Int. J Med. Pharm. Res. (P-ISSN: 2958-3675 | E-ISSN: 2958-3683)
Available on: https://ijmpr.in/

International Journal
of Medical and Pharmaceutical Research

ORGINAL ARTICLE **OPEN ACCESS**

An Open Label Randomized Comparative Clinical Trial on Efficacy and Safety of Bilastine Tablet, Fluticasoneand Mometasone Nasal Spray in Allergic Rhinitis; A Tertiary Care Hospital Based Prospective Interventional Study

Dr.Rohit Chauhan[1]*, Dr.Anamika Thakur[2], Dr. P. K. Kaundal[3], Dr.Jagdeep Thakur[4]

[1]Junior Resident - 3rd Year, Department of Pharmacology, Indira Gandhi Medical College & Hospital (IGMC), Ridge Sanjauli Rd, Lakkar Bazar, Shimla, Himachal Pradesh 171001, India
[2]Professor, Department of Pharmacology, Indira Gandhi Medical College & Hospital (IGMC), Ridge Sanjauli Rd, Lakkar Bazar, Shimla, Himachal Pradesh 171001, India
[3]Professor and Head, Department of Pharmacology, Indira Gandhi Medical College & Hospital (IGMC), Ridge Sanjauli Rd, Lakkar Bazar, Shimla, Himachal Pradesh 171001, India
[4]Professor, Department of Otorhinolaryngology, Indira Gandhi Medical College & Hospital (IGMC), Ridge Sanjauli Rd, Lakkar Bazar, Shimla, Himachal Pradesh 171001, India

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***Corresponding Author**
Dr.Rohit Chauhan

Junior Resident - 3rd Year, Department of Pharmacology, Indira Gandhi Medical College & Hospital (IGMC), Ridge Sanjauli Rd, Lakkar Bazar, Shimla, Himachal Pradesh 171001, India

Received: 02-06-2024
Accepted: 20-08-2024
Available online: 22-08-2024

A B S T R A C T

Background: Corticosteriods nasal sprays are the mainstay of treatment for allergic rhinitis. Most common reasons for patients to be dissatisfied with treatment for allergic rhinitis are inadequate symptom relief and bothersome side effects with intranasal corticosteroids. Bilastine tablet has high specificity and prolong duration of binding to H1 receptor and hence demonstrates antihistamine and antiallergic properties and hence the present study is to compare the efficacy, safety and compliance of bilastine tablet, fluticasone and mometasone nasal spray in allergic rhinitis.

Objective : To determine the efficacy, safety and clinical outcome of bilastine tablet, fluticasone and mometasone nasal spray in allergic rhinitis.

Material and Methods: This single-center, open label randomized interventional clinical trial was conducted in the department ofOtorhinolaryngology (ENT) and department of Pharmacology, Indira Gandhi Medical College and Hospital, Shimla. For this study 240 allergic rhinitis patients aged 18-50 years, satisfying the eligibility criteria were randomized into 3 groups in a 1:1:1 ratio to receive either the bilastine tablet 20mg or fluticasone furoate 50mcg or mometasone furoate 50mcg nasal spray. Baseline lab investigations of absolute eosinophill count, hemoglobin, random blood sugar, renal function test, liver function test, nasal endoscopy and SNOT-22 score were documented. After 6 weeks of active treatment, the study drugs were withdrawn, lab investigations of hemoglobin, renal function test, liver function test were done and documented. SNOT-22 and Medication Adherence Rating Scale (MARS) questionnaire were completed.

Results: In bilastine group the mean baseline SNOT-22 score was 37.85$\pm$ 15.818 which decreased to 3.35 $\pm$ 7.388 after 6 weeks. (P value 0.001). In mometasone nasal spray group the mean baseline SNOT-22 score was 37.79 $\pm$ 11.829 which decreased to 2.8 $\pm$ 4.772 after 6 weeks. (P value 0.001). In fluticasone nasal spray group the mean baseline SNOT-22 score was 37.68 $\pm$ 15.475 which decreased to 2.34 $\pm$ 5.116 after 6 weeks. (P value 0.001). Mean of baseline and post intervention vitals and laboratory parameters in bilastine, mometasone and fluticasone groups was statistically non significant. (P value > 0.05). No ADR/AE reported in any group. Only 1 patient in bilastine and 4 in mometasone and fluticasone group were non-compliant. Hence, 6 weeks of therapy with these three medications, were 100% efficacious and safe.

Conclusion: Bilastine tablet once daily is equally efficacious and safe to use as compared to twice daily regime of fluticasone and mometasone nasal spray. Compliance to intranasal corticosteroids, mometasone and fluticasone nasal spray is

compromised as compared to oral anti histaminic tablet bilastine in allergic rhinitis. Hence therapy may be based on patient preference, convenience and cost.
TrialRegistration : The clinicalTrials.gov Identifier is CTRI/2023/10/058841.

Keywords: Allergic Rhintis, Fluticasone Nasal Spray, Mometasone Nasal Spray, Bilastine Tablet, Clinical Trial, SNOT-22, Efficacy, Safety.

