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ORGINAL ARTICLE

Role of Antileukotrienes in Prevention of Recurrence of Nasal Polyps

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ABSTRACT

Background: Nasal polyps are common in patients with chronic rhinosinusitis, although little is understood about the pathophysiology of nasal polyp production. This study aimed to determine the effect of montelukast (a leukotriene receptor antagonist) as a maintenance therapy for 3 months to prevent recurrent nasal polyps, and detect the relation between cysteinyl leukotrenes (LTC4) in the recurrence of nasal polyposis. **Patient and Methods:** This is a non-randomized phase III clinical trial study included 40 patients with nasal polyposis either primary or recurrent nasal polyps. The study work was done in Otorhiriolaryngology Department in Zagazig University Hospitals in the period from 2010 to 2013. Who were divided into two groups (20 patients in each group) with nasal polyposis either primary or recurrent nasal polyps detected by nasal endoscopy and CT scan of the nose and para nasal sinuses. Functional endoscopic sinus surgery (FESS) was done for all patients to remove nasal polyposis then nasal polyp was taken from all patients during operation to detect the level of tissue leukotriene (LTC4). **Results**: The percentage of female was 22 (55%) and male was 18 (45%). Regarding Nasal Polyp, Bilateral were 40 (100%) and Unilateral were 0 (0%). There was no statistically significant difference between group A and group B regarding Eosinophil. While, there was statistically significant difference between group A and group B regarding Immunohistochemistry expression of LTR. **Conclusions:** Montelukast (a leukotriene receptor antagonist) appears to be beneficial in prevent recurrence of nasal polyps. **Keywords:** Nasal polyps; Montelukast; Antileukotrienes.

INTRODUCTION

Nasal polyps are a common finding in clinical practice; however, the pathogenesis behind polyp formation and its reasons for their recurrence remain obscure [1].

A nasal polyp is a benign tumor that causes irritation of the nasal mucosa and sinuses. Nasal polyps exhibit varying degrees of stromal edema, inflammatory cellular infiltrate, and tissue remodeling of epithelial/stromal components [2].

Extracellular edema and inflammatory infiltrate with more eosinophils are the main histologic features of nasal polypi. In the stroma of nasal polyps, there are few newly formed blood vessels that lack adequate innervations and cell adhesions [3].

Leukotrienes (LTs) are physiologically active products that produced by the enzyme 5-lipoxygenase from arachidonic acid. LTs are conjugated triene compounds with a linear-20 cerban chain [4].

Leukotirenes, active biological compounds produced by eosinophils, monocytes, mast cells and basophils, have piqued the priority of many researchers [1].

Leukotrienes are effective lipid mediators. They are generated as lipid mediators through a series of many enzymatic reactions. The cysteinyl LTs (LTC4, LTD4, and

LTE4) were known as slow reacting compounds [5].

Cysteinyl LTs works in humans via two receptors (the CysLT1 and CysLT2 receptors), both of which have been cloned and mapped for the availability of antibodies to the receptor protein [5].

Leukotrienes (LT) are inflammatory mediators that play a role in the pathogenesis of certain respiratory diseases. Their biological effects include mucous secreation, increased vascular leakage, myofibroblast cellular proliferation, and increased eosinophil tissue recruitment [6].

Eosinophils are the main source of these leukotirenes, causing chronic sinusitis can become a condition of unregulated eosinophil buildup; with eosinophils provide the growth factors required for esinophils recruitment, persistence, activation and proliferation [7]. This study aimed to determine the effect of montelukast (a leukotriene receptor antagonist) as a maintenance therapy for 3 months to prevent recurrent nasal polyps, and detect the relation between cysteinyl leukotrenes (LTC4) in the recurrence of nasal polyposis .

PATIENTS AND METHODS

This is a non-randomized phase III clinical trial study included 40 patients with nasal polyposis either primary or recurrent nasal polyps. The study work was done in Otorhiriolaryngology Department in Zagazig University Hospitals in the period from 2010 to 2013.

We considered the following Inclusion criteria: primary or recurrent nasal polyposis, both sexes were included in the study, age from 20 to 45 was included.

Our exclusion criteria were: Patients who already refuse to participate in the study. Patients have contraindications for interventional endoscopy. Patients have advanced cardiopulmonary illness. Patients have coagulopathy or any sever illness.

Forty Patients were included in the study was divided into two groups (20 patients in each group) with nasal polyposis either primary or recurrent nasal polyps. Then patients were divided after FESS into two groups: Group A: Prednisolone 30 mg for 14 days then reducing by 5 mg every second day for another one week. Budesonde nasal spray metered doses to each nostril for 3 months. Montelukast 10 mg daily for 3 months. Group B: Prednisolene 30 mg for 14 days then reducing by 5 mg every second day for another one week. Budesonde nasal spray metered doses to each nostril for 3 months. Then after 3 months, nasal endoscopy has been done to detect if there is recurrent polyposis or not. If there is recurrent nasal polyp, nasal polyp was taken by nasal endoscopy to detect the level of tissue leukotriene (LTC4)**.**

Ethical Clearance: Written Informed consent was taken from the patient to participate in the study. Approval for performing the study was obtained from Otorhinolaryngology Departments, Zagazig University Hospitals after taking Institutional Review Board (IRB) approval. The work has been carried out in accordance with the code of ethics of the world medical association (Decleration of Helsinki) for studies involving humans.

Statistic analysis

The software SPSS version 16 was used to tabulate and analyze the acquired data (Spss Inc, Chicago, ILL Company).

RESULTS

Table 1; showed that the percentage of female were 22 (55%) and male were 18 (45%). This table shows that the range of age was 20-45 with mean± SD (32 ± 2).

