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ACADEMIC TRIAL WITH CHRONIC ASTHMA PATIENTS USING COMBINATION DRUGS FOR EFFECTIVE PHARMACOTHERAPY

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ABSTRACT

Introduction: Asthma is a chronic disease that affects approximately 300 million people worldwide. A continuous search is on going to identify effective and safe remedies to treat bronchial asthma. Broncorid syrup is composed of Shireesh Chaal (*Albizzia lebbeck*), Kantakari (*Solanum xanthocarpum*), Gokshur (*Tribulus terrestris*), Yashtimadhu (*Glycyrrhiza glabra*), Karkatshringi (*Pistacia integrima*), Vasaka (*Adhatoda vasica*) and is conventionally used to treat asthma.

Objective: To determine the efficiency of Broncorid syrup in minimizing the adverse effects caused by corticosteroids (Fluticasone) and β-agonists (Salmeterol).

Materials and Methods: 63 chronic asthma patients who presented a variety of symptoms for our academic trial were chosen. The biomarkers crucial for the prognosis of the disease like IgE levels, Eosinophils and RBC count were evaluated. Patients who were taking different pharmacotherapies with Corticosteroids (Fluticasone) and β agonists (Salmeterol) or a combination of both (with or without Broncorid syrup) were studied for these biomarkers and compared with healthy controls.

Results: The patients who had taken the Broncorid syrup along with Fluticasone and Salmeterol have shown considerable improvement with respect to IgE levels and Eosinophils count indicating the control of metabolic factors that contribute to allergy causing asthma symptoms. The combination therapy of Fluticasone, with Salmeterol and Broncorid syrup has resulted in overall betterment. The action of Broncorid syrup could be due to the inhibition of mast cell membrane stabilizing effect.

Conclusion: The efficiency of Broncorid syrup in minimizing the adverse effects caused by corticosteroids (Fluticasone) and β-agonists (Salmeterol) was established.

INTRODUCTION

Academic Trials: Academic clinical trials are a valuable component of the health care system, they benefit patients and help determine the safety and efficacy of new drugs and devices. A typical area of academic clinical trials is the advancement and optimization of already existing therapies. Thus, academic clinical trials may for instance test how a combination of registered drugs may improve treatment outcomes. There are many different organizations which have an interest in academic clinical trials and facilitate or take part in their conduct. These organizations include:Hospitals, Universities, Independent Research Organization and Institutions who view trials as a source of income and prestige, and receive private, charitable and government funding. Pharmaceutical or Biotech Companies who view the development and commercialization

of treatments as their business.Regulators who wish to ensure treatments are safe and work effectively.[1]This study is based on phase 3 trials with a limited number of subjects and is sponsored by Bioworld Research and Technologies, Somajiguda which was carried out at Global Hospitals and Laboratories, Hyderabad.Asthma is a disorder of the human respiratory system in which the airways constrict and become narrow, often in response to a "trigger" such as exposure to an allergen, cold air, exercise, or emotional stress. During attacks (exacerbations), the smooth muscle cells in the bronchi constrict, and the airways become inflamed and swollen with difficulty in breathing. Asthma causes 4,000 deaths a year in the US alone. Attacks can be prevented by avoiding triggering factors and by drug treatment. [2]Asthma is diagnosed clinically on the basis of symptoms of wheeze, dysponea, and cough, and by objective evidence of variable airflow obstruction. Allergic asthma can present for the first time at any age, but incidence is highest in childhood. Asthma in childhood frequently remits during adolescence but can recur in adult life. [3]
Diagnosis of asthma still relies on demonstration of variability (measurement of asthma severity) in lung function over time or improvement after a bronchodilator and β-agonist. IgE levels, Eosinophils count and Complete Blood Picture (CBP) with post bronchodilator response should be obtained as the primary test to establish the asthma diagnosis. [4] Majority of the population still have limited access or no access, especially those in remote areas, to modern medicines. Instead, they use traditional medicines for a range of disease complications. [5] There are many natural herbs and herbal supplements that can be used for asthma treatment. Natural Asthma treatment incorporates vitamins, minerals and herbs like *Solanum xanthocarpum, Albizzia lebbeck* to relieve symptoms and prevent further attacks. The Herbal formulation used in the present study for asthma includes

- Shireesh chaal (*Albizzia lebbeck*)
- Kantakari (*Solanum xanthocarpum*)
- Gokshur (*Tribulus terrestris*)
- Yashtimadhu (*Glycyrrhiza glabra*)
- Karkatshringi (*Pistacia integrima*)
- Vasaka leaves (*Adhatoda vasica*)

The present study was aimed to determine the efficiency of Broncorid syrup in combination with Corticosteroids (Fluticasone) and β-Agonists (Salmeterol) to reduce the adverse effects caused Corticosteroids (Fluticasone) and β-Agonists (Salmeterol) in chronic Asthma patients.

