



Short Communication

THE RELATIONSHIP BETWEEN ASTHMATIC PATIENTS NASAL INFECTION WITH *STAPHYLOCOCCUS AUREUS* AND ASTHMA

Mohammed Mousa Atta, Adnan Jawad Ahmed*, Hatim Abd-Al-Kareem and Duaa Yahea Talib

College of Agriculture, University of Sumer, 64005, Rifai DhiQar, Iraq.

Abstract

This study aimed to prove the relationship between nasal infection with *S. aureus* and development of severe clinical signs of asthma, this study is carried out in Al-Hussein teaching hospital / Al-Nasiriya city and other part in animal house / college of Agriculture / Sumer university at the period 1/11/2017-1/2/2018, (20) twenty samples of nasal swabs collected from asthmatic patients transported to the lab. by using transport media for detection of *Staphylococcus aureus* after that this bacteria injected intra-nasally in the lab. animal (Rats) and after one month (10) ten serum samples taken for measurement of (IFN γ , IL-4, IL-5, IL13 and IgE), the results showed existence of *S. aureus* in the nasal cavity of Rats and the concentration of these cytokines as followed :significant increasing in the titters of IFN γ (527.173) ; IL-4 (656.03) ; IL-5 (425.05) ; IL-13 (405.11) and IgE (35.51) compared to control groups (139.32) ; (36.115) ; (46.160) ; (42.25) and (1.6) respectively. concluded there was closely relationship between nasal infection with *S. aureus* and development of severe clinical signs of asthma in asthmatic patients.

Key words : asthmatic, *Staphylococcus aureus*, IFN γ , IgE

Introduction

Airway allergy is a worldwide health problem, an estimated 300 million persons worldwide have asthma and about 400 million persons suffer from allergic rhinitis, the prevalence of both diseases is markedly increasing (Aceves, 2008). Allergic reactions occur to normally harmless environmental substances known as allergen ; these reactions are acquired, predictable and rapid (Adamko *et al.*, 1999). Strictly, allergy is one of four forms of hypersensitivity and is called type I or (immediate) hypersensitivity, its characterized by excessive activation of certain white blood cells called mast cells and basophiles by a type of antibodies known as IgE, resulting in an extreme inflammatory response (Ahmadi *et al.*, 2003). Common allergic reactions include eczema, hives, hay fever, asthma attacks, food allergies and reaction to venom of insect sting such as wasps and bees (Aihara *et al.*, 2004). Many factors take part in the

pathogenicity of asthma as decreasing in IFN γ secreted from (Th1), increasing of (IL-4) which necessary for B cell growth, promoting (Th2) differentiation and IgE synthesis and (IL-5) which responsible for growth, differentiation and survival of eosinophils in bronchi and the source of these two cytokines from (Th2). There are many factors included in asthma pathogenicity as hereditary causes so that the genetic susceptibility of family has greater effect in the incidence of asthma attacks, Scientists found about 25 genes take part in pathogenicity of asthma also environmental factors as air pollution, pollens, vapors added to that some chemicals as formaldehyde (Aihara *et al.*, 2003). But recently the Scientists directed towards clarify the possible role of Rhinosinusitis and nasal polyps as predisposing factors for asthma which caused by several microbes included *Staphylococcus aureus* and its toxins specially (SEB) has greater effect in this disease so that this study aimed to prove that the *Staphylococcus aureus* and its toxins one of causative factors of asthma through applied of Koch

*Author for correspondence : E-mail :Adnanjawad@yahoo.com

Postulate.

Materials and methods

This (case–control) study included (20) twenty asthmatic patients admitted to the Al- Hussein Teaching Hospital / Respiratory and Thoracic diseases department in Al- Nasiriya city from period 1/7/2017 – 1/8/2017 who diagnosed depending on clinical signs and radiological examination.

