

Genetic, environmental and dietary factors affecting the prognosis of allergic rhinitis

Randa S. Hana^{1*}, Bahaa L. Bawi², Nareman S. Eshak³ and Asmaa A. Ahmed⁴

¹Biochemistry Department, Faculty of Medicine, Assiut University, Egypt.

²E.N.T. Department, Faculty of Medicine, Banha University, Egypt.

³Nutrition and Food Science, Faculty of Specific Education, Assiut University, Egypt.

⁴Textile and Clothing Department, Faculty of Specific Education, Assiut University, Egypt.

Accepted 29 April, 2015

ABSTRACT

The transporters associated with antigen presentation (TAP) genes polymorphism could play a role in the pathogenesis of allergic rhinitis. The aim of this study was to investigate the association of TAP genes polymorphism with allergic rhinitis in Egyptian population (by PCR and REFLP), investigate the effect of omega-3 capsules versus fish oil supplementation for treatment, study MCAM (by enzyme-linked immunosorbent assay) as a diagnostic and prognostic biomarker, study the incidence of allergy to textile dyes and the effect of replacement of synthetic by natural dyes on treatment. The results showed that the frequency of TC and AG genotypes were significantly higher in cases than controls, MCAM is a sensitive diagnostic and prognostic biomarker, omega-3 or better fish oil supplements and replacement of synthetic dyes by natural ones could improve allergic rhinitis patients.

Keywords: Allergic rhinitis, TAP1, TAP2 polymorphism, MCAM, omega-3, fish oil.

*Corresponding author. E-mail: mariam132002@yahoo.com.

INTRODUCTION

Allergic rhinitis (AR) is an immunologic nasal response, primarily mediated by immunoglobulin E. It is considered as a heterogenous state, determined by genetic and environmental interactions. Previous studies have shown the relationships between allergies and polymorphisms in many candidate genes such as by immunoglobulin E, T cell receptors, cytokines and their receptors (Chae et al., 2006).

The transporter associated with antigen processing (TAP) gene product is involved in the processing of endogenous peptides that bind to MHC class I molecules. Polymorphism within these genes could alter the efficacy of the immune response which might be relevant for the development of autoimmune diseases (Tamandani et al., 2009). TAP-1 and TAP-2, members of the ATP-binding cassette transporter super family, are composed of two integral membrane proteins, TAP genes polymorphism could influence the selection process that determines which antigen peptides play a role in the pathogenesis of allergic rhinitis (Kim et al., 2007).

The use of omega-3 acid supplements as treatments

for allergic diseases including asthma is controversial. Studies by investigators from Indiana University in the USA have repeatedly demonstrated a beneficial effect of high dose omega-3 fatty acid supplements over 3 weeks in attenuating bronchoconstriction similar or possibly better in potency to what may be expected with regular inhaled corticosteroids (Brannan et al., 2014).

Fish oil is usually made from mackerel, herring, tuna, halibut, salmon, cod liver, whale blubber, or seal blubber. Fish oil supplements often contain small amounts of vitamin E to prevent spoilage. They might also be combined with calcium, iron, or vitamins A, B1, B2, B3, C, or D. Fish oil is used for conditions related to the heart and blood system, diabetes, asthma, developmental coordination disorders, movement disorders, dyslexia, obesity, kidney disease, weak bones (osteoporosis), certain diseases related to pain and swelling such as psoriasis, and preventing weight loss caused by some cancer drugs. A lot of the benefit of fish oil seems to come from the omega-3 fatty acids that it contains (Devereux and Seaton, 2005).

Cell surface glycoprotein MUC18, also known as Melanoma-associated antigen MUC18, CD146 and MCAM, is a single-pass type I membrane protein which belongs to the immunoglobulin superfamily. MCAM expression is detected in endothelial cells in vascular tissue throughout the body and plays a role in cell adhesion. Among molecules at the interendothelial junction, MCAM is involved in cell-cell cohesion and permeability. As a calcium independent cell adhesion molecule involved in heterophilic cell to cell interactions and a surface receptor, it triggers tyrosine phosphorylation, induce signal transduction, proteolysis or immune recognition. It is regulated by the inflammatory cytokine TNF(tumor necrosis factor) and involved in monocyte transendothelial migration during inflammation. It is a key cell adhesion protein in vascular endothelial cell activity and angiogenesis (Kull et al., 2006).

