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Research article

The Effectiveness, Safety and Cost of Different Intranasal Steroid Sprays in Treating Iraqi Patients with Allergic Rhinitis: A Comparative Study

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ABSTRACT

Background: Allergic rhinitis is a common disease that associated with inflammation of the nasal airways resulting in symptoms of sneezing, nasal obstruction, and mucous discharge. Intranasal steroids are the first option for treatment of patients with mild – moderate AR. At which all available intranasal corticosteroids are safe and effective for this indication, differences in efficacy, side effects, and clinical attributes must be considered. So this study aimed to assess and compare the efficacy, safety and cost of different intranasal steroids (bedomethasone dipropionate, budesonide and mometasone furoate monohydrate) that

available in Iraqi pharmacies for the treatment of allergic rhinitis patients.

Subjects & Methods: A randomized single blind clinical trial was done in Al-Diwaniya Teaching Hospital at ENT Unit at which sixty patients of both sexes with allergic rhinitis for at least 1 year were included in this study. The patients were divided into three groups with 20 patients in each group to receive either Bedomethasone dipropionate or mometasone furoate or Budesonide intranasal spray daily for 1 month. Clinical assessment of the allergic rhinitis is done by measuring symptom through the use of visual analog scales at beginning and at the end of the study. Blood samples of AR patients were collected at the beginning and at the end of the study to measure serum Immunoglobulin E (IGE), Interleukin 5(IL5), Eosinophil cationic protein (ECP), Mast cell tryptase (MCT), T-Lymphocyte count.

Results: This study showed a non significant difference among intranasal steroids by their effect on lymphocyte count, IL5, MCT and ECP; however there was a significant difference in the effect of intranasal steroids on VAS, and IGE, at which VAS was significantly reduced by Bedomethasone; while IGE was significantly reduced by mometasone. Additionally there is a non significant difference in the topical side effects among all topical intranasal steroids. Furthermore there is a significantly higher monthly cost for the treatment of allergic rhinitis patients with mometasone nasal spray.

Conclusion: Bedomethasone dipropionate intranasal spray is an effective and cheap therapy when used for short periods for young adult allergic rhinitis patients without any risk from systemic side effects of steroids; while budesonide is a best alternative cheap therapy for Bedomethasone in allergic rhinitis with risk from systemic steroid side effects or who have compliance problems in using nasal steroids twice daily.

KEYWORDS: Allergic rhinitis; intranasal steroids; effectiveness, safety; cost.

Source of support: None

Competing interest / Conflict of interest

The author(s) have no competing interests for financial support, publication of this research, patents and royalties through this collaborative research. All authors were equally involved in discussed research work. There is no financial conflict with the subject matter discussed in the manuscript.

INTRODUCTION

Allergic rhinitis is a common non infectious IgE-antibody mediated inflammation of the nasal airways resulting in symptoms of sneezing, nasal obstruction, and mucous discharge^{1,2}. Although several pharmacological treatment options are available like: decongestants, sedating and non-sedating anti-histamines, mast cell stabilizers (Chromones), leukotriene receptor antagonists, intranasal or systemic corticosteroids, But many studies have shown that intranasal corticosteroids are superior to other modalities for relief of clinical symptoms of AR³, so intranasal steroids become the first option for treatment of patients with persistent mild - moderate AR^{4,5}. The effect of intranasal corticosteroids is directed toward the reduction of the inflammation of the nasal mucosa, through inhibiting both early and late reactions and reducing IgE production and eosinophilia by inhibiting the secretion of cytokines including IL-4, IL-5 and IL-13, which in turn leading to improvement of nasal obstruction, pruritus and sneezing, as well as of rhinorrhea^{6,7}. Whereas all available intranasal corticosteroids are safe and effective for this indication, differences in efficacy, side effects, and clinical attributes must be considered^{8,9}. So the present study aimed to assess and compare the efficacy, safety and cost of different intranasal steroids (beclomethasone dipropionate, budesonide and mometasone furoate monohydrate) that available in Iraqi pharmacies for the treatment of allergic rhinitis patients.

SUBJECTS AND METHODS

STUDY DESIGN

A randomized, single blind clinical trial was done in Al-Diwaniya Teaching Hospital at ENT Unit over 5 months from March 2014 till August 2014. Ethical Approval was obtained from the Ethical Committee of Pharmacy College/ University of Baghdad. Patients who enrolled in this study were diagnosed by a specialist physician to have persistent moderate - severe AR. Patients who have allergic rhinitis symptoms (Sneezing, rhinorrhea, nasal congestion, and conjunctivitis) for at least 1 year were included in this study, after confirmation of that by a positive skin prick test, while those with hypersensitivity to corticosteroids, patients who are already on

steroids, pregnant and breast feeding women, children and patients older than 50 years were excluded from participation in this study. Additionally, any patient who have symptoms like headache, purulent nasal discharge, and fever, which may increase suspicion of rhinosinusitis were excluded from this study.

