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Research Article

N-ASTHEAL®, A HERBAL FORMULA FOR THE TREATMENT OF MILD ASTHMA: AN OPEN, SINGLE CENTRIC, NON-COMPARATIVE PILOT STUDY FOR 3 WEEKS

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ABSTRACT

Objective: The aim was to evaluate efficacy and safety of N-Astheal® in a pilot study on 12 patients with mild to moderate bronchial asthma.

Materials and Methods: The study was an open-label, single centric clinical trial conducted by Ethix Pharma at Clinical Research Center, CMC & H, Bhaisa Khedi, Bhopal, India from 12 March to 30 May 2013. The study was conducted on 12 patients comprised of 8 male and 4 female with an age range of 18-70 years, all the subjects were with mild to moderate bronchial asthma. Patients with another chronic lung disease (other than asthma) and those who are suffering from breathlessness due to cardiovascular disorders were excluded. Pregnant or lactating females were also excluded in the study. The potential subjects were screened and consented. The consented subjects were enrolled in the study and baseline history was obtained in order to determine the patient's eligibility for enrollment in the trail. Thereafter all patients underwent a clinical examination, including hematology, biochemistry, urinalysis and spirometry test. All patients were advised to take N-Astheal twice in a day for a period of 3 weeks. All patients were followed-up twice after giving N-Astheal and during each follow-up visit, physical examination, vitals examination, spirometry, acoustic emission monitoring was done. The final assessment was carried out for decrease in the severity and symptoms of asthma, improvement of forced expiratory volume in one second (FEV1), improvement in forced vital capacity (FVC) and percentage improvement in peak expiratory flow rate (PEFR). Statistical analysis was performed according to intention-to-treat principles.

Results: The overall response to the treatment by N-Astheal® observed a significant reduction in the severity and symptoms of asthma along with significant improvement in FEV1 from 65.2% to 74.9% (*p<0.05), FVC from 96.2% to 105.1% (*p<0.05), PEFR from 44.4% to 64.2% (**p<0.01) was observed from 1st week to 4th week, respectively. This pilot study revealed the beneficial effect of N-Astheal® in acute asthma and similar respiratory condition.

Conclusion: The present pilot study 3 weeks treatment of N-Astheal® had been promising in treating asthma and similar respiratory conditions and at the same time the treatment was proved safe as well with a very good patient compliance.

Keywords: Asthma, N-Astheal®, inflammation, Anti-asthmatic agent, Clinical

INTRODUCTION

Asthma is characterized by a predisposition to chronic inflammation of the lungs in which the airways (bronchi) are reversibly narrowed. Asthma affects total of 300 million in every year worldwide. During asthma attacks (exacerbations of asthma), the smooth muscle cells in the bronchi constrict, the airways become inflamed and swollen, and breathing becomes difficult. This syndrome is characterized by increased responsiveness of the trachea and bronchi to various stimuli and manifested by acute, recurrent, and chronic attacks of widespread narrowing of airways. Because the passages are narrowed, and air flow reduced, mucus also builds up in the lungs, and this makes it even more difficult to breathe. The mucus is also a breeding-ground for bacteria and hence attacks of bronchitis may arise as a complication of the asthma. Many asthma attacks are triggered by allergens, such as dust, mold spores, mites, animal hair or feathers, but the onset may equally be caused by cold air, or it may be preceded by an infection such as a cold. Certainly, stress and more specifically acute anxiety are known to be an immediate trigger for many attacks, and this can sometimes give rise to a vicious circle of asthma - anxiety about the asthma - further attacks [1]. The past decade has witnessed phenomenal increases in the incidences of asthma, asthma-related deaths, and hospitalization.

The pharmacologic agents commonly used for the treatment of asthma can be classified as controllers (medications taken daily on a long-term basis that achieve control primarily through anti-inflammatory effects) and relievers (medications used on an as-needed basis for quick relief of bronchoconstriction and symptoms). Controller medications include inhaled corticosteroids (ICSs), leukotriene receptor antagonists, long-acting beta2-agonists (LABAs) in combination with an ICS, and anti-immunoglobulin E (IgE) therapy. Reliever medications include rapid-acting inhaled beta2-agonists and inhaled anticholinergics [2]. Existing classes of anti-asthmatic agents offer a limited variety of action that can be combined in a complementary and additive manner. Individual oral agents act only on the part of the pathogenic process of bronchial asthma. Hence, they may not produce any cure and may not prevent all complications of bronchial asthma. However, frequent use of these drugs leads to adverse effects along with the emergence of resistance to the therapy.

