

KNOWLEDGE, ATTITUDE AND PRACTICES OF GENERAL PRACTITIONERS AND HOMEOPATHS REGARDING FOOD ALLERGY AND ANAPHYLAXIS IN INDIA- A COMPARITIVE STUDY.

P.Uday Kumar, Priyanka Jain, Vasanthi Siruguri* M V Surekha, **Vishnu Vardhan Rao

Department of Pathology & EM, Department of Food Toxicology*, Department of Biostatistics**
National Institute of Nutrition, Hyderabad, India.

ABSTRACT

Food allergy (FA) is a growing health problem in India and worldwide with notable prevalence in infants when compared with children and adults. Multiple genetic and nutritional factors play an important role in etiology of FA leading to morbidity and mortality. As general practitioners (GPs) and homeopaths are the first persons to be approached by patients with possible FA, the need for evaluating their Knowledge, Attitude and Practices (KAP) towards the same are essential to be studied. A total of 214 participants- 107 GPs with or without specialization in Internal Medicine and 107 homeopaths participated in the study. A validated questionnaire was adopted to assess their KAP. The questionnaire had 31 parameters (demographic details-5, knowledge-21 and attitude and practices-5) regarding symptoms, severity, risk factors, diagnosis and treatment of FA. The score was recorded and results with p -value ≤ 0.05 were considered statistically significant. A significant difference in the perception of FA was observed between GPs (42.1%) and homeopaths (10.3%) regarding the safety of administering influenza vaccines in children with egg allergy ($p=0.003$). 80.4% of GPs and 23.3% homeopaths believed that epinephrine is the 1st line choice for treatment of anaphylaxis ($p=0.035$). 64.5% GPs and 28.1% homeopaths opined that timely administration of epinephrine prevents fatal anaphylaxis which was statistically significant. ($p=0.046$). However no statistically significant difference ($p=0.112$) was found between GPs (65.4%) and homeopaths (58.9%) in their opinion regarding the reliability of positive skin prick test or radioallergosorbent test (RAST) as sufficient FA diagnostic tool. The total scores obtained regarding the knowledge in FA and anaphylaxis by GPs and homeopaths was 66.4% and 46.8% respectively which was not found to be statistically significant ($p=0.172$). Overall knowledge of FA in GPs and homeopaths was comparable with strengths and weakness in each domain. GPs had more precise knowledge than homeopaths, regarding the treatment schedule, in case of anaphylaxis, which in turn reflects the differences in attitude and approach in treating FA among the two groups. Periodic educational programs focused at improving the knowledge regarding food allergy and treatment options is a prerequisite among GPs and homeopaths help them to understand better as well as treat the adverse effects of FA.

KEYWORD: Anaphylaxis, food allergy, general practitioners, homeopaths, KAP, scoring validated questionnaire.

INTRODUCTION

Food allergy (FA) is estimated to affect 1-2% of adult population and 6-8% of children worldwide¹. FA and eczema are common non-communicable diseases which dramatically raise the burden of these diseases in infants and preschool children. Recent surveys reveal that the rate of FA is increasing throughout the world affecting upto 30-35% of people at different stages of their lives². Researchers estimate that upto 15 million Americans are allergic to one or more food items³. The potentially deadly disease affects 1 in every 13 children in USA.¹ In UK, it is estimated that 1-2% of adults and 5-8% of children have FA thus equating to around 2 million people living in UK ³. In Australia recently released FA figures reveal that 4

million people in Australia have reported FA⁴. In Indian scenario the prevalence of reported FA is 6% but after using standard diagnostic tools it turned out to be only 2% as probable FA⁵.

