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Efficacy and Safety Evaluation of Bresol Tablet in Allergic Rhinitis- A Double Blind Placebo Controlled Clinical Study

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Abstract: ***Allergic rhinitis (AR), often considered a trivial disease, is now increasingly being recognized as a cause of significant and widespread morbidity. It is the most common allergic disorder, affecting 10-20 percent of the population. Currently available therapeutic options in the management of AR have major limitations due to low clinical efficacy and associated adverse events. This study was planned to evaluate the clinical efficacy and safety (short- and long-term) of Bresol tablets in AR. The study was a placebo controlled, phase III clinical trial conducted as per the ethical guidelines of Declaration of Helsinki. One hundred subjects from the age group of 15 to 60 years who presented with symptoms of AR were included in the study. At the initial visit, a detailed medical history was obtained by interviewing the subjects, which was followed by thorough clinical examination and all the subjects were investigated by hematological and biochemical tests. Subjects were advised to consume one Bresol tablet, twice-daily for 4 weeks while subjects in placebo group received identical looking placebo in the same dose, for a period of 4 weeks. The predefined primary endpoints were proportion of subjects with rapid symptomatic control and clinical improvement, along with renormalization of laboratory parameters. The results were statistically analyzed by Mann Whitney test and Paired t test. The mean score sneezing, nasal congestion, itching of the eyes, itching of the nose, postnasal drip, rhinorrhea and watery eyes decreased significantly at the end of 4 weeks, when compared to the Placebo and respective baseline values. There was a significant reduction in the Total WBC Count, Neutrophils, Lymphocytes, Eosinophils, Monocytes, ESR and Absolute Eosinophil Count at the end of 4 weeks, when compared to the placebo group. There were no clinically significant adverse reactions; either reported or observed during the entire study period. The overall compliance to the treatment was good and no treatment discontinuations were reported. Therefore, it may be concluded that Bresol tablets are effective and safe in the management of AR.***

Keywords: Bresol Tablet, Allergic Rhinitis, Clinical trial

1. Introduction

Allergic rhinitis, often considered a trivial disease, is now increasingly being recognized as a cause of significant and widespread morbidity.[1] It is the most common allergic disorder, affecting 10-20 percent of the population.[2,3]

Allergic rhinitis had been classified as seasonal, perennial or occupational allergic rhinitis according to the exposed allergens.[4] However, the previous classification had some limitations in that it is common that both seasonal and perennial allergens are sensitized and seasonal allergens cause perennial allergic symptoms or even perennial allergens cause allergic symptoms seasonally.[5,6]

The condition is characterized by continuous or periodic nasal congestion, rhinorrhea, sneezing, pruritis of the conjunctiva, nasal mucosa and oropharynx, allergic shiners, lacrimation, and fatigue. Predisposing factors are a positive family history of similar symptoms and a personal history of collateral allergy manifested as eczematous dermatitis, urticaria, and/or asthma. Clinical presentation may include nasal polyps, pale and boggy (sometimes reddened or excoriated) nasal passages, congested and edematous conjunctiva, injected pharynx, and swelling of the turbinates and membranes of the ear.

Often, there is a temporal relationship between an allergen exposure and an acute episode of allergic rhinitis. Environmental agents that can cause this condition are dust mites, feathers, animal dander, moulds, pollen, grass, and fungus spores. Many people with allergic rhinitis are also allergic to certain foods and may experience symptoms as a result of eating allergy-triggering substances in such foods as eggs, nuts, fish, shellfish, dairy products, or wheat.[7]

Poorly controlled symptoms of allergic rhinitis may contribute to sleep loss, secondary daytime fatigue, learning impairment, decreased overall cognitive functioning, decreased long-term productivity and decreased quality of life. Additionally, poorly controlled allergic rhinitis may also contribute to the development of other related disease processes including acute and chronic sinusitis, recurrence of nasal polyps, otitis media/otitis media with effusion, hearing impairment, abnormal craniofacial development, sleep apnea and related complications, aggravation of underlying asthma, and increased propensity to develop asthma.[8]

Bresol tablets is polyherbal formulations indicated for the management of AR. Bresol tablets contains extracts of *Curcuma longa*, *Ocimum sanctum*, *Adhatoda vasica*, Trikatu, Triphala, *Embelia ribes*, *Cyperus rotundus*, *Cinnamomum zeylanicum*, *Elettaria cardamomum*, *Cinnamomum tamala*, and *Mesua ferrea*. This study was planned to evaluate the efficacy and safety of Bresol tablets in AR.

