Clinical Epidemiology and Global Health xxx (xxxx) xxx–xxx

Contents lists available at ScienceDirect

Clinical Epidemiology and Global Health

journal homepage: www.elsevier.com/locate/cegh

Comparison of tissue level of selenium and zinc in patients with nasal polyposis and healthy people

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ARTICLE INFO

Keywords:
Nasal polyposis
Zinc
Selenium
Ahvaz

ABSTRACT

Background: Nasal polyposis (NP) is an inflammatory condition in nasal and paranasal sinus cavities and its pathophysiology is poorly understood. It seems likely that the trace elements such as zinc and selenium may play a critical role in the genesis of inflammatory sinonasal disease.
Objectives: The aim of this study was to investigate the role of these elements in NP and compare these findings with normal nasal mucosa.
Methods & materials: In this descriptive-analytic cross-sectional study which was done at Imam Khomeini hospital of Ahvaz between July 2018 and June 2019, selenium and zinc levels measured in polyp tissues of 72 patients (47 men and 25 women) and were compared with healthy nasal mucosa of 36 control cases (15 men and 21 women). Hydride generation and flame atom absorption spectroscopy were utilized for selenium and zinc quantifications, consequently.
Results: The mean tissue zinc and selenium levels were, respectively, 18.569 **μg/g** and 68.65 **ng/g** in patients group and 71.015 **μg/g**, 249.53 **ng/g** in control group. It was found that the concentrations of zinc element were significantly lower in polyp tissues than healthy nasal mucosa. In the case of selenium no significant difference was found between patients and controls.
Conclusion: Trace elements are undoubtedly useful, and further studies are needed to determine the effect of zinc and selenium on nasal and sinus polyps.

1. Introduction

Polyps contain inflammatory cells such as Eosinophils, Mast cells, lymphocytes, and cytokines.[1] They usually affect paranasal sinuses bilaterally, especially the anterior ethmoid sinuses, which are in contact with the inhaled air.[2,3] The disease is caused by mucosal edema and sinus epithelium damage.[4]

There is evidence that nasal polyps have been known for thousands of years, but the etiology remains unclear.[5] It is a multifactorial disease. There are several factors involved in its etiology and pathogenesis. Environmental and host-related factors such as: immune barrier defects, fungi, super-antigens, biofilms, atopy, mucociliary dysfunction may be underlying causes of this disease.[6] In general, the prevalence of polyps in adults is estimated to be around 4%.[7] Genetic factors, ethnicity and geographical location, aging and male gender are all contributing factors in increasing the prevalence of the disease.[8] Polyps affect one's quality of life by blocking the nose and reducing the sense of smell. Polyps present in multiple or single-sided large polyps, such as the antrochoanal polyp in the nose.[9] Medical therapy and endoscopic surgery are effective in the treatment of the disease.[10]

Minerals in the body, such as selenium and zinc as a cofactor, have been involved in many processes of the body's immune and defense regulation and are essential nutrients for human health. In other words, antioxidant enzymes require minerals as adjuvants for maximum effectiveness, such as selenium for glutathione peroxidase and zinc and copper for superoxide dismutase.[11–15] Zinc also plays a vital role in protecting the immune system and respiratory function. The role of zinc in the repair of cutaneous and mucosal ulcers and the function of the gastrointestinal tract is well known today.[15] Okur et al., in 2013 reported that these trace elements are found in various tissues. Reducing their levels by increasing the effects of free oxygen radicals leads to cell damage in the nasal mucosal epithelium and is the basis for diseases of the upper respiratory tract such as nasal polyps.[13] Also, Heyland et al., in 2005 in their systematic review found that trace elements and vitamins have an antioxidant function and that high doses of inedible selenium alone or in combination with other antioxidants can reduce

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https://doi.org/10.1016/j.cegh.2020.07.005
Received 2 May 2020; Received in revised form 5 July 2020; Accepted 12 July 2020

mortality in critically ill patients.[16]

As the studies are limited in the field of trace elements, this study aimed to assess the differences in the levels of these elements in patients with polyposis and the control group, which can help us achieve diagnostic and treatment strategies.

