



Effect of a pharmacist intervention on asthma control. A cluster randomised trial

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KEYWORDS

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Summary

Introduction: Achievement and maintenance of good asthma control is a major objective in asthma management. However, asthma control in many patients is suboptimal, due to improper use of asthma medications and non-adherence. The aim of this study was to evaluate the effect of a pharmacist intervention on asthma control in adult patients.

Methods: A 6-month cluster randomized controlled trial was undertaken with allocation of community pharmacies to intervention or control group. Adult asthma patients in the intervention group received a protocol-based intervention addressing individual needs related to asthma control, inhaler technique and medication adherence. Patients in the control group received usual care. Main variables were measured at baseline, 3 and 6 months.

Results: 336 patients completed the study, 150 in the control group and 186 in the intervention group. The intervention resulted in enhanced asthma control: Patients receiving the intervention had an Odds ratio of 3.06 (95% CI: 1.63–5.73; $p < 0.001$) of having controlled asthma six months later. In the intervention group mean ACQ scores significantly improved [0.66 points (SD: 0.78); $p < 0.001$] and the number of controlled asthma patients increased by 30.1% ($p < 0.001$) after 6 months. The intervention also resulted in improved medication adherence (by 40.3%, $p < 0.001$) and inhaler technique (by 56.2%, $p < 0.001$). No significant changes for any of these variables were observed in the control group.

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Conclusion: The AFasma study focused on the important outcomes of asthma management, and showed that through the designed intervention, community pharmacists can increase controlled asthma patients compared to usual care. Trial registration NCT01085474.

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Introduction

In 2006 a new asthma management approach was adopted by the Global Initiative for Asthma (GINA) signalling an important change of philosophy based on asthma control rather than asthma severity or symptoms [1]. Since then, good asthma control has become a primary objective in the management of asthma patients [2], that is an absence of daily symptoms and exacerbations, minimisation of lung function variability or no impairment of quality of life. However, asthma control in many patients is sub-optimal [3,4], with negative implications for the patient's health, quality of life and/or health care costs. Reasons for this poor asthma control are complex including clinical and behavioral issues, such as co-morbidity, ineffective delivery of treatment, low adherence and/or ongoing exposure to triggers [5] among others.

Adherence to preventer medications represents a major challenge [6] since non-adherence to inhaled therapy is common among asthma patients due to intentional or unintentional causes [7]. Despite correct inhaler technique being essential for effective drug delivery, a literature review found that misuse of inhaler devices is frequent in practice [8] contributing to poor asthma control [9–12]. Hence updated asthma guidelines [2,13] highlight the importance of implementing strategies aimed at improving patients' knowledge, skills and aptitudes to self-manage their asthma.

A literature review [14] revealed an increase of pharmacists' participation in outcome-based asthma management programs, with positive impact in symptoms [15–21], pulmonary function [16–23] or severity [16,22–24]. At the time this study was undertaken only one other intervention study [25] in a community pharmacy setting had applied the new asthma management "control" approach. Results showed a positive impact on asthma control only in a subgroup of uncontrolled patients at baseline, suggesting that the impact of a community pharmacist's intervention on asthma control had yet to be established. An additional recently published study in 2012 has found significant improvements in asthma control for patients receiving a pharmacy asthma service during 6 months of follow-up [26].

The objective of the present trial (AFasma study) was to evaluate whether a pharmacist intervention focused on asthma control, medication adherence and inhaler technique would result in an improved asthma control in adult asthma patients.

Methods

Study design

This study was a 6-month cluster randomized controlled trial undertaken between November 2010 and June 2011 in Spain.

Patients

Patients were recruited consecutively in the participant pharmacies (recruitment period: November–December 2010). To be eligible, patients were required to have been prescribed Symbicort (Budesonide/Formeterol, AstraZeneca) for their own use. Inclusion criteria were: aged 18 years or older and have a physician's diagnosis of asthma. Exclusion criteria included: participation in another asthma education program, pregnancy, presence of communication difficulties, suffering from seasonal asthma (asthma symptoms that only occurred in a seasonal pattern) or other pathologies such as Chronic Obstructive Pulmonary Disease, emphysema, lung cancer, respiratory infection and terminal illness (considered as any disease that was reasonably expected to result in the death of the patient).

Sample size was calculated to detect a difference in asthma control of greater than or equal to 20% between study groups. We applied a two-tailed test for comparing two binominal proportions, considering a type II error of 20% ($\beta = 0.80$) and 95% significance ($p = 0.05$). Sample size was adjusted according to standard criteria for cluster randomized trials, using a design effect (DE) of 1.45. The DE was calculated as follows: $DE = 1 + (n_c - 1) \cdot ICC$ (Where n_c is the mean number of individuals in the cluster and ICC the intra-cluster correlation coefficient). The ICC in the present work was considered to be 0.05, and the mean cluster size was assumed to be 10 patients [27]. A potential loss of 20% was estimated. Therefore, a minimum of 342 patients and 35 pharmacies were required.

