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## Treatment of Patients with Airflow Obstruction by General Practitioners and Chest Physicians

*Study of pharmacotherapy of chronic non-specific lung disease supported by the Dutch Asthma Foundation (86.28)*

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The study comprised 223 patients with airflow obstruction and/or bronchial hyperreactivity from 29 general practices in the catchment area of Nijmegen University. Fifty-six patients were treated by 19 chest physicians, the remaining 167 by their general practitioners (GPs), without specialist care. The specialists treated more allergic patients than the GP ( $p < 0.05$ ). No other relevant differences in sex, age, smoking behaviour, and severity of the disease (symptoms, lung function, and bronchial hyperreactivity) could be observed between these two groups of patients.

Chest physicians prescribed almost three times as many drugs as GPs. No immediate response to the prescribed bronchodilators was found in 16% of the patients treated by the GPs, nor in 20% of the patients treated by the specialists. We could identify only a weak relationship between the severity of the disease (symptoms and pulmonary function combined) and the prescribed pharmacotherapy: with growing degrees of severity the GP seems to prescribe more bronchodilators, the specialist more inhaled corticosteroids.

Prescribed pharmacotherapy should be based on the combination of symptoms, pulmonary function, bronchial hyperreactivity, and reversibility on the prescribed bronchodilators.

**Key words:** airflow obstruction, pharmacotherapy evaluation, general practitioner, chest physician, bronchial symptoms, bronchial hyperreactivity.

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### INTRODUCTION

Asthma and chronic bronchitis have a prevalence of 10-20% (1,2) in The Netherlands, a figure comparable with other countries in Europe (3).

Underdiagnosis and undertreatment of patients with airflow obstruction is well-documented (4-8). Therefore it seemed worthwhile to assess the treatment routines of general practitioners (GPs) for patients with chronic airflow obstruction and to compare them with the routines of chest physicians. The present study is part of a larger intervention study of

the effects of continuous bronchodilator pharmacotherapy on the course of the disease and the long-term prognosis. In the first part of the study we selected patients with moderate airflow obstruction and/or bronchial hyperreactivity from general practices and assessed their clinical status and treatment.

The aim of the present paper was to study the pharmacotherapy prescribed by GPs and chest physicians, and to relate the pharmacotherapy to the severity of the disease by assessing symptoms, bronchial hyperreactivity, pulmonary function, and responsiveness to bronchodilators.

Table I. *Exclusion and inclusion criteria for patients concerning lung function and non-specific bronchial hyperreactivity.*

Lung function after eight hours without bronchodilator medication:

*Inclusion criteria:*

FEV <sub>1</sub>	≤ reference value – 2 standard deviations*
or FEV <sub>1</sub> /EVC	≤ reference value – 2 standard deviations*
or FEV <sub>1</sub>	(after bronchodilation) ≥ 15% increase as percentage of initial value
or PC <sub>20</sub>	histamine ≤ 8 mg/ml (Cockcroft method**)

*Exclusion criterion:*

FEV <sub>1</sub>	< 50% reference value*
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- \* see reference 9  
 \*\* see reference 11

## METHODS

Seventy-three GPs in the catchment area of the University of Nijmegen were asked to participate in this study, and 29 GPs accepted. The remaining 44 GPs did not have time or were not able to select at least four patients over 30 years old with symptoms of asthma and/or chronic bronchitis, without other pulmonary or life-threatening diseases. Patients with non-specific bronchial hyperreactivity and/or moderate airflow obstruction were accepted for this study (Table I). Some of the patients were previously difficult to manage and so had been referred to a chest physician.

The data were collected at the end of an eight-week selection period (at the start of the intervention study). This selection period served for baseline testing and was also used to stop any corticosteroid treatment. Patients were only included if – in the opinion of the responsible physician (GP or chest physician) – corticosteroid treatment was not essential for symptom control (no corticosteroid dependency).

### *Selection bias*

In order to overcome 'recruitment-bias' (10) in the selection procedure, we studied a sample of each of the following groups of patients who did not participate in the study.

- patients refusing to take part
- patients excluded by their GP for reasons other than their pulmonary disease
- patients selected by their GP but excluded because of an airflow obstruction of more than 50% of the reference value
- patients selected by their GP but excluded because of no airflow obstruction and no bronchial hyperreactivity.

