Internet-based monitoring of asthma: A long-term, randomized clinical study of 300 asthmatic subjects

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Background: Experience from other fields of internal medicine shows that Internet-based technology can be used to monitor various diseases. The new technology handles complex calculation programs easily, and it is a unique way of communicating. These advantages might be used in optimizing the treatment for asthmatic subjects because undertreatment is a common problem found in European asthmatic subjects.
Objective: We sought to investigate the outcome of monitoring and treatment using a physician-managed online interactive asthma monitoring tool and to assess whether the outcome differs from that of monitoring and treatment in an outpatient respiratory clinic or in primary care.
Methods: Three hundred asthmatic subjects were randomized to 3 parallel groups in a 6-month prospective study: (1) Internet-based monitoring (n = 100); (2) specialist monitoring (n = 100); and (3) general practitioner (GP) monitoring (n = 100). All the patients were examined on entry into the study and after 6 months of treatment.
Results: The treatment and monitoring with the Internet-based management tool lead to significantly better improvement in the Internet group than in the other 2 groups regarding asthma symptoms (Internet vs specialist: odds ratio of 2.64, $P = .002$; Internet vs GP: odds ratio of 3.26; $P < .001$), quality of life (Internet vs specialist: odds ratio of 2.21, $P = .03$; Internet vs GP: odds ratio of 2.10, $P = .04$), lung function (Internet vs specialist: odds ratio of 3.26, $P = .002$; Internet vs GP: odds ratio of 4.86, $P < .001$), and airway responsiveness (Internet vs GP: odds ratio of 3.06, $P = .02$).
Conclusion: When physicians and patients used an interactive Internet-based asthma monitoring tool, better asthma control was achieved. (J Allergy Clin Immunol 2005;115:1137-42.)

Key words: *Asthma, telemonitoring, telemedicine, Internet, outcome assessment, disease management, action plan, self-management*

Abbreviations used
AQLQ: Asthma quality of life questionnaire
GINA: Global Initiative for Asthma
GP: General practitioner
PEF: Peak expiratory flow
PD_{20}: Provocative dose causing a 20% decrease in FEV_1

Over the last 20 years, the prevalence of asthma has increased, especially in the industrialized countries, which imposes a social and economic burden on both the patient and society.[1,2] In spite of effective pharmaceutical treatment and an increasing number of published guidelines, asthma is a growing health problem in countries around the world.[3-5] Undertreatment is currently the most common problem found in European asthmatic subjects.[6,7] Experience from other fields of internal medicine shows that computer- and Internet-based technology can be used to treat and monitor various diseases.[8-10] The new technology handles complex calculation programs and algorithms easily, and it is a unique way of communicating. All these advantages can be amplified in the treatment of asthmatic subjects. Internet-based asthma diaries are available today, but only a few have a feedback system, and to our knowledge, none of them have combined an electronic action plan and a treatment decision support system.[11,12] This has inspired the development of an Internet-based asthma management tool, which was created in a collaboration between Danish physicians, a patient association (The Danish Asthma and Allergy Association), and a pharmaceutical company.[13] The fact that approximately 81% of the Danish population have access to the Internet constitutes an ideal setting for Telemedicine Home Care projects.[14]

The aim of this study was to assess the outcome (symptoms, quality of life, lung function, and airway responsiveness) of an Internet-based management tool in comparison with conventional asthma treatment in a randomized clinical trial over a period of 6 months.

METHODS

Study design

The study was carried out in a 6-month, prospective, randomized comparative design with 3 parallel groups and 2 scheduled visits 6 months apart. At each visit, questionnaires were filled in,

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spirometry was performed, measurement of airway responsiveness with methacholine was conducted, and each patient was interviewed by the physician. The patients were randomized consecutively by using the sealed envelope technique, irrespective of computer experience and smoking status, to one of the following 3 groups: Internet group, treatment by an asthma specialist with the Internet-based management tool (n = 100); specialist group, treatment by an asthma specialist in an outpatient clinic (n = 100); and general practitioner (GP) group, treatment by GPs in primary care (n = 100).

The local ethical committee (of Copenhagen, Denmark) approved the study (KF 01-074/01). All the participants were informed about the study verbally and in writing, and all provided written informed consent before enrollment.