All community pharmacies in the province of Malaga and all members of the Spanish Society of Community Pharmacy in the province of Madrid were invited by letter, with all responders enrolled.

Pharmacies were the unit of randomization and were assigned by an independent researcher after they agreed to participate in the study to either intervention (IG) or control group (CG) using a computer-generated list of random numbers with ratio 1:1. Cluster-randomization was used to minimize cross-contamination. Given the nature of the intervention pharmacists or patients could not be blinded.

Outcome measures

Asthma control was the primary outcome and was assessed using the Asthma Control Questionnaire (ACQ; 5 item version, Spanish) [28,29]. ACQ was self-completed by the patient and the pharmacist calculated the mean of 5 items scored on a 7-point interval scale. For statistical purposes this variable was dichotomized into well-controlled (ACQ score ≤ 0.75) and uncontrolled/partly controlled (ACQ score > 0.75) [30]. A decrease of 0.5 points on the patient's ACQ punctuation was considered clinically relevant [29].

Secondary outcomes included inhaler technique and medication adherence. Inhaler technique was assessed by the pharmacist using a 10-step turbuhaler checklist consistent with the Spanish Guide for Asthma Management-Guide for Asthma Educators (GEMA-Educators) [13]. The patient was asked to perform the inhaler technique with a placebo device in front of the pharmacist. Patients who performed all the checklist steps correctly were classified as having correct inhaler technique. Asthma medication adherence was assessed using the 4-item Morisky–Green–Levine scale [31], which allows the patient to be classified as adherent or non-adherent.

Primary and secondary outcomes were measured at baseline (initial visit), 3 months (intermediate visit) and 6 months (final visit). Demographic variables and other variables related to asthma control were recorded and used for adjustment in the statistical analysis.

Pharmacist training

33 pharmacists allocated to the IG attended a one-day workshop. They were trained to provide education on asthma control, medication adherence and inhaler technique by a respiratory physician and a pharmacist educator/researcher. Training on the study protocol and documentation forms was also delivered. All pharmacists received the Spanish Guide for Asthma Management (GEMA 2009) [32] and the GEMA-Educators [13].

In addition to the training, pharmacists were assisted by a facilitator through regular visits to the pharmacies, to check for compliance with the protocol and solve any problem or query during the study [33]. Counseling via email and phone was also offered.

32 Pharmacists allocated in the CG received instructions by phone about the study protocol before the beginning of the study and were monitored through 2 visits to the pharmacy.

Pharmacist-patient intervention

During the 6 months of follow-up, patients attended 3 scheduled visits to the pharmacy. However, additional visits (up to 6) to intervention patients could be provided if needed. Patient's demographic details were collected in the initial visit and an individualized patient needs analysis on asthma control, medication adherence and inhaler technique was conducted at every visit by the pharmacist in a private counseling area. Control patients received no intervention other than the pharmacist's usual care (normally the safe supply of medicines and medication-taking advice to the patient), whereas patients enrolled in the IG received a protocol based intervention based on GEMA recommendations. Patients were educated using verbal instructions, physical demonstration and written information about turbuhaler use. When appropriate the type of non-adherence (intentional or unintentional) and causes of intentional non-adherence were explored with the Beliefs about Medicines Questionnaire and Health Beliefs Model [34]. Several aspects of asthma control were also covered in each visit. Finally pharmacist and patient jointly agreed goals for the next visit.

Approval for the study was given by the Ethics and Research Committee of the Virgen de las Nieves University Hospital. A written information sheet was provided and informed consent was obtained.

Statistical analysis

Statistical analyses were performed using SPSS for Windows 15.0 (SPSS Inc, Chicago, Illinois, USA) and SAS 9.3 (SAS Institute, 2011). A p -value < 0.05 was considered to indicate statistical significance.

Quantitative variables were expressed as the mean SD and categorical variables were expressed as frequency and percentages. To compare quantitative variables, Student's t -test for independent samples and Student's t -test for paired samples were used. Chi-square analysis was performed for comparisons between groups at baseline and study completion. McNemar test was performed before and after intragroup comparisons to further measure categorical variables.

ACQ scores through the study visits were analysed using a repeated measures multivariate ANOVA. To compare changes on ACQ means through the visits between the study groups, covariance analysis (ANCOVA) was performed, using the study group as the principal effect and baseline ACQ scores as co-variable. A sub-analysis of the effect of the intervention based on asthma control at baseline was also performed.

