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A daily SMS reminder increases adherence to asthma treatment: A three-month follow-up study

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Summary
Background: Poor adherence to asthma treatment is a well-recognised challenge and is associated with increased morbidity, mortality and consumption of health care resources. This study examined the impact of receiving a daily text message reminder on one's cell phone on adherence to asthma treatment.
Methods: A total of 26 subjects aged 18–45 years, with a clinical history of asthma and a positive methacholine challenge test ($PD_{20} \leq 4$ μmol) were randomised to receive, or to not receive, a daily short message service (SMS) reminder on their cell phone to take their anti-asthmatic medication. Inhaled corticosteroids to last for eight weeks and a prescription for four additional weeks were given to the subjects. The primary outcome was adherence to asthma treatment. Secondary outcomes were reimbursement of asthma medication, and change in exhaled nitric oxide levels, lung function, and airway responsiveness.
Results: The absolute difference in mean adherence rate between the two groups after 12 weeks was 17.8%, 95% CI (3.2–32.3%), $p = 0.019$. No significant differences were observed between the two randomisation groups for the secondary outcomes.
Conclusion: Daily text message reminders are already after a short period of observation associated with increased adherence to anti-asthmatic medication.

Introduction

Sufficient asthma control means that the patient has minimal symptoms, no or minimal use of reliever medication, no limitation of daily activities, normal lung function, and few exacerbations.[1] To achieve long-term control of asthma a variety of approaches are needed such as appropriate medication, patient education and lastly sufficient adherence. Adherence is generally defined as the extent to which patients take medications as prescribed by their health care provider. Adherence to treatment in chronic diseases is a well-recognised challenge. Studies have found adherence rates to asthma treatment as low as 50%, which leads to poor asthma control characterised by daily symptoms of breathlessness, decreased lung function, increased inflammation

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and exacerbations.[1] Up to 30% of asthma patients report forgetfulness to be one of the main reasons for their poor adherence indicating an area with room for improvement.[2,3] Non-adherence is often defined as insufficient intake of the prescribed medicine with an adherence rate cut-off at 80%,[4] but there is no consensus as to what constitutes adequate adherence. As modern technology has progressed over the years, this field is now being studied as a possible means to improve adherence. Reminder packaging has been shown to improve adherence to self-administered long-term medications for some time.[5] Recent research now suggests increased adherence to asthma treatment with modern technology devices, such as audiovisual reminder functions, where an electronic audio alarm reminds patients when to take their medication.[6] Electronic patient diaries, where patients daily report peak expiratory flow (PEF) measurements on their cell phones, have also been tested as a possible instrument to improve adherence, and so far with promising results.[7,8] Internet as well as cell phone services, including short message service (SMS), is being implemented more and more in the public health care system — especially by means of optimising communication between health care providers and patients. This study examined the impact of receiving a daily text message reminder on one's cell phone on the adherence to asthma treatment.

Methods

Study design

The study was a follow-up investigation with three clinical examinations at week 0, 4 and 12. At week 0 all patients were given treatment with Seretide® (inhaled corticosteroids, ICS and long acting β_2-agonist, LABA, in combination) 1 dose twice daily. At week 4 the subjects were randomised to either 1) receiving a daily SMS — a reminder to take their asthma medication (the SMS group) or 2) not receiving a SMS reminder (the control group). The SMS reminder was sent daily at 10 a.m. on their cell phone in the following 8 weeks. All participants were informed of the aim of the study and randomisation was done by means of automatic computer generation of randomisation numbers in blocks of six. Discos Seretide® were given twice daily to all subjects at week 0 and 4 (total treatment 60 days). Furthermore, at week 4, all subjects were given a prescription for their treatment in the remaining 4 weeks of the study (from week 8 to 12). All participants were instructed to bring their asthma medicine to the following visit for adherence measurement where medicine dose-count on the discos Seretide® was noted (week 4 and 12). Furthermore, all participants were instructed to start treatment on the day of visit 1 and also not to take their medicine 12 hours before the clinical examination at week 4 and 12. All patients enrolled received a thorough education concerning the necessity of ICS treatment in asthma and all were provided with knowledge of the disease mechanisms and correct inhaler technique. All three visits included an interview conducted by the author, followed by measurement of exhaled nitric oxide (eNO), lung function and airway responsiveness to inhaled methacholine. Furthermore, the first visit included a skin prick test. The scientific ethical committee of Copenhagen, Denmark approved the study (no. H-C-2007-0132) and written consent was obtained from all participants before the first clinical examination.