### *Pathophysiologic data*

- *Symptoms and smoking history:* using the Dutch version of the questionnaire of the Medical Research Council (12). The symptoms were summarized as a score of 0–8 by addition of the symptoms (Table II). The smoking history was assessed in pack years (packages of cigarettes smoked per day per year).
- *Degree of severity:* the symptom score and pulmonary function were combined to give a degree of severity (score 0–5: 5 being the most severe) according to van der Lende (12).
- *Allergy (RAST-test):* pollen (weeds, grasses, trees) animals (cats, dogs), house dust mite, *Aspergillus fumigatus*.
- *Pulmonary function and reversibility of airflow obstruction:* FEV<sub>1</sub> (Forced Expiratory Volume in one second) and EVC (Expiratory Vital Capacity) were assessed after eight hours without bronchodilator medication by means of the (portable) spirometer Microspiro HI-298® (Chest Inc.) (highest of three measurements). The airflow obstruction was assessed on the basis of the FEV<sub>1</sub> as a percent-

Table II. *The questionnaire symptom score.*

Each of the following items counts for one point in the symptom score (total eight points):

- chronic cough on most days or nights in three consecutive months
- chronic phlegm production on most days or nights in three consecutive months
- more than one period of at least three week's cough or phlegm production in the previous three years
- dyspnoea when going upstairs or walking fast on level ground
- weather-influence on cough, phlegm production or dyspnoea
- regular chest-wheezing or -whistling
- attacks of dyspnoea with wheezing (asthmatic attacks)
- 'allergic dyspnoea' after contact with dust, cats, dogs, etc.

Table III. Characteristics of patients.

1 = patients participating in the study, treated by the general practitioner (GP) and chest physician (CP)

2 = refused to take part in the study

3 = excluded by the GP for reasons other than their pulmonary disease

4 = excluded by the researcher because of  $FEV_1 < 50\%$ 5 = excluded by the researcher: no airflow obstruction and no bronchial hyperreactivity ( $PC_{20} > 8$  mg/ml)

Observations have been made in 20% of the group 2, 3 and 4. Mean and standard deviation of the variables are given.

group of patients	1 GP	1 CP	Total	2	3	4	5
n	167	56	223	59	156	81	5
age	53(13)	51(12)	53(12)	58(14)	58(17)	66(10)*	45(15)
sex men (%)	54	64	57	60	55	91*	80
women (%)	46	36	43	40	45	9*	20
pack years	17	15	16	15	20	21	14
symptom score	4.9	5.1	5.0	4.0	3.8	4.1	5.8
allergy (%)	38*	60*	47				
$FEV_1$ (% reference value)	76(17)	72(17)	75(17)	71(14)	67(25)	37 (7)**	103(15)**
$FEV_1/EVC$ (% reference value)	83(14)	82(14)	83(14)	81(16)	79(21)	55(15)**	99 (4)*
Reversibility on							
- salbutamol							
$FEV_1$ (% increase)	9(11)	9 (8)	9 (9)	9 (9)	10(20)	21(16)**	3 (4)*
- ipratropium bromide							
$FEV_1$ (% increase)	9 (8)	9 (8)	9 (8)	11 (8)	12 (9)	19(12)*	3 (4)*

All differences are compared with the patients of group 1, who participated in the study. Significant differences: \* =  $p < 0.05$ , \*\* =  $p < 0.005$ .

age of the reference value (9).

$FEV_1$  and EVC were assessed 30 minutes after inhalation of 40 µg ipratropium bromide (metered dose aerosol: 20 µg/puff). If no response (increase  $FEV_1 < 10\%$ ) occurred, 200 µg of salbutamol (metered dose aerosol: 100 µg/puff) was subsequently inhaled, followed by  $FEV_1$  and EVC testing after 15 minutes. Reversibility was based on the percentage increase of  $FEV_1$  after bronchodilation versus the initial value. If there was an increase in  $FEV_1$  of 10% or more following either ipratropium bromide alone or ipratropium bromide and salbutamol together, the response to salbutamol was assessed on a separate second occasion. Pulmonary function testing and the administration of drugs were all performed by the same investigators.

- *Bronchial non-specific hyperreactivity*: the Histamine Challenge Test, according to Cockcroft et al. (11) was used. Aerosols of histamine were inhaled at five minute intervals in doubling concentrations from 0.03 mg/ml up to 32 mg/ml. Inhalation was discontinued when there was a fall in  $FEV_1$  of  $\geq$

20% of the initial value. This concentration is the  $PC_{20}$ . The  $PC_{20}$  was assessed in an exacerbation-free period, after at least eight hours without bronchodilator medication and after about eight weeks without corticosteroid treatment.