Allergy to textile dyes is not very uncommon. Although the true incidence is unknown, incidence rates range from 0.05 to 15.9% (Hatch and Maibach, 1995; Lazarov et al., 2000). Textiles are made from synthetic or natural fibers, or both. Generally, the actual fibers are not allergenic; rather, the dyes used to color the fabrics are the responsible allergens. The most common sensitizers, disperse orange 3 and disperse red 17, have been reported to cause allergy and serve as good screening allergens for textile allergy (Pratt and Taraska, 2000; Hatch and Maibach, 2000).

Aim of the work

1. Investigate the TAP1 and TAP2 polymorphisms and their association with AR and the most common comorbid disorders in an Egyptian population.
2. Identifying and quantifying a wide spectrum of fatty acids present in a sample of fish oil.
3. Investigate the effect of omega-3 capsules versus fish oil supplementation for treatment of AR patients.
4. Study MCAM as a diagnostic and prognostic marker in allergic rhinitis.
5. Investigate the incidence of allergy to textile dyes in a sample of the Egyptian population and the effect of replacement of synthetic by natural dyes on the course of the disease.

MATERIALS AND METHODS

Subjects

70 female and 30 male patients ranging from 15 to 70 (mean 24.1 years old) with AR were included in this study. Allergic rhinitis was defined as showing symptoms of sneezing, a runny or blocked nose, or itchy, red, and watery eyes after exposure to furred pets or pollen (according to the questionnaire) or having received a physician's diagnosis of allergic rhinitis (Kull et al., 2006). All patients had nasal symptoms such as watery rhinorrhea, sneezing, itching and/or nasal obstruction, and positive skin prick tests (Allergopharma®, Hamburg, Germany) for one or more inhalant

allergens (a positive test is ≥ 2 mm compared to the negative control). From history, patch test reactions were done to paraphenylenediamine, neomycin sulfate, nickel sulfate, cobalt chloride, disperse orange 3, disperse red 17 and they were further classified into mild ($n = 55$) and severe ($n = 45$) according to the disease effect on the quality of life, sleep, daily activities, work performance and the duration of rhinitis (Wallace et al., 2008). The control group consisted of 100 healthy subjects with no personal or family history of allergic diseases, cancers or genetic diseases. There were 70 females and 30 males ranging from 17 to 65 years old (mean 26.2 years old). Randomly, 70 patients in this study were equally divided to receive either Omega-3 capsules once daily or fish oil 2 g/d (equal to omega-3 content of the capsule) (Ghanei et al., 2012) in addition to the traditional therapy and compared to the remaining 30 patients who only received the traditional therapy. The fatty acid content of the capsules is shown in Table 1. The doses were selected according to recommendations of the International Society for the study of Fatty acids and Lipids (Internet: <http://www.issfal.org.uk/Welcome/PolicyStatement3>). The capsules/oil were well tolerated by almost all participants; one subject in the capsule/d group developed abdominal discomfort and was dropped from the study.

DNA extraction

EDTA anti-coagulated 10 ml peripheral blood sample was collected at diagnosis and 2 weeks thereafter from each individual and stored at -70°C before being used. Genomic DNA was extracted with the DNA extraction kit (Promega, Madison, WI, U.S.A.). It was amplified by polymerase chain reaction (PCR), the oligonucleotides used as primers were:

TAP1(C/T intron 7): Forward GTGCTCTCACGTTCCAAGGA, Reverse AGGAGTAGAGATAGAAGAACC TAP2 (A/G exon 11): Forward 3-GGTGATTGCTCACAGGCTGCCG Reverse CACAGCTCTAGGGAAACTC.

Amplification reactions were carried out in 25- μl of reaction mixture containing 100 ng genomic DNA, 0.25 mmol/L dNTPs, 2 mmol/L MgCl_2 , 10 mM Tris-HCl (pH = 8.3), 50 mM KCl, 1.5 units of Taq polymerase (Burlington, Ontario, Canada), and 0.3 mmol/L of each primer (Sigma-Aldrich, USA). PCR was carried out at 95°C for 2.5 min, RFLP assay was performed in a 15 μl reaction mixture containing PCR product (10 μl), buffer (1.6 μl), enzyme (Msp1, 3 units per reaction) and distilled water (3 μl). The reaction mixture was incubated at 37°C for 3 h (Figure 1 and 2).