The primary study outcome was the mean adherence rate to asthma treatment, whereas secondary outcomes were reimbursement of asthma medication and change in exhaled nitric oxide levels, lung function, and airway responsiveness.

Study population

A total of 54 subjects responded to advertisements in free local newspapers. The inclusion criteria were all of the following: 1) A diagnosis of asthma based on a clinical history and daily symptoms, 2) age between 18 to 45 years, and 3) a positive methacholine challenge test with $PD_{20} \leq 4$ μmol. Exclusion criteria included other medical co-morbidities and a smoking history of more than 10 packyears. After a screening session, 30 of the 54 subjects met the inclusion criteria and were enrolled in the three-month follow-up study. Of the 30 asthmatics, 26 subjects were randomised at week 4 (SMS group, $n = 12$ and control group, $n = 14$). A total of 22 subjects completed the study at week 12 (SMS group, $n = 10$ and control group, $n = 12$).

The asthma severity among the randomised subjects was as follows: eight subjects (30.8%) were categorised as mild persistent (GINA 2), 16 subjects (61.5%) as moderate persistent (GINA 3) and two subjects (7.7%) were categorised as severe persistent (GINA 4).[1] Before enrolment into the study, nine subjects (34.6%) had used SABA as monotherapy, nine subjects (34.6%) had used ICS (alone or in combination with LABA and/or SABA) and the remaining eight subjects (30.8%) had not used any treatment at all over the last three months.

Exhaled nitric oxide

Exhaled nitric oxide (eNO) was measured using the Nitric Oxide Analyzer (Niox, Solna, Sweden), which measures the concentration of NO in the expired air. The participants inhaled NO free air and exhaled for 10 s with a constant expiratory flow. The procedure was repeated three times and a mean concentration of NO (ppb) was calculated. NO measurements were performed before any other assessment of pulmonary function.[9,10]

Lung function measurement

Spirometric measurements of the forced vital capacity (FVC) and the forced expiratory volume in 1 s (FEV_1) were used to assess airway limitations among the participants. The FEV_1 and FVC were measured using a 7-L dry wedge spirometer (Vitalograph, Buckingham, UK). At least two measurements of maximal expiratory manoeuvres from total lung capacity to residual volume were performed. The highest FEV_1 and FVC were used in the analysis. Predicted values of FEV_1 and FVC were based on reference values according to Nysom et al.[11]

Methacholine challenge test

Airway responsiveness to inhaled methacholine was measured using the method described by Yan et al.[12] A Morgan nebulizer generated the aerosols of the test solution. Each aerosol was inhaled through the mouth starting with saline (0.9%) and followed by increasing doses of methacholine until a cumulative dose of 7.8 μmol had been reached. The response was measured by determining FEV_1 twice 60 seconds after each inhalation. The test was terminated when the maximum concentration had been reached or when a 20% decline in FEV_1 had occurred before the end of the dosing regimen. If a 10% decrease in FEV_1 occurred, the provocation was performed at half rate. A positive test was defined as a $PD_{20} \leq 4$ μmol. The response dose ratio (RDR) was calculated: $RDR = (\Delta FEV_1/FEV_1(\text{baseline}) \times 100)/PD_{20}$ (μmol).

Skin prick test and blood eosinophils

Skin prick tests were performed with a standard panel of ten allergens consisting of birch, grass, mugwort, horse, dog, cat, house dust mite (*D. Pteronyssinus and D. Farinae*) and fungi (*Alternaria and Cladosporium*) (ALK-Abello, Hoersholm, Denmark). A wheal diameter of at least 3 mm was regarded as positive, and atopy was defined as a positive skin prick test to at least one of the ten allergens. The number of eosinophils (10^9/L) in the peripheral blood was measured in blood samples at week 0.