Aim of the Study

This study was planned to evaluate the clinical efficacy and safety (short- and long-term) of Bresol tablets in Allergic Rhinitis.

Study Design

The study was a placebo controlled clinical trial conducted from January 2011 to May 2011 as per the ethical guidelines of Declaration of Helsinki. The study protocol, CRFs, regulatory clearance documents, product related information and informed consent form were submitted to the Institutional Ethics Committee and were approved by the same.

2. Materials and Methods

2.1 Inclusion criteria

100 subjects of either sex aged between 15 to 60 years and suffering from AR like sneezing, nasal congestion, itching of the eyes, itching of the nose, postnasal drip, rhinorrhoea and watery eyes were included in the study.

2.2 Exclusion criteria

Subjects suffering from severe systemic illness, which necessitated use of other medications, were excluded from the study. Those subjects who had nasal abnormalities causing obstruction, who had acute respiratory infection or severe concomitant disease were excluded from the study. Women having likelihood of pregnancy, pregnant and lactating women were also excluded from the study.

2.3 Study procedures

This study was an open, prospective, non-comparative clinical trial conducted at Department of ENT Grant Medical College & J.J. Hospital Mumbai, India. One hundred subjects from the age group of 15 to 60 years who presented with symptoms of AR (sneezing, nasal congestion, itching of the eyes, itching of the nose, postnasal drip, rhinorrhoea and watery eyes) were included in the study after signing the informed consent document.

Subjects who met the eligibility criteria were enrolled and their informed consent was obtained. At the initial visit, a detailed medical history with special emphasis on family and past medical history, allergy and treatment history was obtained from all subjects. In all subjects, a thorough systemic examination was done, which was followed by a detailed ENT examination. All subjects were investigated by hematological and biochemical tests, which included Total WBC Count, Neutrophils, Lymphocytes, Eosinophils, Monocytes and ESR. Subjects were divided into Drug and Placebo groups (50 each) randomly. Subjects were advised to consume one Bresol tablet, twice-daily for 4 weeks while the subjects in the placebo group received identical looking in same dose, for a period of 4 weeks

All adverse events, either reported or observed by subjects were recorded in the CRF with information about severity, onset, duration and action taken regarding the study drug. Relation of adverse events to the study medication was predefined as "*Unrelated*" (a reaction that does not follow a reasonable temporal sequence from the time of 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). Subjects were allowed to voluntarily withdraw from the study, if they experienced serious discomfort during the study or sustained serious clinical events requiring specific treatment. For subjects withdrawing from the study, efforts were made to ascertain the reason for dropout.

2.4 Follow-up and monitoring

All subjects were investigated for evaluated for symptomatic improvement of AR (sneezing, nasal congestion, itching of the eyes, itching of the nose, postnasal drip, rhinorrhea and watery eyes). Subjects were investigated by hematological and biochemical tests at the end of the study period.

2.5 Primary and secondary end points

The predefined primary endpoints were proportion of subjects with rapid symptomatic control and clinical improvement, along with renormalization of laboratory parameters. The predefined secondary endpoints were incidences of adverse events (short- and long-term) and overall compliance to the drug therapy.

2.6 Statistical analysis

An intent-to-treat analysis was performed for all efficacy evaluations. The changes in the values, before the initiation of study and at the end of the study were analyzed by Statistical test: Mann Whitney test and Paired t test. All values were expressed as Mean ± SEM.

3. Results

One hundred patients were enrolled into the trial with mean age of 25.68 ±10.59 in Bresol group and 28.72±9.84 in Placebo group. Fifty nine female patients and 41 male subjects had participated (Table 1).

There was significant reduction in the mean score of sneezing from 7.16±1.15 at entry to 6.46±1.34, 5.48±1.31, 4.18±1.22 and 3.42±0.91 at the end of 1st week, 2nd week, 3rd week and 4th week of treatment respectively. In the Placebo group the mean score of sneezing were 6.96±1.12 at entry to 6.52±1.27, 5.90±1.06, 5.56±1.20 and 4.98±1.39 at the end of 1st week, 2nd week, 3rd week and 4th week of treatment respectively with significance of p<0.0001 on 3rd & 4th week. Reduction was also observed in nasal congestion from 7.50±1.06 at entry to 6.78±0.95, 5.82±1.02, 4.48±0.99, 3.58±1.09 at the end of 1st week, 2nd week, 3rd week and 4th week of treatment respectively. In the Placebo group the mean score of nasal congestion were 7.46±0.97, 6.82±0.94, 6.18±0.98, 5.68±1.17 and 6.08±1.41 at the end of 1st week,