Fatty acid composition

Fatty acid methyl esters were injected into (HP 6890 series GLC) apparatus. Carrier gas was N_2 with flow rate 2.2 ml/min. The injector temperature was 250°C and that of Flame Ionization Detector was 300°C . Peaks were identified by comparing the retention times obtained with standard methyl esters. Standards were purchased from Nu-Chek Prep, Inc., Elysian, MN, USA. Linoleic acid methyl esters (Catalog n° 47791), FAME mix: C4-C24 unsaturated (Catalog N° 18919) and individual FAMES from 4:0 to 24:1 chain length saturated and unsaturated were obtained from Bellefonte (USA). Sodium chloride, sodium sulfate anhydrous, sodium hydroxide, methanol were purchased from Merck (Hohenbrunn, Germany) and Sigma-Aldrich (St. Louis, MO) and the refined mixture of fish oil from Santiago, Chile (Figure 3).

Plasma concentrations

Plasma concentrations of inflammatory marker MCAM was measured by using enzyme-linked immunosorbent assay (ELIZA)

Table 1. Comparison between the fatty acids composition of omega-3 capsule and fish oil.

Fatty acid composition	Omega-3 capsules (mg/capsule)	Fish oil (g FA/100 g FA)
16:0	3.6	1.1
18:0	5.4	3.20
18:1n-9	15.6	9.63
18:2n-6 (linoleic acid)	2.4	2.03
18:3n-3 (α -linolenic acid)	2.4	0.7
20:1n-9	41.4	0.17
20:4n-3	-	0.84
20:4n-6 (arachidonic acid)	9.6	0.62
20:5n-3 (eicosapentaenoic acid)	252.0	16.78
22:1n-11	11.4	0.84
22:1n-9	5.4	0.09
21:5n-3 (docosapentaenoic acid)	12.6	2.18
22:5n-3	21.0	0.04
22:5n-6 (docosahexaenoic acid)	3.0	10.2

**Figure 1.** TAP2 genotyping by PCR. AA genotype was identified by the presence of 225 bp fragment, AG genotype by the presence of 225, 205, 20 bp fragments and GG genotype by 205 and 20 bp fragments.**Figure 2.** TAP1 genotyping by PCR. T allele gave a product of 183 bp and the C allele gave two fragments of 161 and 22 bp.

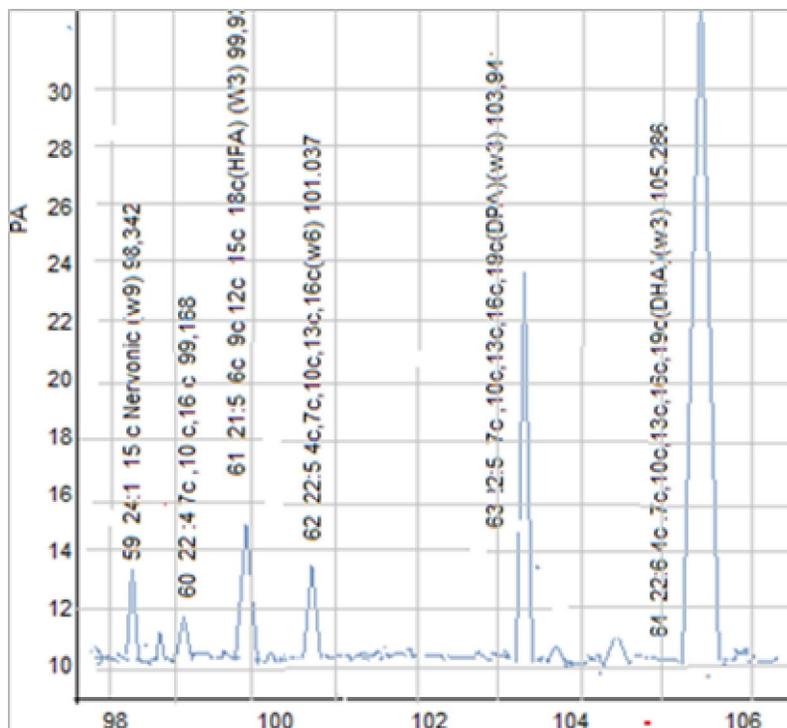


Figure 3. A part of the chromatogram of fish oil.

kits (Catalog Number: SEK10115, Sino Biological Inc.).