FA is hypersensitivity to a specific food and is mediated by immunoglobulin E (IgE).^{6,12} It's incidence has potentially increased in the past decade when compared with other classical allergic diseases.³ In spite of significant understanding regarding the etiology of FA, the mechanism leading to the disease remains undefined. FA may be determined by both genetic and environmental factors.¹ Most of the allergic reactions are to foods like peanut, milk, soya, nuts, eggs and wheat.⁸ It is observed that majority of the children loose allergenicity to foods early in their

Received on : 18-07-2017

Accepted on : 09-08-2017

Address for correspondence

Dr. P. Uday Kumar

Scientist F (Sr. Deputy Director) & HOD

Department of Pathology & EM

National Institute of Nutrition (ICMR),

Hyderabad, Andhra Pradesh, INDIA

Contact no: +91-9247339143

Email:putchaadaykumar@yahoo.com

childhood.^{16,20} Allergic adults typically react to citrus fruits, nuts, fish, peanuts, shellfish and meat. ⁶ Both the severity and complexity of FA is increasing in both developed and developing countries and are also complicated by other allergic diseases such as asthma and atopic eczema.³¹ FA can be fatal if not treated promptly ⁷. Hence appropriate diagnosis of the condition is required. There is a need for more clinical knowledge as well as resources to treat FA including the availability of life saving medications such as epinephrine. Contemplating the current and future public health consequences, prevention and treatment of allergic reactions to foods is a major challenge that ought to be addressed. As GPs and Homeopaths are the most commonly approached health care providers for treatment by the FA patients, this study aimed at evaluating the disparities in knowledge, attitudes and practices concerning food allergies among GPs and homeopaths in India.

METHODOLOGY

Study population

A total of 214 participants: 107 GPs and 107 homeopaths from different private as well as government hospitals and clinics in Hyderabad agreed to participate in the present study which was of 6 months duration. Prior ethical approval was taken from the Institutional Ethics Committee of National Institute of Nutrition, Hyderabad, India, to conduct the study. An Informed oral consent was obtained from the participants of the study.

Study design

GPs and homeopaths were asked to fill the questionnaires which were collected from them on the same day. The participating practitioners and homeopaths did not have prior knowledge of the objectives of the study. The survey consisted of questions that were mainly based on a validated questionnaire^{8,9}. The distributed questionnaires included questions on the demographic characteristics of the participants (5), their knowledge (21), attitudes and approach (5) regarding food allergy and anaphylaxis. The questions were focused on symptoms, triggers and risk factors in food allergy patients and also diagnosis, treatment and utilization of healthcare in case of anaphylaxis. Based on the scoring, already defined in validated questionnaire, the participants (GPs and homeopaths) were awarded a score for each correct response and average score was calculated.

STATISTICAL ANALYSIS

Descriptive statistics were provided for demographic characteristics and response to each question on the questionnaire. Categorical variables and continuous

variables were compared with Chi-square test. A p-value of ≤ 0.05 was considered indicative of statistical significance. SPSS-19 statistical software package was used for the analyses.

RESULTS

Demographic characteristics of the participants: A total of 107 general practitioners and 107 homeopaths completed the questionnaires. It was found that overall most of the participants in both the groups i.e general practitioners and homeopaths were females (50.9%), were in private hospital (53.7%) and had clinical experience of 10-20 years (47.2%). 76% of the participants reported that out of total patient consultation per month more than 10% of them report FA and also most of them were of 5-15 years of age (47.6%). In our study most of the GPs were from private hospital (67.3%) whereas most of the homeopaths were in private practice (58.9%) (p=0.000). 44.9% of the GPs reported that out of the total patient consultation more than 10% of them report FA whereas 37.4% homeopaths reported that out of the total patient consultation less than 5% of them report FA (p=0.017). Most of the patients reporting to GPs were in the age group of 5-15 years (52.3%) whereas majority (43.0%) reporting to homeopaths were in the age group of <5 yrs. (p=0.025). (Table 1).