The chronic nature of asthma and lack of preventive and curative therapy are leading asthma patients in western societies to seek complementary and alternative medicine (CAM) treatment. Although there are wide variations in reported use of CAM, a reasonable estimate is that up to 30% of adults and 60% of children in the US are currently using some form of CAM to treat their asthma. Thus, there is a need for defining and developing reliable CAM therapy for patients [3]. A survey by the National Asthma Campaign found that 60% of people with moderate asthma and 70% with severe asthma have used CAM to treat their condition. Herbal medicine is the third most popular choice of both adults (11%) and children (6%) suffering from asthma. The historical importance of herbal medicine in the treatment of asthma is indisputable. Four of the five classes of drugs currently used to

treat asthma namely, β_2 agonists, anticholinergics, methylxanthines and cromones have origins in herbal treatments going back at least 5000 years. There is a large archive of information on herbal medicine from many cultures for the treatment of asthma. However, a significant proportion of these reports are not based on adequately designed trials [4]. Therefore, much of the early interest in functional foods and nutraceutical was based on medicinal uses of the herbs.

N-Astheal® is a special formulation of standardized extracts derived from *Cassia fistula, Blepharis edulis, Anacylus pyrethrum, Glycyrhiza glabra*. *C. fistula* - The fruits are reported to be used for asthma [5,6]. *B. edulis* - is used in folk medicine to treat asthma [7]. *A. pyrethrum* – mixture with other herbs (Divya Svasari Rasa) is known to treat Bronchitis, cough, coryza, cold, asthma and sinusitis [8]. *G. glabra* – In folk medicine, it is used as a laxative, emmenagogue, contraceptive, galactagogue, anti-asthmatic drug and antiviral agent. Beside this *G. glabra* Linn (Glycyrrhizin, 18β glycyrrhetinic acid and liquiritigenin) have antiallergic activity, which can relieve IgE – induced allergic diseases such as dermatitis and asthma [6,9,10].

The present study was planned to evaluate the safety and efficacy of N-Astheal® in the treatment of mild to moderate bronchial asthma.

MATERIALS AND METHODS

Aim of the study

This study is aimed to evaluate the clinical efficacy, short and long-term safety of N-Astheal® in newly diagnosed and previously treated cases of mild to moderate bronchial asthma.

Study design

The study was an open-label, single centric, non-comparative clinical trial conducted by Ethix Pharma at Clinical Research Centre, CMC & H, Bhaisa khedi, Bhopal, India from 12 March to 30 May 2013 as per the ethical guidelines of the declaration of Helsinki. The study protocol, case report forms, regulatory clearance documents, product-related information and informed consent forms were submitted to the Institutional Ethics Committee and approved by the same on 02.01.13 via ref 2009EP001.

Inclusion criteria

Twelve patients consisting of 8 male and 4 female with an age range of 18-70 years were included in the study conducted by Ethix Pharma at Clinical Research Center, CMC and H, Bhaisa Khedi, Bhopal, India from 12 March to 30 May 2013. A written informed consent was taken from all patients.

Exclusion criteria

Children below 18 years of age, patients with another chronic lung disease (cystic fibrosis or bronchopulmonary dysplasia, pulmonary tuberculosis) severe bronchial asthma, patients who are suffering from breathlessness due to cardiovascular disorders, severe uncontrolled systemic disease, abnormal baseline findings. Patients who received an investigational product or participation in a drug research study within a period of 30 days prior to the first dose of study medication and patients who are not willing to comply with the study protocol were excluded. Pregnant or lactating females were also excluded in the study.

Study procedures

A baseline history was obtained in order to determine the patient's eligibility for enrolment in the trial. The baseline assessment included personal data, a description of symptoms and details of past medical history (family history of asthma, aggravation factor etc.). Thereafter all patients underwent a clinical examination and hematology, biochemistry, urine routine, concomitant medications and electrocardiography. Further, the patients underwent instrumental assessment to verify their vital capacity by using a spirometer. The device measures the volume of air inspired and expired by the lungs. It is the main piece of equipment used for basic pulmonary function tests. Patients were advised to take N-Astheal® twice a day for 21 days.

During the course of treatment, the patients were followed up twice and on first follow-up which is after 10 days of initial IP dispensing the patients are examined on vitals, adverse events, concomitant medications, physical examination. On the second follow-up (on 21st day) the patients were examined on vitals, urine pregnancy test, hematology, biochemistry, urine routine, spirometry test, physical examination and concomitant medications and observations recorded in the structured case record sheet. All patients were reviewed clinically at the end of 3 weeks.

Primary and secondary outcome measures

The predefined primary outcome measures were decreased in the severity and symptoms of asthma, improvement of forced expiratory volume in one second (FEV1), improvement of forced vital capacity (FVC), the percentage improvement of peak expiratory flow rate (PEFR). The predefined secondary outcome measures were incidence of adverse events and compliance to the treatment.