2nd week, 3rd week and 4th week of treatment respectively with significance of $p<0.0001$ on 3rd & 4th week. Significant reduction was also observed in rhinorrhea from 7.28±1.58 at entry to 6.44±1.46, 5.44±1.45, 4.56±1.33, 3.56±1.15 at the end of 1st week, 2nd week, 3rd week and 4th week of treatment respectively with significance of $p<0.0001$in 3rd and 4th week as compared to the values of placebo group. Similarly mean scores for itching of eyes and nose, watery eyes and postnasal drip decreased significantly at the end of 2 weeks, when compared to their respective baseline values (Table 2).

There was a significant reduction in the Total WBC Count from 7202.00±1518.00 at entry to 6460.00±1366.00 at the end of 4 weeks of treatment with Bresol Tablet ($p<0.0001$). Similarly mean scores for neutrophils, lymphocytes, eosinophil, monocyte count, ESR and absolute eosinophil count reduced significantly at the end 4 weeks in the Bresol Group when compared to their respective baseline values (Table 3).

In the Placebo group the Total WBC Count was 7192.00±1528.00 at entry to 6960.00±1498.00 at the end of 4 weeks ($p<0.0184$). Neutrophil Count was 67.82±4.56 at entry to 68.02±4.64 at the end of 4 weeks ($p<0.0399$). Similarly mean scores for lymphocytes, eosinophil, monocyte count, ESR and absolute eosinophil count reduced significantly at the end 4 weeks when compared to their respective baseline values (Table 3).

There were no clinically significant adverse reactions; either reported or observed during the entire study period. The overall compliance to the treatment was good and no treatment discontinuations were reported.

4. Discussion

Allergic rhinitis is characterized by a two-phase allergic reaction, i.e. the initial sensitization phase (IgE formation and triggering of the humoral response) and the clinical disease phase (manifesting symptoms). The clinical disease phase can itself be further subdivided into two distinct phases, namely an early phase (mediated through mast cells) and a late phase (cellular infiltration and mediator release).[9] In the early phase, mast cells release mediators as a result of antigen cross linking of IgE molecules, which results in an explosive degranulation of mast cells, leading to the characteristic symptoms of rhinitis (rhinorrhea, nasal obstruction and itching, sneezing, postnasal drip and loss of sense of smell).[10]

Control of cytokine release from airway epithelial cells is a primary approach in the management of allergic rhinitis and topical corticosteroids with oral antihistamines is the mainstay in the management of allergic rhinitis. In resistant patients, the effects of allergen-specific immunotherapy can be beneficial.[11]

This study observed significant reduction in the mean symptom score for sneezing, nasal congestion, itching of nose, postnasal drip and runny nose. The increased levels of TLC, DLC (polymorphs, lymphocytes, monocytes, eosinophil), ESR and AEC also reduced significantly. These results might be due to the synergistic activities of the ingredients of Bresol tablets, which have been studied in depth by various researchers.

In various studies, curcumins - I, II and III (components of *Curcuma longa*)[12] have been shown to inhibit chemomediators of inflammation (phospholipase, LO, COX-1 and -2, LT, TX, PG, NO, collagenase, elastase, hyaluronidase, monocyte chemoattractant protein-1, interferon-inducible protein, TNF-α, and IL-12.[13,14] Inhibition of these inflammatory chemomediators was shown to be due to the ability of curcumins to bind with phosphatidylcholine micelles.[15] Enhanced suppression of COX-2 expression was observed due to extracellular signal-regulated kinase activity and NF-kappaB activation inhibition, which might be the molecular mechanisms of actions of curcumins.[16]Curcumins significantly inhibits the production of IL-12, reduces induction of γ-IFN, IL-4 in CD4+ T-lymphocytes by macrophages, leading to the inhibition of T-helper cells-1 cytokine profile (IFN-γ and IL-4 production) in CD4+ T-cells.[17] Curcumins are potent antioxidants and inhibit Ca^{2+} entry and PK-C activity.[18] Curcumins also have an immunostimulatory activity, which increases circulating antibody titer, plaque forming cells, alpha-esterase positive cells and phagocytosis.[19,20] Antiallergic property of curcumin in an *in vitro* model of airway hyperresponsiveness in one of the study.[21]

