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Internal Medicine Section

Comparison of Oral Montelukast and Intranasal Fluticasone in Patients with Asthma and Allergic Rhinitis

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ABSTRACT

Introduction: Even though the links between upper and lower airway had been of interest to clinicians since long back, it has not attracted the attention of the researchers till recent past. But the evidence is still far from conclusive, due to limited number of randomized controlled trials available on subjects with concomitant allergic rhinitis and asthma. This gap in the knowledge is even more conspicuous in Indian population.

Aim: The current study is conducted with an objective of comparing the efficacy and tolerability of intranasal Fluticasone and oral Montelukast in treatment of allergic rhinitis and bronchial asthma.

Materials and Methods: The study was a prospective randomized, single blinded, comparative, parallel group study, with two intervention groups conducted in a tertiary teaching hospital in Chennai, Southern India. One hundred and twenty patients diagnosed with concomitant diagnosis of allergic rhinitis and bronchial asthma was randomly allocated to either Fluticasone propionate aqueous nasal spray or oral Montelukast group.

Results: Out of total 120 subjects recruited, 108 subjects were included in the final analysis. The mean reduction in asthma and rhinitis symptom scores and improvement in PEFR was higher for Group A, compared to Group B during all the follow-up periods. No statistically significant difference was observed in proportion of subjects reporting exacerbations in the current study. Both the treatments were well tolerated.

Conclusion: Addition of intranasal Fluticasone propionate to Salmeterol plus Fluticasone is beneficial in improving asthma control, allergic rhinitis control and lung functions as compared to oral Montelukast. Thereby the use of intranasal Fluticasone Propionate in comparison to oral Montelukast in control of Allergic Rhinitis is justified as per the significant improvement in outcome measures.

Keywords: Intra nasal steroids, Leukotriene antagonists, Nasobronchial allergy

INTRODUCTION

Even though the links between upper and lower airway had been of interest to clinicians since long back, it has not attracted the attention of the researchers till recent past. The "Allergic Rhinitis and its Impact on Asthma (ARIA)" workshop conducted in 1999 has clearly outlined study of inter relationship of allergic rhinitis and asthma and impact of treating Rhinitis in asthma control as important research priorities [1]. Since then many studies from across the globe have proved a strong association between upper airway and lower airway diseases [2-5]. Many studies have attempted to explore possible similarities and differences in pathophysiologic mechanism of upper and lower airway disease [5,6].

Wide range of pharmacological substances and their combinations, administered through various routes have been evaluated for their efficacy in allergic rhinitis and asthma individually [7-13]. The therapeutic implications of strong association between upper and lower airways have been explored by very few studies [14-18]. Subsequent ARIA updates and other reviews have made an attempt to summarize the diagnostic and therapeutic implications of this link based on these published evidence [2,19]. But the evidence is still far from conclusive, due to limited number of randomized controlled trials available on subjects with concomitant allergic rhinitis and asthma. This gap in the knowledge is even more conspicuous in Indian population.

The aim of the current study was to compare the efficacy of intranasal Fluticasone and oral Montelukast in treatment of allergic rhinitis and bronchial asthma and also to compare the adverse effects of intranasal Fluticasone and oral Montelukast therapy in patients with allergic rhinitis and asthma.

MATERIALS AND METHODS

Study design: The study was a prospective randomized, single blinded, comparative, parallel group study, with two intervention groups.

Study site: This study was conducted in a tertiary teaching hospital in Chennai, Southern India.

Study period: The study was conducted from March 2013-March 2014.

Study population: Patients diagnosed with concomitant diagnosis of Allergic Rhinitis (According to ARIA guidelines) and Bronchial Asthma (according to GINA guidelines), randomly allocated to the following intervention groups.

Group A: Fluticasone propionate aqueous nasal spray, 200µg one spray in each nostril twice daily.

Group B: Montelukast tablets 10mg in the night time.

