Clinical Trial Protocol
Iranian Registry of Clinical Trials
05 Aug 2019

Effect of inhaled Cromolyn on cough of mild persistent asthma in resistant patients to inhaled Corticosteroid and antileukotriene, A double blind randomized clinical trial.

Protocol summary

Summary
Objectives: The objective of this study is to determine the effect of cromolyn to standard therapy in mild persistent resistant to corticosteroid and anti leukotriene Asthma with normal Spirometry. Design: Prospective randomized controlled clinical trial (active comparator study). Setting and conduct: A pulmonary subspecialty clinic. Participants including major eligibility criteria: Sixty two asthmatic subjects with mild persistent corticosteroid and anti leukotriene resistant Asthma. Subjects suffering from other underlying diseases such as respiratory infection, sever or moderate Asthma, Rhinosinositis, Gastro-Oesophageal Reflux, other obstructive lung disease, vocal cord dysfunction, and reactive airway dysfunction syndrome will be excluded from study. After randomization eligible subjects will receive cromolyn or placebo. Independent pharmacists dispensed either Cromolyn or Placebo according to a computer generated randomization list. Intervention: Each cromolyn or placebo will be consumed for forty days, correct usage of spray and spacer will be educated to patients. After this period they will be evaluated for main parameters. Main outcome (variables) includes: change of clinical finding, change of Spirometry, change of Sputum cytology include inflammatory cell, change of ACT (Asthma control test) Questionnaire and change of FENO (Fractional Exhaled Nitric Oxide). These parameters will be evaluated again after completing the course of treatment.

General information

Acronym
IRCT registration information
IRCT registration number: IRCT201108042695N3
Registration date: 2014-04-13, 1393/01/24
Registration timing: retrospective

Last update: empty
Update count: 0
Registration date 2014-04-13, 1393/01/24

Registerant information
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Recruitment status
Recruitment complete
Funding source
Mashhad branch-Islamic Azad University

Expected recruitment start date
2012-09-28, 1391/07/07
Expected recruitment end date
2013-12-19, 1392/09/28
Actual recruitment start date
empty
Actual recruitment end date
empty
Trial completion date
empty

Scientific title
Effect of inhaled Cromolyn on cough of mild persistent asthma in resistant patients to inhaled Corticosteroid and antileukotriene, A double blind randomized clinical trial.

Public title
Effect of inhaled Cromolyn on persistent asthma
Purpose
Treatment
Inclusion/Exclusion criteria
Inclusion criteria: cough with an intermittent course and history of airway hyper responsiveness; FEV1(Forced Expiratory volume in 1 second) more than 80% (mild asthma); No beneficial effect of inhaled Corticosteroid anti leukotriene during previous treatment. Exclusion criteria: Moderate or severe asthma; FEV1 (Forced Expiratory volume in 1 second) lees than 80%; Asthma
with wheezing; Respiratory infection; Treatment with systemic Corticosteroid; Other Obstructive lung disease; Rhinosinositis; Gastro-esophageal Reflux; Vocal Cord Dysfunction; Reactive airway dysfunction syndrome.

**Age**
No age limit

**Gender**
Both

**Phase**
2

**Groups that have been masked**
None

**Sample size**
Target sample size: 62

**Randomization (investigator's opinion)**
Randomized

**Randomization description**

**Blinding (investigator's opinion)**
Double blinded

**Blinding description**
Placebo
Used

**Assignment**
Parallel

**Other design features**
Due to spontaneous remission of asthma and long term period of treatment with cromolyn double blind randomized clinical trial was used as the best method of study. All recruited asthmatic subjects will randomly divided to two groups of cromolyn inhaler and placebo by computer generated randomization list. One group will be treated by cromolyn or and other group will be received placebo for forty days. Both of them will use spray and the dosage will be 2 puff four times. The physician and pharmacist are blind to the exact drug which the subject will be started with. The cromolyn and placebo form is spray and identical in appearance. They have consecutively numbered for each patient according to the randomization schedule which is not introduced to the physician and pharmacist.

**Secondary Ids**
empty

**Ethics committees**

1

**Ethics committee**
Name of ethics committee
Mashhad branchbranch-Islamic Azad University-
Ethical committee- Department of research

Street address
Shahin Far Building- Sarab Street- Azadi street

City
Mashhad

Postal code
9178673799

Approval date
2011-04-24, 1390/02/04

Ethics committee reference number
A56-21

**Health conditions studied**

1

**Description of health condition studied**
Asthma

**ICD-10 code**
J45.32

**ICD-10 code description**
Mild Persistent Asthma, Status asthmaticus

**Primary outcomes**

1

**Description**
Change of FENO (Fractional Exhaled Nitric Oxide)

**Timepoint**
Before treatment and 40 days after treatment

**Method of measurement**

2

**Description**
Change of FEV1 (Forced Expiratory volume in 1 second)

**Timepoint**
Before treatment and 40 days after treatment

**Method of measurement**

3

**Description**
Change of Sputum Cytology

**Timepoint**
Before treatment and 40 days after treatment

**Method of measurement**
Sputum Cytology for frequency of inflammatory cell (Eosinophil, Neutrophil, Macrophage and Lymphocyte) defined by percentage calculated into 200 cell in each high power field Microscopic in magnification 40x in Sputum.