Subjects

In 2001, a random sample of subjects aged 18 to 45 years, living in the catchment area of H:S Bispebjerg University Hospital of Copenhagen, Denmark, was sent the American College of Allergy, Asthma, and Immunology[15] asthma questionnaire with the purpose of including 300 patients with definite asthma. Letters were posted until 300 asthmatic subjects had been enrolled. Asthma was diagnosed on the basis of a combination of respiratory symptoms and at least one objective measurement of asthma (ie, airway hyperresponsiveness to inhaled methacholine of $\leq$4 μmol, peak expiratory flow [PEF] variability of $\geq$20%, and/or a minimum of 15% [300 mL] increase in FEV_1 after bronchodilation).[16]

Treatment in the 3 groups

All physicians (specialists and GPs) in Denmark are recommended to follow the Global Initiative for Asthma (GINA) guidelines[17] when treating patients with asthma. Those in the Internet group were treated according to the instructions given by the Internet tool based on GINA guidelines. Patients in all 3 groups had to cover the costs of the medication prescribed.

The Internet group

The Internet-based asthma management tool comprised of (1) an electronic diary, (2) an action plan for the patients, and (3) a decision support system for the physician.[13] Patients were given a peak flowmeter (Vitalograph, Ltd, Maid Moriton, Buckingham, United Kingdom) and instructed in the use of the Internet diary. If the patient did not have access to a computer, a push-button telephone was used. Using either option, patients were able to complete the electronic asthma diary and record symptoms, need for rescue medication, and PEF values. The Internet tool's action plan comprised a 3-color warning system accompanied by a written treatment plan.[13] Patients were encouraged to fill in the electronic diary daily and to follow the instructions given by the computer and the physician. Patients with persistent asthma received 1 month of treatment with a high dose of inhaled corticosteroid,[17] and thereafter the decision support system was used to check whether the asthma had been brought under control; the physician then instructed the patient by e-mail or telephone to increase, decrease, or continue the usual treatment. Additional detail on the Internet tool and treatment protocol is provided in the Journal's Online Repository at www.mosby.com/jaci (see also Figs E1-E8).

The specialist group

Patients were treated according to their current severity level,[17] and they were taught how to adjust their medication. A peak flowmeter and a written action plan[18] were given to the patients, and they were asked to use them regularly, preferably daily. The action plan comprised a 3-color warning system based on the symptom score and PEF values.

The GP group

The patients were asked to contact their GP immediately after enrollment and pass on a letter describing the study and giving the test results. The letter did not contain particulars about the recommended therapy, but in 2001, all the GPs in the Copenhagen area had been sent a circular about asthma and GINA guidelines by the local authority. The GP was to assess the patient's asthma symptoms and the test results and from this decide the patient's need for pharmaceutical treatment. The patients in the GP group did not receive any treatment or information about asthma from the study physician.

Questionnaires

All asthmatic subjects filled in questionnaires on asthma quality of life (AQLQ),[19,20] asthma self-care, smoking habits, education, salary, sick leave, and hospitalization. In addition, the study physician conducted a questionnaire-based interview on respiratory symptoms, current medication, compliance (good/poor), and adverse reactions.

Grading of symptoms

The severity of symptom was graded as follows: very mild, respiratory symptoms less than once a week and nocturnal symptoms not more than twice a month; mild, respiratory symptoms 2 to 6 times a week and nocturnal symptoms more than twice a month but not weekly; moderate, respiratory symptoms daily and nocturnal symptoms more than once a week; and severe, respiratory symptoms constantly and nocturnal symptoms more than 4 times a week.[17]

Lung function and methacholine challenge tests

Trained laboratory assistants carried out the lung function test and the test of airway responsiveness with methacholine. Spirometry was performed on a 7-L dry wedge spirometer (Vitalograph), as recommended by the American Thoracic Society.[21] Percentages of predicted normal values for FEV_1 and forced vital capacity were calculated.[22,23] Measurement of FEV_1 was repeated 15 minutes after administration of 0.6 mg of salbutamol.