Inclusion and exclusion criteria: Participants of both genders, aged between 15 –65 years were included in the study. Smokers, pregnant women, people with life threatening/chronic persistent

severe asthma, chronic respiratory illnesses like bronchiectasis, pulmonary tuberculosis and other obstructive airway disease were excluded from the study. The other exclusion criteria included, recent nasal surgery or anatomic defects of the nose, recent two courses of parenteral steroids within 3 months of screening and presence of any co-morbid systemic illness which may affect the assessment directly or indirectly.

Sample size: A total of 120 participants were randomly allocated to both the intervention groups, with 60 subjects in each group.

Random sequence generation: The participants were randomly allocated to one of the two intervention groups by pre-determined computer generated random number sequence using IBM SPSS software version 21 [20].

Allocation concealment: Sequentially Numbered, Opaque Sealed Envelopes (SNOSE) method as described by Doig G.S. et al., has been used for allocation concealment in the study [21]. The allocated intervention sequence was kept in individual, serially numbered sealed opaque covers and was kept under the custody of an independent statistician. The card board with the intervention name was covered with a silver foil to prevent the visibility. Each time when the participant was recruited the opaque cover was opened and the intervention was communicated to the investigator.

Blinding: The study participant blinding could not be achieved, as the route of administration of two interventions were different. The investigator assessing the treatment outcome and the person analysing the data were blinded for the intervention.

Ethical considerations: Ethics approval was obtained from institute Human Ethics Committee. Informed written consent was sought from all the patients, after thoroughly explaining the study objectives, nature of the intervention, risks and benefits of the intervention to the participants. Complete voluntary nature of participation in the study was explained and no undue pressure or coercion was exerted on the patients. Patients were informed that, they are free to withdraw from the study at any point during the course of the trial. Confidentiality of the study participants was maintained throughout the conduction, analysis and reporting of the study findings.

Study procedure: Asthma screening procedure: After obtaining an informed consent, included patients entered a 7 day run in period to document the coexistence of asthma and rhinitis. During this period patients continued their pre study medications and reliever medications as needed for asthma symptoms throughout the study. Asthma symptoms were evaluated using a 1 to 4 point Likert scale, with 1 representing no symptoms to 4 representing severe symptoms, to allow a minimum score of 5 to a maximum score of 20. In addition PEFR monitoring and PFT evaluation was done.

Rhinitis screening procedure: Allergic Rhinitis symptoms were evaluated using a Likert 4 point scale from 1 to 4, with 1 representing no symptoms and 4 representing severe symptoms, for both nasal and non-nasal symptoms of allergic rhinitis. Adding the two scores together gave the total allergic rhinitis score, to allow a minimum score of 12 to a maximum score of 48.

Run in period: It was taken care that patients had not been using any anti-inflammatory medications to control nasal symptoms for 4 weeks prior to or at any time during the study. Additional medications were excluded upto 4 weeks prior to screening and throughout the study including intranasal or ocular cromolyn, short and long acting antihistaminics, nasal decongestants and intranasal anticholinergic. All patients having used the above said medications had extended run in period of 4 weeks of drug free interval with Fluticasone/Salmeterol 125/50 µg for control of Bronchial Asthma.

Out of 142 patients screened, 120 patients who met the eligibility criteria were randomly assigned in to one of the two intervention groups. Sixty patients of Group A received Fluticasone propionate aqueous nasal spray, 200 µg 1 spray in each nostril twice daily. Sixty patients of Group B received Montelukast tablets 10 mg in the night time. All prestudy asthma medications were stopped and all patients of both groups received Fluticasone/Salmeterol combination (125/50 µg) 2 puffs twice daily for 3 months for control of Bronchial Asthma. All patients included in the study underwent a detailed evaluation as per a standard Performa which included spirometry, and peak expiratory flow rate measurement. Drug therapy for allergic rhinitis was stopped after a period of 2 months (60 days). All patients were followed up at intervals of 1 month (Day 30), 2 months (Day 60), and 3 months (Day 90). At each follow-up patients were subjected to objective assessment by peak expiratory flow rate measurement and subjective assessment by questionnaire to assess the symptoms, effect of therapy and appearance of adverse effects if any, in addition to documenting states of exacerbations of both Allergic Rhinitis and Bronchial Asthma. At the end of the study duration the data collected using the questionnaires and the objective assessments was subject to statistical analysis as outlined below.

