Original Research Article

Comparative study of efficacy of intra nasal steroids in combination with antihistamines versus steroids alone as nasal spray in allergic rhinitis - Our experiences

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Abstract

Background: To study and compare the efficacy of intranasal steroids in combination with antihistamines and steroids alone as nasal spray in allergic rhinitis **Materials and Methods:** It is a open design prospective study done between January 2017 to April 2018 on patients of allergic rhinitis data collected from multiple centre. A detailed history was taken and clinical examination of patient was carried out. 100 patients were taken up for study, following ARIA guidelines we classified allergic rhinitis patients and on the clinical severity NOSE Scores were done. **Results:** Pre and post treatment NOSE scores evaluated, statistical significance was evidenced in NOSE score (0.0007429), absolute eosinophil count (0.001612). **Conclusion:** Based on our study Azelastine and fluticasone combination was far superior as assessed by NOSE score. p value of combination group was 0.00074.there was more rapid decline in the AEC in group with azelastine and fluticasone combination and it was well tolerated in adults and adolescence.

Key Words: Allergic rhinitis, intra nasal steroids, antihistamines, nose scores, aec.

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INTRODUCTION

Allergic rhinitis is a global health care problem affecting 10-30% adults.AR is a part of systemic inflammatory process and is associated with other inflammatory disorders including asthma, rhinosinusitis, allergic conjunctivitis. AR is immunoglobulin IgE mediated reaction in nasal mucosa caused by inhaled allergens ,such as pollen, mold, animal dander. It is characterised by nasal congestion, rhinosinusitis sneezing. AR reduces quality of life by affecting sleep, work, productivity and social life.due to it's high prevalence and impact on quality of life AR is considered as major health care problem. Prevalence can be undermined due to misdiagnosis, Underdiagnosis and failure of patient to seek medical attention. The treatment options include allergen avoidance, pharmacotherapy and immunotherapy. Available pharmacotherapy drugs are antihistamines, corticosteroids, decongestants, leukotrine receptor antagonists and anticholinergics. The objective of present study is to evaluate efficacy of nasal steroids alone and in combination with antihistamines.

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MATERIALS AND METHODS

Study Design: It is an open label, prospective study done between January 2017 to April 2018 on patients of allergic rhinitis, Data collected from multiple centres. Sample size: 50 for each drug. Data is recorded at ENT OPD by individual case report form.

Inclusion Criteria: All allergic patients with informed consent.

Exclusion Criteria: People who are already on treatment before the start of study.

Patients visiting the outpatient department of ENT at shadan institute of medical sciences, with symptoms of Allergic rhinitis are enrolled in the study. Written informed consent is taken from the individual and the nature of the study is explained. Once the patient is enrolled into the study, base line investigations like, Complete blood picture, absolute eosinophil count are done. Following ARIA guidelines we classified allergic rhinitis as intermittent or persistent according to the duration of symptoms, and as mild or moderate-severe depending on its severity. The patient is examined with the assessment scales for nasal congestion and obstruction using the Nasal obstruction Symptom Evaluation (NOSE) scale. The follow up is done for checking the alleviation of symptoms after 2weeks of start of the treatment like nasal rhinorrhea, sneezing, nasal obstruction, itching of eyes and nose, itching of posterior pharyngeal wall and dry cough. All the laboratory investigations were done at shadan institute of medical sciences. The end point of study is successful completion of 75 days of treatment. Scales: Nasal Obstruction Symptom Evaluation (NOSE) scale for the assessment of symptoms is given under table 1

Nose scale calculation:

Total score x 5: 0-100

None : 0

Medium : 0-50

Severe :50-100

Dosage:

Fluticasone alone in a dosage of (50mcg) per spray.

Fluticasone 50mcg and azelastine 140mcg per spray available in aerosol form. Administered 2puffs per day in each nostril.

RESULTS AND OBSERVATION

Age Distribution: The overall mean age for 100 subjects was 32.06 years, median was 30 years and mode was 46 years.

Gender distribution: out of total 100 subjects males were 53 and 47 were female.

