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ORIGINAL RESEARCH

Correlates of adherence to respiratory drugs in COPD patients

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Abstract

Aims: To identify the correlates of accidental omissions and intentional interruptions of respiratory therapy in COPD.

Methods: COPD patients (GOLD stages II-IV) were recruited by general practitioners or respiratory physicians. Patients reported in self-report questionnaires their adherence to respiratory drugs (over the past three months) and their perception of therapy.

Results: 179 patients were included (mean age 63 years, 24% females). 45% forgot their respiratory therapy, while 30% interrupted it in the absence of any perceived benefit. The risks of accidental omissions were significantly higher when patients complained about having too many medications to take on a daily basis (OR=2.35; 95%CI=1.13-4.89), and among current smokers (OR=2.14; 95%CI=1.07-4.29). Females were more likely to interrupt therapy intentionally (OR=2.40; 95%CI=1.04-5.53). Surprisingly, there was no significant relationship with the number of drugs actually taken by patients.

Conclusions: Adherence to respiratory drugs is inadequate in COPD patients. In order to improve adherence, patients' perception of the burden of therapy should not be overlooked.

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Keywords adherence, chronic obstructive pulmonary disease, treatment, respiratory therapy, omission, interruptions, supervision

Introduction

Chronic obstructive pulmonary disease (COPD) represents a major public health issue in Western countries[1] given its increasing incidence[1-2] and the detrimental consequences on mortality, quality of life[3] and societal cost.[4-6]

COPD therapy is complex, and consists of oral and inhaled respiratory drugs as well as oxygen therapy. Previous studies have shown inadequate adherence to respiratory therapy – such as inhaled corticosteroids,[7] long-term oxygen therapy,[8] or nebulised therapy[9-10] – in COPD. This inadequate adherence is of concern as it may affect quality of life.[9]

Therefore, improving the effectiveness of COPD management requires a detailed understanding of the factors influencing adherence. These factors comprise patients' personal characteristics as well as factors related to the disease and its management. Correlates of adherence have been little investigated in COPD. Non-adherence has various dimensions such as omission, intentional interruption, or spontaneous change in dosing or refill rates. It is unclear to which extent these different components of non-adherence are correlated.

Data on declared self-reported adherence to respiratory

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drugs were available from the PRE-SPIRO observational study, aimed at improving the understanding of COPD management in the Lyon geographical area of France. In this study, COPD patients' behaviours towards their therapy were investigated, and correlates of accidental omissions and intentional interruptions of respiratory drugs were identified.

Methods

Study design and study population

The cross-sectional PRE-SPIRO study aimed at describing COPD management in the Lyon area and was conducted between March and November 2007. The present analyses correspond to an ancillary objective that had not been planned in the initial protocol. COPD outpatients aged 40-75 (stages II-IV) were recruited by general practitioners (GPs) or respiratory physicians. Other inclusion criteria were: COPD diagnosed ≥12 months before inclusion; smoking history ≥ 20 pack-years; and at least one exacerbation (necessitating a medical contact and/or an increase of therapy) experienced during the past 12 months.

Data collection (self-questionnaires and case-report forms)

During the inclusion visit, the physician reported on COPD-related factors, co-morbid diagnoses and current prescribed respiratory therapy for each patient. Respiratory drugs consisted of inhaled corticosteroids (ICS), long-acting β-agonists (LABA), combined LABA/ICS inhalers, short-acting anticholinergics, short-acting β-agonists (SABA), long-acting anticholinergics, and combined anticholinergics/SABA.

Patients reported in self-questionnaires their sociodemographic characteristics, the overall number of daily drugs they took for any indication at the time of the study, their satisfaction with regard to the information received on COPD and therapy, and their perceived burden of therapy. Adherence was not measured with a validated instrument but by patient replies to the following specific questions regarding recent adherence to respiratory drugs over the past three months: 1) "Have you forgotten any of your respiratory drugs?"; 2) "Have you intentionally interrupted some of your treatments when clinical benefit was not perceived?"; 3) "Have you spontaneously changed the dosing of your drugs?"; and 4) "Have you run out of drug(s) since your last medical visit?".