STATISTICAL ANALYSIS

IBM SPSS statistical software version 21.0 was used for statistical analysis. Clinical symptom scores and PEFR during different follow up periods were taken as primary outcome variables. The two intervention groups were taken as primary explanatory variable. Descriptive analysis of all the explanatory and outcome parameters was done. All the categorical variables were presented in frequencies and percentages. The numerical variables were presented in Means and Standard deviations. The quantitative parameters were checked for normal distribution, using visual inspection of histograms and normal Q-Q plots and also by Skewness and Kurtosis z- values. The Socio demographic variables like age and gender, baseline clinical variables like symptoms and PFT parameters were compared between the two intervention groups, by appropriate cross tabulations. The association between explanatory and outcome parameters was assessed by calculating mean differences and differences in the proportions. Independent sample t-test and chi-square test (Fisher's-exact test) were used appropriately to assess the statistical significance of these associations and 95% Confidence intervals were also calculated for all the parameters. The loss to follow up was 8.3% and 11.6% respectively in group A and B respectively. The analysis of reasons for loss to follow up was totally unrelated to the disease condition, hence least likely to affect the final outcome of the study.

RESULTS

Out of eligible 120 patients, 12 patients dropped out (Group A-5, Group B-7) and 108 patients were included for analysis. Group A -Fluticasone propionate aqueous nasal spray 200µg (n=55) and Group B - Montelukast tablets 10 mg HS (n=53).

Baseline parameters: The baseline sociodemographic, clinical and pulmonary function parameters were comparable between the two study groups. Mean age of patients in Group A being 33.25 years while in Group B being 34.09 years. Male to female distribution in the two groups was comparable. The baseline respiratory function parameters including FEV_1 (73.500 ±20.528 in Group A and 77.643±22.434 in Group B) and Post Bronchodilator reversibility (i.e. the increase noted in the FEV_1 which was used as a criteria for diagnosis of asthma) were also comparable [Table/Fig-1]. The mean reduction in asthma and rhinitis symptom scores was higher for group A, compared to group B during all the follow-up periods. This difference in the mean reduction in scores at 30 day follow up period was only minimal between the two groups and was statistically significant only for the acute total score and

respiratory total score. The difference was higher and statistically significant during 60 day follow-up period for all the scores. The difference in the score reduction between the groups again reduced at 90 day follow up period compared to 60 day follow up period and was not statistically significant [Table/Fig-2].

Parameter	Group A (n=55)	Group B (n=53)	p-value
I. Sociodemographic variables			
Age (Mean± SD)	33.25±12.04	34.09±11.67	0.71
Males (n (%))	27(49.1%)	31(58.5%)	0.32
Female (n (%))	28(50.9%)	22(41.5%)	
II. Baseline Symptom Scores & PEFR			
Acute Total score(Mean± SD)	13.46±3.54	13.19±3.24	0.13
Respiratory Total score Nasal 0(Mean± SD)	10.64±2.89	9.70±3.26	0.11
Respiratory non nasal total score 0(Mean± SD)	10.78±2.94	10.72±2.38	0.90
Peak Expiratory Flow Rate(Mean± SD)	302.18±82.45	295.85±97.71	0.71
III. PFT parameters			
FEV_1/FVC(Mean± SD)	83.79±12.43	86.51±12.25	0.25
FEV_1 (Mean± SD)	73.50±20.53	77.64±22.43	0.31
FVC(Mean± SD)	72.28±18.25	75.69±19.08	0.34
Reversibility(Mean± SD)	17.81±11.81	15.83±10.62	0.55

[Table/Fig-1]: Comparison of all the baseline parameters in two study groups (n=108).