In Ayurveda, black pepper (*Piper nigrum* Linn.), long pepper (*Piper longum* Linn.) and ginger (*Zingiber officinale* Rosc.) are collectively known as *Trikatu*. It is prepared by mixing dried powder of fruits of black pepper, fruits of long pepper and rhizomes of ginger in the ratio of 1:1:1. Various experimental and clinical studies established anti-bacterial[22] and immunomodulatory[23] activities along with its use in the treatment of allergic rhinitis[24]. Further, Gingerols and diarylhepatanoids, the principle active ingredients of *Zingiber officinale* are potent inhibitors of PG synthetase enzyme and 5-LOX enzymes. Potent inhibition of biotransformation of AA (comparable to indomethacin) by *Zingiber officinale* was established in one of the study.[25] The other active ingredients of *Zingiber officinale* (oleoresins-[8]-paradol and [8]-shogaol), have inhibitory effects on COX-2 enzymes[26] and the mechanism of action was hypothesized by the inhibition of COX-1 / TX synthase enzymes.[27] Cyclo-oxygenase-1 and -2 (regulated by the eukaryotic transcription factor NF-kappaB) is the molecular target for the actions of *Zingiber officinale*, and it acts by interfering with the intracellular signaling cascades, those involving NF-kappaB and mitogen-activated PK.[28] Also *Zingiber officinale* possess significant inhibitory effects on PG-E2 production.[29]

Triphala is a traditional Ayurvedic herbal formulation, consisting of equal parts of three medicinal plants namely combining *Terminalia chebula*, *Terminalia belarica* and *Emblica officinalis*. *Triphala* has been used extensively as a drug against a number of diseases including vitiated *Kapha dosha*, that which contributes to the pathogenesis of various respiratory diseases[30, 31]. The research shown that administration of Triphala enhanced the phagocytosis, phagocytic index, antioxidant activities and decreased corticosterone levels in animals thus exhibited significant immunomodulatory activity. Further it also showed

significant antibacterial and anti-inflammatory activities[32]. Further, one of the ingredients of *Triphala* viz., *Terminalia chebula* possesses antitussive, activity against sulphur dioxide gas evoked cough in mice thus validate the popular use of this herb in cough related to numerous respiratory diseases[33]. Further, the principle anti-inflammatory ingredients of *Piper longum* are dihydrokawain, yangonin and methysticin.[34] *Piper longum* inhibits the lipid peroxidation process effectively by its ability to scavenge free radicals involved in initiation and propagation steps.[35] *Piper longum* retards the macrophage recruitment and suppress cytokines production.[36] Inhibition of TNF-α release was observed using isolated kawapyrones of *Piper longum*.[37]

The principle ingredients of *Emblica officinalis* are tannoids (emblicanin A and B, punigluconin, and pedunculagin).[38] In addition to the antitussive activity, it was observed that *Emblica officinalis* has anti-inflammatory, antispasmolytic and antioxidant efficacy and it reduces the mucus secretion in the airways.[39] *Emblica officinalis* also possesses superoxide-scavenging and prolyl endopeptidase inhibitory activity. Also this herb significantly inhibits the free radical production, restores the anti-oxidant status,[40] inhibits apoptosis and DNA fragmentation, relieves the immunosuppressive effects on lymphocyte proliferation and even restores the IL-2 and γ-IFN production.

Terminalia belirica possess anti-peroxidative activity[41] *and* inhibits lipid peroxide formation by scavenging hydroxyl and superoxide radicals.[42] Antioxidant potential of *Terminalia belerica* (stronger than alpha-tocopherol) is attributed to hydroxybenzoic acid and hydroxycinnamic acid derivatives, flavonol aglycones and their glycosides.[43]

Ocimum sanctum has an immunostimulatory effect on the humoral immunologic response (an increase in antibody titer), as well as of the CMI response (E-rosette formation and lymphocytosis).[44] Another study documented a decrease in histamine release from mast cells (humoral immune response) and a decrease in leucocyte migration inhibition (CMI response). This immunomodulatory effect was postulated as mediated by GABAergic pathways.[45] Significant inhibition of leucocyte migration in the pleural exudates, which suggest that the *Ocimum sanctum* inhibits the enhancement of the vascular permeability and leucocyte migration following inflammatory stimulus.[46] Analgesic action of *Ocimum sanctum* is exerted both centrally as well as peripherally.[47] Free radical scavenging potential of ursolic acid isolated from *Ocimum sanctum* against lipid peroxidation was observed *in vitro*.[48] Also *Ocimum sanctum* possess potent free radical scavenging activity[49] and antioxidant activity.[50]