NEED FOR THE STUDY: The usage of Broncorid syrup has been found to be beneficial as it possess good activity to prevent recurrence of asthma attacks and minimizing adverse effects of corticosteroids and β-agonists such as syncope, ear, nose and throat infections, laryngitis, oral lesions, edema, immediate, delayed hypersensitivity reactions, osteoporosis, dyspnea, facial oropharyngeal edema and immediate bronchospam.

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 is not based on adequately designed trials. Definitive evidence for any of the herbal preparations has not emerged till now. Considering the popularity of herbal medicine with asthma patients, there is urgent need to design clinically relevant randomised trials for herbal preparations in the treatment of asthma. We want to test the efficacy and safety of Broncorid syrup given along with Pharmacotherapy in this disease. Hence, we have taken up an academic trial to get an insight into how herbal formulation is effective in bringing down the suffering of the patients mainly by improving the lung health and minimizing the adverse effects of corticosteroids (Fluticasone) and β-agonists (Salmeterol).

Information obtained from this study would be beneficial to other patients with the same disease.

OBJECTIVE OF THE STUDY :

To determine the efficiency of Broncorid syrup in reducing the adverse effects caused by corticosteroid (Fluticasone), β agonist (Salmeterol) and their combinations with or without Broncorid syrup by estimation of following parameters: IgE levels and Eosinophils count, RBC count

MATERIALS AND METHODS: In the present study, 63 chronic asthma patients were selected who presented a variety of symptoms for the academic trial. The study was intended to evaluate the biomarkers crucial for the prognosis of the disease. The patients who were taking different pharmacotherapies with Corticosteroids (CS therapy) and β-agonists or a combination of both (with or without herbal formulation) were tested for the three biomarkers along with healthy controls.

Information to Participants

PROTOCOL NO: BRTGH91

SPONSOR: BIOWORLD

INVESTIGATORS (Principal and at least one Co-Investigator): Dr. Rajyalakshmi, Dr. Naik, Dr. Syed Tufail.

Title: Academic Trial With Chronic Asthma Patients Using Combination Drugs For Effective Pharmacotherapy: You are invited to take part in this research study which is basically a single, randomized trial to determine the efficacy and safety of asthma patients using combination drugs for effective pharmacotherapy**.** The information in this document is meant to help you decide whether or not to take part. Please feel free to ask if you have any queries or concerns.

You are being asked to participate in this study being conducted in Global Hospitals/NIMS /DDH RC. because you satisfy our eligibility criteria which are:

(1) Diagnosis of ASTHMA

(2) Age between …25-60 … years

(3) No contraindication to the use of the agents to be used in the study, which means absence of any disease or condition likely to get worsened by the drugs under study, which is Dabur Broncorid syrup(Herbal Formulation).

(4) Taking or taken therapy for asthma with corticosteroids.

(5) Neither pregnant nor breast-feeding in case of female patients.

You will be one of the 60 (give total number of patients to be enrolled in the study) patient recruited. we plan to recruit in this study. You will be assigned to either of the TWO study groups. One group of patients will receive standard medication(s), which are Corticosteroid therapy-1 with Advair & Corticosteroid therapy-2 with salmetrol, different pharmacotherapies with Corticosteroids (CS therapy).placebo - controlled studies, add the following statement: A placebo is an inactive or a dummy medication, which is given to increase the scientific validity of our study. Moreover, a placebo is needed so that it does not become known either to patient or patient's investigator to which group patients are being assigned. This method, in scientific terms is known as blinding. This is important for unbiased evaluation of the study medication.

A survey by the National Asthma Campaign found that 60% of people with moderate asthma and 70% with severe asthma have used complementary and alternative medicine 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 is not based on adequately designed trials. A critical analysis of herbal medicinal products used in the treatment of asthma symptoms that have been the subject of randomised clinical trials is

absolutely necessary. There is a high prevalence of usage of complementary medicine for asthma. Herbal preparations have been cited as the third most popular complementary treatment modality by asthma sufferers. This academic trial was undertaken to determine if there is any evidence for the clinical efficacy of herbal preparations for the treatment of asthma symptoms in terms of reducing recurrence of asthma attacks and minimizing side effects. We want to test the efficacy and safety of Herbal preparation given along with Pharmacotherapy in this disease. This usage of herbal medicines has been found to be beneficial and found to possess good activity to prevent recurrence of asthma attacks and minimizing side effects of corticosteroid bronchodilators such as Dysphonia and Adrenal Gland Suppression.

Information obtained from this study would be beneficial to other patients with the same disease.