Parameter	Group	Mean	Mean difference	p-value	95% CI	
					Lower	Upper
I. Asthma Symptom Score						
Difference 30 days	Group A	6.20±3.27	0.747	0.248	-0.529	2.024
	Group B	5.45±3.41				
Difference 60 days	Group A	8.20±4.85	2.823	0.005	0.886	4.759
	Group B	5.38±5.29				
Difference 90days	Group A	8.38±4.13	0.967	0.200	-0.520	2.454
	Group B	7.42±3.63				
II. Rhinitis Nasal Symptom Score						
Difference 30 days	Group A	4.20±2.96	1.860	0.004	0.612	3.109
	Group B	2.34±3.56				
Difference 60 days	Group A	4.54±4.04	3.262	0.000	1.597	4.928
	Group B	1.28±4.67				
Difference 90days	Group A	3.02±3.67	0.5465	0.417	-0.784	1.877
	Group B	2.47±3.27				
III. Rhinitis Non Nasal Symptom Score						
Difference 30 days	Group A	4.38±3.11	0.891	0.139	-0.294	2.076
	Group B	3.49±3.09				
Difference 60 days	Group A	4.51±4.21	1.434	0.054	-0.023	2.890
	Group B	3.08±3.35				
Difference 90days	Group A	3.65±3.85	-0.57187	0.366	-1.820	0.676
	Group B	4.23±2.52				
IV. Rhinitis Total score						
Difference 30 days	Group A	8.82±4.82	2.988	0.004	0.955	5.021
	Group B	5.83±5.80				
Difference 60 days	Group A	9.64±5.51	5.278	0.000	2.811	7.745
	Group B	4.36±7.32				
Difference 90days	Group A	7.31±5.75	0.517	0.617	-1.526	2.559
	Group B	6.79±4.89				

[Table/Fig-2]: Comparative analysis of changes in various symptom scores between the two studies groups using independent sample t-test (n=108).

The mean improvement in PEFR values was higher in group A compared to group B during 30 day and 60 day follow-up periods. The difference between two Groups at 30 day follow-up period was very minimal (2.84 L/min) and was statistically not significant. The difference in improvement in PEFR was highest during the 60 day follow-up period and was statistically significant. The difference at 90 day follow-period was more in group B and was statistically not significant [Table/Fig-3].

Exacerbations: The frequency of acute exacerbations was more in group B compared to Group A during 30 day and 60 day follow-up periods and was more in Group A at 60 day follow up period. The frequency of acute exacerbations was very less during 90 days follow-up and not statistically significant. The overall frequency of acute exacerbations was higher in Group B compared to Group A [Table/Fig-4].

Adverse Effect Profile: In Montelukast group there were 10 (18.9%) participants reported headache and 7(13.2%) of the patients reported GI disturbances at 30 and 60 day follow up periods. There were no adverse events reported at 90 day follow up period in this group. In Fluticasone group the most commonly reported adverse effects were nasal irritation, throat infection, sneezing and headache but by lesser number of subjects. All these adverse effects were reported more during the 60 day follow up period [Table/Fig-5].

Improvement in PEFR	Group	Mean	Mean difference	p-value	95% CI	
					Lower	Upper
At 30 day follow-up	Group A	59.63±52.77	2.844	0.79	19.08	-24.77
	Group B	56.74±61.97				
At 60 day follow-up	Group A	93.27±106.84	39.311	0.05	1.49	80.11
	Group B	53.96±107.01				
At 90 day follow-up	Group A	76.54±83.95	-11.002	0.49	42.59	-20.59
	Group B	87.54±81.56				

[Table/Fig-3]: Comparative analysis of changes in PEFR values between the two study groups using independent sample t-test. (n=108).