Statistical analysis

The association between polymorphism in TAP1 and TAP2 genes with the risk of AR was estimated by computing odds ratio (OR) and 95% confidence intervals (95% CI), using a multivariate logistic regression analysis. The Statistical analysis was performed using software SPSS version 10.0 (SPSS, Chicago, IL). Group results are expressed as means \pm SDs. ANOVA was used to compare treatment effects. Significance was set at $P < 0.05$.

RESULTS

The genotype of the TAP1 and TAP2 genes in AR cases and healthy controls derived from Egyptian population were analyzed. Demographic variables for cases and controls have been summarized in Table 2. The distribution of TAP1 genotypes among cases and controls was shown in Table 3. The frequency of TC genotype was greater in cases (49.0%) than controls (10.0%, OR = 8.7, 95% CI = 4.08 to 18.7, $P < 0.0001$). In case of TAP2, the frequency of AG genotype (50%) were greater in cases than controls (6%, OR = 13.8, 95% CI (4.06 to 47.21), $P < 0.0001$). The frequency of TT and AA genotypes was significantly lower in patients (20% for both) when compared to controls (89%, 91% respectively, $P < 0.0001$). Table 2 demonstrates the frequency of comorbid disorders among allergic rhinitis patients and controls. The most common comorbid

disorder of allergic rhinitis was nasal polyps (46%) followed by asthma (35%) and sinusitis (5%, $P < 0.05$). Table 4 demonstrates the distribution of TAP genotypes among allergic rhinitis patients in association with comorbid disorders. The frequency of TC, AG alleles were significantly higher among allergic rhinitis patients with nasal polyps, asthma than other comorbid disorders ($P < 0.001$). When the genotypes of TAP were stratified according to the severity, there was no significant association between both genotypes and the severity of AR.

The treatment with fish oil reduced AR symptoms up to 45% of cases without reporting any side effects, in the omega-3 group; symptoms were reduced up to 25% compared to 14% in the remaining group. The pretreatment mean level of MCAM in the patient group was 426 ± 35.5 pg/ml compared to 126 ± 32.1 pg/ml in the control ($P < 0.001$) (Figure 4). Moreover, the level of MCAM was significantly higher in severe compared to mild cases ($P < 0.01$) (Figure 5). The mean level in fish oil treated group decreased significantly compared to omega-3 treated group (225 ± 18.5 , 296 ± 21.3 pg/ml, $P < 0.05$) and both compared to pretreatment levels ($P < 0.001$ for both). The sensitivity and the specificity of MCAM were 84 and 85.7% respectively (area under the curve was 0.890). Figure 6 showed the hypersensitivity of allergic rhinitis patients to the different tested allergens by the skin prick test. The most common allergens in these patients were synthetic dye (48%), The least common allergens included fish and milk ($\approx 1\%$ for each one).

Table 2. Demographic and clinical characteristics of allergic rhinitis cases and controls.

Variables	Allergic rhinitis, n=100 (%)	Control subjects, n=100 (%)	P- value
Residence			
Rural	18	28	N.S
Urban	82	72	
Socioeconomic status			
High or moderate level	60	43	N.S
Low level	40	57	
Smoking			
+ve	35	6	$P < 0.01$
ve-	65	94	
History of skin allergy			
+ve	36	0.0	N.S
ve-	64	100	
Family history of allergic rhinitis			
+ ve	47	6	$P < 0.01$
-ve	54	95	
Comorbid disorders			
Nasal polyps			
+ ve	46	9	$P < 0.05$
-ve	54	91	
Asthma			
+ ve	35	14	$P < 0.05$
- ve	65	86	
Sinusitis			
+ ve	5	0	N.S
- ve	95	100	