We have obtained permission from the Institutional Ethics Committee [and the Drug Controller General of India] for conducting this study.

The study design

All patients in the study will be divided into two or more groups. Patient will be assigned to either of the two groups. One group will receive herbal medicine in the form of broncorid syrup at a dosage of two teaspoonfuls two times a day with luke warm water for a period of 30 days. Standard treatment will be given to all patients.

For randomized study, which treatment group patient will be assigned to determined purely by chance, which, in scientific language, is called 'randomization'. Randomization improves the scientific quality of research.

Study Procedures

The study involves monitoring patient's symptoms / blood levels of Biomarkers which mostly consist of an ELISA procedure for IgE analysis and visualization of complete blood pictures and get an idea of eosinophil counts.

Once patients are enrolled in the study, they will be required to follow the instructions [diet / take the drugs as instructed and detailed on the envelope / avoid alcohol / smoking / any other precautions].

Patient will be told about patient's visit schedules and patient will have to report to the hospital (study site). The planned scheduled visits involve weekly visits at NIMS/GLOBAL HOSPITALS /DDH/GH. Patient will be required to visit the hospital 4 times during the study. Patients are not allowed to take any medications other than the ones prescribed by the investigator. If patient need to take some treatment (drug / physiotherapy / other), patient must consult the investigator before taking that treatment. At each visit, the study physician will examine patient. Some [blood / urine / other tests will be carried out at each visit. 6 ml of blood will be collected at each visit. Blood collection involves prick with a needle and syringe. Patient will have to completely refrain from smoking / alcohol during the 30 days of study. Potential risks of providing blood may very rarely include pain, bruising, fainting or a small infection at the Puncture site. These tests are essential to monitor patient's condition, and to assess the safety and efficacy of the treatment given to patient.

Patient Consent Form

Title of the study:

Academic Trial with Chronic Asthma Patients Using Combination Drugs For Effective Pharmacotherapy

Name of the participant: _____

_____

Name of the Principal (Co-) Investigator: Dr. Pradeep Naik

Name of the Institution: Global clinical research services pvt ltd.

Name and address of the sponsoring (funding) agency: Bioworld Research technologies

Documentation of the informed consent

I… have read the information in this form (or it has been read to me). I was free to ask any questions and they have been answered. I am over 18 years of age and, exercising my free power of choice, hereby give my consent to be included as a participant in "**Academic Trial**

With Chronic Asthma Patients Using Combination Drugs For Effective Pharmacotherapy."

(1) I have read and understood this consent form and the information provided to me.
(2) I have had the consent document explained to me.
(3) I have been explained about the nature of the study.
(4) My rights and responsibilities have been explained to me by the investigator.
(5) I have been advised about the risks associated with my participation in the study.
(6) I have informed the investigator of all the treatments I am taking or have taken in the past …… . months including any desi (alternative) treatments.
(7) I agree to cooperate with the investigator and I will inform him/her immediately if I suffer
unusual symptoms.
(8) I have not participated in any research study within the past … ..month(s).
(9) I have not donated blood within the past …… months — Add if the study involves extensive blood sampling.
(10) I am aware of the fact that I can opt out of the study at any time without having to give any
reason and this will not affect my future treatment in the hospital.
(11) I am also aware that the investigators may terminate my participation in the study at any
time, for any reason, without my consent.
(12) I hereby give permission to the investigators to release the information obtained from me as
result of participation in this study to the sponsors, regulatory authorities, Government agencies, and ethics committee. I understand that they may inspect my original records.
(13) My identity will be kept confidential if my data are publicly presented.
(14) If, despite following the instructions, I am physically harmed because of any substance or any procedure as stipulated in the study plan, [my treatment will be carried out free at the investigational site / the sponsor will bear all the expenses], if they are not covered by my insurance agency or by a Government program or any third party.
(15) I have had my questions answered to my satisfaction.
(16) I have decided to be in the research study.

I am aware, that if I have any questions during this study, I should contact at one of the INVESTIGATORS listed above. By signing this consent from, I attest that the information given in this document and the HIV consent form has been clearly explained to me and apparently understood by me. I will be given a copy of this consent document.
SIGNATURE OF THE PARTICIPANT

Materials Used

1. Dabur Broncorid Syrup
2. Azrol inhaler Salmeterol 25 μg/ puff NATCO
3. Serobid inhaler Salmeterol 25 μg/ puff CIPLA
4. Advair Diskus 100/50 Salmeterol + Fluticasone GSK
5. Hemocytometer, diluting pipette for red blood cells, light microscope, for blood sample collection: cotton balls, alcohol, sterile needles, rubber gloves.