Analyses

Correlates of any accidental omissions of therapy during the past three months were identified in univariate analyses of socio-demographic characteristics, the overall number of co-morbid diagnoses, and disease- and management-related factors including patients' perception of their COPD management and therapy. In addition, we also studied the impact of any associated depression given its well-known impact on adherence.[11,12] The burden of therapy was assessed by the overall number of drugs taken on a daily basis by the patient (for any indication). Chi-square and Wilcoxon tests were used, and then a multivariate logistic model was computed. The risk of accidental omission during the past three months was studied. The model was systematically adjusted for age, gender, COPD stage, the type of supervision

Table 1. Patients' main characteristics.

	n	% [1]
Overall	**179**	**100.0**
Gender		
Males	136	76.0
Females	43	24.0
Age (years)		
40-59	60	33.7
60-69	71	39.9
70 et +	47	26.4
Current smoking (vs. No)	88	49.2
Pack-years		
20-30	71	40.1
31-40	41	23.2
> 40	65	36.7
Education level		
Less than A-level	136	76.4
A-level and more	42	23.6
Associated depression	36	20.2
COPD stage		
II	111	62.0
III-IV	68	38.0
Type of supervision		
Primary care	116	65.2
Specialist	26	14.6
Both	36	20.2
Hospitalisations due to respiratory problems (past 12 months)	31	17.3
Main respiratory drug classes		
Short-acting β-agonist (SABA)	78	45.9
Long-acting β-agonist (LABA)	36	21.4
Combined LABA-Inhaled corticosteroids	111	65.3
Long-acting anticholinergic	76	44.2
Short-acting anticholinergic	17	10.1
Combined anti-cholinergic-SABA	32	18.8
Inhaled costicosteroids	35	20.7
Fenspiride	32	18.3
Oral corticosteroids	70	40.9
Overall number of daily drugs (any indication)		
< 4	63	35.6
4-5	52	29.4
6 and more	62	35.0
Perception of COPD management		
Feeling to be adequately informed about disease	140	78.6
Feeling to be adequately informed about therapy	141	78.6
Feeling to have too many drugs to take daily	63	35.2
Declared adherence toward respiratory therapy (past 3 months)		
Any accidental omission	79	44.6
Any intentional interruption when clinical benefit was not perceived	54	30.2
Any spontaneous change in doses	86	48.0
Has been running out of medication since the last visit	28	15.6

[1] Percentages do not always refer to 179 due to missing data for some variables

(primary care, respiratory medicine, or both) and any associated depression. Other correlates were entered in the models if they showed a univariate association with the studied variable (p<0.10). Other declared behaviours toward therapy were not included in the models, as they were not considered to be explanatory variables.

Similar analyses were conducted for any intentional interruption of therapy during the past three months in the absence of any perceived efficacy.

Results

Patients' baseline characteristics

The 179 patients (mean age 63 years, SD=8.4) included in the study were mostly males (Table 1). In terms of educational level obtained, over three quarters did not exceed high school level (Table 1). Half of the patients were still smoking, and the overall cumulated smoking pack-years averaged 40.6 (SD=16.9). The mean number of co-morbid diagnoses was 2.3 (SD=1.9) – most commonly hypertension (54%), diagnosed emphysema (34%), arthrosis (31%) and depression (20%).

Management of COPD

COPD stage II was prevalent (Table 1), and patients were mostly managed by their GP only. About 17% of patients had been hospitalised due to respiratory problems during the previous 12 months. The most common prescribed respiratory drugs were combined LABA/ICS, SABA, long-acting anticholinergics and LABA (Table 1). About 21% of patients received ICS not combined with LABA, despite the absence of labelling or marketing authorisation. About 12% of the patients received long-term oxygen therapy. The mean number of daily drugs taken for any indication was 4.9 (SD=2.9).

More than a fifth of the patients felt inadequately informed about their disease or therapy. Over one third of the patients complained about having too many drugs to take on a daily basis (see Table 1).

Declared adherence to respiratory therapy

During the previous three months, 45% of patients forgot their respiratory therapy at least once, and 30% reported at least one intentional interruption in the absence of perceived clinical benefit. About half of the patients spontaneously changed the dosage of their medication. Lastly, 16% had run out of respiratory drugs since their last medical visit.