It is recommended that the analysis of cluster randomised trials takes account of clustering, even where the ICC is small [35]. The regression analysis of the primary outcome used the mixed model approach recommended by Murray [35]. However, accounting for clustering had little impact on estimates or precision, possibly because of the extremely small ICC and small number of patients per pharmacy. Consequently, analysis of the secondary outcomes (deemed to be part of the causal pathway to the primary endpoint) used simpler methods which assumed no clustering by pharmacy.

A multivariate logistic regression analysis was performed to explore the association between asthma control and study group; estimation was by maximum likelihood using the SAS GLIMMIX procedure. This analysis included a random intercept for pharmacy nested within group to account for clustering of patients within pharmacies and was adjusted by covariates that could affect asthma control (Asthma control at baseline, gender, age, Body Mass Index, smoking status, number of asthma drugs and living area). This analysis was repeated using an intention to treat approach (ITT) assuming a worst-case scenario (patients in the CG ended with controlled asthma and patient in the IG ended with uncontrolled asthma) for patients with missing outcomes data.

Results

Study sample

Initially 65 pharmacies were enrolled, and after withdrawals, 51 pharmacies (22 in the CG and 29 in the IG) completed the study. 384 patients were offered to enter

the study and 373 patients accepted, of which 346 finished the study (160 in the CG and 186 in the IG). However one pharmacy and its 10 patients were excluded from the analysis due to lack of reliable data, leaving 50 pharmacies (21 in the CG and 29 in the IG) and 336 patients analysed (150 in the CG and 186 in the IG). There were 7 patients per pharmacy on average ranging from 2 to 10. 107 out of 186 patients in the IG attended more than three times to the pharmacy, and 51 (27.4%) completed 6 visits (Fig. 1).

Patients in both IG and CG had similar demographic and clinical characteristics (Table 1). However percentage of uncontrolled patients, mean number of anti-asthmatic

drugs and percentage of patients living in an urban area were significantly higher in the IG ($p = 0.005$, $p = 0.038$ and $p < 0.001$ respectively).

Primary outcome: asthma control

Mean ACQ scores significantly decreased from the initial to the intermediate visit in both IG (0.32 points, SD: 0.91, $p < 0.001$) and CG (0.16 points, SD: 0.73, $p = 0.017$), while between the intermediate visit and the final visit the decrease was only observed in the IG (0.34 points, SD: 0.65,

