



Infections to allergies via antibiotics: A triangular scenario.

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ABSTRACT

Antibiotics could upset the body's normal balance of Th₁ and Th₂ immune functions. Such an imbalance could possibly result in increased occurrence of allergies. Estimation of Total serum IgE, which is a product of Th₂ function, is the primary diagnostic test for Type I allergic diseases. The present study compares total serum IgE levels in 'on antibiotic' versus 'not on antibiotic' random population. 200 subjects (aged 18 – 50 years) from general population were randomly recruited for the study. Their total serum IgE levels were estimated using enzyme immuno assay technique. To blind the study the subjects' history of 'antibiotic consumption' and 'allergy symptoms and diagnosis' was taken post estimation of total serum IgE levels. The subjects were categorized in two groups: those who had not taken any antibiotics for ≥ 1 year formed the 'not on antibiotic' group and rest were the ones who had taken antibiotics within one year and formed 'on antibiotic' group. Total serum IgE levels, allergy symptoms and diagnosis of allergic disease were compared between these two groups. The total serum IgE levels of the 'on antibiotic' group were significantly greater as compared to the 'not on antibiotic' group ($p < 0.001$). Symptoms and diagnosis of allergic disease were also significantly higher in the 'on antibiotic' group as compared to the 'not on antibiotic' group ($p < 0.001$). To conclude use of antibiotics might deviate the immune-system towards allergies.

Keywords: Antibiotics, Allergy, IgE

INTRODUCTION

Allergies and asthma has increased globally. But pinning down the causes of the rise has proved difficult. Physicians from any faculty would readily agree that it is very common to find patients suffering alternatively from infections and allergies. It will be certainly interesting to find out clues to understand this congruent events of disease. The current study was aimed to find out if use of antibiotics may have a role to play in patients who get tossed between infections and allergies¹. Mairi Noverr and Gary Huffnagle² has provided an experimental evidence in mice that antibiotics can upset the gut flora which can provoke an allergic response. A study from Poland has suggested that maternal use of antibiotics during pregnancy may prove to be a risk factor for persistent wheezing and development of allergy in early infancy³. A birth

cohort study based on the West Midlands General Practice Research Database had investigated records of 29,238 children for early exposure to infections, use of antibiotics and the incidence of allergic disease. This study could find no evidence supporting exposure to infections and reduced incidence of allergic disease, and concluded that the use of antibiotics to treat infections might be associated with early diagnosis of allergic disease⁴. A recent study published in the Journal of Epidemiology has reported that early antibiotic use was associated with asthma and allergy at 6 years of age⁵. The current study was taken up to evaluate if use of antibiotics in adult population over a defined period could have a role in raised occurrence of allergic diseases.

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Conflict of Interest—none

MATERIALS AND METHODS

The study was carried out at a Mumbai city hospital over the period of 2 years. 200 subjects from general population (aged 18 – 50 years) were randomly recruited for the study. 5 mL blood was collected in a plain vacutainer and total serum IgE levels were estimated using enzyme immuno assay (VIDAS bioMérieux)⁶. 25 known positive and known negative samples for total serum IgE served as controls. To blind the study the subjects' history of 'antibiotic consumption' and 'allergy symptoms and diagnosis' was taken post estimation of total serum IgE levels. The subjects were categorized in two groups: those who had not taken any antibiotics for ≥ 1 year formed the 'not on antibiotic' group and rest were the ones who had taken antibiotics within one year and formed 'on antibiotic' group. Total serum IgE levels and allergy status were compared between these two groups. Descriptive statistics was used to analyze the data.

RESULTS

The results indicated significantly high ($p < 0.001$) prevalence of allergic diseases in the 'on antibiotic group' as compared to the 'not on antibiotic group' (Table 1). Out of 200 randomly recruited subjects

126 (63%) were on antibiotic within one year period and 74 (37%) were not on antibiotic for ≥ 1 year. Amongst the 'on antibiotic group' of 126 subjects 110 (87%) had history of doctor diagnosed allergic disease. Amongst the 'not on antibiotic group' of 74 subjects 24 (32.4%) had history of doctor diagnosed allergic disease. This difference was statistically significant $p < 0.001$ (Table 1).

The 'on antibiotic group' ($n=126$) had consumed antibiotics for various reasons like fever, common cold, sore throat, cough, dental problems, gastro intestinal discomforts, fall and pimples (Figure 1). They could not be segregated based on the type of antibiotic due to different types, varying dosage, different time gap, etc.