#### Data of treatment

The GP provided data on the medication in the preceding year: drug(s) prescribed, dose, treatment strategy: continuous or occasional (occasional means: following complaints/symptoms).

- \* *Referred patients*: patients under specialist treatment had been referred by the GP to the specialist in the past. It was not possible – retrospectively – to assess exactly the reason for referral. Usually it was uncertainty on the part of the GP of the diagnosis and/or treatment. The selection period (see above) was scheduled to establish the homogeneity of the study sample, regardless of the place of treatment.

GP = General Practitioner (167 patients)  = not prescribed  
 CP = Chest Physician (56 patients)  = permanent use  
 = occasional use

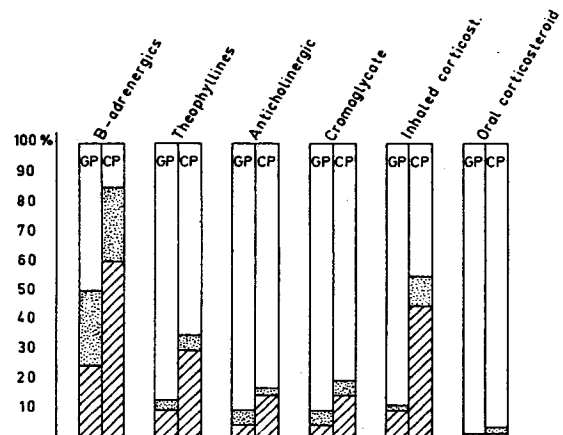


Fig. 1. Prescribed pharmacotherapy in percentages of patients.

\* *Pharmacotherapy* (at the entry of the study) was categorised in the following way:

- none
- bronchodilators ( $\beta_2$ -agonists, anticholinergics and theophyllines)
  - one bronchodilator
  - two or more bronchodilators
- cromoglycate
- corticosteroids: - inhalation
  - oral

#### Analysis

The level of pharmacotherapy was related to:

- bronchodilation on ipratropium bromide and salbutamol
- degree of severity of the disease
- bronchial hyperreactivity

These relationships were studied separately for patients treated by their GP and by the specialist.

Data are expressed in terms of mean  $\pm$  standard deviation. Student's t-test was used in the statistical evaluation of the data. The ethical committee of the university approved this study. The patients gave oral consent.

## RESULTS

All patients with symptoms of asthma and/or chronic bronchitis were considered for this study. Two hundred and twenty-three patients (127 men, 96 women) of the 524 patients with symptoms were finally selected. Characteristics of these patients and of patients who refused or were excluded are given in Table III. No significant differences were observed between these groups of patients. There was thus no evidence of recruitment bias in the selection of patients.

Of the 223 patients, 167 were treated by their GP and 56 by 19 chest physicians (Table III). Significantly ( $p < 0.05$ ) more patients with allergy were under specialist care, but otherwise the two groups were very similar. The mean value of the degree of severity was 3.7 and 3.6 for specialist-treated and GP-treated patients, respectively. The geometric mean  $PC_{20}$  for specialist-treated patients was 11.7 mg/ml, while it was somewhat higher, 14.6 mg/ml (less hyperreactive), for the GP-treated patients. This difference was not significant.

The GP and the chest physician differed in the treatment strategy (Figure 1). Patients without pharmacotherapy were more frequently found in the subgroup treated by the GP. Patients treated by the specialist received the greatest number of drugs, the mean being 2.2 (0.8 for the patients in primary care).

$\beta_2$ -adrenergics were prescribed most frequently by both GP and specialist, followed by the inhaled corticosteroids; specialists, however, prescribed six times more corticosteroids than GPs.

Almost a quarter of the patients (52 of 223) did

Table IV. Prescribed pharmacotherapy for 223 patients related to the degree of severity of their disease.

(prescriptions in percentages of patients)

GP = General Practitioner

CP = Chest Physician

degree of severity	0-3		4		5	
	GP	CP	GP	CP	GP	CP
total numbers of patients	67	19	65	27	35	10
no medication	34	5	32	0	23	10
one bronchodilator	43	15	40	15	51	30
two or more bronchodilators	6	11	4	15	14	0
cromoglycate	10	32	12	22	6	0
inhaled corticosteroids	7	32	9	41	0	60
oral corticosteroids	0	5	3	7	6	0

Table V. Prescribed pharmacotherapy for 216 patients related to their bronchial hyperreactivity.