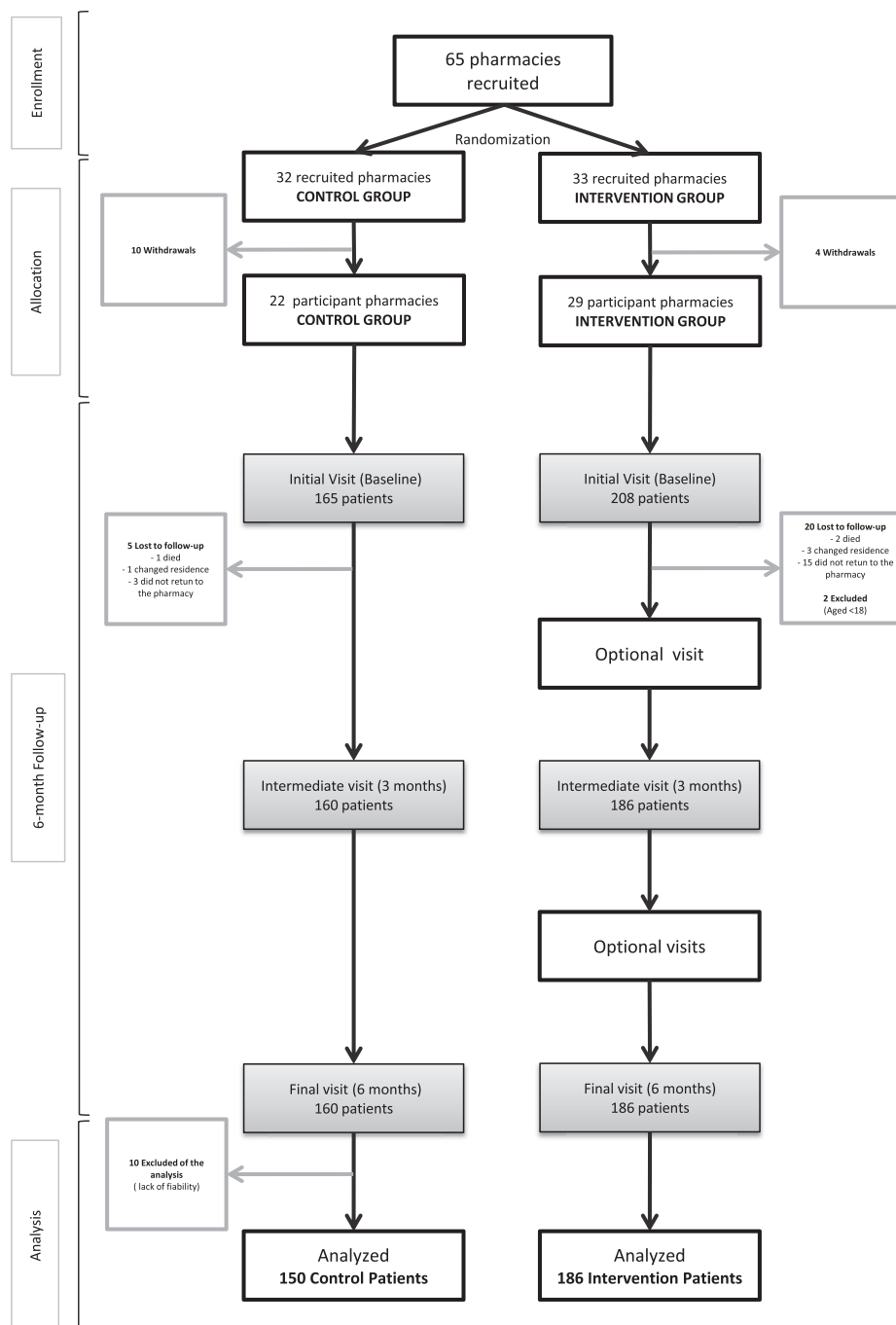


Figure 1 Flowchart of patients and pharmacies during the AFasma study.

Table 1 Baseline characteristics of study patients.

	Total (n = 336)	IG (n = 186)	CG (n = 150)	p Value
Primary variables				
ACQ punctuation; mean (SD)	1.4 (1.1)	1.4 (1.1)	1.3 (1.2)	0.444
Controlled asthma; n (%)	116 (34.5)	52 (28.0)	64 (42.7)	0.005
Correct inhaler technique; n (%) ^a	72 (21.4)	36 (19.5)	36 (24.0)	0.302
Adherence to asthma treatment; n (%) ^b	130 (38.7)	71 (38.2)	59 (39.3)	0.828
Other variables				
Male; n (%)	155 (46.1)	82 (44.1)	73 (48.7)	0.402
Age (years); mean (SD)	55.8 (19.1)	54.3 (19.1)	57.8 (19.0)	0.097
BMI (kg/m ²); mean (SD)	27.1 (5.3)	27.0 (5.5)	27.2 (5.1)	0.676
Current smoker; n (%)	70 (20.8)	40 (21.5)	30 (20.0)	0.736
Urban living area; n (%)	242 (72.0)	112 (66.2)	130 (86.7)	<0.001
Marital status (with partner); n (%)	185 (55.1)	98 (52.7)	87 (58.0)	0.331
Level of education				
No education; n (%)	50 (14.9)	23 (12.4)	27 (18.1)	0.351
Primary; n (%)	123 (36.7)	66 (35.5)	57 (38.3)	
Secondary/Vocational education; n (%)	86 (25.7)	52 (28.0)	34 (22.8)	
University; n (%)	76 (22.7)	45 (24.2)	31 (20.8)	
Employment status				
Unpaid worker; n (%)	103 (30.7)	54 (29.0)	49 (32.7)	0.711
Paid worker; n (%)	112 (33.3)	65 (34.9)	47 (31.3)	
Unemployed or retired person; n (%)	121 (36.0)	67 (36.0)	54 (36.0)	
Anti-asthmatic drugs; mean (SD)	1.5 (0.7)	1.6 (0.7)	1.4 (0.7)	0.038
Type of controller treatment				
Low-dose ICS plus long-acting β 2 agonists	13 (3.9)	7 (3.8)	6 (4.0)	0.275
Medium-dose ICS plus long-acting β 2 agonists	276 (82.1)	158 (84.9)	118 (78.7)	
High-dose ICS plus long-acting β 2 agonists	47 (14.0)	21 (11.3)	26 (17.3)	
Use of other ICS; n (%)	8 (2.4)	5 (2.7)	3 (2.0)	0.681
Use of oral corticosteroids; n (%)	2 (0.6)	1 (0.5)	1 (0.7)	0.879
Use of anticholinergic drugs; n (%)	36 (10.7)	24 (12.9)	12 (8.0)	0.149
Use of antileukotriene drugs; n (%)	34 (10.1)	24 (12.9)	10 (6.7)	0.060
Use of short-acting β 2 agonists; n (%)	99 (29.5)	59 (31.7)	40 (26.7)	0.312

CG: control group; IG: intervention group; SD: standard deviation; Kg: kilograms; m: meters; BMI: body mass index; ICS: inhaled corticosteroids.