Parameter	Group (n=55)	Group B (n=53)	p-value (Fisher-exact test)
Acute Exacerbation 0	0 (0.0%)	0 (0.0%)	-
Acute Exacerbation 30 days	2(3.6%)	3 (5.7%)	0.67
Acute Exacerbation 60 days	3 (5.5%)	8 (15.1%)	0.12
Acute Exacerbation 90 days	2 (3.6%)	0 (0.0%)	0.49
Acute Exacerbation total	8(14.5%)	11(20.8%)	0.5

[Table/Fig-4]: Comparison of acute exacerbation with different durations in two study groups (n=108).

Adverse effect	Montelukast n(%)			Fluticasone n(%)		
	Day 30	Day 60	Day 90	Day 30	Day 60	Day 90
Headache	10(18.9)	10(18.9)	0(0)	2(3.6)	2(3.6)	1(1.8)
Throat Infection	0(0)	0(0)	0(0)	2(3.6)	4(7.2)	2(3.6)
Nasal Irritation	0(0)	0(0)	0(0)	2(3.6)	5 (9.0)	1(1.8)
Sneezing	0(0)	0(0)	0(0)	1(1.8)	2(3.6)	2(3.6)
Cough	0(0)	0(0)	0(0)	1(1.8)	1(1.8)	1(1.8)
Skin Rash	0(0)	0(0)	0(0)	0(0)	1(1.8)	0(0)
GI disturbance	7 (13.2)	7 (13.2)	0(0)	0(0)	0(0)	0(0)

[Table/Fig-5]: Descriptive analysis of the adverse effects in both the study groups (n=108).

DISCUSSION

Control of Asthma Symptoms: In this study one of the primary end points was to evaluate the effect of good rhinitis control exerting an indirect controlling effect on asthma control and the lasting effect of intranasal steroids as compared to oral leukotriene antagonists if any. In this study it was observed that asthma control displayed

by a higher difference in baseline to follow-up symptom score was more significant in the intranasal Fluticasone as compared to Montelukast at Day 60. Although not statistically significant, a carryover effect was noted for asthma symptom control in both the groups between day 60 and 90 (post withdrawal of the rhinitis drug). The symptom score at Day 90 was consistently lower than baseline.

In a similar design study conducted by Nathan et al., on 1551 patients no significant differences were reported for asthma control from baseline to follow-up, furthermore no difference in improvements between Fluticasone and Montelukast groups were noted [22]. However this mentioned study did not make use of any standard LABA/ ICS combinations for the treatment of Asthma symptoms and only as and when required SABA was used for treatment. This could be the probable reason for the improved asthma control in the present study. Studies by Day J and Nathan RA et al., T Carrillo, Di Lorenzo G et al., and Maspero J et al., have reported improved therapeutic outcomes with fluticasone and other steroids, given as nasal spray [22-25]. But most of these studies have not done any comparative analysis with oral monteleukast. Studies by Reed et al., and Watson et al., also reported similar findings in their study utilizing intranasal administration of steroids [26,27].

But in their Cochrane data base review of 14 trials, Taramarcaz P et al., concluded that "Intranasal corticosteroids were well tolerated. While INCS tended to improve asthma symptoms and forced expiratory volume in one second, the results did not reach significance [28]. They have suggested intranasal and intrabronchial corticosteroid combination as main stay of treatment pending further evidence.

Control of nasal symptoms: The current study shows, significantly enhanced improvements in Rhinitis nasal symptom score at all follow ups in the intranasal Fluticasone group as compared to the groups of patients treated with oral Montelukast. It is evident from the data that there is some sustained activity of both drugs with clinical supremacy of Fluticasone even after withdrawal of the drugs. These findings concur with the findings of Nathan et al., who reported clinical superiority of nasal Fluticasone with Salmeterol/ Fluticasone combination over Montelukast in combination with Salmeterol/Fluticasone and placebo Salmeterol/ Fluticasone combination over a period of 4 weeks [22]. Weiner et al., established the superiority of intranasal steroids even over antihistamines in controlling the nasal symptoms like sneezing, runny nose, blocked nose, and nasal itch [29]. As per the ARIA guidelines also recommend intra-nasal steroids as the treatment of choice in patients presenting with predominantly symptoms of nasal congestion [19].