INTRODUCTION

Evidence suggest that the prevalence of allergic diseases is increasing globally, including in the Asia-Pacific region [1]. The reported prevalence of allergic rhinitis ranging from 10–40% in United States, 10–13% in India [2], 8-10% in South Korea, to more than 50% among adults in Vietnam and Thailand, depending on the method of assessment [3]. Allergic rhinitis is IgE-mediated inflammation of nasal mucosa.

It has four cardinal symptoms namely sneezing, rhinorrhea, nasal obstruction, and itching [4]. It is diagnosed clinically on the presence of at least two of the four nasal symptoms of sneezing, rhinorrhea, nasal obstruction, and itching, along with a relevant history of triggering factors and the presence of pale and gray nasal mucosa visible on anterior rhinoscopy. It is typically triggered by environmental allergens such as pollen, pet hair, dust mites etc. The impact and frequency of allergic diseases are often underestimated [5]. Antihistamines have been in clinical use for >70 years, and the pharmacological characteristics of these agents have been evolving over the time [6].

Mometasonefuroate and Fluticasone furoate nasal spray(FFNS), a glucocorticoid, both exhibit greater anti-inflammatory activity with longer duration of action and low bioavailability when administered intranasally in allergic rhinitis patients.

Hence the current study to find out the clinical results of bilastine, a new antihistamine that is highly selective for the H_1 histamine receptor. Most common reasons for patients to be dissatisfied with treatment for allergic rhinitis are inadequate symptom relief and bothersome side effects with intranasal corticosteroids [7].Currently, allergic rhinitis is an highly under diagnosed and undertreated condition with questionable compliance to the treatment and hence the present study is to compare the efficacy, safety and compliance of bilastine tablet, fluticasone and mometasone nasal spray in allergic rhinitis.

Methods

Study Design

This phase 3**,** an open label randomized interventional clinical trial was conducted in the department of Otorhinolaryngology (ENT) and department of Pharmacology, Indira Gandhi Medical College and Hospital, Shimla, which is a tertiary care institute in Himachal Pradesh and caters to the needs of the majority of the population of this state.

Patients

Patients aged 18–50 years of either sex, attending ENT OPD irrespective of type of allergic rhinitis were enrolled for the study after obtaining written informed consent.

Patients were excluded from the study if they had hypersensitivity to bilastine tablet, fluticasone and mometasone nasal spray, had acute or chronic sinusitis, chronic purulent postnasal drip, rhinitis sicca, atrophic rhinitis, rhinitis medicamentosa, nasal structure abnormalities, active pulmonary disorder including asthma, had a history of narrow-angle glaucoma, increased intraocular pressure, and posterior sub capsular cataract, patients with RBS of >140 mg/dL, serum transaminases of twice upper normal limit, serum bilirubin of ≥2.0 mg/dL, and /or serum creatinine ≥2.5 mg/dL, pregnant or lactating females, patients who had received the following medications in the given time frame: nasal/oral decongestants, nasal/antihistamines: 72 hours;nasal/inhaled corticosteroids, leukotriene receptor anatagonists, 5-lipoxygenase inhibitors, methylxanthines, nonprescription drugs: 7days; MOA inhibitors: 14 days; oral corticosteroids: 12 weeks.

Safety Assesment

The safety of the study medication were assessed by recording the vitals, adverse drug reaction and events occurring during the course of the study and at the end of the clinical trial including routine hematological and biochemical laboratory investigations hemoglobin, renal function test, liver function test. These investigations were available free of cost resulting in zero out of pocket expenditure from patient.

Efficacy Assessments

Efficacy values included SNOT-22. It is a validated patient-reported outcome tool used to delineate the presence and severity of sinonasal disorders and the impact of these on health-related quality of life. It assesses 22 symptoms, which are related to nasal, sleep quality, otologic, and/or emotional symptoms, on an integer scale of 0-"no problem", 1-"very mild problem," 2-"mild to slight problem," 3-"moderate problem," 4-"severe problem," or 5-"problem as bad as it can be." SNOT-22 questionnaire was completed for each patient on day 0 and then after end of 6 weeks.

Treatment compliance were assessed telephonically on regular basis and using Medication Adherence Rating Scale (MARS) questionnaire.

Patients who fulfilled the eligibility criteria were enrolled for the study and were subjected to focused history and physical examination as per structured questionnaire to record information. Patients satisfying the eligibility criteria were randomized in a 1:1:1 ratio, as per the 'Paper Chit System' randomization by preparing 240 chits of paper indicating schedule to receive either the bilastine tablet 20mg or fluticasone furoate 50mcg or mometasonefuroate 50mcg nasal spray. Patients allergic to bilastine, fluticasone, mometasone and/or any other drug of same class were excluded. SNOT-22 score was applied on the patients to assess the baseline symptomatology. Baseline lab investigations of absolute eosinophill count, hemoglobin, random blood sugar, renal function test, liver function test, nasal endoscopy and SNOT-22 score were documented. Thereafter, the patients were followed up regularly on weekly phone calls and diary maintained by the patients, with last scheduled visit after 6 weeks. Patients, as per the groups, were instructed to take two sprays of the study drug (nasal spray 50mcg) in each nostril twice daily and oral bilastine tablet 20mg at bedtime for 6 weeks, starting from the day of randomization. After 6 weeks of active treatment, the study drugs were withdrawn, lab investigations of hemoglobin, renal function test, liver function test were done and documented. SNOT-22 and Medication Adherence Rating Scale (MARS) questionnaire were completed.