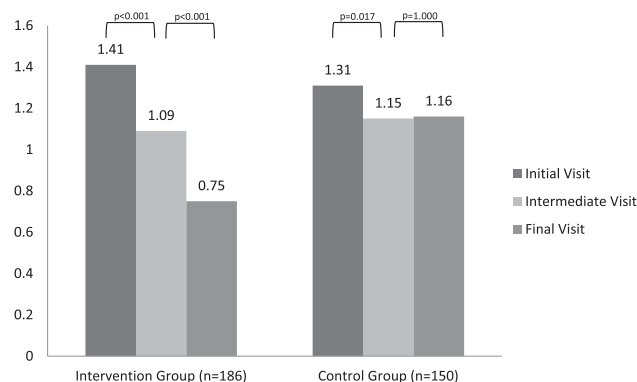
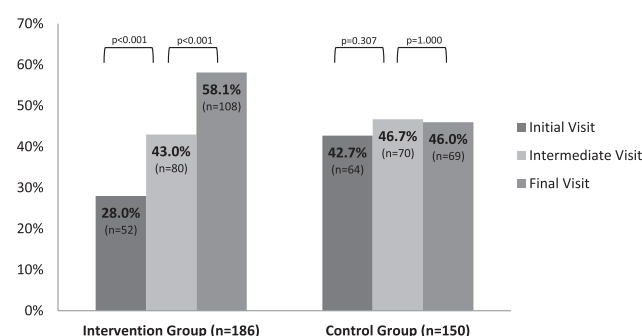
^a Correct performance of all steps for Turbuhaler inhaler technique. 10-step Turbuhaler checklist.

^b Morisky-Green-Levine test.

$p < 0.001$). In the IG a final clinically relevant reduction of 0.66 (SD: 0.78, $p < 0.001$) in mean ACQ scores was observed (Fig. 2).

In the IG, the proportion of patients with controlled asthma significantly increased from baseline (28.0%, $n = 52$)

to the intermediate visit (43.0%, $n = 80$) and from the intermediate visit to the final visit (58.1%, $n = 108$), while this proportion in the CG remained similar (Fig. 3). At the end of the study, asthma was controlled in significantly more patients in the IG than in the CG (58.1% versus 46.0%, $p = 0.028$), with an Odds Ratio of 3.06 (95% CI: 1.63–5.73;

**Figure 2** Mean ACQ scores across the study visits.**Figure 3** Proportion of patients with controlled asthma across the study visits.

$p < 0.001$) (Table 2). The Intrapharmacy correlation coefficient was found to be very small (<0.001), signaling there was no cluster effect. The results for the ITT approach, where patients with missing outcomes were included (20 IG and 5 CG) showed an adjusted odds ratio of 1.94 (95% CI: 1.06–3.55; $p = 0.032$).

Table 2 Multivariate logistic regression analysis to assess the effect of pharmacist intervention on asthma control at the endpoint ($n = 327$, missing data on age and BMI of 9 patients).

Variable	Adjusted OR	95%CI	p Value
Group assignment			
Control	Reference		
Intervention	3.059	1.632–5.733	<0.001
Sex			
Female	Reference		
Male	1.254	0.724–2.173	0.418
Age			
Older than 78	Reference		
From 18 to 30	0.958	0.293–3.130	0.943
From 30 to 42	0.831	0.243–2.837	0.766
From 42 to 54	0.468	0.140–1.562	0.216
From 54 to 66	0.712	0.240–2.108	0.538
From 66 to 78	0.398	0.137–1.159	0.091
Smoking status			
Non-smoker	Reference		
Smoker	0.859	0.429–1.719	0.0667
Living area			
Urban	Reference		
Rural	1.386	0.746–2.574	0.301
BMI			
Obese ($\text{BMI} \geq 30 \text{ kg/m}^2$)	Reference		
Normal weight ($18.5 \leq \text{BMI} \leq 24.99 \text{ kg/m}^2$)	1.545	0.733–3.257	0.252
Overweight ($25 \leq \text{BMI} \leq 29.99 \text{ kg/m}^2$)	1.291	0.628–2.654	0.487
Number of anti-asthmatic drugs			
Three or more	Reference		
One	0.902	0.378–2.147	0.814
Two	0.687	0.275–1.715	0.420
Asthma control at baseline			
Controlled	Reference		
Uncontrolled	0.057	0.028–0.114	<0.001

OR: Odds Ratio; 95%CI: 95% confidence interval; BMI: body mass index.