Specific Reagent For Estimation Of Biomarker

1. IgE using ELISA kit reagents
2. Eosinophils count reagent
3. Complete Blood Count (CBC) reagent

Reagents used for Elisa Technique

1. Antibody-coated wells (1plate, 96wells)
   Microtiter wells coated with mouse monoclonal anti-IgE
2. IgE zero Buffer,13ml
   Contains bovine serum with yellow dye and preservative
3. Enzyme conjugate reagent (18ml)
   Contains bovine serum with yellow dye and preservative
4. Reference standard set (1mL/vial)

Contains 0, 10, 15, 100, 400 and 800IU/mL (WHO) of Immunoglobulin E in bovine serum with preservative liquid ready to use

5. TBM Reagent (1bottle, 11ml) Contains 3,3', 5, 5' tetramethylbenzidine (TMB) stabilized in buffer solution
6. Stop solution (1N Hcl) (1 bottle, 11ml) Contains diluted hydrochloric acid

Reagent Preparation

1. All reagents should be allowed to reach room temperature(18-25℃)before use
2. All reagents should be mixed by gentle inversion or swirling prior to use
3. Do not induce foaming
4. Samples with expected values greater than 800 IU/ml should be diluted with Zero standard prior to assaying. A 1:100 initial dilution is recommended

RESULTS AND DISCUSSION: In the present study, 63 chronic asthma patients who presented a variety of symptoms were chosen for academic trial and were divided in to 5 Groups and results are tabulated.

Tabulation of Results: The IgE, Esinophils counts, Complete Blood Count values for the subjects are recorded along with their age and gender. The values are then compared and evaluated.

Group1 Healthy control group without asthma			
Ige Level (IU/L)	**Eosinophil Count(%)**	**RBC Count(Mil/Cmm)**	
30	1	4.3	
34.7	1.3	4.5	
33.9	1.4	4.12	
35.9	3.4	4.14	
45.8	3.3	5.12	
33.23	3.5	5.79	
45.67	3.6	4.67	
46.98	2.4	5.68	
47.3	2.6	4.65	
45.98	3.5	5.67	
46.12	2.5	4.32	
47.15	2.8	4.36	
41.0608333	2.608333333	4.776666667	mean
6.7861831	0.930745872	0.625856988	Std Div

Group 2- Corticosteroid therapy with fluticasone + salmeterol			
The age group of patients is 32-65.Main symptoms are allergic rhinitis,wheezing,active pneumonia infections			
IgE Level (IU/L)	**Eosinophil Count (%)**	**RBC Count (Mil/Cmm)**	**Patient**
100	10	4.5	F
111.3	10.9	4.55	F
120.9	9.92	4.57	M
120.2	9.95	4.59	M
113.89	10.34	4.43	M
114.78	10.23	4.9	M
115.67	10.42	4.89	M
111.45	10.25	4.67	M

119.2	10.21	4.56	M
116.8	11	4.65	M
109	10.45	4.89	M
108	10.24	5.57	M
106	10.12	5.89	M
104.56	11	5.43	M
120	11	5.23	M
112.7833333	10.402	4.888	Mean
6.33607209	0.389215328	0.443705179	Std Deviation

Group 3- β-agonist therapy with salmeterol			
The age group of patients is 35-72.The symptoms are upper respiratory tract infections, acute asthma and wheezing			
IgE Level (IU/L)	**Eosinophil Count (%)**	**RBC Count (Mil/Cmm)**	**Patient**
70.77	8	4.3	F
70.33	8.01	4.5	F
70.98	8.09	4.12	F
71	8.6	4.14	F
72.67	8.4	5.12	M
72.98	8.7	5.79	M
75.56	8.1	4.67	M
76	8.5	5.68	M
78	8.99	4.65	M
80.97	9.1	5.67	M
80.78	9.11	4.32	M
89	8.44	4.36	M
83	8.77	4.4	M
87.45	8.32	4.56	F
90.89	9	4.43	F
78.02533333	8.542	5.284636236	Mean

Group 4- Corticosteroid therapy with fluticasone + salmeterol + Broncorid syrup			
Age group:34-62. Common symptoms are acute allergic asthma and shortness of breath, wheezing and pneumonia			
IgE Level (IU/L)	**Eosinophil Count (%)**	**RBC Count (Mil/Cmm)**	**Patient**
80.23	9	4.5	F
80.99	9.11	5.32	M
80.97	9.23	5.12	M
81.89	9.45	5.22	M
81.56	9.1	4.43	F
82.88	9.12	5.1	M
83	9.15	4.89	M
84.6	9.19	4.35	M

87.9	9.18	4.56	M
88.34	9.45	4.22	M
82	9.78	4.89	M
84	9.07	4.11	F
85.98	9.08	5.89	M
87.2	9.67	5.43	M
88.23	9.98	5.44	M
90.87	10	4.88	M
84.415	9.3475	4.896875	Mean
3.266131249	0.334893018	0.503702541	Std Deviation