Sixty eligible patients who fulfill the inclusion criteria were randomly allocated into one of the 3 groups: The patients in the first group were given beclomethasone dipropionate aqueous nasal spray 42µg (2 sprays into each nostril twice daily). The patients in the second group were given Budesonide aqueous nasal spray 64 µg (2 sprays in each nostril once daily) and the patients in the third group were given Mometasone furoate monohydrate nasal spray 0.05% (64µg) (2 sprays in each nostril once daily). Patients were evaluated at baseline and after one month from starting treatment.

EVALUATION OF CLINICAL, IMMUNO - INFLAMMATORY AND ECONOMIC PARAMETERS

Clinical evaluation of disease activity was done through patient self-assessment (Visual analog scale, VAS) of their rhinitis symptoms. Blood specimen collection was done at baseline and after 1 month of starting treatment for measuring the following parameters: Serum total immunoglobulin E (IGE), Interleukin 5(IL5), Eosinophil cationic protein (ECP), Mast cell tryptase (MCT), and T-lymphocyte count. T-lymphocyte was measured by a hematology auto-analyzer (Ruby-CELL-DYN 08H56-02 Abbott Company, Abbott Park, IL, USA), while IGE, IL5, ECP, and MCT were measured by using ELISA technique. All laboratory analysis was done by specialized laboratory researchers who were blind to this study.

Additionally the monthly cost of each intranasal steroid was calculated based on the average price of the spray in different Iraqi drug stores and the total number of puffs in each spray.

STATISTICAL ANALYSIS

Statistical package for social sciences (SPSS) version 20 was used for data input and analysis. Continuous variables were presented as mean ±

standard deviation (SD) and discrete variables were presented as numbers and frequencies. Chi square test for independence was used to test the significance of association between discrete variables. ANOVA test was performed to test the significance of difference in the mean of 3 independent samples in normally distributed continuous variables. Findings with P value less than 0.05 were considered significant.

RESULTS

There is a non significant difference in all demographic parameters for patients in the 3 treated groups as shown in table 1.

Table 2, showed a nonsignificant difference in the baseline level of all studied clinical and immune hematological parameters for patients in the 3 treated groups except the baseline level of IGE at

Table 1. Demographic data of allergic rhinitis patients.

Parameter	Beclomethasone (n=20)	Budesonide (n=20)	Mometasone (n=20)	P-value
Age (years)	25.05±10.03	25.35±6.67	25.65±8.22	>0.05
Disease duration (years)	12.40±6.76	14.95±5.62	13.80±6.81	>0.05
Female/Male n (female %)	8/12(40%)	6/14(30%)	8/12(40%)	>0.05
Family Hx of AR n (%)	12(60%)	8(40%)	11(55%)	>0.05
Social Hx smoking: no smoking percentage (%)	7(35%)	6(30%)	7(35%)	>0.05

which it was significantly higher among patients in mometasone group.

After one month of treatment with either beclomethasone, budesonide and mometasone, it was found that there is a nonsignificant difference among nasal steroids by their effect on lymphocyte count, IL5, MCT and ECP; however there was a significant difference in the effect of intranasal steroids on VAS, and IGE, at which VAS was significantly reduced by Beclomethasone; while IGE was significantly reduced by mometasone as shown in table 3.

Table 4, showed that there is a nonsignificant difference in the topical side effects among all topical intranasal steroids.

Table 5, showed that there is a significantly higher monthly cost for the treatment of allergic rhinitis patients with mometasone nasal spray.

Table 2: Baseline hematological & clinical parameters of the patients.

Parameter	Baseline Value			p value
	Mometasone	Beclomethasone	Budesonide	
VAS	7.75 ±1.01	8.25±1.20	7.75±1.06	0.262
Lymphocyte	1025±429.65	1195±374.13	1125.8±331.02	0.371
MCT	12.85±2.17	11.95±1.46	12.015±0.84	0.145
ECP	23.91±4.03	24.549±4.77	26.107±4.17	0.267
IL5	7.32±3.55	8.83±2.85	9.705±3.17	0.668
IGE	749.75±417.41	391.3±108.26	580.1±394.15	0.006

VAS = Visual analogue scale; IGE = serum immunoglobulin E; IL5 = interleukin 5; ECP = eosinophil cationic protein; MCT = mast cell tryptase.

Table 3. Changes in hematological & clinical parameters after one month.

