STUDY PROTOCOL

Aim: To assess the effectiveness of sending reminders to mobile phones and patient counselling to improve adherence among patients with chronic respiratory disease using inhalers in a tertiary care centre in Puducherry

Background

Adherence is the key to the success of any treatment. The rate of adherence is low for chronic diseases. Inhalers are the mainstay of treatment for chronic respiratory conditions like asthma and COPD. The adherence rate is low for inhalers compared to other dosage forms. The reasons for non-adherence could be numerous. Forgetting to take medications is the most common reason for non-adherence. Lack of knowledge about disease and drugs also leads to non-adherence. Multiple interventions addressing the above issues have proved effective in improving adherence. This study was carried out in a tertiary care hospital, which gives patients free treatment and drugs. The effectiveness of cost-effective and pragmatic interventions like patient counselling and recorded voice call reminders to patients' mobile phones were tried in this study.

1 Methodology

1.1 Study design

This study is a 2 x 2 factorial randomized controlled trial and an open labelled study since both participants and researchers knew the intervention type.

1.2 Study Setting

The institute ethics committee approved this study. Adult patients who had had an established diagnosis of either asthma or COPD followed up in General Medicine or Pulmonary Medicine Outpatient Department (OPD) in JIPMER, Puducherry, South India, and had used inhalers at least for the preceding three months were eligible to participate in the study.

1.3 Sample size

The sample size was determined by effect sizes observed in previous research and meta-analyses. Moderate effect sizes (Cohen's d=0.60) were estimated from self-reported adherence for the inhaler.[104] We assumed 80% retention and estimated 110 participants in each study arm to achieve a 90% chance of detecting differences in the main effects of counselling and voice call reminders and 80% for counselling x voice call reminder interaction.

1.4 Randomization

A randomization table was created using the Random Allocation Software. A computer-generated randomized sequence was made by a person not involved in the study. This random sequence was placed in sequentially numbered opaque sealed envelopes and handed over to the investigator.

2 Study participants

Inclusion criteria

- Patients diagnosed with asthma or COPD and followed up in JIPMER Medicine or Pulmonary Medicine OPD three months prior to the study period with or without other chronic co-morbid conditions
- The patients should own a mobile phone and be able to use it

Exclusion criteria:

- Patients who should refrain from performing PFT, as in the case of patients with pneumothorax, history of recent MI or pulmonary embolism, abdominal or cerebral aneurysm
- Patients who had undergone recent surgery
- Patients who were hard of hearing or mentally disabled.

3 Interventions:

They were randomized into any one of the four groups, as shown below. Patient counselling and voice call reminders were the two interventions. The grouping was done in a 2 x 2 factorial design. The training in the inhaler technique was given to all groups and was considered as the baseline treatment.

Group 1	Baseline treatment + patient counselling + Voice call reminders
Group 2	Baseline treatment + Patient counselling
Group 3	Baseline treatment + Voice call reminders
Group 4	Baseline treatment

3.1 Baseline treatment

Patients were shown a video explaining the technique of inhaler use. This video was downloaded from YouTube (https://www.youtube.com/watch? v=fVPKNl2tNu4) with the title “Learn how to use a Rotahaler Inhale” on demonstration of Rotahaler that M/s Cipla uploaded.

This video explains the steps in the use of Rotahaler. After watching the video, patients were asked to demonstrate the technique. Any steps that were missed or done incorrectly were rectified on the spot.

3.2 Patient counselling

This involves face-to-face counselling with the recruited patients in groups 1 and 2. This counselling focuses on clarifying patients' beliefs about disease, which were identified as barriers to adherence. The topics to be discussed during patient counselling were identified by semi-structured interviews conducted before the start of the study. In brief, the topics discussed were:

(1) The disease process in chronic respiratory diseases (CRD) and its chronic nature
(2) The role of allergy in asthma and their belief about food-induced allergy. The role of smoking in COPD patients
(3) The need to take drugs regularly
(4) The need to follow a healthy lifestyle with balanced nutrition and exercise
(5) Any other doubts the patients may raise were also clarified

3.3 Voice call reminders

Patients in groups 1 and 3 received recorded voice calls. A recorded voice call message was sent twice a week to their mobile phones in their vernacular language, encouraging them to take their medications regularly. The message was for 20 seconds. Voice call messages would advise patients to take their steroids (red rotacaps) regularly and a note to contact their healthcare provider in case of uncontrolled disease.

4 Data collection and trial endpoints

Socioeconomic, medical and non-medication-related data were obtained during the interview. Self-reported assessments were obtained during their hospital visit at baseline. The third- and sixth-months data were obtained either during their follow-up visits or over the phone. The PFTs were done at baseline and third month, and sixth-month follow-up visits. Patients with at least one PFT done during one of the above follow-up visits were included for analysis.

4.1 Primary outcome variables

MMAS-8 scores and proportion of days covered (PDC) were the primary outcome variables. The description of these two variables is given in objective 1. In addition, PDC values were calculated six months before starting the treatment and during the six months of the intervention period.

4.2 Secondary outcome variables

Predicted FEV_1(%) and ACT or CAT score were the secondary outcome variables. The description of these two variables is given in objective 1.

5 Trial schedule:

- Patients screened: Patients visiting the OPD who were fitting the inclusion and exclusion criteria were screened.
- Patients recruited: The eligible patients willing to participate in the study were recruited
- Informed consent: The trial procedures were explained, and informed consent was obtained from each patient.
- Randomized to one of four groups: Recruited patients were randomized using the randomization table prepared before starting the study.
- Baseline data collected: Once recruited, the baseline demographic, disease-related, and drug-related data were obtained from the patient and their case record.
- The intervention was given for six months:
- Data collected at the third month and the sixth month. M1, M3 and M6 are used to indicate data collected at followup during first month, third month and sixth month.

6 Statistical analyses

The continuous variables were expressed as mean±SD, and categorical variables were expressed as frequency and percentage. The continuous and categorical variables at baseline in all four groups were compared using ANOVA and Chi-square test. Generalized estimating equations logistic regression model was used to predict the adherence outcome (good and poor) based on treatment and time period with exchangeable correlation structure. Chi-square test was used in this study to assess the statistical significance of differences in treatment and differences over time. Factorial ANOVA was also used to assess the main effects and interactions of the interventions. MMAS-8 scores, PDC values and predicted FEV_1(%) were taken as continuous variables for the factorial ANOVA. Statistical tests were performed with IBM SPSS version 19, and adjustment for multiple comparisons was made using the Bonferroni test.