**Secondary outcomes**

1

**Description**
Change of IL-8

**Timepoint**
One year later

**Method of measurement**
Enzyme-linked immunosorbent assay (ELISA)
### Description
- **Change of INF-GAMMA**

#### Timepoint
- One year later

#### Method of measurement
- Enzyme-linked immunosorbent assay (ELISA)

### Description
- **Change of IL-17**

#### Timepoint
- One year later

#### Method of measurement
- Enzyme-linked immunosorbent assay (ELISA)

### Description
- **Change of TLR-2**

#### Timepoint
- One year later

#### Method of measurement
- Enzyme-linked immunosorbent assay (ELISA)

### Intervention groups

#### 1

##### Description
Steps before starting the study: Asthmatic subjects referred with cough and history of recurrence with or without reactive airway hyper responsiveness and without wheezing will be treated with one puff spray fluticasone 250 twice a day with spacer. Spacer usage will be educated. If they do not improve after one week oral Montelukast will be added to previous drug. Afterward chest x ray will be taken, if they do not improve again. In case of infiltration in favor of infection, they will cure with Doxycycline 100 mg or clarythromycin 500 mg two twice a day for 10 days. In subjects with normal chest X ray anti reflux therapy will be added to previous drugs including Fluticasone and montelukast. Patients whom do not improve with these regimes will be entered to our study. Phase one: Recruitment of subjects: Informed consent will be given after oral discussion. Parameters which will be evaluated before intervention include clinical physical exam and paraclinical evaluations such as Spirometry (with Spirometry super Spiro, Micro medical company, England), FENO (Chemilumine scence instrument, No Breath, Bed font company, England), Sputum Cytology for frequency of inflammatory cell (Eosinophile, Neutrophile, Macrophage and Lymphocyte) defined by percentage calculated into 200 cell in each high power field Microscopic in magnification 40x in Sputum and ACT ( Validated Asthma control test Questionnaire). Some of the sputum will be freezed for secondary parameters evaluation including Toll like receptor 2, IL-8, IL-17 and INF-Gamma. These parameters will be evaluated by enzyme-linked immunosorbent assay (ELISA) method.

### Category
- **Diagnosis**

### 2

##### Description
After pretest evaluations, patients will be randomly divided in two groups and will be received cromolyn spray or placebo for 40 days four time daily two puff with spacer. Cromolyn and placebo have similar shape and have provided from Sina Daru company in Tehran, Iran by manager of study. Subjects will be educated for drug usage with spacer and mode of administration. Patients will follow for 10 days for exacerbation of Asthma which may be occurred in subjects whom will receive placebo. After 40 days post test study will be performed. In this step subjects will be evaluated again for clinical exam and paraclinical parameters including Spirometry, FENO, Sputum Cytology and ACT Questionnaire. Some of the sputum will be freezed for secondary parameters evaluation including Toll like receptor 2, IL-8, IL-17 and INF-Gamma.

### Category
- **Treatment - Drugs**

### Recruitment centers

#### 1

##### Recruitment center

- **Name of recruitment center**
  - Mashhad branch-Islamic Azad University

- **Full name of responsible person**
  - Mojtaba Meshkat

- **Street address**
  - Shahin Far building, Sarab street, Azadi Avenue

- **City**
  - Mashhad

### Sponsors / Funding sources

#### 1

##### Sponsor

- **Name of organization / entity**
  - Mashhad Branch-Islamic Azad University

- **Full name of responsible person**
  - Mojtaba Meshkat

- **Street address**
  - Shahin Far building, Sarab Street, Azadi avenue

- **City**
  - Mashhad

##### Grant name

- **Grant code / Reference number**

- **Is the source of funding the same sponsor organization/entity?**
  - Yes

##### Title of funding source

- **Mashhad Branch-Islamic Azad University**

##### Proportion provided by this source

- **100**

##### Public or private sector

- **Public**
Person responsible for general inquiries

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Sharing plan

Deidentified Individual Participant Data Set (IPD)
empty
Study Protocol
empty
Statistical Analysis Plan
empty
Informed Consent Form
empty
Clinical Study Report
empty
Analytic Code
empty
Data Dictionary
empty