Parameter	Value			p value
	Mometasone	Beclomethasone	Budesonide	
VAS	-4.5±1.70	-6.3±1.62	-4.75±1.58	0.002

Lymphocyte count	-757.5±373.20	-812.5±389.62	-927.6±325.14	0.327
MCT	-1.13±2.21	-0.62±1.85	-0.79±1.28	0.664
ECP	-4.84±2.70	-5.9345±3.54	-4.464±2.46	0.269
IL5	-1.77±4.34	-1.515±2.64	-2.7±3.19	0.528
IgE	-611±433.66	-244.35±102.01	-451.05±390.69	0.005

VAS = Visual analogue scale; IgE = serum immunoglobulin E; IL5 = interleukin 5; ECP = eosinophil cationic protein; MCT = mast cell tryptase.

Table 4. Topical side effects of intranasal steroids.

Spray	Bedomethasone (n=20)	Budesonide (n=20)	Momtasone (n=20)	p-value
Burning N (%)	4(20%)	5(25%)	2(10%)	0.45
Epistaxis N (%)	2(10%)	4(20%)	1(5%)	0.32
Bad taste in throat N (%)	1(5%)	3(15%)	4(20%)	0.36

N = number of cases; % = percent of cases.

Table 5. Monthly cost of treating allergic rhinitis by different intranasal steroids.

Parameter	Bedomethasone	Budesonide	Mometasone
Cost of 1 piece	8500 IQD	17000 IQD	20800 IQD
Total number of puffs in 1 piece	200	200	140
Cost of each puff	42.5 IQD	85 IQD	148.6 IQD
Number of puffs needed in each day	8	4	4
Cost of treatment for 1 month	10200 IQD	10200 IQD	17832 IQD

IQD=Iraqi dinar.

DISCUSSION

Of the available and most effective medications for the treatment of AR are intranasal steroids¹⁰. Yet the availability of wide variety of intranasal steroids in the Iraqi pharmaceutical market complicates the selection of a preferred agent for an allergic rhinitis patient. So this study aimed to find the appropriate intranasal steroid in term of effectiveness, safety and cost.

Although many studies in the world assess the effectiveness of different intranasal steroids by measuring inflammatory parameters in the nasal lavage^{11,12}; but some other studies depend on measuring immune inflammatory parameters in the blood for evaluating the effectiveness of different intranasal steroids^{13,14}; Anyhow measuring immuno-inflammatory parameters in the blood is easier and more convenient to the patient, so this study compare the effectiveness among different intranasal steroids by measuring these parameters in patient's blood sample.

This study showed a non significant difference among intranasal steroids on most of the studied immune-inflammatory parameters like lymphocyte

count, MCT, ECP and IL5, similarly many studies confirm that there is a similar clinical efficacy for all INS¹⁵. Regarding IgE, despite that this study showed a significant higher reduction of IgE by mometasone but actually there may be non significant difference among INS, since this significant difference in the effect of mometasone on IgE may be resulted from the already significant difference in the baseline level of IgE among patients in mometasone group with other groups. Furthermore VAS for patients' reported symptoms (sneezing, rhinorrhea, nasal congestion and eye itching) which was reduced significantly by Beclomethasone more than other intranasal steroids, while some studies suggest that there is only very few differences among intranasal steroids on VAS scores¹⁶, while other studies agree in that there is pharmacological differences between INS, yet if they are used regularly and correctly there is no clear evidence that any INS is superior to any other for AR symptom relief^{17,18}. This difference from these studies may be explained in that VAS score is a subjective

parameter which is mainly dependent on patient response that can be affected by many factors like drug onset of action, and drug effectiveness which is mainly related to regular and correct usage of the nasal spray; although it is well known that drugs once daily regimen are better to ensure patient compliance but on the other hand if the patient forget to use it this means that the probability of missing the treatment in that day will be high while for drugs with twice daily regimen the chance of forgetting the application of the nasal steroid at one time don't mean complete missing of the daily treatment. So this means that there is little actual differences in the effectiveness of intranasal steroids in treating allergic rhinitis, besides that this study showed that there is a non significant difference in the topical side effects among all topical intranasal steroids, this finding is consistent with finding in other studies¹⁹. The systemic side effects of INS were not examined in this study, since many other studies showed very limited systemic side effects with all INS especially with mometasone and Budesonide if used in the therapeutic doses and for short period of time²⁰. But since results of this study showed that there is a significantly higher monthly cost for the treatment of allergic rhinitis patients with mometasone nasal spray. So we can conclude that Beclomethasone therapy is a best and cheap therapy when used for short periods for young adult patients without any risk from systemic side effects of steroids; Based on above data mometasone is expensive and no more effective than Budesonide with no more safety²¹, so Budesonide is a best alternative cheap therapy for Beclomethasone in allergic rhinitis with risk from systemic steroid side effects or who have compliance problems in using nasal steroids twice daily.

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