Education: Majority of patients were found in the secondary level of education followed by primary and uneducated category.

Marital Status: Majority of the subjects in the sample were married.

Socio Economic Status: Most of the patients fall under lower socio economic status i.e. 36%.According to kuppuswamy scale all subjects were divided into following groups, 22 of the subjects fell under lower middle SES,36 subjects fell under lower SES.26 of the subjects fell under middle SES, and 16 of the subjects fall under upper middle SES. Nose score evaluation only for fluticasone nasal spray: It was found that 50 patients who have taken fluticasone nasal spray on day 0 i.e., before the drug was prescribed have NOSE scores in the range of around 70 to 95 median being around 85.(table 2) On the day 15 i.e.2weeks after the course was started there was a gradual decline in the score and the range was found to be around 70 to 85 median being around 75. On day 30 i.e,4 weeks after the course was started there was a gradual decline in the score and the range was found to be around 55 to 80 median being around 70. On day 45 i.e., 6 weeks after the course was started there was much decline in the score and the range was found to be around 45 to 75 median being around 60. On day 60 i.e., 8 weeks after the course was started there was still gradual decline in the score and range was found to be around 35 to 70 median being around 55. Finally on day 75 i.e. 10 weeks after the course was started there was a gradual decline in the score and the range was found to be around 25 to 60 median being around 40.(table 3) Nose score evaluation for combination of fluticasone and azelastine nasal spray: It was found that 50 patients who have taken combination of fluticasone and azelastine nasal spray on day 0 i.e. before the drug was prescribed have NOSE scores in the range of around 70 to 95 median being around 85.(table 2) On day 15 i.e., 2 weeks after the course was started there was a gradual decline in the score and the range was found to be around 70 to 85 median being around 75. On day 30 i.e., 4 weeks after the course was started there was a gradual decline in the score and range was found to be around 40 to 65 median around 55. On day 45 i.e., 6 weeks after the course was started there was a much decline in the score and the range was found to be around 30 to 55 median around 40. On day 60 i.e. 8 weeks after the course was started there was a still decline in the score and the range was found to be around 20 to 35 median around 25. Finally on day 75 i.e., 10 weeks after the course was started there was a gradual decline in score and range was found to be around 10 to 25 median around 15.(table 3) Complete blood picture of the patients taking fluticasone nasal spray: It was found that patients who were put on fluticasone nasal spray before the start of treatment 30 subjects i.e. 60 % have eosinophilia along with lymphocytosis and remaining 20 subjects i.e. 40 % have only eosinophilia in their blood picture. After the

end of treatment it was found that patients who were put on fluticasone nasal spray 33 subjects i.e. 66 % were totally normal and remaining 17 subjects i.e. 34 % have only lymphocytosis in their blood picture. Complete blood picture of patients taking fluticasone and azelastine nasal spray combination: It was found that patients who were put on fluticasone and azelastine nasal spray combination before the start of treatment 34 subjects i.e. 68 % have eosinophilia along with lymphocytosis and remaining 16 subjects i.e. 32% have only eosinophilia in their blood picture. After the end of treatment it was found that patients who were put on fluticasone nasal spray 39 subjects i.e. 78% were totally normal and remaining 11 subjects i.e. 22% have only lymphocytosis in their blood picture. Absolute eosinophil count (AEC) evaluation for fluticasone nasal spray: It was found that 50 patients who have fluticasone on day 0 i.e. before the drug was prescribed have absolute eosinophil count (AEC) in the range of around 450 to 600 median being around 460.(table 4) On day 15 i.e. 2 weeks after the course was started there was a gradual decline in the AEC and the range was found to be around 400 to 520 median being around 450. On day 30 i.e. 4 weeks after the course was started there was a gradual decline in the AEC and the range was found to be around 350 to 500 median being around 400. On day 45 i.e., 6 weeks after the course was started there was a much decline in the AEC and the range found to be around 300 to 480 median being around 380. On day 60 i.e,8 weeks after the course was started there was still a gradual decline in the AEC and the range was found to be around 220 to 440 median being around 320. Finally on the day 75 i.e. 10 weeks after the course was started there was a gradual decline in the AEC and the range was found to be around 200 to 430 median being around 300.(table 5) Absolute eosinophil count (AEC) evaluation for fluticasone and azelastine nasal spray: It was found that 50 patients who have fluticasone and azelastine combination on day 0 i.e., before the drug was prescribed have AEC in the range of around 360 to 580 median being around 480.(table 4) On day 30 i.e. 4 weeks after the course was started there was a gradual decline in the AEC and the range was found to be around 250 to 430 median being around 350. On day 45 i.e. 6 weeks after the course was started there was a much decline in the AEC and range was found to be around 200 to 380 median being around 300 On day 60 i.e. 8 weeks after the course was started there was still gradual decline in the AEC and the range was found to be around 120 to 320 median being around 200. Finally on day 75 i.e.10 weeks after the course was started there was a gradual decline in AEC and the range was found to be around 100 to 230 median being around 180 (table 5)