Knowledge of the participants: The rates of correct

Table I: Demographic characteristics of the participants (N= 214)

Variables	Overall (N=214)	Sample Population		p-value
		GPs (n=107) n (%)	Homeopaths (n=107) n (%)	
Gender				
• Males	105(49.1)	51(47.7)	54(50.5)	0.682
• Females	109(50.9)	56(52.3)	53(49.5)	
Practice type				0.000*
• Private clinic	85(39.8)	22(20.6)	63(58.9)	
• Private hospital	115(53.7)	72(67.3)	43(40.2)	
• Govt. Hospital	14(6.5)	13(12.1)	1 (0.9)	
Years in practice				0.344
• <10	67(31.4)	30(28.1)	37(34.5)	
• 10 -20	101(47.2)	50 (46.7)	51(47.7)	
• >20	46(21.4)	27(25.2)	19(17.8)	
Food allergic patients load/month				0.017*
• <5%	69(32.2)	29(27.1)	40(37.4)	
• 5-10%	69(32.3)	30(28.0)	39(36.4)	
• >10%	76(35.5)	48(44.9)	28(26.2)	
Age group of food allergic patients seen				0.025*
• <5 years	42(19.6)	14 (13.1)	28 (26.2)	
• 5-15 years	102(47.6)	56 (52.3)	46 (43.0)	
• 15-50 years	60(28.2)	29(27.1)	31(29.0)	
• >50 years	10(4.6)	8 (7.5)	2 (1.8)	

GPs: General Practitioners

Significance level by chi-square test*, p-value<0.05

responses for each question are summarized in Table 2. Regarding questions on knowledge of participants to food allergies the average score to questions testing

Table II: Comparison of knowledge of the participants regarding food allergy (N= 214)

Questions pertaining to knowledge about FA	Overall (N=214)	GPs (n=107) n(%)	Homeopaths (n=107) n(%)	p-value
Symptoms and severity				
Child can die from milk allergy reaction (N)	212(99.0)	107(100.0)	105(98.1)	0.155
Chronic nasal problems are symptom of FA (N)	159(74.2)	74(69.2)	85(79.4)	0.085
Triggers and environmental risk				
Asthma is an important risk factor for severe anaphylaxis (Y)	199(92.9)	101(94.4)	98(91.6)	0.422
Food component that causes allergic reaction (protein)	204(95.3)	104(97.2)	100(93.5)	0.195
Food allergens are passed from maternal diet into breast milk (Y)	205(95.7)	106(99.1)	99(92.5)	0.017*
Children with IgE-mediated milk allergies can eat yoghourts/cheese with milk (N)	198(92.5)	104(97.2)	94(87.9)	0.009*
Okay for children with egg allergies to eat egg yolks (N)	199(92.9)	101(94.4)	98(91.6)	0.422
Vaccines are unsafe for children with egg allergy (influenza)	179(83.6)	95(88.8)	84(78.5)	0.042*
Moderate/severe atopic dermatitis is associated with FA (25%-50%)	185(86.4)	96(89.7)	89(83.2)	0.162
Age group most likely to have food allergies (0-5 y)	200(93.4)	103(96.3)	97(90.7)	0.097*
Teenagers are at higher risk for fatal FA vs. younger children (Y)	184(85.9)	95(88.8)	89(83.2)	0.237
Diagnosis, treatment and utilization of healthcare				
There is a cure for FA (N)	189(88.3)	99(92.5)	90(84.9)	0.079
Daily antihistamine prevents FA reaction (N)	157(73.3)	72(67.3)	85(79.4)	0.044*
I would prescribe epinephrine autoinjector for a child who had anaphylaxis (Y)	165(77.1)	83(77.6)	82(76.6)	0.871
The first treatment of choice is epinephrine in case of anaphylaxis(Y)	181(84.5)	98(91.6)	83(77.6)	0.005*
The rate of preference of IM route for epinephrine injection(Y)	172(80.3)	101(94.4)	71(66.4)	0.000*
No contraindication to prescribing self-injectable epinephrine (Y)	191(89.2)	100(93.5)	91(85.0)	0.047*
Timely administration of epinephrine prevents fatal anaphylaxis (most of the time)	184(86.4)	97(90.7)	87(81.3)	0.049*
Epinephrine injection location (lateral thigh)	140(65.4)	79(73.8)	61(57.0)	0.010*

their knowledge on food allergies and anaphylaxis was 75.2% and 81.7% for GPs and homeopaths respectively with no statistical difference between them. 93.4% of participants had correct knowledge that children less than 5 years were most likely to have food allergies, when compared most of the GPs (96.3%) had correct knowledge in comparison to homeopaths (90.7%) regarding the same.(p=0.097). More than half of the participants (83.6%) responded correctly to the question that influenza vaccines are unsafe for children with egg allergy, where GPs (88.8%) had more knowledge regarding the same than