Airway responsiveness to inhaled methacholine was measured in all patients with FEV_1 values of greater than 70% of the predicted value.[24] The provocative dose causing a 20% decrease in FEV_1 (PD_{20}) was calculated, and airway hyperresponsiveness was defined as a PD_{20} of 4 μmol methacholine or less. The dose-response slope was calculated as the decrease in FEV_1 divided by the highest dose of methacholine administered.[25] A constant of 3 was added to all dose-response slopes to eliminate negative and zero values, and logarithmically transformed values were used for analysis.

Statistical analyses

The data were analyzed with the statistical program SPSS (version 12). Means and SDs were calculated for the normally distributed data, whereas medians and ranges were used to describe the skewed distributed data. For the continuous variables, data were analyzed by means of ANOVA, followed by the 2-sample *t* test to compare the groups and a paired *t* test for the paired data. The χ^2 or Fisher exact test was used to analyze categoric data, and the McNemar test was applied for paired data. Furthermore, logistic regression was conducted to calculate the odds ratio with a 95% CI. *P* values of less than .05 were considered significant.

Asthma quality of life was chosen for the power calculations on the basis of data from the article by Juniper et al.[20] On a 95% power to detect a significant difference, 80 patients were required in each group. An estimated loss of 20% in each group at follow-up was expected, resulting in enrollment of 300 asthmatic subjects, 100 in each group.

TABLE I. Patients' characteristic at baseline

Characteristics	Internet group (n = 85)	Specialist group (n = 88)	GP group (n = 80)	Dropouts (n = 47)
Sex (F/M)	58/27	58/30	58/30	33/14
Age (y)*	28 (18-44)	30 (19-45)	30 (20-45)	30 (20-45)
Symptoms grading				
Very mild (%)	1	1	1	4
Mild (%)	49	48	50	45
Moderate (%)	25	19	24	32
Severe (%)	25	32	25	19
AQLQ†	6.17 (3.86-7)	6.20 (3.25-7)	6.13 (1.89-7)	6.26 (3.62-7)
FEV_1, % predicted‡	91 (14)	93 (13)	92 (12)	91 (15)
AHR logDRS‡	1.03 (0.5)	1.05 (0.4)	1.02 (0.5)	1.16 (0.6)

AHR, Airway hyperresponsiveness; *logDRS*, logarithmically transformed values of the dose-response slope of methacholine.
*Median (range).
†The overall AQLQ score contains 4 domains: activities, symptoms, emotions, and environment.
‡Mean (SD).

TABLE II. Treatment effect at follow-up

	Internet vs specialist		Internet vs GP		Specialist vs GP	
Variables	Odds Ratio (95% CI)	*P* value	Odds Ratio (95% CI)	*P* value	Odds Ratio (95% CI)	*P* value
Improved symptoms	2.64*(1.43-4.88)	.002	3.26*(1.71-6.19)	<.001	1.23*(0.66-2.30)	NS
Improved AQLQ	2.21†(1.09-4.47)	.03	2.10†(1.02-4.31)	.04	0.95†(0.43-2.07)	NS
Improved FEV1 ≥300 mL	3.26‡(1.50-7.11)	.002	4.86‡(1.97-11.94)	<.001	1.49‡(0.55-4.05)	NS
Improved AHR	1.26§(0.57-2.79)	NS	3.06§(1.13-8.31)	.02	2.44§(0.89-6.72)	NS

NS, No significant difference between groups; *AHR*, airway hyperresponsiveness.
*Odds for improvement in asthma symptoms at follow-up: the improvement in symptoms was defined as improvement of one or more severity steps: 64% (Internet group), 40% (specialist group), and 35% (GP group) of the patients improved.
†Odds for improvement in AQLQ score at follow up: improvement in AQLQ score was defined as improvement of 0.5 (minimal important change) or more in the overall score: 33% (Internet group), 18% (specialist group), and 19% (GP group) of the patients improved.
‡Odds for improvement in FEV_1 of 300 mL or more at follow-up: 32% (Internet group), 13% (specialist group), and 9% (GP group) of the patients improved.
§Odds for improvement in airway responsiveness by one or more dosage step at follow-up: 21% (Internet group), 17% (specialist group), and 8% (GP group) of the patients improved.