Control of non nasal symptoms: A significant improvement in the non nasal symptoms of allergic rhinitis was observed in both the treatment arms when compared to baseline. However after withdrawal of the drugs we observed a continued protective action in the Montelukast group whereas the Fluticasone group demonstrated a relative fall in the control of non nasal symptoms. The efficacy of Leukotriene antagonists in controlling the non nasal symptoms especially the itchy throat and palate [19]. Similar evidence for the effectiveness of oral leukotriene inhibitors in controlling the ocular manifestations of allergic rhinitis is provided by a multitude of studies done by Pullerits T et al, Ratner PH et al., and Weiner JM [11,12,29].

No statistically significant difference was observed in proportion of subjects reporting exacerbations in the current study. There was statistically significant improvement in the Peak Exploratory Flow Rates (PEFR), in both the intervention groups with most significant intergroup difference being demonstrated at Day 60 with increase in PEFR of 93.27 in Fluticasone group versus 53.96 ml in Montelukast group ($p<0.001$). These study findings corroborate with the study findings by Lyseng-Williamson KA et al., and Martin BG et al., [9,30]. A study by O'Connor RD et al., have proposed that oral monteleukast may have better effect on preventing exacerbations and overall improvement in symptoms [31].

Adverse effect profile: None of the groups reported any serious side effects warranting the withdrawal of the drug or the patient from the study. The most commonly reported adverse effect in the Montelukast group were headache 18.9% and GI disturbances 13.2% patients, while in Fluticasone group a wide array of local effects of the administration including nasal irritation, throat infection, sneezing and headache were reported but in a relatively lesser number of patients. These short term side effects noted are in line with the comparative study by Nathan et al., reporting headache, sore throat, epistaxis, dyspepsia as the most common side effects observed comparably with both Montelukast and Fluticasone. Studies by Nathan RA et al., Maspero J et al., have reported better tolerability of intra nasal steroids [22,25]. Cochrane data base review by Taramarcaz P et al., had also reported Intranasal corticosteroids are well tolerated [28].

LIMITATION

Considering the different route of administration of the drug, efficient blinding could not be achieved in the study, hence would have resulted in some bias in estimation of the outcome. The direction and magnitude of this bias could not be established. Even though the random allocation of participants had resulted in good balance in all the base line variables, the role of residual confounding is not documented, due to inadequate sample size to conduct multivariate analysis.

CONCLUSION

This study demonstrates that addition of intranasal Fluticasone propionate to Salmeterol plus Fluticasone is beneficial in improving asthma symptom control; allergic rhinitis (nasal and non nasal symptoms) control and enhances the improvement in lung functions as measured by PEFR, as compared to oral Montelukast.

The sporadically observed adverse effects are insignificant and thereby the use of concomitant intranasal Fluticasone Propionate to control Allergic Rhinitis in patients of Nasobronchial Allergy is justified as per the significant improvement in outcome measures.

Whether this action has prolonged and lasting effects to allow discontinuation of the drugs following short courses or prolonged administration is required for continued activity needs to be studied further with continuous monitoring for adverse effects over a long period of time.