Results

Asthma is consider as one of the common inflammatory disorders (chronic inflammatory disorders) which increase in spreading in our environment as a result of exposure to many effectors or environmental allergens or there was genetic susceptibility that combined with excessive production of IgE antibodies specifically to stimulated antigens as Chinopodium which result in Allergic bronchitis, Rhinosinusitis, Contact dermatitis added to that increase stimulation of (Th2) which secrete large quantity of cytokines as (IL-4, IL-5 and IL-13) which consider as chief key to develop of hyper responsiveness. This study depend on measurement of (IgE, IL-4, IL-5 IL-13 and IFN γ) in the serum samples taken from (10) ten of lab. animals (Rabbits). this study showed statistically significant increasing ($p=0.05$) in IFN γ level which was in lab. Animals (527.173) and in control group was (139.32) ; statistically significant increasing in titter of IL-4 ($p=0.05$) which was (656.03) and in control group (36.115); in case of IL-5 there was statistically significant increasing($p=0.05$) was (425.05) and in control group (46.166) also in case of IL-13 was (405.11) and in control group (42.25) added to that IgE antibody titter was (35.51) and in control group (1.6). microbial examination of this study revealed to isolation of *Staphylococcus aureus* from nasal cavity of asthmatic patients and from nasal cavity of Rabbits after month of intra nasal injection.

Discussion

This study showed statistically significant increasing in IFN γ compared with control group and this agreed with many studies that found significant increasing in IFN γ in asthmatic patients infected with nasal *Staphylococcus aureus* and this fact explained by that the increasing in IFN γ necessary in immunological response against bacterial infections which act as activator and stimulator of the macrophage, NK, antigen presentation on the surface of the macrophage and stimulation of WBC transmigration from blood vessels to the site of infection, increasing in titter of IL-4 in asthmatic patients and this

type of interleukins consider as important one in growth, survival and differentiation of B lymphocytes also plasma cells and production of antibodies specially IgE and increase of no. of eosinophils in respiratory tract added to that IL-13 which has same effect, increasing of IL-5 agreed with many studies on asthmatic patients which responsible for increase no. of eosinophils growth and differentiation so that, its responsible for greater part of asthma pathogenicity due to its presence in large no. in respiratory tract and in case of IgE there was significant increasing in serum of lab. animals specially those infected with *S. aureus* compared with control group. further studies for elucidating mechanisms and for confirming their relationships between asthma and infection with *S. aureus* in large scale population there are many different studies proved that *S. aureus* and its toxins have major role in asthma as following :

1. Bachert *et al.*, (2012), found enterotoxin IgE positivity was significantly greater in patients with severe asthma than in healthy control subjects so that they proved SE IgE antibodies but not IgE against inhalant allergens are risk factors for asthma severity and hypothesize that the presence of enterotoxin IgE in serum indicates the involvement of Staphylococcal super antigens in pathophysiology of patient with severe asthma.
2. Yang *et al.*, (2005), proved that the asthma is closely related with sinusitis by taking 85 asthmatic patients they found 51 of 85 patients with high serum anti staphylococcus enterotoxin B antibody before treatment obtained satisfactory results for both sinusitis and asthma.
3. Kowalski *et al.*, (2011), observed that total IgE had a strong correlation with specific IgE to SEs in serum from asthma patients that was independent of atopic status and these two factors significantly correlated with asthma severity markers.
4. Xin Yan *et al.*, (2015), found positive rate and level of SEB specific IgE significantly higher in the serum from Chinese patients with Chronic Rhinosinusitis without nasal polyp than that from healthy control so, the positive rate and level of SEB – specific IgE in Chronic Rhinosinusitis with nasal polyp showed an increasing trend but didn't reach significance.
5. Lara *et al.*, (2010), proved that the *S. aureus* is correlated with the development of persistent severe inflammatory diseases of the upper airway including Chronic Rhino sinusitis with nasal polyp.
6. Tomassen *et al.*, (2013), in first large – scale population – based epidemiological study to demonstrate the

sensitization to *S. aureus* enterotoxins in European volunteers, they are demonstrated that IgE sensitization to SE is common in Europe, may occur in the absence of sensitization to other allergens (aeroallergens such as house dust mite), probably reflecting a different pathophysiologic basis, this effect may be mediated through its association with strongly increased total IgE concentration via polyclonal super antigen action of enterotoxins.