Raw data OR (simple logistic regression analysis): 1.625 (95%CI: 1.054–2.507; $p = 0.028$).

Assuming mean values for age and BMI ($n = 336$); OR: 3.117; IC: 1.669–5.823; $p < 0.001$.

Intention to treat ($n = 352$); OR: 1.942; IC: 1.061–3.553; $p = 0.032$.

Intention to treat assuming mean values for age and BMI ($n = 361$); OR: 1.997; IC: 1.089–3.662; $p = 0.026$.

Hosmer–Lemeshow test (Chi-squared = 6.038; $p = 0.643$); Nagelkerke R-squared: 0.407.

A subgroup analysis of uncontrolled asthma patients at baseline showed a greater effect of the intervention on both proportion of controlled patients and mean ACQ scores after 6 months of follow up compared to those patients that were well-controlled at baseline (Table 3).

Secondary outcomes: inhaler technique and medication adherence

Proportion of patients with incorrect performance of steps for Turbuhaler inhaler technique at baseline is summarised in Table 4.

The percentage of intervention patients with correct inhaler technique significantly increased between baseline (19.5%) and intermediate visit (57.0%, $p < 0.001$), and between intermediate visit and final visit (75.7%, $p < 0.001$). Significant increase was also observed in patients included in the CG between baseline (24.0%) and intermediate visit (46.0%, $p < 0.001$), but not between intermediate visit and final visit (50.0%, $p = 0.286$). Proportion of patients with correct inhaler technique at the end of the study was significantly higher in the IG (75.8% versus 50.0%, $p < 0.001$) (Fig. 4).

When compared with the CG, proportion of patients in the IG who performed steps 2, 4, 6, 7, 8, and 10 of the inhaler technique correctly was significantly higher at the final visit (Table 5).

In the IG, proportion of patients adherent to asthma treatment significantly increased from baseline (38.2%) to intermediate visit (60.8%; $p < 0.001$), as well as between intermediate visit and final visit (78.5%; $p < 0.001$). In the CG this increase was observed between baseline (39.3%) and intermediate visit (53.3%; $p < 0.001$), but not between intermediate visit and final visit (52.0%; $p = 0.839$). Proportion of adherent patients at the end of the study was significantly higher in the IG (78.5% versus 52.0%, $p < 0.001$) (Fig. 5).

Discussion

The results show that the educational intervention in this 6-month study significantly improved asthma control in patients allocated in the IG, compared to usual care. Secondary outcomes important for asthma management were also improved, and the results remained significant when a more restrictive ITT analysis was used.

Within the first 3 months of follow-up, a significant improvement in ACQ scores, inhaler technique and medication adherence among patients in both study groups was observed. These positive results in the CG could be attributed to several factors; patients may have modified their behavior because they knew they were being studied (Hawthorne effect) or because as part of the measurement of the main variables, they were asked questions about their asthma control, medication adherence and inhaler technique, activities that may not usually have been performed in the pharmacy. Additionally, even though control pharmacists were asked not to change their usual care during the study, they might have provided more information than the one usually provided. Although community pharmacists have specific medication and disease knowledge, they usually demand and are provided additional

Table 3 Sub-analysis of the effect of the intervention based on asthma control at baseline.

	Patients with controlled asthma at baseline (<i>n</i> = 116) ^a			Patients with uncontrolled asthma at baseline (<i>n</i> = 220) ^b		
	IG	CG	<i>p</i> -Value	IG	CG	<i>p</i> -Value
Controlled asthma (final visit); <i>n</i> (%)	47 (90.4)	54 (84.4)	0.337	61 (45.5)	15 (17.4)	<0.001
Correct Turbuhaler inhaler technique (final visit); <i>n</i> (%) ^c	38 (73.1)	36 (56.3)	0.061	103 (76.9)	39 (45.3)	<0.001
Difference between groups in adjusted mean changes for ACQ from baseline to intermediate visit; points (IC95%) ^c	0.05 (−0.15–0.25)		0.634	−0.21 (−0.01–0.44)		0.065
Difference between groups in adjusted mean changes for ACQ from baseline to final visit; points (IC95%) ^c	−0.18 (−0.37–0.02)		0.079	−0.62 [−0.80 –(−0.43)]		<0.001

CG: control group; IG: intervention group; 95%CI: 95% confidence interval.

^a Intervention group (*n* = 52), Control group (*n* = 64).

^b Intervention group (*n* = 134), Control group (*n* = 86).