Short message service

The participants randomised to the SMS group received the following short text message daily at 10 a.m. from week 4: ''*Remember to take your asthma medication morning and evening. From the Respiratory Unit*''. The service was administered via the Internet by CIM mobility.

Medicine count and pharmacy reports

The medicine administration count on the inhaler device was registered at week 4 and 12 and adherence rate was registered as the percentage of the medicine actually taken by the patients, calculated from the medicine dose-count on the discos Seretide® and the number of days between clinical examinations: $(60 - \text{dose-count})/2 \times \text{days} \times 100\%$. Pharmacy reports were collected from www.sundhed.dk, where all pharmaceutical transactions within the last two years are registered. In the present study, the time to collect the prescribed medicine was noted.

Statistical analysis

The data were analysed with the statistical package SPSS (SPSS Inc., Chicago, IL). Continuous data were analysed by *t*-tests whereas categorical data were compared using chi squared and Fisher's exact tests. The Wilcoxon signed rank test and the Mann-Whitney test was used to compare non-parametric data. A *p*-value <0.05 was considered statistically significant.[13]

Results

Descriptives

There were no significant differences between the basic characteristics of the two randomisation groups at the time of enrolment (Table 1). Furthermore, there was no

Table 1 Characteristics of two randomisation groups at enrolment.

Variable	SMS group ($n = 12$)	Control group ($n = 14$)	Total ($n = 26$)	*P*-value
Male sex	6 (50.0)	8 (57)	14 (54)	0.72
Age	34.4	30.7	32.2	0.22
Height (cm)	173.3	175.0	174.2	0.64
Weight (kg)	89.5	81.8	85.3	0.28
BMI	30.1	26.5	28.1	0.14
Age at onset	17.8	16.7	17.2	0.82
Duration	16.9	15.6	16.2	0.78
Packyears	0.8	1.3	1.1	0.59
Eosinophils (10^9/L)	0.21	0.29	0.26	0.14
Atopy	9 (75)	12 (86)	21 (81)	0.64
eNO (ppb)	32.6	45.3	39.5	0.31
FEV_1 (L)	3.32	3.28	3.30	0.89
FVC (L)	4.38	4.27	4.32	0.81
FEV_1% of predicted	84.5	80.0	82.1	0.46
FEV_1/FVC	76.4	77.3	76.9	0.82
PD_{20} (μmol), median	0.75	1.00	1.00	0.99
LogRDR	1.59	1.59	1.59	0.99
ACQ, median	1.71	1.93	1.79	0.52
MiniAQLQ, median	5.67	5.47	5.53	0.70

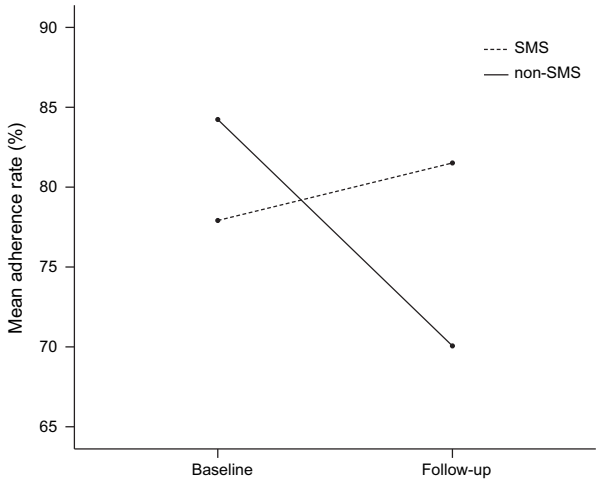

Figure 1 Change in mean adherence rate in the SMS group and the control group between week 4 and week 12.

difference between the groups in their use of asthma medication prior to enrolment ($p = 0.30$).