Correlates of non-adherence to respiratory therapy

Univariate analyses

- General and COPD characteristics

A nearly-significantly higher percentage of women intentionally interrupted therapy, whereas accidental omissions did not noticeably change between genders. Despite a global non-significant effect of age, patients over 70 tended to intentionally interrupt therapy more frequently (see Table 2). Accidental omissions were significantly more common among current smokers, while the difference was less marked for intentional interruptions. The number of co-morbid diagnoses did not substantially vary with accidental omissions (2.5 vs. 2.2,

Table 2. Univariate correlates of forgetting therapy and of interrupting respiratory therapy in the absence of perceived efficiency (patients'characteristics).

	Any accidental omission			Any intentional interruption in the absence of perceived efficiency		
	n	% [1]	p	n	% [1]	p
Overall	**177**	**44.6**	-	**179**	**30.2**	-
Gender						
Males	135	43.0	0.42	136	26.5	0.06
Females	42	50.0		43	41.9	
Age (years)						
40-59	58	51.7	0.37	60	26.7	0.21
60-69	71	43.7		71	26.8	
70 et +	47	38.3		47	40.4	
Current smoking			0.0004			0.14
Yes	86	58.1		88	35.2	
No	91	31.9		91	25.3	
Smoking history (Pack-years)						
20-30	71	49.3	0.55	71	40.0	0.83
31-40	39	46.1		41	26.8	
> 40	65	40.0		65	32.3	
Education level						
Less than A-level	134	42.5	0.39	136	29.4	0.63
A-level and more	42	50.0		42	33.3	
Associated depression						
Yes	35	57.1	0.10	36	47.2	0.01
No	141	41.8		142	26.1	

[1] Percentages do not always refer to 179 due to missing data for some variables

Table 3. Univariate correlates of forgetting therapy and of interrupting respiratory therapy in the absence of perceived efficiency (management-related factors and declared adherence to therapy).

	Any accidental omission			Any intentional interruption in the absence of perceived efficiency		
	n	% [1]	p	n	% [1]	p
Overall	**177**	**44.6**	-	**179**	**30.2**	-
COPD stage						
II	109	51.4	0.02	111	32.4	0.40
III-IV	68	33.8		68	26.5	
Type of supervision						
Primary care	116	50.0	0.02	116	31.0	0.13
Specialist	26	19.2		26	15.3	
Both	34	47.1		36	38.9	
Hospitalisations due to respiratory problems (past 12 months)						
Yes	31	41.9	0.74	31	22.6	0.31
No	146	45.2		148	31.8	
Overall number of daily drugs (any indication)						
< 4	63	49.2	0.65	63	31.7	0.95
4-5	51	45.1		52	30.8	
6 and more	61	41.0		62	29.0	
Perception of COPD management						
Feeling to be adequately informed about disease						
Yes	138	41.3	0.12	140	29.3	0.78
No	38	55.3		38	31.6	
Feeling to be adequately informed about therapy						
Yes	139	41.0	0.06	141	28.4	0.31
No	38	57.9		38	36.8	
Feeling to have too many drugs to take daily						
Yes	63	55.6	0.03	63	38.1	0.09
No	114	38.6		116	25.9	
Declared adherence toward respiratory therapy (past 3 months)						
Any intentional interruption when clinical benefit was not perceived						
Yes	54	85.2	<0.0001	———	———	———
No	123	26.8		———	———	———
Any spontaneous change in doses						
Yes	85	65.9	<0.0001	86	48.8	<0.0001
No	92	25.0		93	12.9	
Has been running out of medication since the last visit						
Yes	28	89.3	<0.0001	28	53.6	0.0033
No	149	36.2		151	25.8	

[1] Percentages do not always refer to 179 due to missing data for some variables

p=0.55), nor with intentional interruptions (2.7 vs. 2.1, p=0.20). In contrast, non-adherence was associated with depression, with a significant difference for intentional interruptions (Table 2). There was no evidence that non-adherence was influenced by the patient's smoking history or education level.

- Factors related to COPD and disease management

Forgetting therapy was more common among stage II patients, whereas intentional interruption of therapy showed no difference between different disease stages. At least a two-fold decrease in the rates of reported accidental omissions and intentional interruptions were observed among patients supervised by hospital specialists, although global statistical association was not significant for intentional interruptions (see Table 3).