RESULTS

We enrolled 300 subjects who fulfilled the criteria for asthma. There were no significant differences among the 3 groups at baseline (Table I). Two hundred fifty-three subjects completed both the screening and follow-up visits. No significant difference was found in the dropout rate of the 3 groups (15, 12, and 20 subjects, respectively; $P = .26$, χ^2).

Asthma symptoms, AQLQ, lung function, and airway responsiveness

At follow-up, the odds for improvement in symptoms, AQLQ, and lung function were significantly in favor of the Internet group compared with the other 2 groups (Table II).

The improvements in FEV_1 observed over the 6 months for the 3 groups were 0.187 mL (SEM 0.04) in the Internet group, 0.035 mL (SEM 0.03) in the specialist group, and 0.004 mL (SEM 0.03) in the GP group ($P < .001$, ANOVA; Internet vs specialist: $P = .001$, *t* test; Internet vs GP: $P < .001$, *t* test; data not shown). Finally, a significant odds ratio for an improvement in airway responsiveness was observed between the Internet group and the GP group (Table II). Additional statistical analyses besides odds ratios are provided in the Journal's Online Repository at www.mosby.com/jaci (see also Tables E1 and E2).

The number needed to treat (on the basis of the improvement in AQLQ) for the Internet group compared with the specialist group was 5.46, and that compared with the GP group was 5.69, as calculated according to the method of Guyatt et al.[26]

Pharmaceutical treatment, side effects, and compliance

On entry, 51% were not taking any medication for asthma. At follow-up, an increase was noted in the use of inhaled corticosteroids in all groups, but significantly more patients in both the Internet and specialist groups used inhaled corticosteroids at the follow-up visit (Table III). The recommended daily dose of inhaled corticosteroids was calculated on the severity of the patient's asthma at the time of enrollment and found to be 800 μg, with an average range 400 to 1600 μg, for all patients, with no difference between the groups (data not shown). At follow-up, it was shown that only the Internet group had received the recommended treatment (Table III). Side

TABLE III. Medication, compliance, and use of action plan at baseline and at follow-up*

	Internet group (n = 85)			Specialist group (n = 88)			GP group (n = 80)		
Variables	**Baseline**	**Follow-up**	**McNemar**	**Baseline**	**Follow-up**	**McNemar**	**Baseline**	**Follow-up**	**McNemar**
No asthma medication	44%	0%	<.001	57%	1%	<.001	53%	26%	<.001
Take ICS	21%	91%	<.001	20%	83%	<.001	17%	29%	.04
Daily dose of ICS,† μg		866 (0-1600)			400 (0-1600)			0 (0-1200)	
Good Compliance‡	32%	87%	<.001	25%	79%	<.001	36%	54%	<.001
Use of action plan§	2%	88%	<.001	3%	66%	<.001	0%	6%	NS

NS, No significant difference between groups; ICS, inhaled corticosteroids.
*No significant difference was seen among the 3 groups at baseline.
†The daily dose of inhaled corticosteroids actually taken by the patients during the study (median [range]).
‡Good compliance is defined as use of medication always or almost always.
§The patients were asked whether they used their action plan (yes/no).

effects reported at follow-up showed that dysphonia was more common in the Internet group (17% vs 4% and 9%; $P = .002$, χ^2), as was oropharyngeal candidiasis (18% vs 3% and 4%; $P < .001$, χ^2). No significant differences were found between groups in respect to tachycardia and tremor (data not shown). A significant improvement in compliance was observed for all groups, but good compliance was significantly higher ($P < .001$, χ^2) for both the Internet versus the GP group and the specialist versus the GP group (Table III).

Scheduled and unscheduled visits and patients' use of action plan

All patients had 1 scheduled visit at the clinic during the 6 months. However, acute unscheduled visits were made by 3.7% of the patients in the Internet group versus 2.1% of the patients in the specialist group and 1.3% of the patients in the GP group ($P = .05$, χ^2) on a monthly basis. The patients in the GP group visited their physician on average once (95th percentile, 1-3). Patients in the Internet group used the management tool on average 4 times in 2-week blocks (range, 1-6) during the 6-month follow-up period (data not shown). Two patients in the Internet group and one in the GP group visited the emergency department in the study period. One patient in the specialist group was hospitalized because of an exacerbation. At the time of enrollment, 2% had a written action plan. At follow-up, a difference in the 3 groups was found in the use of an action plan (88%, 66%, and 6%, respectively; $P < .001$, χ^2; Table III).