Table 1: Nasal obstruction symptoms evalutation scale

	Not a problem	Very mild problem	Moderate problem	Fairly bad problem	Severe problem
1. Nasal congestion or stuffiness	0	1	2	3	4
2. Nasal blockage or obstruction	0	1	2	3	4
3. Trouble breathing through nose	0	1	2	3	4
4.Trouble sleeping	0	1	2	3	4
5.Unable to get enough air through nose during exercise/exertion	0	1	2	3	4

Table 2: Base line NOSE score (day 0) (Table 2)

NOSE score	Sample size	Mean	Standard deviation
Fluticasone only	50	84.7	6.6555
Fluticasone and Azelastine	50	84.5	5.9974

P=0.46889

The base line scores in both groups is comparable and no statistically significant score was observed in both the groups after applying two sample independent t-test

Table 3: NOSE score after 10 weeks (day 75) (Table 3)

NOSE score day 75	Sample size	Mean	Standard deviation
Fluticasone only	50	44.8	7.7565
Fluticasone and Azelastine	50	20.2	4.7337

P =0.0007429

After the end of treatment (75 days) NOSE score on both groups is comparable and statistically significant score was observed in both the groups as p value was found to be 0.0007429,($p<0.005$) This signifies combination of fluticasone and azelastine is superior in terms of alleviation of symptoms.

Table 4: Base line AEC (DAY 0)

AEC DAY 0	Sample size (N)	Mean	Standard deviation
Fluticasone only	50	515.64	4698.45
Fluticasone and azelastine	50	471.86	51.1768

P=0.5519

Table 5: AEC (DAY 75)

AEC DAY 75	Sample size (N)	Mean	Standard deviation
Fluticasone only	50	280.8	51.9057
Fluticasone and azelastine	50	163.34	32.7486

P = 0.00161210

After 75 days of treatment AEC in both groups is comparable and statistically significant score was observed in both the groups after applying two sample independent t- test and p value was found to be 0.001612($p<0.005$).This signifies that after the completion of treatment for a specified period of 10 weeks the combination of azelastine and fluticasone was far better in decreasing the AEC.