Ethical approval and Clinical trial registration

The study was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines. The institutional ethical committee approved the protocol dated 16/08/23 No.HFW(MC-II)B(12)ETHICS/2020/15093. Written informed consent was obtained from all the participants. The clinicalTrials.gov Identifier is CTRI/2023/10/058841.

RESULTS

Study Population

Among total 240 patients, 101 were female patients. Among which 31 female patients were in bilastine group, 36 female in mometasone nasal spray group and 34 female were in fluticasone nasal group.

Out of 240 total patients, 139 were male patients. Among which 49 male patients were in bilastine group, 44 in mometasone nasal spray group and 46 female were in fluticasone nasal group.

Gender	Bilastine Tablet	Mometasone Nasal Spray	Fluticasone Nasal Spray	P value (Chi-Square)
Female	31	36	34	0.723
Male	49	44	46	

Efficacy

Comparison of SNOT-22 in different groups

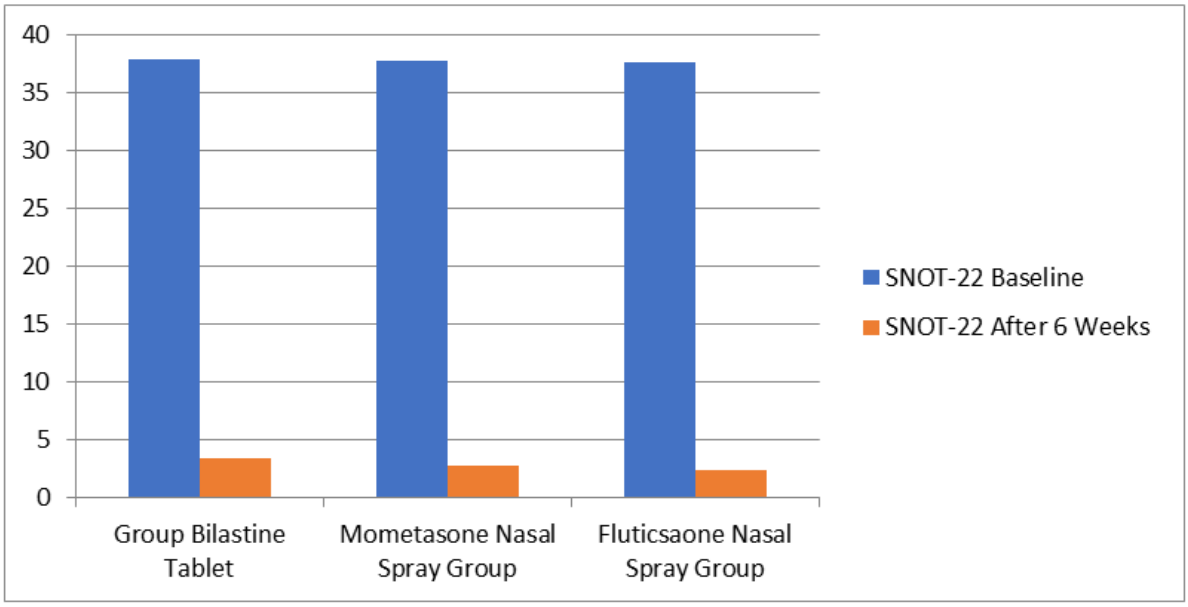


Figure: Comparison of SNOT-22 in different groups

SNOT-22	Group Bilastine Tablet Mean & Standard deviation	Mometasone Nasal Spray Group Mean & Standard deviation	Fluticsaone Nasal Spray Group Mean & Standard deviation	P value
SNOT-22 Baseline	37.85 ± 15.818	37.79 ± 11.829	37.68 ± 15.475	0.997
SNOT-22 After 6 Weeks	3.35 ± 7.388	2.8 ± 4.772	2.34 ± 5.116	0.552

SNOT-22 score has decreased in all the study groups which is significant (0.001). However, comparative P value for SNOT-22 before intervention was 0.997 in all the study groups and SNOT-22 post intervention was 0.552 which is statistically non-significant.