Group 5- Corticosteroid therapy with salmeterol with Broncorid syrup			
Age Group 34-67,Common Symptoms Are Upper Respiratory Tract Infections With Acute Allergic Asthma.			
IgE Level (IU/L)	**Eosinophil Count (%)**	**RBC Count (Mil/Cmm)**	**Patient**
60.75	8	4.55	F
60.23	8.1	4.98	F
60.25	8.12	4.89	F
60.89	8.15	4.23	F
61.2	8.14	5.12	M
61.7	8.34	5.21	M
66.5	8.45	5.14	M
67.8	8.19	5.15	M
68.2	8.09	4.56	M
68.34	8.5	4.98	M
71.45	8.6	4.89	M
78.9	7.9	5.83	M
76.89	8.35	5.31	M
73.7	8.57	5.72	M
74.56	8.65	5.5	M
80.12	9	5.1	M
68.2175	8.321875	5.0725	mean
7.039561066	0.289947553	0.415844522	std deviation
60.75	8	4.55	F

Statistical Analysis: Graph pad Prism software was used to calculate statistical significance. Prism offers four related tests that compare three or more groups. The choice of a test depends on two choices.

Repeated measures: It tests when the columns of data are matched. Here are some examples:

Measure a variable in each subject several times, perhaps before, during and after an intervention. Recruit subjects as matched groups, matched for variables such as age, ethnic group, and disease severity.

Nonparametric test: Nonparametric tests, unlike ANOVA are not based on the assumption that the data are sampled from a Gaussian distribution. But nonparametric tests have less power, and report only P values but not confidence intervals. Deciding when to use a nonparametric test is not straightforward. In the present study, the statistical analysis One-way ANOVA was carried out as it compares the means of three or more unmatched groups.

Effect of Serum IgE levels in IU/L

S.NO	Group	MEAN±SEM
1	G1(Control)	41.06±1.959
2	G2 (Fluticasone+salmeterol)	112.8±1.636*
3	G3(Salmeterol)	78.03±1.814**
4	G4(Fluticasone+salmeterol+Broncorid syrup)	84.69±0.8204***
5	G5(Salmeterol+Broncorid syrup)	67.42±1.679***

Groups show significance when compared to Control group

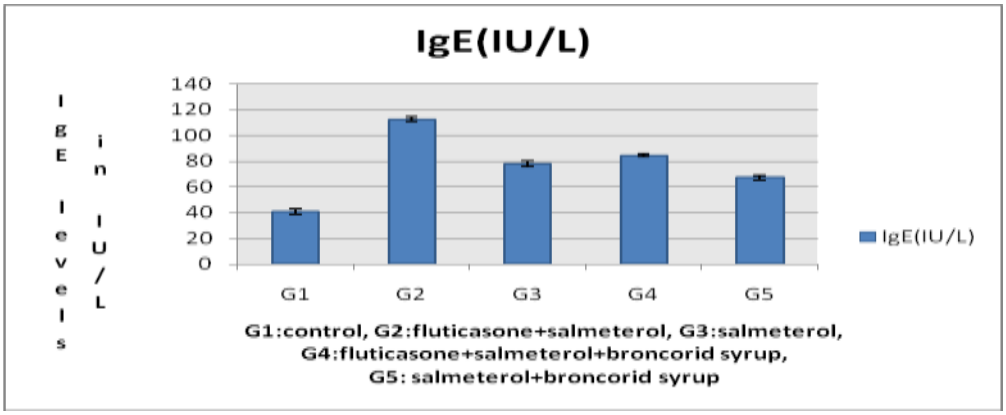

Fig: Graph showing effect of Serum IgE levels in IU/L

*=p<0.05 compared with Control group.
** =p<0.01 compared with Control group.
***=p<0.001 compared with Control group

All values were expressed in Mean±SEM. Results were analyzed using one way-ANOVA following Dunnett's post test.

One-way ANOVA, and related nonparametric tests compare three or more sets of measurements (data expressed using an interval or ratio scale). All values were expressed in Mean±SEM. Results were analyzed using one way-ANOVA following Dunnett's post test. Our results have shown that the mean IgE level in Group2 patients treated with fluticasone+salmeterol is 112.8±1.636* IU/L(International Unit per Litre) where as the IgE levels in patients treated with salmeterol was shown to be 78.03±1.814**IU/L. A different picture of the results were observed when the patients in Group4 and 5 who took combination therapy with fluticasone+salmeterol as corticosteroid therapy and broncorid syrup. The results of the biomarker study in the combination therapy groups have shown that G4 patients who had taken fluticasone+salmeterol as corticosteroid therapy and broncorid syrup had mean IgE level reduced to 84.69±0.8204*** IU/L whereas G3 patients who had taken salmeterol as β-agonist therapy and broncorid syrup had mean IgE levels reduced to 67.42±1.679***IU/L. Thus there is decrease in IgE levels of serum.