DISCUSSION

Allergic rhinitis is a disease caused by inhalant exogenous antigens such as dyes and house dust mites and others; the preferential pathway of antigen processing is known to be MHC class II. However, inhalant antigenic peptides can be routed into the MHC class I pathway, involving TAP molecules in allergic rhinitis, this complex is expressed on the cell surface, where it is recognized by CD T cells (Cresswell, 1996; Trowsdale et al., 1990). Polymorphism in the TAP genes was assessed for evidence of association with allergic rhinitis. From this assessment, a significant difference was observed between allergic rhinitis and controls in subjects with the TC and AG genotypes carriers. These results suggest that TAP polymorphism is associated with the development of allergic rhinitis in Egyptians. On the other hand, the frequency of TT and AA genotypes were

significantly lower in patients (20% for both) when compared to controls (89 and 91%, respectively) presenting negative association of these genotypes with the disease group ($P < 0.001$). Ismail et al. (1997) reported similar results in Tunisian patients with atopy and asthma but Takeuchi et al. (2002) reported that the TAP1 gene is not primarily involved in susceptibility to allergic rhinitis in the Japanese population (Takeuchi et al., 2002). However, further population and functional studies are necessary to clarify the roles of the polymorphisms in allergic rhinitis. The addition of omega-3 capsules or fish-oil significantly decreased the plasma inflammatory biomarker MCAM because increase in the blood n-3 FA lowers plasma arachidonic acid concentrations, thus decreasing the synthesis of inflammatory prostaglandins, as seen in the present study (Bjorneboe et al., 1989). Ghanei et al. (2012) reported similar results in patients with pruritus and

Table 3. *TAP1* and *TAP2* genotypes in patients with allergic rhinitis and healthy controls.

<i>TAP1</i> genotypes	Case, n = 100 (%)	Control, n = 100 (%)	Odds ratio (95% confidence interval) P < 0.0001*	<i>TAP2</i> genotypes	Case, n = 100 (%)	Control, n = 100 (%)	Odds ratio (95% confidence interval) P < 0.0001*
TT	20	89	0.03 (0.01 - 0.06) P < 0.0001*	AA	20	91	0.02 (0.01 -0.05) P < 0.0001*
TC	49	10	8.7 (4.08 - 18.7) P < 0.0001*	AG	50	6	13.8 (4.06 - 47.21) P < 0.0001*
CC	31	1	44.4 (5.9 - 333.6) P = 0.02	GG	30	3	40.4 (17.4 - 93.8) P < 0.0001*

ORs were adjusted for age.

Table 4. Distribution of *TAP* genotypes among allergic rhinitis patients with comorbid disorders.

	AR with nasal polyps	AR with asthma	AR with sinusitis
TT	5(10%)	4 (11.4%)	1 (20%)
Odds ratio	1.6	3.8	0.8
95 % CI	0.5 -5.4, P = 0.3	1.5 - 9.3, P = 0.030	0.3 - 2.3, P = 0.7
TC	28 (56%)	15 (42.8%)	4 (80%)
Odds ratio	25.4	3.8	0.7
95 % CI	9.8 - 66.04, P < 0.0001*	1.5- 9.3, P = 0.04	0.2 - 2.4, P = 0.6
CC	13 (34%)	16 (45.7%)	
Odds ratio	14.8 - 74.8	121.8	--
95 % CI	P < 0.0001*	14.8 - 996.4, P < 0.0001*	
AA	6 (10%)	5 (14.3%)	1 (20%)
Odds ratio	0.03	0.77	0.74
95 % CI	0.009 - 0.1, P < 0.0001*	0.2 - 2.4, P = 0.6	0.2- 2.3, P = 0.755
AG	27 (54%)	16 (45.7%)	3 (60%)
Odds ratio	32.5	7.3	1.0
95 % CI	11.2 - 93.7, P < 0.0001*	2.6 - 20.3, P = 0.0001*	0.2- 4.1, P = 1 .0
GG	13 (36%)	14 (40%)	1 (20%)
Odds ratio	48.5	28.2	1.1
95 % CI	12.4 -189.2, P < 0.0001*	7.3 - 109.6, P < 0.0001*	0.1-11.6, P = 0.8