REFERENCES

[1] Bachert C, van Cauwenberge P, Khaltaev N. Allergic rhinitis and its impact on asthma. In collaboration with the World Health Organization. Executive summary of the workshop report. 7-10 December 1999, Geneva, Switzerland. *Allergy*. 2002;57(9):841-55.
[2] Cruz AA, Popov T, Pawankar R, Annesi-Maesano I, Fokkens W, Kemp J, et al. Common characteristics of upper and lower airways in rhinitis and asthma: ARIA update, in collaboration with GA(2)LEN. *Allergy*. 2007;62 Suppl 84:1-41.
[3] Dixon AE. Rhinosinusitis and asthma: the missing link. *Current Opinion in Pulmonary Medicine*. 2009;15(1):19-24.
[4] Thomas M. Allergic rhinitis: evidence for impact on asthma. *BMC Pulmonary Medicine*. 2006;6 Suppl 1:S4.
[5] Volcheck GW. Does rhinitis lead to asthma? Evidence for the one-airway hypothesis. *Postgraduate Medicine*. 2004;115(5):65-68.
[6] Yamauchi K, Shikanai T, Nakamura Y, Kobayashi H, Ogasawara M, Maeyama K. [Roles of histamine in the pathogenesis of bronchial asthma and reevaluation of the clinical usefulness of antihistamines]. *Yakugaku zasshi: Journal of the Pharmaceutical Society of Japan*. 2011;131(2):185-91.
[7] Esteitie R, deTineo M, Naclerio RM, Baroody FM. Effect of the addition of montelukast to fluticasone propionate for the treatment of perennial allergic rhinitis. *Ann Allergy, Asthma Immunol*. 2010;105(2):155-61.
[8] Katial RK, Oppenheimer JJ, Ostrom NK, Mosnaim GS, Yancey SW, Waitkus-Edwards KR, et al. Adding montelukast to fluticasone propionate/salmeterol for control of asthma and seasonal allergic rhinitis. *Allergy and Asthma Proc*. 2010;31(1):68-75.