Table 2; showed that regarding Eosinophil, >440 cell/mm were 37 (92.5%) and <440 cell/mm were 3 (7.5%).

Table 3; showed that there was statistically significant difference between group A and group B regarding Recurrence.

Table 4; showed that there was no statistically significant difference between group A and group B regarding Eosinophil.

Table 5; showed that there was statistically significant difference between group A and group B regarding Immunohistochemistry expression of LTR.

Table (1): Sex among the studied cases.

		No.	%
Sex	**Female**	22	55
	Male	18	45
Age (years)	20 - 45	32 ± 2	

Table (2): Eosinophil among the studied cases.

		No.	%
Eosinophil	**>440 cell/mm**	37	92.5
	<440 cell/mm	3	7.5

Table (3): Comparison between group A and group B regarding recurrence.

			group A	group B	X^2	P. value
Recurrence	**yes**	**No.**	0	5	3.657	0.04
		%	0.0%	25%		
	no	**No.**	20	15		
		%	100.0%	75%		

Table (4): Comparison between group A and group B regarding Eosinophil

			group A	group B	X^2	P. value
Eosinophil	**>440**	**No.**	19	18	0.360	0.548
		%	95%	90%		
	>440	**No.**	1	2		
		%	5%	10%		

Table (5): Comparison between group A and group B regarding tissue leukotriene LTC4.

			group A	group B	X^2	P. value
Immunohistochemistry expression of LTR	**High (strong cytoplasmic stain)**	**No.**	2	7	2.294	0.029
		%	10%	35%		
	High (strong cytoplasmic stain)	**No.**	18	13		
		%	90%	65%		

DISCUSSION

This study showed that, the percentage of female were 22 (55%) and male were 18 (45%). Since it helps to explain the sex variations in inflammation, immunity to infection, and autoimmune disease, the regulation of inflammation by sex hormones like estradiol is crucial. Progesterone and estradiol, two sex hormones, are also engaged in a variety of physiological and pathological processes, including lung health. Asthma and ASA intolerance have been found to be more common in men than women. Hormonal changes may be the cause for nasal allergy sensitivity and asthma attacks in females [8].

The link between female sex hormones and nasal polyps is still unproved [9]. According to some researches, nasal polyps are more common in women [10].

This was in contradicting with that reported by **Rugina et al**[11] who found the frequency of nasal polyposis is believed to be around 4%, with a slight male-to-female ratio. According to a Danish study, the incidence rate of symptomatic nasal polyposis is 0.86 male patients and 0.39 female patients per 1,000 people per year [12].

In this study, regarding Eosinophil, >440 cell/mm were 37 (92.5%) and <440 cell/mm were 3 (7.5%).

Vuralkan et al[13] who studied fifty patients diagnosed with nasal polyposis. They discovered that 94% of the polyps were eosinophilic. Eosinophils' role in allergic illnesses has been studied, and this may be related to polyp etiology. Stimulation of such effector capabilities by structure cell-derived cytokines would likely represent a primary inflammatory response amplification mechanism in nasal polyps[14].

In the current study, Percentage of recurrence was higher among group B than group A (25%versus 0%).

San Nicoló et al[15] who aimed to determine the efficacy of postoperative antileukotriene therapy in preventing nasal polyposis recurrence. They discovered that MT had considerably fewer polyp recurrences than the other therapy groups. Postoperative treatment with leukotriene-receptor antagonists effectively reduces the recurrence of nasal polyps. Over time, MT has a positive influence on subjective sinonasal outcomes and patients' quality of life.

In this study, There was no statistically significant difference between group A and group B regarding Eosinophil**.**

Schäper et al[16] who aimed to investigate the effect of montelukast, a cysteinyl-leukotriene receptor antagonist, on clinical symptoms and inflammatory markers in nasal lavage fluid in individuals with nasal polyps. In a blinded, placebo-controlled study, twenty-four individuals (7 women, 17 men; median age, 55.5 years) with nasal polyps were given 10 mg montelukast once daily for 6 weeks. The placebo phase was assigned at random four weeks before (n=12) or after therapy (n=12). A symptom score, rhinoendoscopy, rhinomanometry, eosinophil smears, and nasal lavages were done to determine the presence of various mediators. They discovered that, when compared to placebo, there were substantial improvements in nasal symptom score and airflow limitation following treatment, as well as a reduction in inflammatory mediators in nasal lavage fluid. Furthermore, decreased eosinophils were found in nasal smears and peripheral blood 2 and 6 weeks following treatment. Leukotriene 1 receptor blockage reduced eosinophil inflammation and other mediators such as neurokinin A and substance P in nasal lavage fluid from patients with nasal polyps and asthma, with or without aspirin intolerance.

In this study, There was statistically significant difference between group A and group B regarding Immunohistochemistry expression of LTR.

Increased amounts of leukotrienes (LTs) and their receptors have been found in nasal polyps in studies. Cysteinyl-LTs, which are generated by arachidonic acid metabolism in CRS inflammatory cells such as eosinophils and mast cells, bind to G-protein coupled receptors to enhance localized inflammation such as eosinophil infiltration, mucous secretion, collagen deposition, and mast cell cytokine release [17].

This process can be stopped by either blocking the receptor with an LT receptor antagonist like montelukast or stopping the synthesis of cysteinyl-LTs with a 5-lipoxygenase inhibitor like zileuton. LTAs have been shown to be effective in chronic inflammatory illnesses of the airways, such as allergic rhinitis, asthma, and aspirin-exacerbated respiratory disease (AERD), all of which frequently occur with CRSwNP. Several trials have found LTAs to be effective as a main treatment for CRSwNP [18,19] .

CONCLUSIONS

Montelukast (a leukotriene receptor antagonist) appears to be effective in prevent recurrence of nasal polyps.

Conflict of interest: No

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