The median IgE value for 'not on antibiotic group' ($n=74$) was 85 IU/mL and for 'on antibiotic group' ($n=126$) was 320 IU/mL (Figure 2). The varied allergy symptoms in both the groups as noted from the patients' clinical history and their doctors diagnosis were atopic dermatitis, hives, food allergy, drug reactions, allergic rhinitis and extrinsic asthma (Table 2).

Table 1 Antibiotic v/s not on antibiotic subjects and occurrence of allergy

Category	Allergic	Not allergic	Total
On antibiotic	110	16	126
Not on antibiotic	24	50	74
Total	134	66	200

Chi-square: 63.48, Degree of freedom:1, $p < 0.001$

Table 2 Antibiotic consumption and distribution of allergy symptoms

Allergy Symptoms	'not on antibiotic group' ($n=74$)	'on antibiotic group' ($n=126$)
Atopic dermatitis	1	2
Hives	5	10
Food allergy	1	12
Drug reactions	2	16
Allergic rhinitis	5	30
Extrinsic asthma	10	40

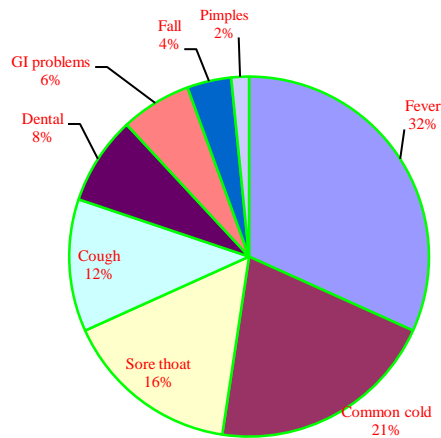


Figure 1 Symptoms and antibiotic consumption

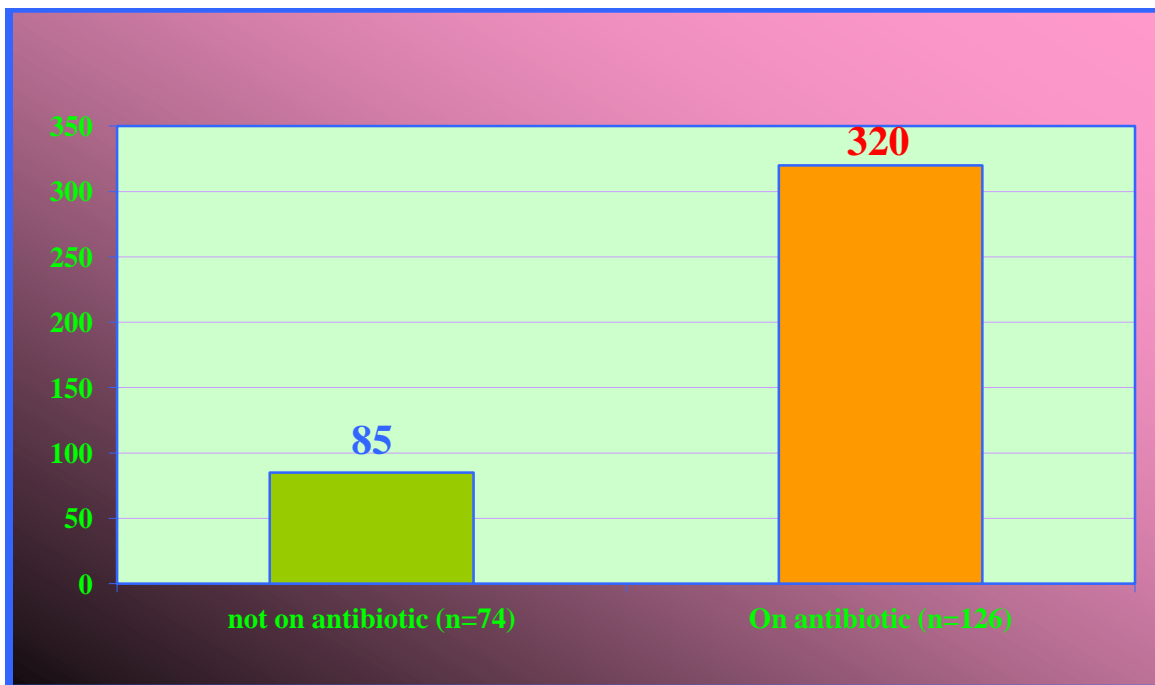


Figure 2 Comparison of median IgE IU/mL

DISCUSSION

Immune system comprises of two types of immunity: cell-mediated (T-helper cell 1) or Th1 which is infection oriented, and humoral (T-helper cell 2) or Th2 which is allergy oriented immunity. At