Table III: Comparison of Attitude and practices of participants regarding food allergy (N= 214)

Questions pertaining to attitude and practices about FA	Overall (N=214)	GPs (n=107) n (%)	Homeopaths (n=107) n (%)	p-value
How often do you refer your patients with suspected FA to a subspecialist (allergist) • Mostly • Rarely	142(66.4) 72(33.6)	67 (62.6) 40 (37.4)	75 (70.1) 32 (29.9)	0.247
Age group most likely to have food allergies • 0 - 5 years • 5 - 15 years • >15 years	75(35.1) 127(59.3) 12(5.6)	26 (24.3) 70 (65.4) 11 (10.3)	49 (45.8) 57 (53.3) 1 (0.9)	0.000*
I am confident of my ability to care for patients with FA(Y)	166(77.5)	82(76.6)	84(78.5)	0.743
Which of the following do you think is the most important to help people with food allergies? • Promote public awareness campaigns about FA • Identify the cause of FA • Develop a cure for FA	80(37.5) 94(43.9) 40(18.6)	36 (33.6) 53 (49.6) 18 (16.8)	44 (41.1) 41 (38.3) 22 (20.6)	0.255
Would you like periodic training sessions for allergic diseases (Y)	191(89.2)	94(87.9)	97(90.7)	0.508

**Y: Yes, GPs: General Practitioners
Significance level by chi-square test*, p-value<0.05**

homeopaths (78.5%) (p=0.042). Variations in the number of correct answers given by the participants was observed in relation to triggers, risk factors and treatment of food allergies i.e more number of GPs had correct knowledge that food allergens passes from maternal diet into breast milk (99.1%), daily antihistamine intake cannot prevent food allergy reaction (79.4%), in case of anaphylaxis epinephrine is the 1st treatment of choice (91.6%), intramuscular route should be preferred for epinephrine injection (94.4%), there is no contraindication in prescribing self injectable epinephrine (93.5%), timely administration of epinephrine prevents fatal anaphylaxis (90.7%), lateral thigh is the correct location for epinephrine injection (73.8%), correct dose of epinephrine (63.6%) in comparison to homeopaths (92.5%, 67.3%, 77.6%, 66.4%, 85%, 81.3%, 57%, 49.5% resp.) and which were statistically significant too with the corresponding p values. (p=0.017, 0.044, 0.005, 0.000, 0.047, 0.049, 0.010, 0.039 resp.).

Attitude and approach of the participants to FA: It was observed that most of the participants (66.4%) refer their patients with suspected FA to a subspecialist. Most of them (77.5%) were confident of their ability to care for patients with FA. 43.5% of the total participants reported that identification of cause of FA should be the most important step to help people with FA, 89.2% of the participants showed interest for periodic training sessions for allergic diseases. No significant difference was observed between both the groups (GPs vs homeopaths) in referring patients with suspected food allergy to subspecialist or allergist

(62.6% vs 70.1% resp.), their confidence on their ability to care for patients with food allergy (76.6% vs 78.5% resp.) and need for periodic training session for allergic disease (87.9% vs 90.7% resp.)