(prescriptions in percentages of patients)  
GP = General Practitioner  
CP = Chest Physician

PC <sub>20</sub> histamine (mg/ml)	< 2.0		2.0–8.0		> 8.0	
	GP	CP	GP	CP	GP	CP
total numbers of patients	36	15	47	18	80	20
no medication	4	0	8	0	20	2
one bronchodilator	10	8	13	9	20	2
two or more bronchodilators	6	11	4	15	14	0
cromoglycate	2	4	4	11	3	8
inhaled corticosteroids	2	13	1	9	3	17
oral corticosteroids	1	4	1	0	1	2

not show a direct improvement in FEV<sub>1</sub> of more than 10% on either salbutamol or ipratropium bromide. When the responses were related to the prescribed bronchodilators, it appeared that 38 patients (17%) were given drugs to which they did not respond (increase FEV<sub>1</sub> = 2.1%, s.d. = 2.0), at least not at the time of testing. Of these patients, 27 were GP-treated (16%) and 11 specialist-treated (20%).

Only a weak relationship was found between the severity of the disease and the pharmacotherapy (Table IV). GPs appeared to prescribe more medication (mainly bronchodilators) when the condition was more severe. The specialists prescribed relatively more inhaled corticosteroids for patients with a more serious condition.

No correlation was found between the degree of bronchial hyperreactivity and medication by either GPs or specialists (Table V).

## DISCUSSION

This study was concerned with the level of treatment of patients with moderate airflow obstruction and/or bronchial hyperreactivity. There is strong evidence for a beneficial effect of continuous pharmacotherapy treatment on the prognosis of patients with serious airflow obstruction (13, 14). For patients with moderate airflow obstruction this is not yet clear. Kaptein et al. (4) assessed the adequacy of treatment by relating the symptoms to the therapy prescribed. In our study three other factors were included: pulmonary function, reversibility of obstruction, and degree of bronchial hyperreactivity. These clinical features were assessed at the same

time. It is unlikely that they are stable characteristics of the patients, and the data must therefore be interpreted with care.

In general, the pharmacotherapy of our group was representative for the pharmacotherapy prescribed for obstructive pulmonary disease in The Netherlands (15). The chest physician prescribed overall three times more drugs than the GP. At the time of examination the severity of the disease showed hardly any differences (except for allergy) between the GP- and specialist-treated patients. However, this study did not give insight into the severity of the disease before treatment, nor into the possible benefits of previous therapy. Assessing the severity of the disease after one year in the intervention study will have to confirm that the patients treated by the GP and the specialist were fully comparable.

There was no relation between medication prescribed and bronchial hyperreactivity. Several recent studies confirmed a relationship between bronchial hyperreactivity and the severity of the disease (16,17). Therefore hyperreactive patients seem to be liable to undertreatment. The medication prescribed showed a slight correlation with the severity of the disease: with growing severity the GP seemed to prescribe somewhat more bronchodilators, the specialist more inhaled corticosteroids. The GP seemed to be more occupied with treating symptoms, the specialist with preventing exacerbations.

The best way to assess 'under-' and 'overtreatment' is to prescribe new or withdraw used medication and follow the clinical condition of the patients. This will be a subject of further studies. Another way is to evaluate the response to drugs that have a direct measurable effect, such as bronchodilators. In this study 17% of the patients were treated with a bronchodilator without an immediate relevant reaction in bronchial obstruction. This could not be explained by the absence of bronchial obstruction at the moment of measuring: most of the patients had a FEV<sub>1</sub> of less than 90% of the reference value and might have been improved by bronchodilation with either salbutamol or ipratropium bromide. Although about half of these patients had a positive Histamine Challenge Test (the same proportion as in the total study group), thus far no study showed that bronchodilator therapy would improve the bronchial hyperreactivity (18,19). Corticosteroid treatment is probably more appropriate for these patients.

In the selection procedure we identified a subgroup whose condition was underdiagnosed and pos-

sibly undertreated: patients excluded by the investigator for too serious airflow obstruction. This subgroup reported fewer symptoms on the standard questionnaire than the group of patients studied, but the pulmonary function showed alarming impairment: the average FEV<sub>1</sub> was 37% of the reference value; FEV<sub>1</sub>/FVC was 58% of the reference value. None of the 20% sample studied received corticosteroids, and 24% received no medication at all. As none of these patients were treated by a specialist the pulmonary function impairment was probably unknown. It is important that the GP should be able to identify this subgroup in the future.

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