Adhatoda vasica possess potent antiallergic activity[51]**.** The widely used mucolytics, namely benzylamines (bromhexine and ambroxol) are the semi-synthetic derivatives of vasicine, extracted from *Adhatoda vasica* and these benzylamines enhance lysozyme levels in the respiratory-tract secretions and clear bacilli-laden mucus.[52] Results of the study showed that the potent antiinflammatory activity of *Adhatoda vasica* was equivalent to that of hydrocortisone.[53]
The principle ingredients of *Cyperus rotundus* are sesquiterpenes (beta-selinene, isocurcumenol, nootkatone and aristolone) and a triterpene (oleanolic acid).[54] Inhibition of NO and O_2- production *in vitro* by *Cyperus rotundus was* observed in a study and the inhibition was found to be due to the suppression of iNOS protein and iNOS mRNA expression.[55]

Embelin, a benzoquinone-derivative isolated from *Embelia ribes*, when tested for its antibacterial potential exhibits significant inhibition against five and moderate activity against three stains of 12 bacteria tested.[56] Embelin and its 2, 5-isobutylmine salts have been reported to possess anti-inflammatory activity in carrageenan-induced paw edema and cotton pellet granuloma formation.[57]

The bark of *Cinnamomum zeylanicum*, showed a very low inhibitory concentration value ranging from 0.14 to 0.26 mg/ml, efficiency concentration value from 6.1 to 11.6 mg/mg DPPH and reducing power value from 0.6 to 2.8 ascorbic acid equivalents (ASE/ml), and reasonably high values (8.5–16.2) of anti-radical power (ARP), indicating their strong Free radical scavenging activity. They also showed better inhibition of hydroxyl radical induced deoxyribose degradation.[58] The anti-inflammatory effect of these plants was determined by xylene-induced ear oedema in mice and cotton pellet granuloma test in rats.

Leaves of *Cinnamomum tamala* inhibited significantly and dose dependently edema induced by carrageenan in rats and also reduced significantly acetic acid induced vascular permeability in mice. When tested in vitro, it exhibited significant membrane stabilizing property.[59]
Elettaria cardamomum significantly increased WBC count. Similarly bone marrow cellularity and Alpha esterase positive cells which are lowered by radiation, were partly restore by *Elettaria cadimomum*.[60]

The xanthones of *Mesua ferrea* namely, dehydrocycloguanandin , calophyllin-B, jacareubin 6-desoxy jacareubin mesuaxantbone-A mesuaxanthone-B and euxanthone produced varying degrees of C.N.S. depression and also exhibited anti-inflammatory activity both by intraperitoneal and oral routes in rats as tested by carrageenin induced hind paw oedema, cotton pellet granuloma and granuloma pouch techniques, in normal and adrenalectomised rats.[61] The antibacterial efficacy of the methanol extract of flowers of *Mesua ferrea* could inhibit a large number of Gram-positive and Gram-negative bacteria at concentration ranges of 100 to 50 µg/ml, or even lower, as against vibrios and *Escherichia coli*. In *in vivo* tests, used at concentrations of 100 and 200 µg/g of body weight, it offered significant protection to Swiss strain of albino mice when challenged with 50 MLD of a virulent strain *Sulmonella typhimurium*.[62]

5. Conclusion

Increasing prevalence of AR is a global health issue and AR has a severe impact due to associated long-term compromises in the quality of life. The available treatment options for AR have major limitations due to fewer efficacies and associated adverse events. This study observed a highly significant reduction in the mean scores for sneezing, nasal congestion, itching of nose, postnasal

drip and rhinorrhea. The increased levels of TLC, DLC (polymorphs, lymphocytes, monocytes, eosinophil), ESR, and AEC reduced significantly at the end of the study. The significant results might be due to the synergistic activities of the ingredients of Bresol tablets. There were no clinically significant adverse reactions during the entire study period. The overall compliance to the treatment was good and no treatment discontinuations were reported. Therefore, it may be concluded that Bresol tablets and syrup are effective and safe in the management of AR.