Adverse events

All local and systemic adverse events, reported or observed by patients were recorded with information about severity, time of onset, duration and action taken regarding the study drug.

The adverse events were graded as follows:

Grade 1: Mild, easily tolerated by the patient, causing minimal discomfort and not interfering with everyday activities.
Grade 2: Moderate, sufficiently discomforting to interfere with normal everyday activities.
Grade 3: Severe, prevents normal everyday activities.
Grade 4: Life-threatening, places the patient at immediate risk of death.
Grade 5: Fatal.

Relation of adverse events to study medication was predefined as "unrelated" (a reaction that does not follow a reasonable temporal sequence from the administration of the drug), "possible" (follows a known response pattern to the suspected drug, but could have been produced by the patient's clinical state or other modes of therapy administered to the patient), and "probable" (follows a known response pattern to the suspected drug that could not be reasonably explained by the known characteristics of the patient's clinical state). Patients were allowed to voluntarily withdraw from the study if they had experienced serious discomfort during the study or sustained serious clinical events requiring specific treatment. For patients withdrawing from the study, efforts were made to ascertain the reason for dropout. Non-compliance (defined as failure to take <80% of the medication) was not regarded as treatment failure, and reasons for non-compliance were noted.

Statistical analysis

Statistical analysis was performed according to intention-to-treat principles. Changes in various parameters from baseline values and values after the 0, 1, 2 and 3 weeks were analyzed by "paired t-test." The minimum level of significance was fixed at 99% confidence limit, and a 2-sided $p<0.05$ was considered to be significant. The values are expressed in the sequence as: Mean score (M) at 0, 1, 2 and 3 weeks, standard deviation at baseline 1, 2 and 3 weeks. In all graphs, the baseline value is 0.00.

RESULTS

A total of 16 patients were screened for enrollment, 4 of whom were excluded because of failure to meet the inclusion criteria, questionable drug compliance and time commitment. During the treatment period, 1 patient dropped out from the N-Astheal® treated group and 1 lost to follow-up. Ten patients completed the 3 weeks trial period. The age range was 18-70 years (Table 1). There was a male predominance in the study and total 8 (67%) males and 4 (33%) females were enrolled in the study. Baseline characteristics of these patients are presented in Table 2.

It was observed that by the end of regimen there was significant reduction in the severity and symptoms of asthma along with significant improvement in FEV from 65.2% to 74.9% (*p<0.05; Fig. 1), FVC from 96.2% to 105.1% (*p<0.05; Fig. 2), PEFR from 44.4% to 64.2% (**p<0.01; Fig. 3) was observed from 1st week to 4th week respectively.

There were no clinically significant mild or severe adverse reactions (either reported or observed), during the entire period of the study and excellent patient compliance to N-Astheal® was observed.

Table 1: Subjects demographics

Age	Number of patients	Percentage
18-34	5	41.7
35-52	6	50.0
53-70	1	8.3

Table 2: Blood chemistry of N-Astheal®

Blood chemistry	Treatment	
	1st week	4th week
Urea	18.44±11.04	14.76±9.74
Creatinine	0.93±0.35	0.63±0.43
Total bilirubin	0.51±0.06	0.44±0.30
D-bilurubin	0.26±0.16	0.23±0.19
SGOT	16.7±10.33	24.18±18.34
SGPT	19.07±13.21	22.5±17.09
Alkaline phosphatase	52.47±32.32	72.18±67.29

Values expressed in Mean±SD for n=12, SD: Standard deviation, SGOT: Serum glutamate oxaloacetate transaminase, SGPT: Serum glutamate pyruvate transaminase