Effect of Eosinophils count in %

S.NO	Group	MEAN±SEM
1	G1(Control)	2.608±0.2687
2	G2 (Fluticasone+salmeterol)	10.4±0.1005*
3	G3(Salmeterol)	8.542±0.102*
4	G4(Fluticasone+salmeterol+Broncorid syrup)	9.304±0.07647**
5	G5(Salmeterol+Broncorid syrup)	8.277±o.06057**

Groups show significance when compared to Control group

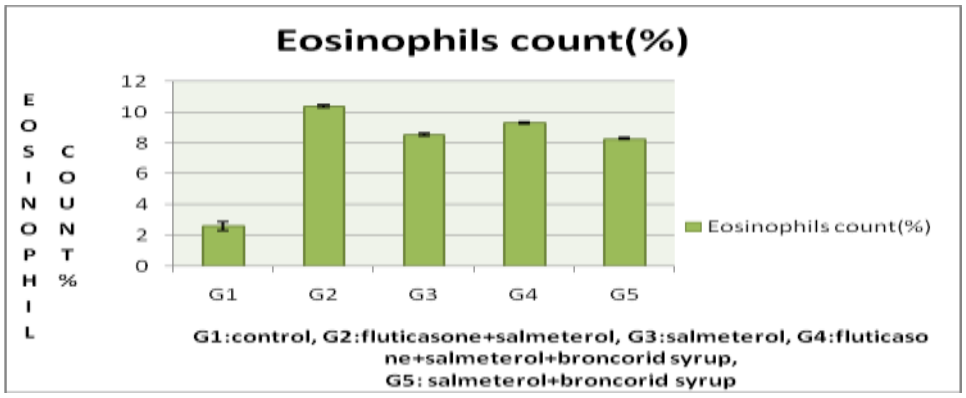

Fig: Graph showing effect of Eosinophils count in %

*=p<0.05 compared with Control group.

** =p<0.01 compared with Control group.

All values were expressed in Mean±SEM. Results were analyzed using one way-ANOVA following Dunnett's post test. Our results have shown that the mean Eosinophils count level in Group2 patients treated with fluticasone+salmeterol is 10.4±0.1005*% whereas the IgE levels in patients treated with salmeterol was shown to be 8.542±0.102*%. A different picture of the results were observed when the patients in Group4 and 5 who took combination therapy with fluticasone+salmeterol as corticosteroid therapy and broncorid syrup. The results of the biomarker study in the combination therapy groups have shown that G4 patients who had taken fluticasone+salmeterol as corticosteroid therapy and broncorid syrup had mean Eosinophils count level reduced to 9.304±0.07647** % whereas G3 patients who had taken salmeterol as β-agonist therapy and broncorid syrup had mean Eosinophil count levels reduced to 67.42±1.679***%.

Effect of RBC count in mil/cmm

S.NO	GROUP	MEAN±SEM
1	G1(Control)	4.777±0.1807
2	G2(Fluticasone+Salmeterol)	4.888±0.1146
3	G3(Salmeterol)	4.714±0.1473
4	G4 (Fluticasone+Salmeterol+Broncorid syrup)	4.898±0.1346*
5	G5 (Salmeterol+Broncorid syrup)	5.071±0.1111*

Group2 and Group3 show No significance when compared to Control group whereas Group4 and Group5 shows significance.

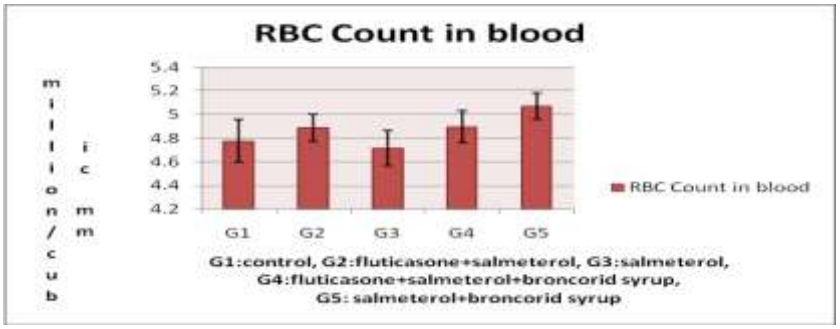

Fig: Graph showing effect of RBC count in mil/cmm

*=p<0.05 compared with Control group. All values were expressed in Mean±SEM. Results were analyzed using one way-ANOVA following Dunnett's post test.