2. Methods and materials

2.1. Participants

This descriptive-analytic cross-sectional study was conducted at Imam Khomeini Hospital of Ahvaz between July 2018 and June 2019 to evaluate tissue zinc and selenium levels in patients with and without nasal polyposis. According to Okur,[13] the mean and the standard deviation in the patient group for zinc and selenium were 2.55 ± 2.32 μg/g and 30.03 ± 24.32 pg/g, respectively, and in healthy groups were 4.37 ± 2.91 μg/g and 44.95 ± 26.48 pg/g, respectively. Based on the probability of a Type I error of 0.05 and the probability of a Type II error of 0.2, the sample size were determined 36 for the control and 72 for the patient group, based on the ratio of one to two (healthy group per patient). Patients with cystic fibrosis, allergic fungal sinusitis, and Kartagener syndrome were excluded. Patients with a confirmed diagnosis of nasal polyposis by endoscopy and CT (Computed Tomography) included in this study. Polyp specimens were taken during the endoscopic operation from 72 (47 men and 25 women) cases with ages ranged from 12 to 70 years. Normal nasal mucosa specimens from inferior turbinate were taken during the surgery for other causes, such as septal deviation, rhinoplasty, concha bullosa, and dacryocystorhinostomy from 36 (15 men and 21 women) cases with ages ranged from 11 to 38 years.

The protocols and all experimental procedures of the study were approved by the local Ethics Committee of AJUMS (Ahvaz Jundishapur University of Medical Sciences), Ahvaz, Iran which were in complete accordance with the ethical regulations of human studies set by the Helsinki declaration.

2.2. Procedure

Tissue samples were washed in 0.9% NaCl serum and were dried with clean gauzes and placed in plastic bags. The samples were stored in the freezer at −30 °C until microwave digestion. Microwave digestion was adapted from Pechova et all[17] with slight modification. The specimens were defrosted, weighed, and transferred to the microwave Teflon vessel, then a mixture of HNO3 (11 mL), H2O2 (5 mL), and H2O (1 mL) was added, microwave program was started after closing the vessels. Ethose 1 Milestone oven was operated at a controlled-pressure mode. The microwave program is given in Table 1.[17] The digested samples were dried on a hot plate, and the dried residue was redissolved in 10 mL HCl (10% HCl), and divided into two portions, one portion for zinc and the other for selenium quantitation's. Hydride generation and flame atomic absorption spectroscopy used for selenium and zinc quantifications, consequently. A 5FL ZEISS flame atomic absorption apparatus used for all atomic absorption measurements.

Table 1
Microwave timing program for tissue samples.

Phase	Tension	Time of duration
Step 1	250W	2 min
Step 2	0W	2 min
Step 3	250W	6 min
Step 4	400W	5 min
Step 5	650W	5 min
Ventilation	–	12 min

2.3. Statistical analysis

The Mean, median, and standard deviation parameters were determined to describe the data in quantitative variables. Frequency and percentage were used to describe the data in qualitative variables. The data were analyzed using a chi-square test, an independent *t*-test, a Mann-Whitney test and a univariate logistic regression. A multivariate logistic regression was used to analyze the data. Significance level was set at 0.05. All analyzes were performed using SPSS 22 software.

3. Results

Table 2, in univariable part, indicates significant relationship between age, gender and zinc content between the patient and the control groups, while no significant relationship between selenium and control groups was found. In the univariable part, the risk of developing nasal polyps decreased by 9.4% per each unit increase in zinc levels. With age, the likelihood of developing nasal polyps increased about 21% per each year increasing, and the likelihood of having a nasal polyp in men is more than 2.5 times (2 fold and 63%) higher than women, and there is no statistically significant relationship between selenium and nasal polyps. The multiple logistic regression model using the Enter method to control the influence of other gender and zinc variables on age, was significantly related to the age variable and the likelihood of developing nasal polyps increased 14% for each year increase in age. Regarding the control of the disruptive effects of other gender and age variables, the likelihood of developing nasal polyps decreased by about 8% for each unit increase in zinc level.