Baseline vitals in different study groups

Baseline Vitals	Bilastine Tablet Mean & Standard Deviation	Mometasone nasal Spray Mean & Standard Deviation	Fluticasone Nasal Spray Mean & Standard Deviation
Pulse	78.8 ±8.024	78.49 ± 8.624	79.61 ± 8.059
Respiratory Rate	13.93 ±1.230	14.14 ± 1.421	14.24 ± 1.334
Systolic Blood Pressure	124.35 ±10.137	124.18 ± 9.794	126.38 ± 10.583
Dystolic Blood Pressure	79.23 ±6.479	79.55 ± 6.482	81.73 ± 5.743

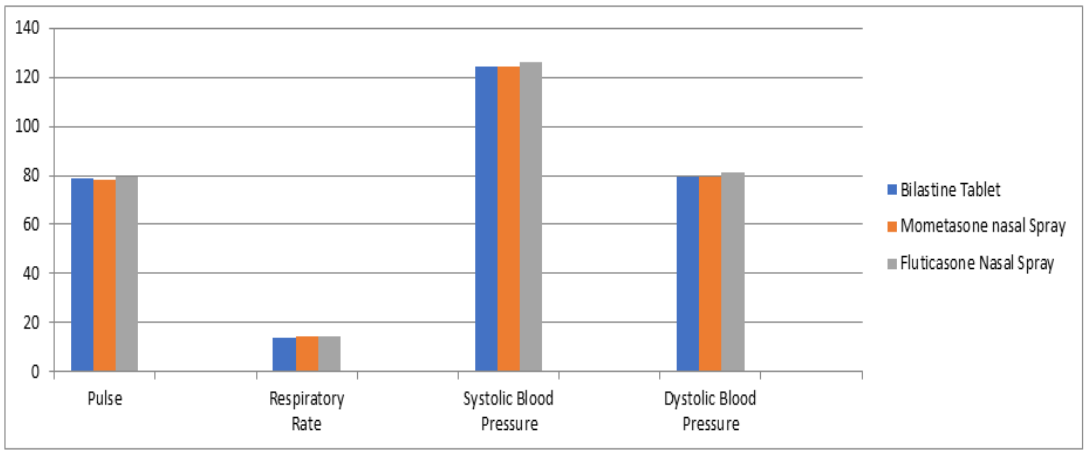


Figure: Baseline vitals in different study groups

After 6 weeks post intervention vitals in different study groups

After 6 weeks Post Intervention	Bilastine Tablet	Mometasone nasal Spray	Fluticasone Nasal Spray
Vitals	**Mean & Standard Deviation**	**Mean & Standard Deviation**	**Mean & Standard Deviation**
Pulse	77.83 ± 7.817	77.58 ± 9.644	80.33 ± 8.671
Respiratory Rate	13.94 ± 1.325	14.26 ± 1.329	14.05 ± 1.221
Systolic Blood Pressure	125.13 ± 10.791	124.33 ± 9.517	126.5 ± 10.803
Dystolic Blood Pressure	79.63 ± 6.188	79.83 ± 6.039	81.23 ± 6.344