DISCUSSIONS

In present study conducted on one hundred patients on allergic rhinitis whether fluticasone propionate intranasal steroids to a combination of fluticasone and azelastine nasal spray, several parameters were considered including age, gender, education, marital status, socioeconomic status, NOSE score, CBP, and AEC. This is an open labelled study. there was no control group or a placebo group. Baseline NOSE score was recorded after the diagnosis of allergic rhinitis is established and treatment was started with fluticasone nasal spray for 50 subjects and a combination of fluticasone and azelastine nasal spray in another 50 subjects where alleviation of symptoms was more with combination of fluticasone and azelastine nasal spray using NOSE score. These findings were similar to a study conducted by wood *et al*[36,] in monash university the effectiveness of INS vs oral antihistamines on nasal symptoms, eye symptoms, and nasal resistance, whenever results were reported.INS produce greater relief of nasal blockage than did oral antihistamines.INS produce greater relief of nasal discharge than did oral antihistamine.INS were also more effective in sneezing. though our study did not involve any oral antishistamine. In the current study combination spray with AzeFlu was found to be far superior than the individual which is in accordance with a study conducted by Klimek *et al*[18] where it was found that the superiority of AzeFlu over AZE and FP was seen for each individual symptoms of the rhinitis, and the onset of action of AzeFlu was rapid, within 30 minutes. AzeFlu also provided clinically important in the health related quality of life. post hoc efficacy analyses of the extent of response and time to response showed that more patients treated with AzeFlu achieved greater improvements compared to patients treated with AZE or FP, and perhaps more importantly, achieved these response significantly faster. This was an open label, multicenter study in Germany that included 1781 patients with AR, treatment with AzeFlu resulted in higher response rates than seen in the double blind trials[18.] Similar findings were found in a study conducted by Ratner *et al*[19].proof of concept study showed that azelastine nasal spray and fluticasone nasal spray in combination provided a substantial therapeutic benefit for patients with SAR(seasonal allergic rhinitis) compared with therapy with either agent alone. However in our study the results showed that azelastine nasal spray and fluticasone nasal spray in combination provided significant benefit compared with fluticasone alone. Moreover in our study the combination nasal spray was compared only with fluticasone alone but in the study conducted by Ratner *et al*, combination was compared with both azelastine and fluticasone independently and there was no particular focus on SAR Safety in long and short term trials in adults and adolescence: In the present study the age range was from 7yrs to 62 yrs and the younger age population from the age of 7 to 20 were 18 in number. The study conducted was a short term one i.e. 75days, safety and efficacy was well established with no adverse reactions were reported as nasal administration was clearly demonstrated and most of the subjects were adults none of the patients developed epistaxis, bitter taste because of clear method of administration of nasal spray.This is in accordance with the review conducted by Bousquet J *et al*.[20], included SAR patients 12 years and older with moderate/severe disease treated for 14 days. within this time frame, AzeFlu was well tolerated. The number of adverse events reported by patients was low in all active groups, with dysgeusia most often reported in the AzeFlu and AZE groups and epistaxis more commonly reported in the FP group. These events were usually mild in intensity and transitory in nature. Bitter taste is a common side effect with AZE nasal spray however proper administration of the nasal spray will enable retention of the medication in the nasal mucosa and reduce the potential for taste problems[20]. Similarly in a study conducted by Berger WE *et al*.,[21] which was a long term study conducted outside of the US and showed that AzeFlu was well tolerated after 1 year of continuous use, eith no safety signal, this would preclude its long term use[21] and similar findings as compared to our study was seen in a study conducted by Klimek L *et al*[22] The safety of Azeflu in adults and adolescents has been comprehensively reviewed[22].

Oral vs intranasal antihistamines: In current study the combination of antihistamine, azelastine and intranasal steroid, fluticasone was used and compared with

fluticasone INS alone which showed increased clinical benefit with the combination nasal spray and oral antihistamines were not used. This is in accordance with the study conducted by Weiner *et al* [23], with oral antihistamines in combination with intranasal corticosteroids showed no increased clinical benefit with these drugs in combination. Onset of action of Azelastine vs INS In the current study the efficacy of combination was far better with the combination of azelastine and fluticasone nasal spray, it was evident statistically only at the end of the study i.e, after 75 days. Hence the onset of action showed significant p-value <0.005 only at the end of 75 days. However with the study conducted y Berkowitz *et al*[24], it showed azelastine has a faster onset of action compared with INS in patients of SAR. The resson for lack of evaluation of onset of action is because in our study combination of azelastine and fluticasone was used. Hence onset of action could not be attributed to individual drug.

Conclusion and limitations

CONCLUSIONS

Based on our study it appears azelastine and fluticasone combination was far superior as assessed by NOSE score P value of the combination group was 0.00074. Efficacy of the combination group was found to statistically significant on 75th day**.** Both the groups were found to have no eosinophilia at end of study. There was more rapid decline in AEC in the group with Azelastien and fluticasone combination i.e. p value was found to ebe 0.0016 There was no much difference in CBP in both groups**.** It was found that combination was well tolerated in adults and asolescence

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