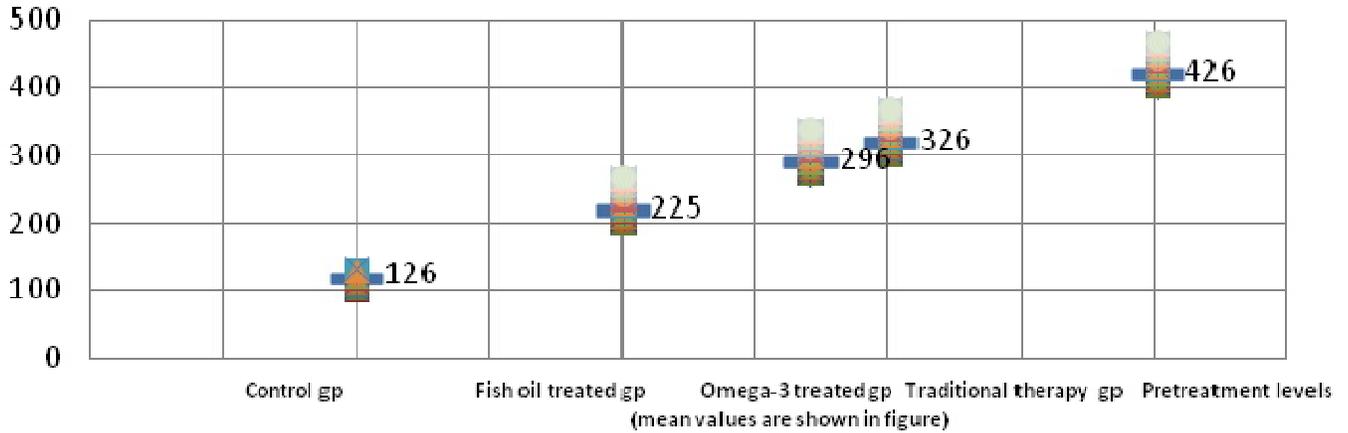


Figure 4. Scattergram showing the levels of MCAM in control group, fish oil treated group, Omega-3 treated group, the traditional therapy group and the pretreatment levels.

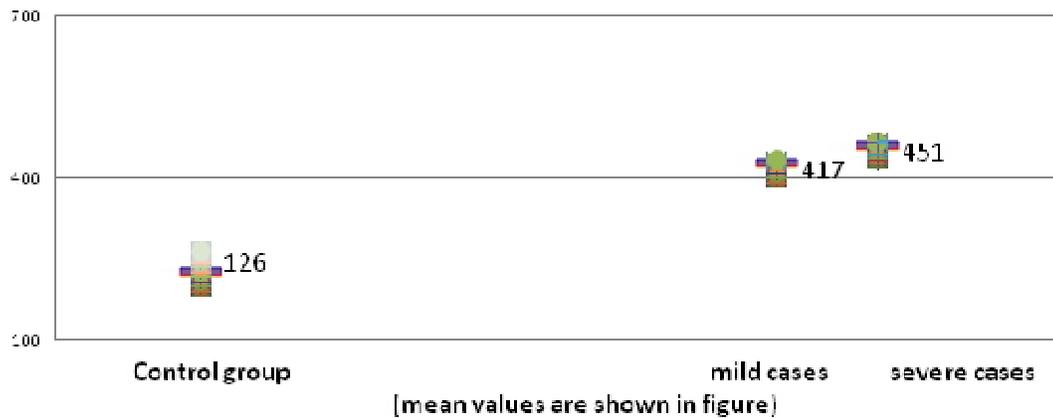


Figure 5. Scattergram showing the levels of MCAM in controls group, mild and severe cases before treatment.