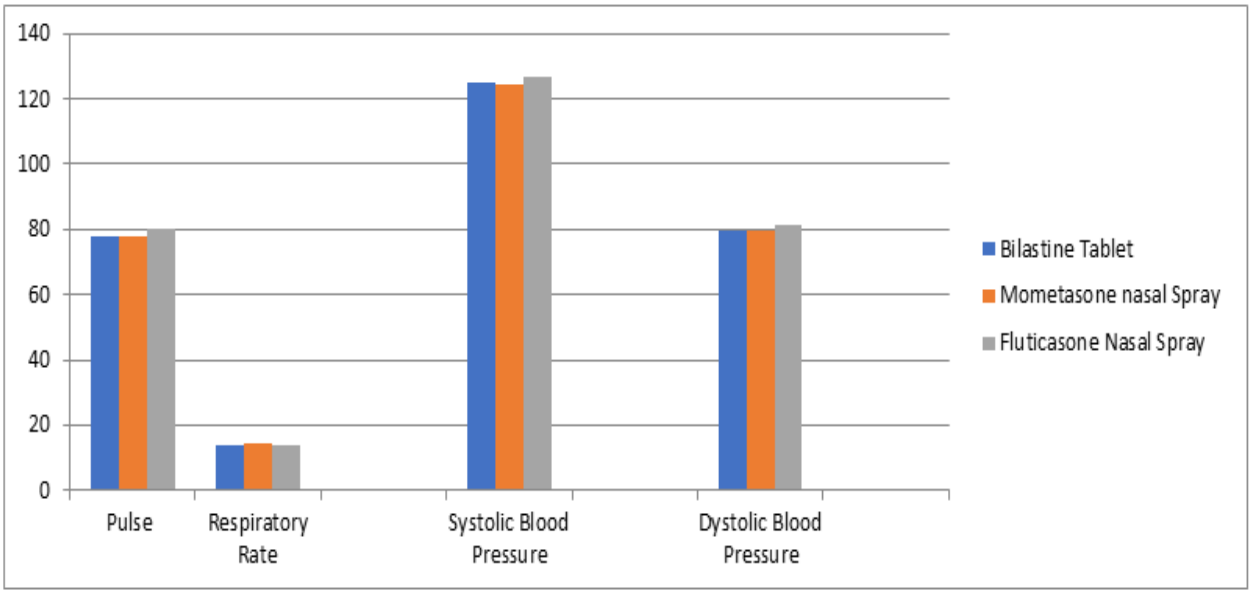


Figure: After 6 weeks post intervention vitals in different study groups

Laboratory tests baseline of the different study groups

Base line	Bilastine Tablet	Mometasone nasal Spray	Fluticasone Nasal Spray
Laboratory tests	**Mean & Standard Deviation**	**Mean & Standard Deviation**	**Mean & Standard Deviation**
Hemoglobin	12.441 ± 1.8246	12.374 ± 1.7621	12.235 ± 1.7126
SGPT	29.95 ± 12.859	30.26 ± 13.473	31.26 ± 10.809
SGOT	30.6 ± 9.192	30.78 ± 10.964	32.86 ± 12.325
Bilirubin	0.6824 ± 0.30235	0.6520 ± 0.30140	0.6842 ± 0.35413
Urea	25.634 ± 7.7148	25.197 ± 8.3394	26.388 ± 7.6481
Creatinine	0.6494 ± 0.22149	0.6712± 0.24919	0.6781 ± 0.23963

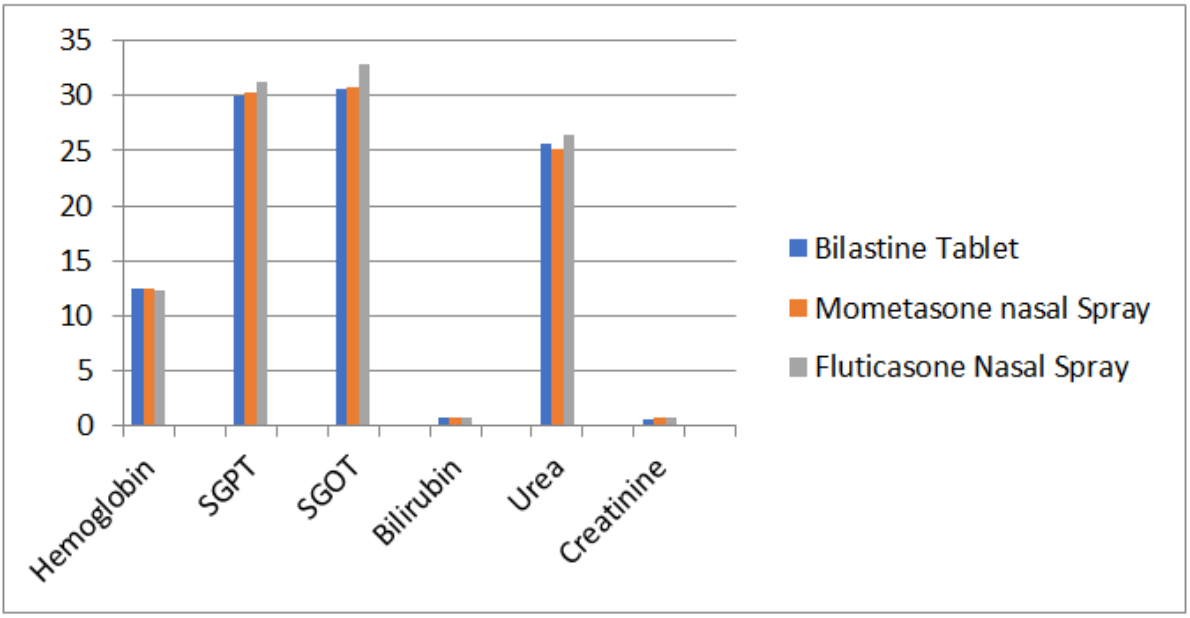
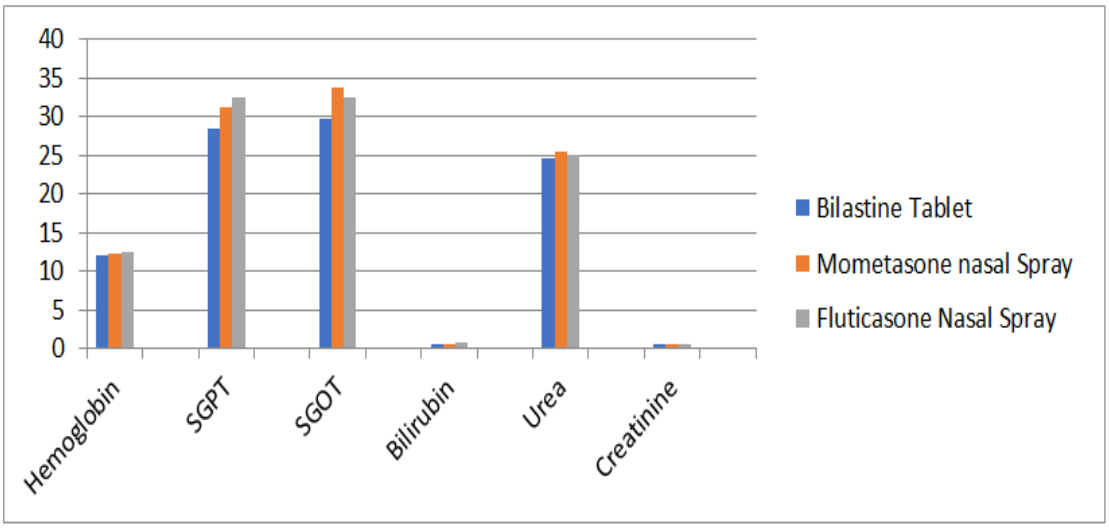