Primary outcome

From week 4 to week 12 the mean adherence rate in the SMS group increased from 77.9% to 81.5%; mean change = 3.6%, 95% CI (−8.5−15.7%), $p = 0.52$, whereas the mean adherence rate in the control group decreased from 84.2% to 70.1%; mean change = −14.2%, 95% CI (−24.2−4.1%), $p = 0.01$ (Fig. 1). The absolute difference in mean adherence rate between the two groups after 12 weeks was 17.8%, 95% CI (3.2−32.3%), $p = 0.019$.

Secondary outcomes

We did not observe any significant differences in the secondary outcomes between the SMS group and control group after 12 weeks (Table 2). Notably, a total of 17 (65%) of the randomised subjects had collected their prescribed anti-asthmatic medication at the pharmacy at follow-up. Of these, nine subjects were from the SMS group and eight subjects were from the control group ($p = 0.68$). Also, we found no significant differences in the number of days for the subjects in each group to collect their medicine; a median of 29 days (range 13 to 49 days) in the SMS group vs. a median of 32 days (range 13 to 50 days) in the control group ($p = 0.56$).

During the study, we observed overall improvements in eNO ($p < 0.001$), airway responsiveness (RDR) ($p < 0.001$) and FEV_1 ($p = 0.015$). The change in these parameters were, however, not differential in the two groups.

Discussion

This 12-week follow-up study showed that asthmatic patients who receive a daily SMS reminder on their cell phone remember to take, on average, about 18% more doses of their anti-asthmatic medication compared with asthmatic patients who do not receive such an SMS reminder.

Improvement of the generally poor adherence rates in treatment of asthma is essential to obtain adequate asthma control. As demonstrated by Suissa et al. poor adherence to asthma treatment is correlated with increased morbidity and mortality and an increased consumption of health care resources.[6] A daily SMS reminder is thought to create a higher awareness of asthma control and treatment and by implementing this awareness in a patient's daily routine the adherent behaviour is improved. For example, forgetfulness has been reported by 30% of patients in recent studies to be one of the main reasons for non-adherence.[14] Non-intentional and intentional non-adherence often co-exist in the same individual, and guidelines advice a combination of various interventions to achieve and sustain sufficient adherence. All subjects in this study were thoroughly instructed in the necessity of ICS treatment for asthma and provided knowledge of the disease and correct inhaler technique − all interventions known to be associated with improved adherence to treatment.[1] However, despite frequent examinations during the 12-week study period, these interventions together did not seem to be sufficient in the control group, suggesting a general need for a broader approach in improving adherence to treatment.

The effects of a daily SMS reminder on adherence appear to be somewhat larger than the effects on the clinical outcomes in the present study. To some extent, this was to be expected, as modest amounts of non-adherence may still leave patients within a well-treated therapeutic window. Furthermore, as no consensus exists for what constitutes adequate adherence, a poorer adherence may still be sufficient for a short period of time to improve clinical outcomes in steroid-naïve or undertreated patients. Some of the clinical outcomes are known to improve rather quickly, i.e. eNO, after initiating treatment with ICS, however it is difficult to stipulate the period of time it

Table 2 Secondary outcomes in the two randomisation groups.

Variable	Total ($n = 22$)		SMS group ($n = 10$)		Control group ($n = 12$)		SMS = control[1)]
	Difference (95% CI)	*P*-value	Difference (95% CI)	*P*-value	Difference (95% CI)	*P*-value	
eNO (ppb)	−19.4 (−29.5−9.5)	<0.001	−18.0 (−33.6−2.3)	0.029	−20.6 (−35.6−5.6)	0.012	0.795
FEV_1% of predicted	5.66 (1.24−10.07)	0.015	3.28 (−1.94−8.50)	0.189	7.65 (0.22−15.07)	0.045	0.318
FEV_1/FVC	2.02 (−0.49−4.54)	0.109	0.72 (−1.89−3.33)	0.548	3.11 (−1.28−7.50)	0.147	0.337
LogRDR	−0.87 (−1.17−0.57)	<0.001	−0.76 (−1.18−0.35)	0.003	−0.99 (−1.52−0.46)	0.003	0.453
ACQ	−0.73 (−1.03−0.44)	<0.001	−0.87 (−1.40−0.34)	0.005	−0.62 (−1.01−0.23)	0.005	0.392
MiniAQLQ	0.58 (0.27−0.90)	<0.001	0.57 (0.05−1.10)	0.035	0.59 (0.13−1.05)	0.016	0.961