Adherence did not significantly vary with past hospital admissions, the overall number of daily drugs, and satisfaction about information received on disease. A nearly-significantly lower rate of omissions was noted when patients were satisfied about the information they had received on therapy. Accidental omissions, and to a lesser extent intentional interruptions, were more common when patients complained about having too many drugs to take on a daily basis. Lastly, accidental and intentional interruptions were both closely correlated with other declared behaviours toward therapy (Table 3).

Multivariate analyses

A non-significant trend observed for elderly patients in the univariate analyses was shown (see Table 4). Women were more likely to interrupt respiratory therapy intentionally, whereas there was no convincing effect of gender on accidental omissions. For both outcomes, increased risks were observed for depressed patients, but not significantly so (Table

Table 4. Logistic models for omitting or interrupting drug during the past 3 months (Logistic regressions).

	MODEL 1: any accidental omission (n=174)		MODEL 2: Any intentional interruption when clinical benefit was not perceived (n=176)	
	OR	95%CI	OR	95%CI
Age (years)				
40-59	1.00	-	1.00	-
60-69	0.76	0.35-1.69	1.07	0.47-2.42
70 et +	0.57	0.22-1.45	1.99	0.81-4.86
Gender				
Males	1.00	-	1.00	-
Females	1.17	0.50-2.73	2.40	1.04-5.53
Associated depression	1.91	0.79-4.60	1.86	0.80-4.32
Current smoking	2.14	1.07-4.29	———	———
COPD stage				
II	1.00	-	1.00	-
III-IV	0.51	0.25-1.04	0.67	0.32-1.39
Type of supervision				
Primary care	1.00	-	1.00	-
Specialist	0.23	0.07-0.76	0.31	0.09-1.09
Both	1.03	0.43-2.49	1.60	0.70-3.66
Feeling to have too many drugs to take daily	2.35	1.13-4.89	1.86	0.90-3.82
Feeling adequately informed about therapy	0.42	0.18-0.98	———	———

——— No significant univariate association ($p \geq 0.10$)

4). The risk of accidental omissions was significantly increased for current smokers (Model 1). A significantly lower risk of forgetting therapy was observed among patients supervised by a respiratory physician, whilst the three-fold decreased risk for intentional interruptions approached significance level (Table 4). Complaining about having too many drugs to take on a daily basis was a major correlate of accidental drug omissions, whilst the significance threshold was not reached for intentional interruptions. Patients who felt adequately informed about their therapy were less likely to omit it.

Discussion

Declared adherence to respiratory drugs was inadequate in this sample of treated COPD patients. Differences in adherence patterns were noted depending on the type of supervision, gender, current smoking status, and the perceived burden of therapy. In contrast, the actual burden of therapy, smoking history, or education level had a more limited impact. Although non-adherence behaviours were highly associated, interestingly some differences in the correlates of intentional and of accidental interruption were observed, particularly in terms of age and gender. The inadequate adherence observed in our data is in line with the conclusions of previous studies in COPD[10,11] and in other chronic diseases.[13] In addition, our univariate analyses suggest that non-adherent behaviours and erroneous beliefs toward respiratory therapy tended to be associated rather than isolated.

Elderly patients tended to interrupt therapy more often, but this did not reach significance level (as shown in Table 4). The relationship between age and adherence to respiratory drugs has yielded discordant findings. Some studies have reported better adherence in older patients,[10,14] while others have not.[15,16] Even though no significant association was identified with education level, our result requires caution as the impact of education on adherence has been established.[10,16] Our sample comprised a majority of poorly educated patients, which could account for our finding. Although not significant, an increased risk of intentional non-adherence was detected with depression; the detrimental impact of depression on adherence is clearly established.[12]

In this study, women were more likely to interrupt therapy, but most studies have failed to detect any convincing effect of gender on adherence.[9,10,16-18] Women with COPD tend to be more depressed than men.[19] Nevertheless, Model 2 (adjusted for depression) showed an independent effect for gender, suggesting that, in our data, the higher risk of drug interruptions exhibited by women may not be driven by depression alone.