4. Discussion

Nasal polyposis is a chronic, common inflammatory disease of the nose and sinuses with many symptoms that affect the patient's overall quality of life. It requires effective and continuous treatment. In a study of the role of free radicals and antioxidants in nasal polyps, Dagli and colleagues found that serum and tissue antioxidant levels in polyposis patients were lower than controls and that malondialdehyde-thiobarbituric acid (MDA) levels as an oxidant increased. Their study showed that oxidative stress plays an important role in the pathogenesis of nasal polyps and that antioxidants can prevent tissue damage caused by free radicals in polyps.[4] Truong-Tran et al. examined the role of zinc in the respiratory epithelium. According to a review of their articles, zinc has an antioxidant and anti-inflammatory effect and protects the respiratory epithelium from free radicals and pollutants and indicates the effect of zinc on asthma and other inflammatory diseases of the respiratory tract that damage the physical mucosal barrier.[18]

Okur and his colleagues conducted a study on trace elements in nasal polyps in which the selenium, zinc, and superoxide dismutase tissue levels were lower in polyposis patients than in the control group.[13] Heyland and colleagues in their systematic review found that trace elements and vitamins have an antioxidant function and that high doses of inedible selenium alone or in combination with other antioxidants can reduce mortality in critically ill patients.[16]

Rostkowska et al. concluded that the copper, zinc, selenium, and lead levels in the polyp tissue were below the normal mucous membrane.[19] Dabbaghmanesh and his colleagues concluded that zinc and copper serum levels were lower in nasal polyp patients than in healthy subjects. Serum iron levels were also lower in patients, but this difference was not statistically significant.[20]

In the present study, tissue levels of zinc and selenium were compared in the case and control groups. In the case of selenium, unlike previous studies, no significant difference was found between patients and controls. It can be noted that the amount of data on selenium is much lower than expected, and this low number of data undermines the results of the selenium analysis. This difference between the two groups may be due to the small number of data. The reason for the low sample

Table 2
Relationship of a variable and multivariate age, gender, zinc and selenium to the response variable.

		Patients				Control				P-value	Type of Test	Univariable		Multivariable	
		Number	%	Mean	SD	Number	%	Mean	SD			OR (95% CI)	P-value	OR (95% CI)	P-value
Age		72	67%	38.305	11.677	36	33.3	24.333	5.56	< 0.001	Independent *t*-test	1.208 (1.12–1.30)	< 0.001	1.144 (1.046–1.252)	0.003
Sex	Female	25	54.3			21	45.7			0.02	Chi-square	2.632 (1.153–5.983)	0.02	1.83 (0.471–7.11)	0.383
	Male	47	75.8			15	24.2								
Zinc		71	66.4	18.569	14.071	36	33.6	71.015	64.497	< 0.001	Mann-Whitney	0.906 (0.873–0.940)	< 0.001	0.919 (0.881–0.958)	< 0.001
Median (Range)		16.424 (385.38)				56.90 (70.81)									
Selenium		25	89.3	68.65	38.69	3	10.7	249.53	200.61	0.149	Mann-Whitney	0.948 (0.948–1)	0.07		
Median (Range)		67.82 (138.41)				230.321 (399.83)									

size of selenium may be the low weight of the specimens presented, especially for the control group due to the ethical limits of obtaining healthy mucosal tissue and for patients also due to polyp tissue restriction.

In the study without adjusting for age and sex, there was a significant difference between the tissue level of zinc in the patient and control groups. The likelihood of developing nasal polyps decreased by 9.4% per unit increase in zinc levels. Also, with age, the odds of getting sick are about 21% per unit increase in the age variable (every year). Moreover, men are more than twice as likely as women to have a nasal polyp (2 fold and 63%) and about the limitations of our study, the amount of data on selenium is much lower than expected, and this low number of data undermines the results of the selenium analysis. It was noticed that the reason for the small sample size of selenium can be the low weight of the presented samples, especially for the control group due to the ethical limits of obtaining healthy mucosal tissue.

5. Conclusion

The role of antioxidant and trace elements in the prevention of mucosal injury and polyps is discussed. Further studies are needed to prove or disprove this relationship.

Funding

Funding is provided by the Vice President of the University of Research and the Center for Hearing Research and the Comprehensive Laboratory of the University.

Declaration of competing interest

There are no conflicts of interests among the authors.

Acknowledgment

This article is the result of an assistant dissertation number HRC-9702 registered with the University's Ethics Committee at IR.AJUMS.REC.1397.277.

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