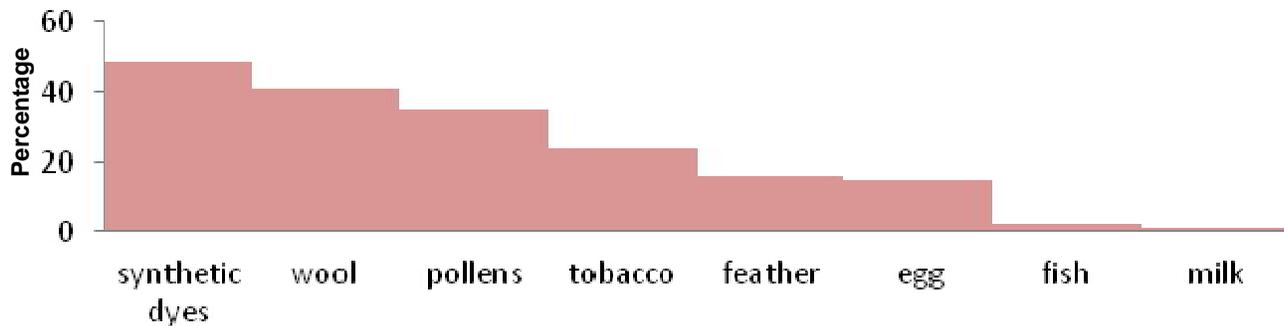


Figure 6. Results of skin prick test to the different tested allergens among allergic rhinitis patients.

concluded that fish oil contains EPA and DHA that have a pivotal role in maintaining the normal function of the nerve tissue and cellular membranes and could relieve skin disease such as eczema and even psoriasis (Ghanei

et al., 2012). Many other randomized trials have been demonstrative of the lowering effects of fish oil on the circulating endothelial dysfunction markers (Robinson and Stone, 2006; Kris-Etherton et al., 2002).



Figure 7. Samples of the textile stained with natural stains and used in the current study.

In summary, the current study clearly shows that supplementation of omega-3 can sufficiently improve AR. On the other hand, as expected, fish-oil supplementation also showed a better beneficial effect (may be due to the antioxidant content of vitamin E, A, B1, B2, B3, C, D, calcium and iron (Devereux and Seaton, 2005)). In addition, it was well-tolerated without any complications which suggest that dietary ingestion of plant-derived n-3 FAs could be effective in improving the treatment outcome of allergic rhinitis in humans.

Management of textile dye allergy includes use of topical and systemic glucocorticoids, avoidance of offending dye sources, tight synthetic Lycra clothing, 100 percent polyester linings, and nylon stockings. Instead, patients should wear 100 percent natural-based fabrics (that is, cotton, linen, silk, wool) (Hatch and Maibach, 1995). In the current study, five patients tried cotton textiles (damour textiles) as scarfs {stained with red onion (anthocyanidin dye) and *Punica granatum*, their dried peels boiled in water for 15 min, then the textile was added, boiled for another 15 min and dried, stabilized with NaCl, $\text{AlK}_2\text{O}_8\text{S}_2$ and $\text{KAl}(\text{SO}_4)_2$, they were stable during washing for one week} and reported marked improvement in allergic symptoms. Joe (2001) reported similar results and concluded that patients should wear 100% natural-based fabrics, undershirts, slip pants and loose-fitting clothing. In the current study, natural dyes allow the product to be completely natural in textile and dyeing, without any toxic or allergic substances, environmental friendly, healthy and safe to get rid of its waste products (Figure 7).

Conclusion

The study results indicated that the TAP alleles belong to the predictor gene set for allergic rhinitis and could be used in genomic analysis, MCAM is a sensitive biomarker. Omega-3 or better fish oil supplements (as a possible natural alternative source for omega-3 without side effects) and replacement of synthetic dyes by natural ones could improve allergic rhinitis patients.