Unlike the overall smoking history, current smoking was found to be associated with accidental omission of therapy, which confirms Turner *et al.*'s conclusions.[10] Current smoking may be considered as a marker of limited involvement in healthy behaviours.

Despite non-significant multivariate associations, patients with more severe COPD (stages III/IV) tended to forget their therapy less often, probably due to the higher burden of

symptoms they encounter, and this also is consistent with Turner *et al*.'s findings.[10] Likewise, accidental and intentional interruptions were less common in patients managed by respiratory physicians. Interpreting this finding requires caution and further confirmation, as there were only six specialists in our study. Nonetheless, better adherence patterns have been described among elderly patients supervised by specialists, irrespective of their disease.[20] It may be that respiratory physicians devote more time and give more explanation on the disease and its therapy to their COPD patients; however, although no significant difference in COPD grade was noted in our data according to the type of supervision (p=0.22), patients followed-up by hospital specialists might have more severe disease. Conversely, compared with exclusive supervision in primary care, adherence patterns were not enhanced in COPD patients followed-up by both GPs and specialists. This could suggest that occasional referral to specialists, notably during severe exacerbations, may not substantially heighten patients' awareness of adherence issues. Similarly, better adherence patterns could have been expected in patients who experienced recent hospitalisation due to respiratory problems.

Adherence did not vary significantly with the overall number of drugs taken daily by patients. Although a previous survey yielded similar conclusions,[20] our findings should not be over-interpreted. Poly-pharmacy leads to complicated regimens, and confusion about medications is a well-known causative factor of poor adherence in chronic diseases,[21] notably in COPD.[11,15] Similar caution is required in interpreting the absence of impact of the overall number of co-morbid diagnoses.

Conversely, complaining about the overall amount of daily drugs was a significant predictive factor for accidental omissions, whilst a nearly two-fold increased risk of interruption (although not significant) was observed (Table 4). This suggests that the perception of the burden of therapy may influence adherence more than the actual burden itself. The critical role on adherence of patients' perceptions, beliefs and experiences about illness and treatments has been underlined in COPD.[15,22] A key prerequisite of adherence is patients' conviction of the necessity to use the drug.[11,23] The significantly decreased risk of accidental omission when patients were satisfied with the information received on therapy supports the necessity of good communication with caregivers – as already advocated by previous studies[15,16] – and the need for therapeutic education.

This study has some methodological limitations. Adherence was not measured with a validated instrument, and the corresponding questions on adherence were not focused on any specific respiratory drug class. COPD respiratory therapy is heterogeneous, comprising numerous drug classes with various administration routes. In addition, the duration and frequency of declared non-adherence episodes were not examined.

Self-completion questionnaires tend to overestimate patients' real adherence.[10] Furthermore, memory bias regarding drug interruptions during the past three months cannot be excluded; even poorer adherence patterns might have been observed using direct measures. A further limitation is that some factors which might potentially influence adherence – such as drug tolerability,[11] ethnicity, level of resource, duration of respiratory therapy,[10] or patients' level of cognitive impairment[22] – were not documented. Finally, the limited number of patients in our survey might explain some of our non-significant findings.

Our findings have clinical implications. The quality of communication between caregivers and patients is a key factor in improving adherence.[11,16] Specific attention should be paid to patients at higher risk of using therapy irregularly, such as current smokers. Patients' reasons for intentional interruptions should be better understood. Whenever possible, simplification of dosing regimens should be carried out.[21]

The influence of patients' perceived burden of therapy on adherence may be modified by a better understanding of therapy, and therefore education may help reduce interruptions of therapy, as has been shown in COPD[7] and asthma.[24] Interestingly, education of patients, along with better co-ordination of care, showed significant improvements on COPD patients' adherence[25] as well as fewer hospitalisations.[26]

In conclusion, the PRE-SPIRO study enabled us to verify the inadequate adherence level in COPD outpatients and to identify some of its correlates. The differences in adherence patterns that we have observed in the present study require more elaborate investigations. Further studies are needed to enhance the knowledge of adherence patterns in COPD.

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Conflict of interest declarations

F Denis is an employee of Boehringer-Ingelheim France, but he was not involved at any stage of the analyses and interpretation of results, which were performed by the Pharmacoepidemiology Unit in Lyon. There is no conflict of interest for any other author.

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