Our results have shown that the mean RBC count in blood of Group2 patients treated with fluticasone + salmeterol is 4.888±0.1146 mil/cmm whereas the RBC count in patients treated with salmeterol was shown to be 4.714±0.1473mil/cmm. A different picture of the results was observed. When the patients in Group4 and 5 who took combination therapy with fluticasone+salmeterol as corticosteroid therapy and broncorid syrup. The results of the biomarker study in the combination. Therapy groups have shown that G4 patients who had taken fluticasone+salmeterol as corticosteroid therapy and broncorid syrup had mean RBC count has increased to 4.898±0.1346*mil/cm whereas G3 patients who had taken salmeterol as β-agonist therapy and broncorid syrup had mean RBC count has increased to 5.071±0.1111*mil/cmm. Thus there is increase in RBC counts in blood.

Comparison of All Parameters:

We have assessed these three markers in the blood of patients in Groups 1 to 5 to understand how thecombination therapy works. Dabur's Broncorid syrup is a herbal formulation which seems to be effective in reducing the intensity of the chronic illness in asthma patients. The results of our biomarker study is shown below

S.no	GROUP	IgE levels(IU/L)	Eosinophils count(%)	RBC count(mil/cmm)
1	G1(Control)	41.06±1.959	2.608±0.2687	4.777±0.1807
2	G2(Fluticasone+Salmeterol)	112.8±1.636*	10.4±0.1005*	4.888±0.1146
3	G3(Salmeterol)	78.03±1.814**	8.542±0.102*	4.714±0.1473
4	G4(Fluticasone+Salmeterol+Broncorid syrup)	84.69±0.8204***	9.304±0.07647**	4.898±0.1346*
5	G5 (Salmeterol+Broncorid syrup)	67.42±1.679***	8.277±o.06057**	5.071±0.1111*

IgE levels (IU/L) Group 1 vs. Group 2, $p < 0.05$; and Group 1 vs. Group 3, $p < 0.01$; however, Group 1 vs. Group 4 and Group 5, $p < 0.001$.

Eosinophils count(%).Group 1 vs. Group 2 and Group 3, $p < 0.05$; and group 1 vs. group 4 and Group 5, $p < 0.01$.

RBC count (mil/cmm) Group 1 vs. Group 2, Group 3 NS whereas Group 4 and Group 5, $p < 0.05$

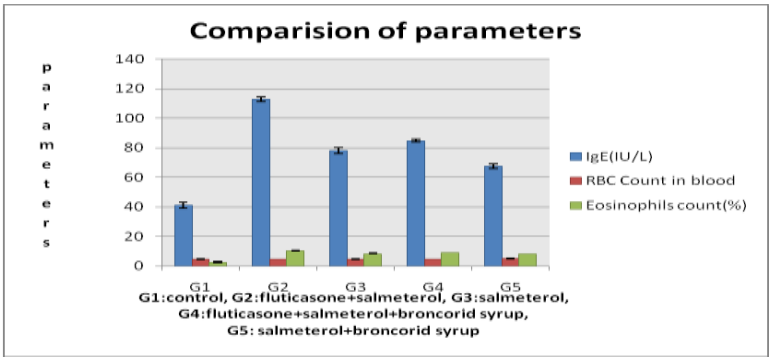

Fig: Graph showing comparison of results

S.NO	GROUP	IgE levels(IU/L)	Eosinophils count(%)	RBC count(mil/cmm)
1	G1(Control)	41.06±1.959	2.608±0.2687	4.777±0.1807
2	G2(Fluticasone+Salmeterol)	112.8±1.636*	10.4±0.1005*	4.888±0.1146
3	G3(Salmeterol)	78.03±1.814**	8.542±0.102*	4.714±0.1473
4	G4 (Fluticasone+Salmeterol+Broncorid syrup)	84.69±0.8204***	9.304±0.07647**	4.898±0.1346*
5	G5 (Salmeterol+Broncorid syrup)	67.42±1.679***	8.277±o.06057**	5.071±0.1111*

IgE levels(IU/L)

Group 1 vs. Group 2, $p < 0.05$; and Group 1 vs. Group 3, $p < 0.01$; however,
Group 1 vs. Group 4 and Group 5, $p < 0.001$.

Eosinophils count(%).

Group 1 vs. Group 2 and Group 3, $p < 0.05$; and group 1 vs. group 4 and Group 5, $p < 0.01$.