DISCUSSION

A Cochrane review[27] demonstrates that asthma is better controlled if patients, self-monitoring their symptoms and peak flow, follow a written action plan and attend regular control visits to their physician's office. But it can be quite complicated to handle for both patients and physicians, and therefore Internet-based management systems have been developed to try to improve user-friendliness in self-management and monitoring.

This randomized controlled study is one of a very few similar studies. We demonstrated that an Internet-based management tool had the potential of improving asthma outcome compared with conventional treatment over a period of 6 months.

The last few years have seen the development of various kinds of tools for improving asthma care. Guendelman et al[12] demonstrated that interactive telephone-based education for 12 weeks produced better asthma control than did the use of a conventional asthma diary. This asthma education tool differs considerably from our asthma management tool in that ours contains an action plan for the patient and a decision support system to help the physician decide the level of treatment. An Internet-based asthma monitoring system was developed by Finkelstein,[11] who used portable spirometers and pocket-sized palmtop computers for registering lung function and symptoms. The system was found to be user-friendly in a study of 31 asthmatic subjects.[28] However, the study was not designed to assess the ability of the system to improve asthma treatment. These 2 studies nevertheless indicate that Internet-based asthma monitoring and education form a promising tool to improve asthma outcomes.

Our management tool proved to be user-friendly in a pilot study of 90 asthmatic subjects,[29] and the present study shows that it can improve asthma care in the setting of a randomized clinical trial. The improvement in asthma control was more pronounced in the Internet group than in the other 2 groups, which suggests that Internet management of asthma is beneficial. In addition, the number needed to treat was calculated to be 6. In other words, for patients using Internet-based asthma management, 1 out of 6 patients experiences a significant improvement in asthma quality of life compared with traditional management. The FACET study found the number needed to treat to be 12.[30] We believe that the benefit deriving from implementation of the Internet tool is to some extent caused by the opportunity to register symptoms continually and thereby obtain a more accurate picture of disease severity. The difference in the asthma control of the Internet group and that of the specialist group might be

explained by patients' reluctance to alter their medication or consult a physician because the patients in the specialist group used their action plan and made unscheduled visits less often. Other studies indicate that compliance is better with electronic peak flow monitoring than with conventional paper recording.[31,32] Furthermore, a cardiologic review has shown that telemonitoring can facilitate early detection of deterioration.[10] Both of these results could explain our findings. Moreover, only the Internet group received the recommended daily dose of inhaled steroid, and this was probably because of a more adequate evaluation of the asthma severity, better compliance, and closer and more efficient monitoring. However, the higher consumption caused significantly more local side effects in the Internet group. This could suggest that some of the patients were overtreated. Consequently, further analyses are needed to assess whether the treatment algorithm incorporated in the Internet tool should be adjusted.

Implementation of the tool in clinical practice might be impeded by physicians' lacking confidence in the use of computer technology[13] and a tendency among the physicians to think that the decision support system of the Internet tool interferes with their own treatment practice. The latter will reduce the compliance to the treatment recommendations incorporated in the tool. But even more problematic is the underdiagnosis and undertreatment of asthma found at baseline. There remains a huge amount of work in improving asthma management in primary care before an Internet-based asthma management system can be applied effectively in clinical practice.

We do not believe that the Internet tool per se provided better asthma control, but our study showed that its use resulted in closer monitoring, immediate feedback, adequate medication, and better compliance and that all these initiatives together produced better asthma control. Our study also indicates that asthma treatment could be improved in both the specialist and the GP setting and that the Internet could be a helpful tool here, too.

In conclusion, we found that physician-managed and Internet-based monitoring produced better control of asthma, but the costs were scheduled Internet monitoring in periods of 2 weeks, more unscheduled visits, a higher consumption of inhaled steroids, and more side effects. Nonetheless, we believe that Internet-based monitoring is effective in controlling asthma over a period of 6 months and that the future will see further developments of such monitoring and electronic devices to the benefit of both patients and physicians.

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