REFERENCES

- Bjorneboe A, Soyland E, Bjorneboe GE, Rojka G, Drevon CA, 1989.** Effect of n-3 fatty acid supplement to patients with atopic dermatitis. *J Intern Med Suppl*; 731:233–236.
- Brannan JD, Bood J, Alkhabaz A, Balgoma D, Otis J, Delin I, Dahlén B, Wheelock CE, Nair P, Sven-Erik D, O'Byrne PM, 2014.** The effect of omega-3 fatty acids on bronchial hyperresponsiveness, sputum eosinophilia, and mast cell mediators in asthma. *Chest*, 147(2):397-405.
- Chae SC, Park YR, Li CS, Lee JH, Yang YS, Zhang Q, Kim KS, Chung HT, 2006.** Analysis of the variations in IL-28RA gene and their association with allergic rhinitis. *Exp Mol Med*, 38:302–309.
- Cresswell P, 1996.** Invariant chain structure and MHC class II function. *Cell*, 23:505–507.
- Devereux G, Seaton A, 2005.** Diet as a risk factor for atopy and asthma. *J Allergy Clin Immunol*, 115:1109–1117.
- Ghanei E, Zeinali J, Borghei M, Homayouni M, 2012.** Efficacy of omega-3 fatty acids supplementation in treatment of uremic pruritus in hemodialysis patients: a double-blind randomized controlled trial. *Iran Red Crescent Med J*, 14(9):515–522.
- Hatch KL, Maibach HI, 1995.** Textile dye dermatitis. *J Am Acad Dermatol*, 32(4):631-639.
- Hatch KL, Maibach HI, 2000.** Textile dye allergic contact dermatitis prevalence. *Contact Dermatitis*, 42(4):187-195.
- Ismaïl A, Bousaffara R, Kaziz J, Zili J, El Kamel A, Tahar Sfar M, Remadi S, Chouchane L, 1997.** Polymorphism in transporter antigen peptides gene (TAP1) associated with atopy in Tunisians. *J Allergy Clin Immunol*, 99(2):216-23.
- Joe EK, 2001.** Allergic contact dermatitis to textile dyes. *Dermatol Online J*, 7(1):9.
- Kim KR, Cho SH, Choi SJ, Jeong JH, Lee SH, Park CW, Tae K, 2007.** TAP1 and TAP2 Gene Polymorphisms in Korean Patients with Allergic Rhinitis. *J Korean Med Sci*, 22(5):825–831.
- Kris-Etherton PM, Harris WS, Appel LJ, 2002.** Fish consumption, fish oil, omega-3 fatty acids, and cardiovascular disease. *Circulation*, 106(21):2747–2757.
- Kull I, Bergstrom A, Melen E, Lilja G, van Hage M, Pershagen G, Wickman M, 2006.** Early-life supplementation of vitamins A and D, in water-soluble form or in peanut oil, and allergic diseases during childhood. *J Allergy Clin Immunol*, 118:1299–1304.
- Lazarov A, Trattner A, David M, Ingber A, 2000:** Symptoms and signs reported during patch testing. *Am J Contact Dermat*, 11(1):26-29.
- Pratt M, Taraska V, 2000.** Disperse blue dyes 106 and 124 are common causes of textile dermatitis and should serve as screening allergens for this condition. *Am J Contact Dermat*; 11(1):30-41.
- Robinson JG, Stone NJ, 2006.** Antiatherosclerotic and antithrombotic effects of omega-3 fatty acids. *Am J Cardiol*, 98(4A):39i–49i.
- Takeuchi K1, Abe S, Masuda S, Yuta A, Majima Y, Sakakura Y, 2002.** Lack of association between gene polymorphism of transporters associated with antigen processing and allergic rhinitis in a Japanese population. *Ann Otol Rhinol Laryngol*, 111:460-463.
- Tamandani DMK, Sobti RC, Shekari M, Hussein SA, Suri V, 2009.** No association of TAP1 and TAP2 genes polymorphism with risk of cervical cancer in north Indian population. *J Assist Reprod Genet*, 26(4):173–178.
- Trowsdale J, Hanson I, Mockridge I, Beck S, Townsend A, Kelly A, 1990.** Sequences encoded in the class II region of the MHC related to the "ABC" superfamily of transporters. *Nature*, 348:741–744.
- Wallace DV, Dykewicz MS, Bernstein DI, Blessing-Moore J, Cox L, Khan DA, Lang DM, Nicklas RA, Oppenheimer J, Portnoy JM, Randolph CC, Schuller D, Spector SL, Tilles SA, 2008.** The diagnosis and management of rhinitis: An updated practice parameter. *J Allergy Clin Immunol*, 122:S1.

Citation: Hana RS, Bawi BL, Eshak NS, Ahmed AA, 2015. Genetic, environmental and dietary factors affecting the prognosis of allergic rhinitis. *Biochem Biotechnol Res*, 3(2): 30-37.