Figure: Laboratory tests baseline of the different study groups

Laboratory tests after 6 weeks post intervention vitals in different study groups

After 6 weeks Post Intervention	**Bilastine Tablet**	**Mometasone nasal Spray**	**Fluticasone Nasal Spray**
Laboratory tests	**Mean & Standard Deviation**	**Mean & Standard Deviation**	**Mean & Standard Deviation**
Hemoglobin	12.151 ± 1.695	12.355 ± 1.7548	12.455 ± 1.4175
SGPT	28.38 ± 12.958	31.16± 13.838	32.44 ± 14.175
SGOT	29.7 ± 10.177	33.65 ± 13.280	32.56 ± 13.755
Bilirubin	0.6841 ± 0.26516	0.6773 ± 0.26267	0.7174 ± 0.30448
Urea	24.649 ± 7.3293	25.563 ± 8.2090	25.1 ± 8.6794
Creatinine	0.6562 ± 0.22087	0.6851± 0.25138	0.6685 ± 0.24402



Absolute eosinophill count, mean & standard deviation among all study groups was 0.364 ± 0.166. It was done for confirmation of diagnosis, post intervention absolute eosinophill count was not done. Nasal smear eosinophill count was not done as it was not feasible. No ADR/AE reported.

Medication Adherence Rating Scale (MARS)
Compliance comparison among Bilatine tablet, Mometasone Nasal Spray and Fluticasone nasal Spray Group

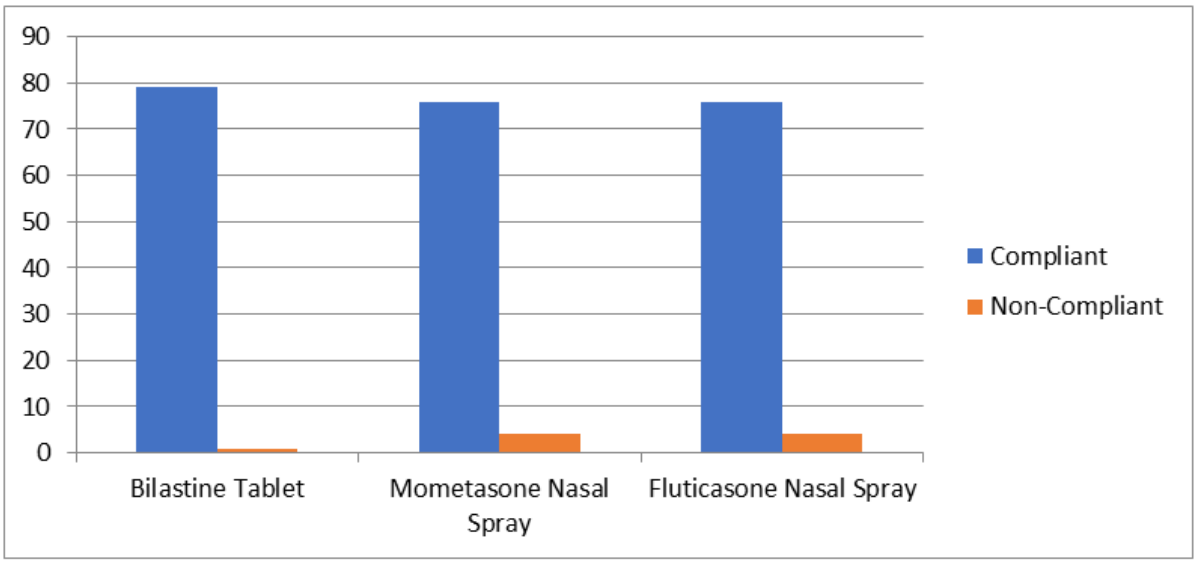


Figure: Compliance comparison different study groups

MARS	Bilastine Tablet	Mometasone Nasal Spray	Fluticasone Nasal Spray
Compliant	79	76	76
Non-Compliant	1	4	4
P value	0.354	0.289	0.213

Only 1 patient in bilastine and 4 in mometasone and fluticasone group were non-compliant.

DISCUSSION

In our awareness, present study is the only study which has compared oral antihistamine tablet bilastine, with intranasal corticosteroids (INCS), mometasone and fluticasone nasal spray. The present study was on Efficacy and Safety of bilastine tablet, fluticasone and mometasone nasal spray in allergic rhinitis.