P-value for test of differential effect in SMS and control group.

takes - and how much medicine *not* to be taken for the individual patient — before the initial improvement in clinical outcomes begins to revert. Seasonal variation in symptoms followed by changeable needs in medication regimens does not simplify these questions. Charles et al. demonstrated a significant improvement in adherence to treatment with an audiovisual reminder device, but at the end of the 6-month study period no differences in clinical outcomes (PEF) between the groups were observed.[6] In that study the proportion of adherent subjects (≥80% of their medication taken) after 6 months were 88.6% in the study group compared to 39.1% in the control group. PEF may therefore be a too stable measure, whereas eNO probably would have shown differences even when only 39% were taken their medication. The low proportion of adherent subjects in the control group in the study indicates, that after a short period of increased adherence among all patients and improvements in clinical outcome — as commonly seen in the beginning of a clinical trial — it may take a period of more than 6 months before the initial improvements has reverted in non-adherent subjects.

The time to collect the prescribed medicine at the pharmacy was longer in the control group, compared with the study group, however, not statistically significant, and it would therefore have been interesting to evaluate the collecting time over a longer period of time. The adherence rate in the control group was reduced significantly during the study period, and it may only be a matter of time before this also affects the adherent behaviour regarding the reimbursement of medication. Firstly, and most obviously, because the patients do not require refill as often because of lower adherence rates equal to a lower consumption of medicine and secondly, due to a generally poor adherent behaviour with minor focus on preventative asthma treatment. Furthermore, it is not uncommon among non-adherent patients to have a high use of SABA and low use of ICS. A Danish study described undertreatment among almost 50% of asthmatic patients with persistent asthma, receiving only SABA or LABA as monotherapy.[15] Therefore, together with the collecting time of prescribed medication, the *type* of medicine collected (SABA, LABA and/or ICS) is also an important factor to keep in mind.

Overall, the perception of receiving a daily SMS was positive (data not shown), although the majority found the SMS receiving time at 10 o'clock in the morning unsuitable, which implies room for improvement in further studies. It would be advisable to adjust the SMS receiving time individually to each patient to optimise the effect, as patients differ greatly in daily routines. A daily SMS reminder is, thus, easily implemented within clinical settings, as most adult patients have a cell phone.

This study had a limited sample size and a short follow-up period, therefore further studies with more participants and a longer follow-up are required before any unambiguous conclusions and a cost-benefit profile can be made regarding the effect on clinical outcomes. A potential adaptation to the SMS message may also be observed during a study period longer than three months. However, most of the participants in the intervention group noticed the SMS daily at receiving time, but stopped reading it after some weeks, indicating that over time the function of an SMS is to be compared with a simple alarm clock on a cell phone, creating a higher awareness of asthma control in the patient's adherent behaviour. In this study the adherence measurement method has the limitation of dose-dumping, where participants could empty their medicine devices prior to the visits. Hence, the validity of adherence measurement was based upon participant credibility regarding possible dose-dumping on the discos Seretide®, and is a possible limitation of the study. We found no reason to believe that the validity of adherence differed between the intervention and control group based upon interviews with the participants at week 12 and furthermore as both study groups were aware of the aim of the study. However, by implementing a smartinhaler as done by Charles et al., this limitation would be reduced in future studies.

In conclusion, a daily SMS reminder was found to have a significant effect on adherence to asthma treatment. Our findings expand upon those described by Charles et al. where an audiovisual reminder device significantly improved adherence to treatment.[6] As non-adherence is not only problematic in respect to asthma treatment, it also opens the possibility for a daily SMS reminder to improve adherence to treatment regimens across a larger spectrum of chronic diseases.

Conflict of interest statement

None of the authors have a conflict of interest to declare in relation to this work.

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