^c Analysis of covariance (ANCOVA), using the patient's group assignment as the primary effect and baseline ACQ punctuation as the co-variable (differences are expressed compared to the CG).

specific training prior to the delivery of a specific pharmaceutical care service. Intervention pharmacists were provided with training above and beyond the usual training a pharmacist would receive on asthma management and so that they could effectively address patients needs based on asthma control, medication adherence and/or inhaler use. However, it should be noted that these improvements were sustained at 6 months only in intervention patients, suggesting that to detect an impact in patient outcomes, future similar research should be carried out during at least that period of time.

Our overall findings agree with other published research [15–24]. Two studies in a community pharmacy setting [25,26] were found to measure asthma control as the primary outcome, reflecting the GINA 2006 shift of paradigm in asthma management. Armour et al. [26] assessed asthma control using a symptom/activity tool and the ACQ for

patients receiving either a three- or four- visit asthma pharmacy service. They found an increase in patients classified as having good asthma control by 32% (for the three-visit group) and by 38% (for the four-visit group) and a mean decrease in ACQ scores of 0.57 and 0.56 respectively. Similar results in both increase percentage of controlled patients and mean decrease of ACQ scores were also found in our study. Mehuys et al. [25] measured asthma control with a clinically validated tool (Asthma Control Test, ACT) and found that the intervention significantly improved ACT scores only in a subgroup of patients having insufficiently controlled asthma at baseline. However in the present study, positive results were found not only in a subgroup of uncontrolled patients at baseline but also in the aggregated data. As previously suggested [9], this greater improvement in asthma control on uncontrolled patients at baseline can establish a different interventional approach in asthma

Table 4 Proportion of patients with incorrect performance of steps for Turbuhaler inhaler technique at baseline.

Turbuhaler inhaler technique step	Total (<i>n</i> = 336)	IG (<i>n</i> = 186)	CG (<i>n</i> = 150)	<i>p</i> Value
1 Unscrew and lift off the cover	9 (2.7)	2 (1.1)	7 (4.7)	0.043
2 Hold the inhaler upright	81 (24.1)	37 (19.9)	44 (29.3)	0.044
3 Twist the red grip fully to the right as far as it will go and twist it back again to the left. A "click" will be heard	41 (12.2)	26 (14.0)	15 (10.0)	0.268
4 Breathe out gently taking care not to breathe into the Turbuhaler	157 (46.7)	90 (48.4)	67 (44.7)	0.497
5 Place mouthpiece between teeth and lips	52 (15.5)	27 (14.5)	25 (16.7)	0.588
6 Inhale forcefully and deeply	75 (22.3)	51 (27.4)	24 (16.0)	0.012
7 Remove the inhaler from the mouth, hold breath for 8 s and exhale away from the mouthpiece	140 (41.7)	86 (46.2)	54 (36.0)	0.058
8 If further doses are needed wait 30 s and repeat steps from 2 to 7 ^a	59 (50.0)	35 (53.0)	24 (46.2)	0.458
9 Replace white cap	22 (6.5)	15 (8.1)	7 (4.7)	0.211
10 Rinse mouth with water. Do not swallow	142 (42.3)	77 (41.4)	65 (43.3)	0.721

^a This step was assessed in those patients prescribed with two consecutive inhalations (118 patients: CG = 52; IG = 66).

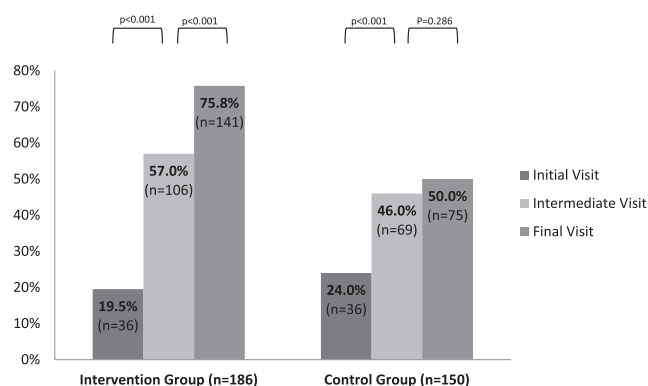


Figure 4 Proportion of patients with correct inhaler technique across the study visits.