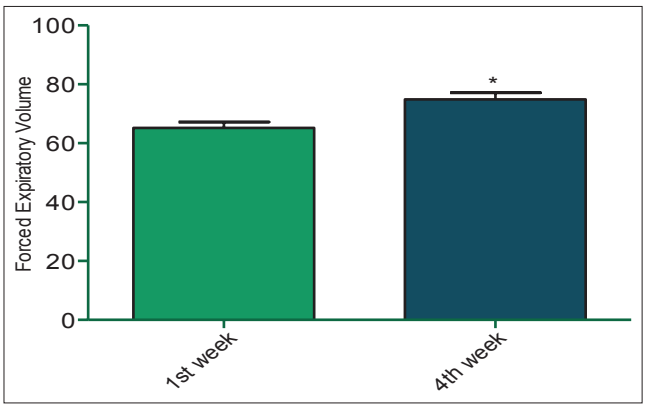

Fig. 1: Effect of N-Astheal® on forced expiratory volume

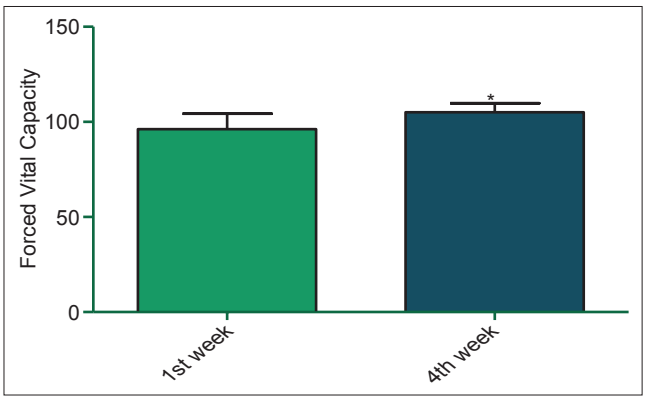

Fig. 2: Effect of N-Astheal® on forced vital capacity

DISCUSSION

Asthma is a chronic disease characterized by acute exacerbation of coughing, dyspnea, wheezing and chest tightness. Patients usually have reduced FEV1 as well as reduced airflow. This open-label, single centric, non-comparative pilot trial compared the effects of 3 weeks of treatment with the tablet herbal mixture N-Astheal® on lung function, asthma control and cough related health status. It was shown that N-Astheal® therapy could improve pulmonary efficiency. The primary outcome of the study was lung function. Significant improvement in lung function was found in the N-Astheal® group in 3 weeks of treatment. It was, therefore, very likely that N-Astheal® alleviated asthmatic attacks through a direct influence on lung functions. Prior reports suggest that CAMs may have some therapeutic effects on allergic asthma [11]. This study was conducted to determine the safety and efficacy of N-Astheal® on patients with mild asthma. In the Indian community, people often wish to use herbal therapy to supplement conventional medical treatment for a person suffering from asthma so that the dosage of steroids could be reduced to lessen their side-effects [12]. Our present study may have given them some assurance. N-Astheal® was safe and effective in improving lung functions. We chose changes in FEV1 as the first efficacy end point on account of their validity for the monitoring of airway obstruction. By the end of the study, FEV1 was significantly improved in N-Astheal®-treated patients. Moreover, a marked progression in lung function of more than 10 compared with baseline was achieved for most patients. With the increasing popularity of herbal remedies, N-Astheal® showed a marked easing effect. The overall symptoms and emotions domains of the patients showed significant improvement. The factors possibly contributing towards the easing effect could be the increased nurse – patient interactions (e.g., reminder calls and monthly study visit for proper asthma management) leading to better self-cares and thus improved outcome measures.

CONCLUSION

N-Astheal® showed an overall improvement in asthma symptoms and had a good patient compliance, even improvement in diagnostic parameters FVC and PEFR (FEV1/FVC) which are clinically used as an index of lung functions. The result showed that there were significant differences in FVC and PEFR before and after the treatment. FVC will be diminished in both obstructive and restrictive diseases. The improvement in FVC and PEFR of the patients after N-Astheal® treatment for 3 weeks supports the postulation of decreased airway obstruction. In addition, there was a prominent reduction in severity and symptoms of asthma. There were no clinically significant mild or severe adverse reactions (either reported or observed), during the entire period of study and excellent patient compliance to N-Astheal® was also observed. This anti-asthmatic effect of N-Astheal® could be achieved because of the unique formula and its highly efficient broad spectrum activity for respiratory conditions. N-Astheal® shows prompt relief from shortness of breath, thus, it can be used in the

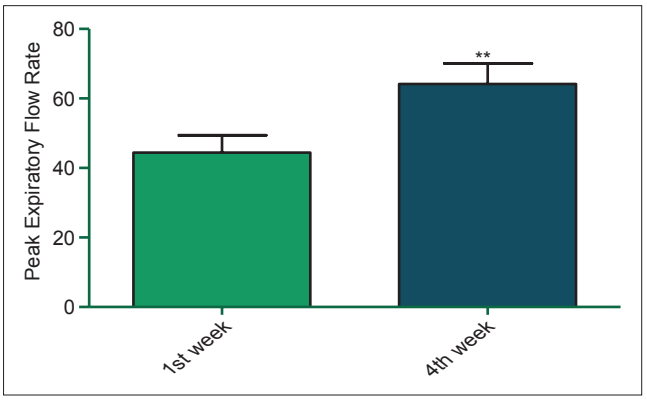

Fig. 3: Effect of N-Astheal®on peak expiratory flow rate

treatment of Asthma, chronic obstructive pulmonary disease or any similar conditions.

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