the time of birth neonates have humoral or Th2 type immunity as the intrauterine environment is predominantly Th2⁷. After birth as one comes across various infections the cell-mediated or Th1 immunity develops. And at the time of 2-3 years of

age a balanced Th₁-Th₂ status is achieved. Once balanced the immune system becomes dynamic, now when it comes across any infection it goes back and forth between Th₁ and Th₂- fights of the infection - regains the balance and restores health. In chronic infectious diseases when the immune system fails to combat the infection, the Th₁ function goes on increasing leading to an imbalance between the Th₁ and Th₂ immunity. In such situation antibiotics are given to the sufferer to get rid of the infection. Ideally therapy with antibiotics should fight of the infection, lower the Th₁ and resumes balance with Th₂. But, antibiotics can not differentiate the infection from the healthy common flora of the body resulting in dysbiosis or killing of the common body-friendly microflora. This

results in undue reduction in Th₁ that further results in reversing of the imbalance from Th₁ predominance to Th₂ predominance⁸. Besides, when antibiotics are prescribed and administered in anticipation of an infection, or for mild infections, or for prophylactic purpose or without checking for antibiotic sensitivity test it could result in further undue reduction of Th₁, and further Th₂ domination. On the other hand, when the antibiotics are given without checking patient's allergic skin reaction, and if the patient ends up with an allergic reaction, this too would add to the Th₂ dominance.

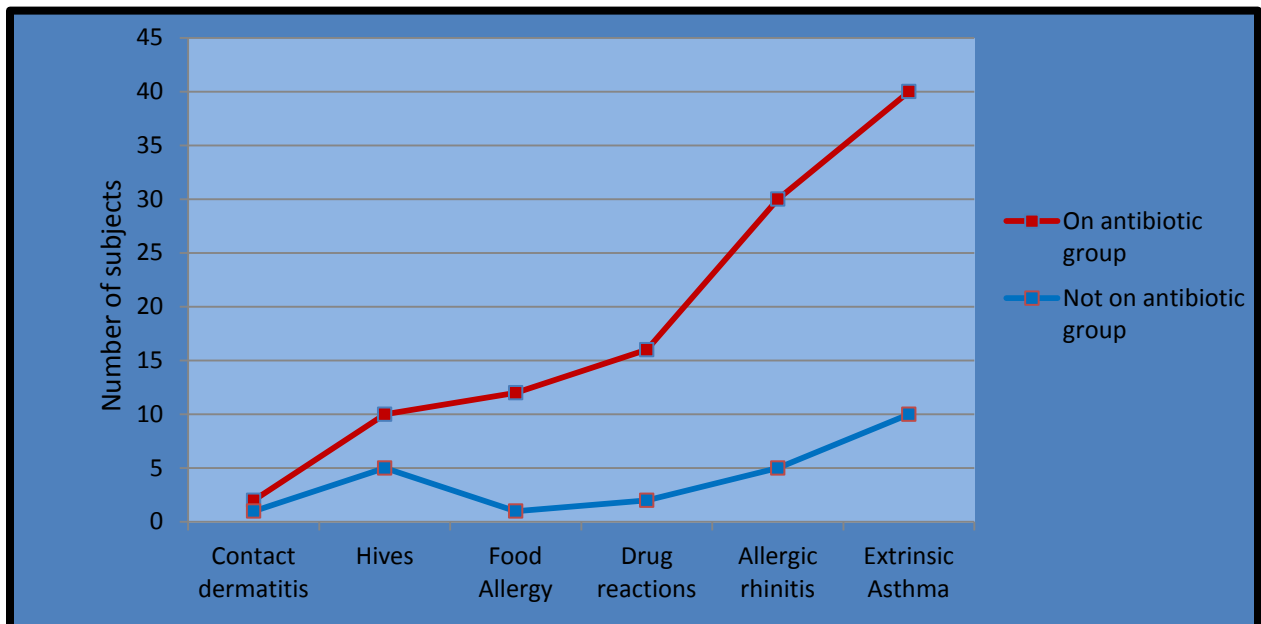


Figure 3 Symptoms of allergy and number of subjects in 'On antibiotic' v/s 'Not on antibiotic' group

