjects underwent induced sputum analysis at the follow-up visit since this testing was not yet routinely carried out at the time of diagnosis.

Table 3. Questionnaires

		M ± SD
Asthma severity *		330 ± 186
Quality of life **		
Total score		4.5 ± 1.4
Respiratory symptoms		4.6 ± 1.5
Limitation in daily activities		4.1 ± 1.3
Emotional aspects		4.9 ± 1.8
Reactions to environmental stimuli		4.3 ± 1.6
Psychological distress (PSI)	> 25	
Depression	19 (47.5%)	27.1 ± 23.2
Anxiety	21 (52.5%)	30.1 ± 21.2
Anger	16 (40%)	23.4 ± 20.7
Cognitive disturbance	18 (45%)	27.7 ± 23.9
Total	19 (47.5%)	28.1 ± 19.9
Psychiatric syndromes (MCMI-III)	< 75 / 75- <85 / ≥85	
Anxiety disorders		
Anxiety	26/5/9	44.0 ± 38.9
PTSD	38/2/0	29.3 ± 27.6
Somatoform disorder	38/1/1	50.5 ± 29.0
Mood disorders		
Major depression	37/1/2	44.6 ± 27.4
Dysthymia	31/7/2	35.2 ± 32.4
Bipolar disorder	38/2/0	46.0 ± 23.3
Substance abuse disorders		
Alcohol dependence	40/0/0	24.6 ± 23.5
Drug dependence	39/1/0	34.8 ± 20.8
Severe psychotic disorders		
Psychosis	40/0/0	31.4 ± 29.8
Delusional disorder	39/0/1	32.9 ± 28.5

Legend: * scale from 0 to 662.5 (severe); ** scale from 1 (bad) to 7 (excellent); PSI = Psychiatric Symptom Index; MCMI-III = Millon Clinical Multiaxial Inventory-III; PTSD = post-traumatic stress disorder.

Table 4. Patterns of outcomes at time of follow-up assessment

Pattern	No abnormality	Bronchial obstruction	Hyper-responsive-ness	Sputum neutrophilia > 60%	Sputum eosinophilia ≥ 2%	Number of subjects
1	X					5
2		X				2
3			X			9
4				X		3
5					X	1
6		X	X			6
7		X		X		4
8			X	X		1
9			X		X	3
10				X	X	2
11		X	X	X		2
12		X	X		X	2
TOTAL	5	16	23	12	8	40

Table 5. Relationships between clinical, functional and inflammatory parameters

	PC_{20}	Sputum eosinophilia	Sputum neutrophilia	Daily dose of inhaled steroids	Quality of life	Asthma severity
FEV_1 (% pred)	r = 0.18 p=0.31	r =0.05 p=0.78	**r =-0.37** **p=0.03**	**r =-0.42** **p=0.007**	r =0.2 p=0.21	**r =-0.51** **p=0.01**
PC_{20}		r =-0.28 p=0.16	r =0.11 p=0.58	**r =-0.39** **p=0.027**	**r =0.41** **p=0.016**	r =-0.32 p=0.08
Sputum eosinophilia			r =-0.2 p=0.27	**r =0.30** **p=0.009**	r =-0.15 p=0.39	**r =0.39** **p=0.03**
Sputum neutrophilia				r =0.16 p=0.36	r =-0.21 p=0.24	r =0.27 p=0.15
Daily dose of inhaled steroids					r =-0.09 p=0.95	**r =0.53** **p=0.001**
Quality of life						r =-0.05 p=0.75

Legend: Asthma severity assessed with the St. George's Asthma Severity Questionnaire (reference no.16) and quality of life according to the questionnaire proposed by Juniper EF and coworkers (reference no. 15); daily dose of inhaled steroids in beclomethasone equivalent; sputum neutrophilia and eosinophilia in %; log transformation of PC20.

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