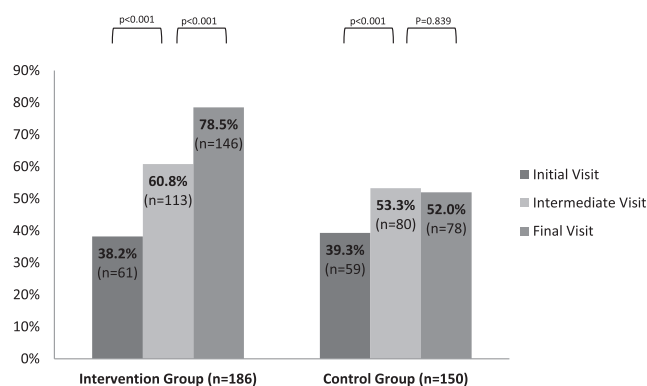


Figure 5 Proportion of adherent patients to asthma treatment.

management. The identification of uncontrolled patients through health initiatives in different settings would allow targeting asthma management strategies and probably reducing asthma-related costs over time.

The intervention delivered to patients allocated to the IG was effective, individualized and tailored to the patients' current asthma control, following GEMA recommendations. Adherence education was provided using different strategies according to the kind of non-adherence identified in the patient. The intervention was individualised, taking into account specific barriers to medication adherence, using validated tools for patients presenting intentional non-adherence. This allowed the assessment of necessity beliefs and concerns about asthma treatment and effectively addressed them. Inhaler training was delivered using written and verbal counselling plus physical demonstration (proven to be the most effective way of delivering such education [36]), improving the percentage of patients

performing correct inhaler technique. As medication adherence and inhaler technique are both critical issues for successful asthma management, their improvement probably contributed to the enhancement of asthma control in 30.1% of patients allocated in the IG. Unfortunately, neither assessment nor training on inhaler technique is regularly being performed in many clinical settings, increasing the risk of misuse of inhaler devices [10]. Nevertheless at the end of the study there still were non-adherent patients (21.5%) and patients failing to use the inhaler device correctly (24.2%). Whether these issues in association with other factors, such as smoking status or exposure to triggers, may have contributed to 41.9% of patients failing to achieve good asthma control is unknown.

Some limitations of this study must be mentioned. Firstly, only patients treated with Symbicort were included in the study; therefore, our sample may not be representative of the whole asthma population. Secondly, significant

Table 5 Proportion of patients with incorrect performance of steps for Turbuhaler inhaler technique at final visit.

Turbuhaler inhaler technique step		IG (n = 186)	p Value ^a	CG (n = 150)	p Value ^a	p Value ^b
1	Unscrew and lift off the cover	1 (0.5)	1.000	0 (0.0)	d	0.368
2	Hold the inhaler upright	6 (3.2)	<0.001	34 (22.7)	0.076	<0.001
3	Twist the red grip fully to the right as far as it will go and twist it back again to the left. A "click" will be heard	2 (1.1)	<0.001	6 (4.0)	0.035	0.080
4	Breathe out gently taking care not to breathe into the Turbuhaler	20 (10.8)	<0.001	37 (24.7)	<0.001	0.001
5	Place mouthpiece between teeth and lips	9 (4.8)	0.001	10 (6.7)	<0.001	0.471
6	Inhale forcefully and deeply	12 (6.5)	<0.001	20 (13.3)	0.481	0.033
7	Remove the inhaler from the mouth, hold breath for 8 s and exhale away from the mouthpiece	14 (7.5)	<0.001	31 (20.7)	<0.001	<0.001
8	If further doses are needed wait 30 s and repeat steps from 2 to 7 ^c	4 (6.0)	<0.001	14 (26.4)	0.012	0.002
9	Replace white cap	3 (1.6)	0.004	8 (5.3)	1.000	0.057
10	Rinse mouth with water. Do not swallow	9 (4.8)	<0.001	36 (24.0)	<0.001	<0.001

^a For intra-group comparisons between baseline and end point (McNemar test).

^b For comparisons between groups (Chi-Square test).

^c This step was assessed in those patients prescribed with two consecutive inhalations (120 patients: CG = 53; IG = 67).

^d McNemar test was not calculated since at least one of the variables used for the calculation of measures of association was a constant.

differences between study groups were found at baseline in mean number of anti-asthmatic drugs and percentage of patients living in an urban area. Although patients had similar ACQ scores at baseline, when categorized according to their level of asthma control, significant differences were also observed. This concern was controlled for by adjusting the statistical analysis to take these baseline differences into account. Finally, since patient's outcomes were achieved after a 6-month intervention, sustainability of these results on a longer term follow-up cannot be assured.

In conclusion, asthma represents a worldwide problem and public health initiatives are essential to encourage asthma education for patients and healthcare providers. The AFasma study focused on the important outcomes of asthma management, and showed that through the designed intervention, community pharmacists can increase controlled asthma patients compared to usual care. Although the intervention delivered seemed to be compatible with the pharmacists' daily practice, additional research would be needed to define the core issues for a future implementation of the service in a community pharmacy setting.

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Conflict of interest statement

All the authors have declared that they have no conflict of interest.

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