IgE is the signature antibody of Th₂ functions⁹ and is the principal diagnostic test for Type I allergic diseases. Significantly raised ($p < 0.001$) total serum IgE levels of the 'On antibiotic group' v/s 'not on antibiotic group' (Figure 2) are indicative of a possible role of antibiotics in causing Th₂ predominance leading to allergies^{10,11}. Allergic march is the progression of allergic conditions from the primary symptoms of allergy like atopic

dermatitis to the complicated allergic conditions like asthma¹². When the study findings of allergy symptoms in the 'On antibiotic group' v/s 'not on antibiotic group' (Table 2, Figure 3) are compared it is very obvious that the expression of allergic symptoms and the progression of allergic march is more in the 'On antibiotic group' subjects.

Further if allergies are not treated Th2 predominance with low Th1 immunity makes the human body an easy target for infection. Such infection could again catch patient's and the treating physician's attention and might get treated with an antibiotic. Thus, these patients enter a vicious condition and perennially suffer from infections, allergies or both.

CONCLUSION

Use of antibiotics might deviate the immune-system towards allergies. And this could be an important reason for rise in allergic diseases. The study indicates need for justified use of antibiotics. Prophylactic application of antibiotics calls for cautious attention with regards of immunity balance.

REFERENCES

1. Gaash, B. 2008: Irrational Use of Antibiotics. *Indian J Practising Doctor* 5: 2008-03 – 2008-04.
2. Mairi, C. N. and Gary, B. H. 2004: Does the microbiota regulate immune responses outside the gut? *Trends in Microbiology* 12: 562-568.
3. Jedrychowski, W., Gałaś, A., Whyatt, R., and Perera, F. 2006: The prenatal use of antibiotics and the development of allergic disease in one year old infants: A preliminary study. *Int J Occup Med Environ Health* 19: 70-76.
4. McKeever, T.M., Lewis, S. A., Smith, C., Collins, Heatlie JH, Frischer, M., and Hubbard, R. 2002: Early exposure to infections and antibiotics and the incidence of allergic disease: a birth cohort study with the West Midlands General Practice Research Database. *J Allergy Clin Immunol* 109: 43-50.
5. Risnes, K.R., Belanger K., Murk W., and Bracken M.B. 2011: Antibiotic exposure by 6 months and asthma and allergy at 6 years: Findings in a cohort of 1,401 US children. *Am J Epidemiol* 173: 310-318.
6. Seka-Seka, J., Brouh, Y., Yapó-Crézoit, A.C., and Atseye N.H. 2004: The Role of Serum Immunoglobulin E in the Pathogenesis of Plasmodium falciparum Malaria in Ivorian Children. *Scandinavian Journal of Immunology* 59: 228-230.
7. Raghupathy, R. 1997: Th-1 type immunity is incompatible with successful pregnancy. *Immunol Today* 18: 478-482.
8. Bamias, G., Marini, M., Moskaluk, C., Odashima, M., Ross, W., Rivera-Nieves J., et al. 2002: Down-Regulation of Intestinal Lymphocyte Activation and Th1 Cytokine Production by Antibiotic Therapy in a Murine Model of Crohn's Disease. *The Journal of Immunology* 169: 5308-5314.
9. Shah, S., and Bapat, M. 2006: Parental history of allergy, maternal serum IgE & cord serum IgE. *Indian journal of medical sciences* 60: 1: 13-18.
10. Williams, C.A., Galley, H.F., Watt, A.M., and Webster, N.R. 2005: Differential effects of three antibiotics on T helper cell cytokine expression. *Journal of Antimicrobial Chemotherapy* 56: 502-550.
11. Oyama, N., Sudo, N., Sogawa, H., and Kubo, C. 2001: Antibiotic use during infancy promotes a shift in the TH1/TH2 balance toward TH2-dominant immunity in mice. *J Allergy Clin Immunol*, 107: 153-159.
12. Wahn U. 2001: Review. Series VI: The immunology of fetuses and infants: what drives the allergic march? *Allergy* 55: 591-599.

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