7. The effects of *S. aureus* nasal carriage on nasal cytokines environment was noticed by Riechelmann *et al.*, (2015) and Refaat *et al.*, (2008) who found that *S. aureus* nasal carriage in allergic rhinitis patients was associated with high levels of nasal IL-4 and IL-13 (Th2 cytokines) and low level of IFN γ (Th1 cytokines) and its associated with high nasal IgE level suggesting that nasal *S. aureus* can augment Th2 bias and promote local IgE production thus can actively modulate the allergic reaction in affected tissues.
8. Ensaf *et al.*, (2015) found significant positive correlation between SEB – specific IgE level in patients and markers of severity of allergic reaction including blood eosinophilia, ECP and total IgE levels, So that, they suggest that nasal carriage of enterotoxin producing *S. aureus* has a potential role in the development and severity of allergic airway diseases.

References

- Aceves, S.S. and D.H. Broide (2008). Airway fibrosis and angiogenesis due to eosinophil trafficking in chronic asthma. *J. Exp. Med.*, **53(2)**:894-920.
- Adamko, D.J., B.L. Yost, A.D. Fryer and D.B. Jacoby (1999). Ovalbumin sensitization changes the inflammatory response to subsequent para influenza infection. Eosinophils mediate airway hyperresponsiveness, m(2) muscuranic receptor dysfunction, and antiviral effects. *J. Exp. Med.*, **53(2)**: 884-901.
- Ahmadi, K.R., J.S. Lanchbury, P. Reed, M. Chiano, D. Thompson, M. Galley, A. Line, E. Lank, H.J. Wong, D. Strachan and T.D. Spector (2003). Novel association suggests multiple independent QTLs within chromosome 5q21-33 region control variation in total humans IgE levels. *Genes Immun.*, **4(4)**: 289-97.
- Aihara, M., K. Dobashi, K. Iizuka, T. Nakazawa and M. Mori (2003). Comparison of effects of Y-27632 and Isoproterenol on release of cytokines from human peripheral T cells. *Clin. Exp. Allergy.*, **7(12)**:444-475.
- Aihara, M., K. Dobashi, K. Iizuka, T. Nakazawa and M. Mori (2004). Effect of Y-27632 on release of cytokines from peripheral T cells in asthmatic patients and normal subjects. *Clin. Exp. Allergy.*, **2(9)**: 175-195.
- Akbari, O., R.H. Dekruyff and D.T. Umetsu (2001). Pulmonary dendritic cells producing IL₁₀ mediate tolerance induced by respiratory exposure to antigen. *Nat. Immunol.*, **2**: 725_731. {pub Med}.
- Akdis, M. *et al.*, (2004). Immune responses in healthy and allergic individuals are characterized by a fine balance between allergen -specific T regulatory 1 and T helper2 cells. *J. Exp. Med.*, **199**: 1567_1575.
- Akpinarli, A., D. Guc, O. Kalayci and E. Yigitbas (2002). Increased interleukin-4 and decreased interferon gamma production in children with asthma: function of atopy or asthma? *Asthma.*, **39(2)**:159-65.
- Akuthota, P., J.J. Xenakis and P.F. Weller (2011). Eosinophils : Offenders or general bystanders in allergic airway disease and pulmonary immunity? *J. Innate immune*, **37(1)**: 94-111.
- Al-Zubadi, A.A. (2013). Interferon gamma gene polymorphism as predisposing factor to tuberculosis in Babylon Province. pH thesis.
- American Thoracic Society (1995). Standardization of spirometry. *Am. J. Respir. Crit. Care Med.*, **152(3)**:1107-36.
- Anderson, H.R. (2005). Prevalence of asthma. *Br. Med. J.*, **330(5)**: 1037_8.
- Arzu, D., B. Yalcin, B. Atil and M. Reginald (2012). IL-8, IL-10, TGF β and GCSF levels were increased in severe persistent allergic asthma patients with anti IgE treatment.
- Asher, I., E. Dagli, S.G. Johansson, H. Karen and H. Tari (2004). Environmental Influences on Asthma and Allergy Prevention of Allergy and Allergic asthma. World Allergy Organization Project Report and Guidelines. *ChemImmunol Allergy. Basel, Karger*, 36-101.
- Bachert, C., P. Gevaert, N. Zhang, T. Van-Zele and C. Perez-Novo (2007). Role of staphylococcal superantigens in upper airway disease super-antigens and Allergens. *Chem. Immunol. allergy.*, **93**: 214
- Bachert, C., K. Vansteen, N. Zhang and G. Holtappels (2012). Specific IgE against *S. aureus* enterotoxins : an independent risk factor for asthma. *J. Allergy. Clin. Immunol.*, **130(2)**: 376–381.
- Badthoorn, E., A. Limburg, J.J. Bouwman, A.W. Bossink and S.F. Thijsen (2011). Diagnostic potential of an enzyme-linked immunosorbent assay in Tuberculous Pericarditis. *Clin. Vaccine Immunol.*, **18**: 874_877.
- Bailey, T., S. Stark, A. Grant, C. Hartnett, M. Sang and A.A. Kalyuzhny (2002). Multi-donor ELISPOT study of IL_{1B}, IL₂, IL₄, IL₆, IL₁₃, IFN γ and TNF α release by cryopreserved human peripheral blood mononuclear cells. *J. Immunol. Methods.*, **270**: 171_182.
- Bakolis, I., J. Heinrich, J.P. Zock, D. Norback, C. Svanes, C.M. Chen, S. Accordini, G. Veriato, M. Olivieri and D. Jarvis (2015). House dust – mite allergen exposure is associated with serum specific IgE but not with respiratory outcomes. *Indoor Air.*, **25(3)**: 235 – 244.