[9] Lyseng-Williamson KA, Plosker GL. Inhaled salmeterol/fluticasone propionate combination: a pharmacoeconomic review of its use in the management of asthma. *PharmacoEconomics*. 2003;21(13):951-89.
[10] O'Connor RD, Stanford R, Crim C, Yancey SW, Edwards L, Rickard KA, et al. Effect of fluticasone propionate and salmeterol in a single device, fluticasone propionate, and montelukast on overall asthma control, exacerbations, and costs. *Ann Allergy, Asthma Immunol*. 2004;93(6):581-88.
[11] Pullerits T, Praks L, Ristioja V, Lotvall J. Comparison of a nasal glucocorticoid, antileukotriene, and a combination of antileukotriene and antihistamine in the treatment of seasonal allergic rhinitis. *The Journal of Allergy and Clinical Immunology*. 2002;109(6):949-55.
[12] Ratner PH, Howland WC, Arastu R, Philpot EE, Klein KC, Baidoo CA, et al. Fluticasone propionate aqueous nasal spray provided significantly greater improvement in daytime and nighttime nasal symptoms of seasonal allergic rhinitis compared with montelukast. *Ann Allergy, Asthma Immunol*. 2003;90(5):536-42.
[13] Zeiger RS, Bird SR, Kaplan MS, Schatz M, Pearlman DS, Orav EJ, et al. Short-term and long-term asthma control in patients with mild persistent asthma receiving montelukast or fluticasone: a randomized controlled trial. *The American Journal of Medicine*. 2005;118(6):649-57.
[14] Aubier M, Neukirch C, Peiffer C, Melac M. Effect of cetirizine on bronchial hyperresponsiveness in patients with seasonal allergic rhinitis and asthma. *Allergy*. 2001;56(1):35-42.
[15] Baena-Cagnani CE, Berger WE, DuBuske LM, Gurne SE, Stryszak P, Lorber R, et al. Comparative effects of desloratadine versus montelukast on asthma symptoms and use of beta 2-agonists in patients with seasonal allergic rhinitis and asthma. *International Archives of Allergy and Immunology*. 2003;130(4):307-13.
[16] Berger WE, Schenkel EJ, Mansfield LE. Safety and efficacy of desloratadine 5 mg in asthma patients with seasonal allergic rhinitis and nasal congestion. *Ann Allergy, Asthma Immunol*. 2002;89(5):485-91.
[17] Corren J, Manning BE, Thompson SF, Hennessy S, Strom BL. Rhinitis therapy and the prevention of hospital care for asthma: a case-control study. *The Journal of Allergy and Clinical Immunology*. 2004;113(3):415-19.
[18] Crystal-Peters J, Neslusan C, Crown WH, Torres A. Treating allergic rhinitis in patients with comorbid asthma: the risk of asthma-related hospitalizations and emergency department visits. *The Journal of Allergy and Clinical Immunology*. 2002;109(1):57-62.
[19] Bousquet J, Khaltaev N, Cruz AA, Denburg J, Fokkens WJ, Togias A, et al. Allergic Rhinitis and its Impact on Asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA(2)LEN and AllerGen). *Allergy*. 2008;63 Suppl 86:8-160.
[20] Corp I. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.
[21] Doig GS, Simpson F. Randomization and allocation concealment: a practical guide for researchers. *Journal of Critical Care*. 2005;20(2):187-91; discussion 91-93.
[22] Nathan RA, Yancey SW, Waitkus-Edwards K, Prillaman BA, Stauffer JL, Philpot E, et al. Fluticasone propionate nasal spray is superior to montelukast for allergic rhinitis while neither affects overall asthma control. *Chest*. 2005;128(4):1910-20.
[23] Day J, Carrillo T. Comparison of the efficacy of budesonide and fluticasone propionate aqueous nasal spray for once daily treatment of perennial allergic rhinitis. *The Journal of Allergy and Clinical Immunology*. 1998;102(6 Pt 1):902-08.
[24] Di Lorenzo G, Pacor ML, Pellitteri ME, Morici G, Di Gregoli A, Lo Bianco C, et al. Randomized placebo-controlled trial comparing fluticasone aqueous nasal spray in mono-therapy, fluticasone plus cetirizine, fluticasone plus montelukast and cetirizine plus montelukast for seasonal allergic rhinitis. *Clinical and experimental allergy: journal of the British Society for Allergy and Clinical Immunology*. 2004;34(2):259-67.
[25] Maspero J, Guerra F, Cuevas F, Gutierrez JP, Soto-Ramos M, Anderton S, et al. Efficacy and tolerability of salmeterol/fluticasone propionate versus montelukast in childhood asthma: A prospective, randomized, double-blind, double-dummy, parallel-group study. *Clinical Therapeutics*. 2008;30(8):1492-504.
[26] Reed CE, Marcoux JP, Welsh PW. Effects of topical nasal treatment on asthma symptoms. *The Journal of Allergy and Clinical Immunology*. 1988;81(5 Pt 2): 1042-47.
[27] Watson WT, Becker AB, Simons FE. Treatment of allergic rhinitis with intranasal corticosteroids in patients with mild asthma: effect on lower airway responsiveness. *The Journal of Allergy and Clinical Immunology*. 1993;91(1 Pt 1): 97-101.
[28] Taramarcaz P, Gibson PG. Intranasal corticosteroids for asthma control in people with coexisting asthma and rhinitis. *The Cochrane Database of Systematic Reviews*. 2003(4):Cd003570.
[29] Weiner JM, Abramson MJ, Puy RM. Intranasal corticosteroids versus oral H1 receptor antagonists in allergic rhinitis: systematic review of randomised controlled trials. *BMJ* (Clinical research ed). 1998;317(7173):1624-29.
[30] Martin BG, Andrews CP, van Bavel JH, Hampel FC, Klein KC, Prillaman BA, et al. Comparison of fluticasone propionate aqueous nasal spray and oral montelukast for the treatment of seasonal allergic rhinitis symptoms. *Ann Allergy, Asthma Immunol*. 2006;96(6):851-57.
[31] O'Connor RD, Nelson H, Borker R, Emmett A, Jhingran P, Rickard K, et al. Cost effectiveness of fluticasone propionate plus salmeterol versus fluticasone propionate plus montelukast in the treatment of persistent asthma. *Pharmaco Economics*. 2004;22(12):815-25.

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