Of the total of 240 patients, 101 were female of which 31 were in bilastine tablet group, 36 in mometasone nasal spray group and 34 were in fluticasone nasal group. Of the 139 male patients 49 were in bilastine group, 44 in mometasone nasal spray group and 46 in fluticasone nasal group a total of 80 patient in each group. The mean age of the patients in bilastine group was 34.65 $\pm$ 10.118 years, in mometasone nasal spray group was 34.9 $\pm$ 10.031 years, in fluticasone nasal group was 38.11 $\pm$ 9.374 years.

In study done by Mak*et al*., (2013) [10] different age groups were enrolled and, findings were consistent with our study. Ninty four perennial allergic rhinitis were randomly assigned to two treatment groups: anmometasone group and an fluticasone group. Treatment was provided for 4 weeks. A detailed TSS analysis showed mometasone to be more effective for relieving nasal symptoms, whereas FP was more effective for relieving non-nasal symptoms. Patient questionnaire scores suggested a significant reduction in symptoms for both the MFM ($P < 0.01$) and FP ($P < 0.01$) groups. In a study conducted by Aneeza, *et al*., (2013) [11] all measurements were taken at baseline and at 4 and 8 weeks of treatment. 63 patients who were randomized into the either mometasonefurate group (n=36) or fluticasone furoate group (n=27) completed the study. 76% patients had mild ocular symtoms, 20.5% had moderate symptoms and only 2.6% had severe symptoms at baseline based on the iTOSS; 65.1% had mild nasal symptoms and 3% had severe nasal symptoms. There was significant reduction in the symptom scores after 1 week ($p<0.05$). Both groups had significant improvement in RQOLQ scores after 1 month, which further improved at 2 months ($p<0.05$). The nasal dimensions also improved in both groups ($p<0.05$) but there was no statistically significant difference between groups. Both mometasonefuroate and fluticasone furoate are effective as single-modality treatment of allergic rhinitis.

SNOT-22 is a validated patient-reported outcome tool used to delineate the presence and severity of sinonasal disorders and the impact of these on health-related quality of life.; it considers both the severity and frequency of 22 individual symptoms. Individual items are scored on a 6-point scale, with a higher score indicative of greater impairment (ie, 0 = “no problem” and 5 = “problem as bad as it can be”). The total score is the composite of each of the 22 items, criteria used in study conducted by SF Weinstein *et al*., (2018) [10] and is indicative of overall sinonasal health (range, 0-110). Among the individual items of SNOT-22, the following items are typically associated with AR: postnasal discharge, nasal blockage, runny nose, and sneezing [13].

In our study, the reduction in SNOT-22 was statistically significant in all study groups. In bilastine tablet group the mean baseline (Before Intervention) SNOT-22 score was 37.85 ± 15.818. The mean decrease in SNOT-22 was to a level of 3.35 ± 7.388 after 6 weeks of post intervention (P value 0.001). In mometasone nasal spray group the mean baseline (Before Intervention) SNOT-22 score was 37.79 ± 11.829. The mean decrease in SNOTT-22 was 2.8 ± 4.772 after 6 weeks of post intervention (P value 0.001). In fluticasone nasal spray group the mean baseline (Before Intervention) SNOT-22 score was 37.68 ± 15.475. The mean decrease in SNOTT-22 was 2.34 ± 5.116 after 6 weeks of post intervention (P value 0.001).

In a study done by Okubo *et al*., (2017) [12]bilastine showed an overall favorable effect on relieving the symptoms of AR compared to placebo as measured by total symptom score, nasal symptom score, and non-nasal symptom score with 20mg bilastine for 2 weeks. In our study bilastine tablet was effective in reducing SNOT -22 score in allergic rhinitis over 6 weeks of post intervention.

However, in our study, the change in vitals and laboratory parameters in different study groups were statistically non significant (P>0.05) from baseline (before intervention) to after 6 weeks (post intervention). No ADR/AE reported during the period in all the study groups. Hence, bilastine tablet and newer generation intranasal corticosteroids mometasone and fluticasone nasal spray are safe to use. Previous studies done by Mandl*et al*., (1997) [13], Okubo ***et al***., **(2017) [12]** and Juvekar, *et al*., (2024) [14 has also confirmed the safety of bilastine tablet, mometasone nasal spray and fluticasone nasal spray in allergic rhinitis which is consistent with the result of our study.

In our study, out of 80 patients in bilastine study group 79 were compliant and 1 was non-compliant (1.3%). In mometasone nasal spray study group, 76 patients were compliant and 4 were non-compliant (5.0%) and of the total of 80 patients in fluticasone nasal spray study group, 76 patient were compliant and 4 were non-compliant (5.0%).

After 6 weeks of therapy with these three medications, shows them to be 100% efficacious and safety using more rigrous SNOT-22 testing with 22 symptom criteria. All study group shows improvement in SNOT-22 score after 6 weeks therapybut there was no statistically significant difference between groups. All three medications bilastine tablet, mometasone and fluticasone nasal spray are effective as single-modality treatment of allergic rhinitis. Bilastine tablet once daily is equally efficacious and safe to use as compared to twice daily regime of fluticasone and mometasone nasal spray. Compliance to intranasal corticosteroids, mometasone and fluticasone nasal spray is compromised as compared to oral anti histaminic tablet bilastine in allergic rhinitis. Hence therapy may be based on patient preference, convenience and cost.