Bresol tablets significantly reduced the symptoms of AR namely sneezing, nasal congestion, itching of nose, postnasal drip and rhinorrhea and also significantly reduced elevated TLC, DLC (polymorphs, lymphocytes, monocytes, eosinophil), ESR and AEC levels without causing clinically significant adverse reactions. The observed effect might be due to the synergistic effect of the ingredients of Bresol tablets. Thus it can be concluded that the Bresol tablets are effective and safe in the management of AR and can be effectively used in allergic rhinitis patients.

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Tables:

Table 1: Demographic data

	Drug	Placebo
Age	25.68±10.59	28.72±9.84
Males	18	23
Females	32	27

Table 2: Daily individual symptoms of rhinitis

		Drug	Placebo	Significance
Sneezing	Baseline	7.16±1.15	6.96±1.12	NS
	1 week	6.46±1.34	6.52±1.27	NS
	2 weeks	5.48±1.31	5.90±1.06	NS
	3 weeks	4.18±1.22	5.56±1.20	P<0.0001
	4 weeks	3.42±0.91	4.98±1.39	P<0.0001
Nasal congestion	Baseline	7.50±1.06	7.46±0.97	NS
	1 week	6.78±0.95	6.82±0.94	NS
	2 weeks	5.82±1.02	6.18±0.98	NS
	3 weeks	4.48±0.99	5.68±1.17	P<0.0001
	4 weeks	3.58±1.09	6.08±1.41	P<0.0001
Itching of the eyes	Baseline	0.30±1.07	0.32±1.00	NS
	1 week	0.28±0.99	0.30±0.99	NS
	2 weeks	0.22±0.76	0.22±0.76	NS
	3 weeks	0.18±0.66	0.20±0.73	NS
	4 weeks	0.14±0.50	0.18±0.60	NS
Itching of the Nose	Baseline	0.24±1.26	0.24±1.26	NS
	1 week	0.24±1.26	0.24±1.26	NS
	2 weeks	0.20±1.07	0.20±1.07	NS
	3 weeks	0.14±0.76	0.18±1.02	NS
	4 weeks	0.12±0.63	0.18±1.02	NS
Post-nasal drip	Baseline	3.94±3.14	3.96±3.12	NS
	1 week	3.46±2.78	3.48±2.76	NS
	2 weeks	2.90±2.37	3.08±2.42	NS
	3 weeks	2.42±2.08	3.20±2.57	NS
	4 weeks	1.96±1.68	3.42±2.81	P<0.0041
Rhinorrhea	Baseline	7.28±1.58	7.26±1.54	NS
	1 week	6.44±1.46	6.58±1.43	NS
	2 weeks	5.44±1.45	5.94±1.35	NS
	3 weeks	4.56±1.33	5.78±1.45	P<0.0001
	4 weeks	3.56±1.15	5.94±1.45	P<0.0001
Watery Eyes	Baseline	1.82±3.09	1.88±3.10	NS
	1 week	1.56±2.67	1.60±2.72	NS
	2 weeks	1.40±2.38	1.56±2.66	NS
	3 weeks	1.10±1.87	1.58±2.70	NS
	4 weeks	0.94±1.62	1.58±2.73	NS
Statistical Test: Mann Whitney test, NS: Not Significant				

Table 3: Laboratory Investigations

		Baseline	After treatment.	Significance
Drug	Total WBC Count	7202.00±1518.00	6460.00±1366.00	P<0.0001
	Neutrophils	67.82±4.56	69.24±4.22	P<0.0001
	Lymphocytes	26.78±1.54	28.02±0.98	P<0.0001
	Eosinophils	4.60±1.20	1.94±0.87	P<0.0001
	Monocytes	1.42±0.61	1.40±0.73	NS
	ESR	8.66±1.81	8.66±1.61	NS
	Absolute eosinophil count	339.90±123.00	126.70±67.59	P<0.0001
Placebo	Total WBC Count	7192.00±1528.00	6960.00±1498.00	P<0.0184
	Neutrophils	67.82±4.56	68.02±4.64	P<0.0399
	Lymphocytes	26.78±1.54	26.86±1.59	NS
	Eosinophils	4.58±1.23	4.48±1.15	NS
	Monocytes	1.38±0.53	1.36±0.60	NS
	ESR	8.84±1.28	8.72±1.39	NS
	Absolute eosinophil count	339.90±123.00	321.70±130.20	P<0.0489
Statistical Test: Paired t test NS: Not Significant				