- Baldacci, S., E. Omenaas and M. Oryszczyn (2001) : Allergy markers in respiratory epidemiology. *Eur. Respir. J.*, **17**:773-90.
- Barrat, F.J. *et al.*, (2002). In vitro generation of interleukin 10 producing regulatory CD4(+) T cells is induced by immunosuppressive drugs and inhibited by T helper type 1(Th1) and Th2 inducing cytokines. *J. Exp. Med.*, **195**: 603_616.
- Bassuny, W.M., K. Ihara, Y. Sasaki, R. Kuromaru, H. Kohno and N. Matsuura (2003). Functional polymorphism in the promoter/enhancer region of the FOXP3/Scurfin gene associated with type I diabetes. *Immunogenetics*. **55**: 149_56.
- Belkaid, Y., C.A. Piccirillo, S. Mendez, E.M. Shevach and D.L. Andsacks (2002). CD4+CD25_ regulatory T cells control leishmania major persistence and immunity. *Nature*, **420**: 502_507.
- Beltrani, V.S. and M. Boguniewicz (2003). Atopic Dermatitis. *Dermatol. Online J.*, **9(2)**:1.
- Bener, A., W. Safa, S. Abdulhalik and C.G. Lestringant (2002). An analysis of skin prick test reactions in asthmatics in a hot climate and desert environment. *Allergy Immunol.*, **34(8)**: 281-6.
- Bernstein, I.L., J.T. Li, D.I. Bernstein, R. Hamilton, S.L. Spector and R. Tan (2008). *An Allergy Asthma Immunol.* **100**: s15-s66
- Bettiol, J., P. Bartsch, R. Louis, D. De Groote, Y. Gevaerts, E. Louis and M. Malaise (2006). Cytokine production from peripheral whole blood in atopic and non atopic asthmatics: relationship with blood and sputum eosinophilia and serum IgE levels. *Allergy*, **55**:1134-41.
- Blease, K., S.I. Kunkel and C.M. Hogaboam (2000). Acute inhibition of nitric oxide exacerbates airway hyperresponsiveness, eosinophilia and C₂C chemokine generation in a murine model of fungal asthma. *Inflamm. Res.*, 49,297-304.10.1007-pl0000210 {pub Med} {cross ref}
- Borish, L., A. Aarons, J. Rumblyrt, P. Cvvietusa, J. Negri and S. Wonzeal (2004). IL-10 regulation in normal subjects and patients with asthma *J. Allergy Clin. Immunol.*, **97**: 1288 96.