REFERENCES

1. Björkstén, B., Clayton, T., Ellwood, P., Stewart, A., Strachan, D., & Phase III Study Group, T. I. (2008). Worldwide time trends for symptoms of rhinitis and conjunctivitis: Phase III of the International Study of Asthma and Allergies in Childhood. *Pediatric Allergy and Immunology*, *19*(2), 110-124.
2. Dykewicz, M. S., &Fineman, S. (1998). Executive summary of joint task force practice parameters on diagnosis and management of rhinitis. *Annals of Allergy, Asthma & Immunology*, *81*(5), 463-468.doi: 10.1016/S1081-1206(10)63152-3.
3. Lâm, H. T., VănTường, N., Ekerljung, L., Rönmark, E., &Lundbäck, B. (2011). Allergic rhinitis in northern vietnam: increased risk of urban living according to a large population survey. *Clinical and Translational Allergy*, *1*, 1-8.
4. Canonica, G. W., Bousquet, J., Mullol, J., Scadding, G. K., & Virchow, J. C. (2007). A survey of the burden of allergic rhinitis in Europe. *Allergy*, *62*, 17-25.
5. Pawankar, R., Canonica, G. W., Holgate, S. T., Lockey, R. F., &Blaiss, M. S. (2013). WAO white book on allergy: update 2013. Miwaukee, WI; world allergy organization; 2013.
6. Church, D. S., & Church, M. K. (2011). Pharmacology of antihistamines. *World Allergy Organization Journal*, *4*, S22-S27.
7. Katelaris, C. H., Lai, C. K., Rhee, C. S., Lee, S. H., De Yun, W., Lim-Varona, L., ... & Sacks, R. (2011). Nasal allergies in the Asian–Pacific population: results from the Allergies in Asia–Pacific Survey. *American journal of rhinology & allergy*, *25*(5_suppl), S3-S15.
8. Mak, K. K., Ku, M. S., Lu, K. H., Sun, H. L., &Lue, K. H. (2013). Comparison of mometasonefuroate monohydrate (Nasonex) and fluticasone propionate (Flixonase) nasal sprays in the treatment of dust mite-sensitive children with perennial allergic rhinitis. *Pediatrics& Neonatology*, *54*(4), 239-245. doi:10.1016/j.pedneo.2013.01.007
9. Aneeza, W. H., Husain, S., Rahman, R. A., Van Dort, D., Abdullah, A., &Gendeh, B. S. (2013). Efficacy of mometasonefuroate and fluticasone furoate on persistent allergic rhinoconjunctivitis. *Allergy & Rhinology*, *4*(3), ar-2013. doi:10.2500/ar.2013.4.0065
10. Weinstein, S. F., Katial, R., Jayawardena, S., Pirozzi, G., Staudinger, H., Eckert, L., ...&Teper, A. (2018). Efficacy and safety of dupilumab in perennial allergic rhinitis and comorbid asthma. *Journal of Allergy and Clinical*

Immunology, *142*(1), 171-177. doi: 10.1016/j.jaci.2017.11.051. Epub 2018 Jan 31. PMID: 29355679.

11. Salo, P. M., Calatroni, A., Gergen, P. J., Hoppin, J. A., Sever, M. L., Jaramillo, R., ...&Zeldin, D. C. (2011). Allergy-related outcomes in relation to serum IgE: results from the National Health and Nutrition Examination Survey 2005-2006. *Journal of Allergy and Clinical Immunology*, *127*(5), 1226-1235.
12. Okubo, K., Gotoh, M., Asako, M., Nomura, Y., Togawa, M., Saito, A., ...&Ohashi, Y. (2017). Efficacy and safety of bilastine in Japanese patients with perennial allergic rhinitis: a multicenter, randomized, double-blind, placebo-controlled, parallel-group phase III study. *Allergology International*, *66*(1), 97-105. doi: 10.1016/j.alit.2016.05.014. Epub 2016 Jul 14. PMID: 27421817.
13. Mandl, M., Nolop, K., Lutsky, B., & Participants in the 194-079 Study Group. (1997). Comparison of once daily mometasonefuroate (Nasonex) and fluticasone propionate aqueous nasal sprays for the treatment of perennial rhinitis. *Annals of Allergy, Asthma & Immunology*, *79*(4), 370-378. doi: 10.1016/s1081-1206(10)63030-x. PMID: 9357385.
14. Juvekar, M. R., Vaidya, G. K., Majumder, A., Pendharkar, A. D., Irudhayarajan, A., Kundu, A., ...& Mehta, R. T. (2024). A Real-World Observational Study to Evaluate the Safety and Effectiveness of Fluticasone Furoate–Oxymetazoline Fixed Dose Combination Nasal Spray in Patients with Allergic Rhinitis. *Clinical Drug Investigation*, *44*(2), 123-130. doi:10.1007/s40261-023-01338-8