RBC count(mil/cmm)

Group 1 vs. Group 2, Group 3 NS whereas Group 4 and Group 5, $p < 0.05$

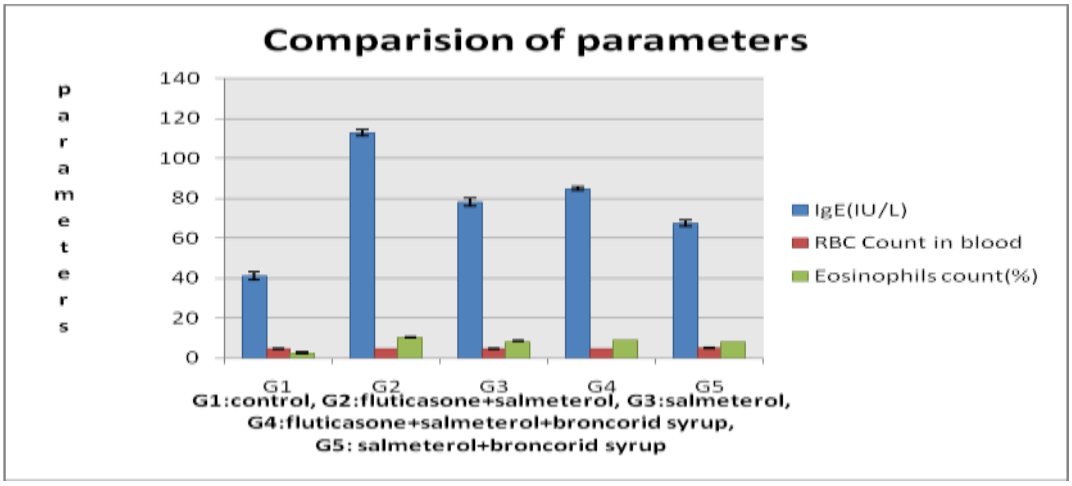

Fig: Graph showing comparison of results

All values were expressed in Mean±SEM. Results were analyzed using one way-ANOVA following Dunnett's post test and are statistically significant.

The patients who were taking different drugs like fluticasone+salmeterol as Corticosteroids (CS therapy) and salmeterol as β-agonists and their combination with or without Broncorid syrup were evaluated with the biomarkers*=p<0.05 compared with Control group. All values were expressed in Mean±SEM. Results were analyzed using one way-ANOVA following Dunnett's post test.

Our results have shown that the mean RBC count in blood of Group2 patients treated with Fluticasone+salmeterol is 4.888±0.1146mil/cm whereas the RBC count in patients treated with salmeterol was shown to be 4.714±0.1473mil/cm. A different picture of the results were observed when the patients in Group4 and 5 who took combination therapy with fluticasone+salmeterol as corticosteroid therapy and broncorid syrup. The results of the biomarker study in the combination therapy groups have shown that G4 patients who had taken fluticasone+salmeterol as corticosteroid therapy and broncorid syrup had mean RBC count has increased to 4.898±0.1346*mil/cmm whereas G3 patients who had taken salmeterol as β-agonist therapy and broncorid syrup had mean RBC count has increased to 5.071±0.1111*mil/cmm. Thus there is increase in RBC counts in blood.

Comparison of All Parameters: We have assessed these three markers in the blood of patients in Groups 1 to 5 to understand how the combination therapy works. Dabur's Broncorid syrup is a herbal formulation which seems to be effective in reducing the intensity of the chronic illness in asthma patients. The results of our biomarker study is shown below which are crucial for the prognosis of the disease. The plasma IgE levels reflects the proportion of allergic antibodies produced against the triggers for asthma whereas the Eosinophils counts also give an idea about the extent of allergens in the blood. The RBC counts had increased and Eosinophils counts have come down in groups G4 and G5 who took the broncorid syrup when compared to groups G1 and G2 who took corticosteroids and β-agonists alone.

Our results have shown that the patients who had taken the Broncorid syrup along with CS therapy and β-agonist have shown considerable improvement with respect to IgE levels and Eosinophils counts indicating the control of metabolic factors that contribute to allergy causing asthma symptoms whereas the drugs like fluticasone+salmeterol (corticosteroid therapy) and salmetrol (β-agonists therapy) without Broncorid syrup could not show considerable improvement with respect to IgE levels and Eosinophil counts indicating decreased levels of control of metabolic factors that contribute to allergy causing asthma symptoms. The combination therapy of Corticosteroids, β-agonists and Broncorid syrup has resulted in overall betterment and improvement in the health and quality of life of the patients which was evident by replies of the patients to our questionnaire and the clinicians reports.

CONCLUSION

The adverse effects caused by combination therapy of corticosteroids (Fluticasone) and β agonists (Salmeterol) were reduced when taken in combination with Broncorid syrup which was evident by significant reduction in the levels of IgE, Eosinophils and increased RBC count. The action of Broncorid syrup could be due to the inhibition of mast cell membrane stabilizing effect.

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