DISCUSSION

Although many studies similar to our study have been carried out on general physicians, pediatricians, nutritionists, adolescents and general public in different parts of the globe but comparative studies between the physicians and homeopaths with regard to allergy are limited.^{9, 10} In a study conducted on 407 physicians, 58% of them reported that less than 5% of their patient load consisted of food allergic patients.⁹ Another study done on 297 physicians in Turkey reported that 92% percent of physicians reported to treating patients with food allergies, although such patients only compromised <5.0% of their total patient load.¹⁰ A clinic based study done on homeopaths reported that in homeopathic practice FA was a frequent presenting complaint accounting for almost 20% cause of consultation. In spite of prevalence of large number of allergic disorders with many patients being treated by homeopaths, there are however only very few well-documented studies /case reports.¹¹ In our study it is reported that more number of food allergic patients (5-10%) consult homeopaths as compared to GPs (<5%) with most of the patients who consult GPs being in the age group of 5-15 years and those approaching homeopaths being <5 years of age. Earlier studies have reported that a child will achieve tolerance i.e outgrow an allergy, after 5 years of age. A study found that 3,188 children surveyed had a FA, while 1,245 had outgrown between five to eight years of age.¹² Another Canadian research team reports that children are most likely to outgrow their FA by the age of six. After 10 years of age, the chance of spontaneous resolution was reported to be much lower. It's unknown why some children develop a tolerance to food allergens while others continue to suffer from them into adulthood. Researchers speculate that multiple allergies, the types of allergenic proteins, and a diet of strict avoidance vs. gradual introduction of the offending foods may play a key role. From our study it is revealed that more than half of the participants had correct knowledge about the fact that children less than 5 years are most likely to have food allergies.

According to a recent study childhood immunization is one of the greatest public health successes of the last century and will play a vital and technical role in upcoming years.¹³ Influenza vaccine is egg derived and has been contraindicated in people with egg allergy.¹⁴ However, no study has shown that residual ovalbumin content can cause adverse events

(including anaphylaxis related morbidity or mortality) in egg allergic recipients, or that vaccination is riskier for these recipients than for the general population. Similarly in our study less than half of the participants had correct knowledge that influenza vaccines are generally not recommended for children suffering from egg allergy and when compared to homeopaths GPs gave comparatively better response.

Large variations were observed in the correct responses among GPs and homeopaths regarding passage of food allergens from maternal diet to breast milk. Some studies report protection with exclusive and prolonged breastfeeding, particularly in children prone to atopy.^{15,16} Whereas other reports have suggested breast milk could be responsible for early sensitization to food^{17,18}. The flavours, proteins and other food chemicals from the mother's diet go through breastmilk.¹⁹ This may lead to allergic or adverse reaction for a hypersensitive child. A recent study done in Spain concluded that a allergen/s free maternal diet should be recommended only if FA is confirmed in breastfed babies.²⁰ In our study GPs gave correct response which was clinically significant than homeopaths that food allergens pass through maternal diet. Antihistamines, known as H1 blockers, are prescribed to relieve mild allergy symptoms, although they cannot control a severe reaction. A study reported that H1 receptors and their clinical efficacy is not completely explored with regard to their contribution of anti-allergic effects.²¹ There is no data available suggesting superior allergic properties of H1 histamine compared to those are not extensively investigated. In our study both GPs and homeopaths gave correct replies that daily intake of histamines cannot prevent FA. Food-induced anaphylaxis is a serious allergic reaction that is rapid in onset and may cause death. Typically, IgE-mediated food-induced anaphylaxis is believed to involve systemic mediator release from sensitized mast cells and basophils. Epinephrine is the only medication that can reverse the symptoms of anaphylaxis. It is available in an auto-injector (EpiPen® or Adrenaclick®).²² IM epinephrine is recommended over subcutaneous injection because it provides a more rapid increase in plasma and tissue concentrations of epinephrine.²³ According to studies by Bewick & Wright IM injection into the thigh may be impossible in overweight or obese individuals, especially women who have thicker subcutaneous fat tissue.²⁴ When an epinephrine auto-injector is used, children weighing less than 25 kg should receive the 0.15 mg dose.²⁹⁷ Children over 25 kg through adults should receive the 0.3 mg dose autoinjector. When a 1:1,000 epinephrine solution is used, patients should receive a dose of 0.01 mg/kg with

a maximum dose of 0.5 mg. It is the drug of choice for anaphylaxis and should be administered as first-line therapy.²⁵ Failure to administer epinephrine early in the course of treatment has been repeatedly implicated in anaphylaxis fatalities.^{26,27} Despite this fact, physicians often fail to prescribe epinephrine. In our study also 80.4% GPs and 23.3% homeopaths believed that epinephrine is the first choice of treatment of anaphylaxis. Food allergies are usually diagnosed using methods that include medical histories, clinical examinations, skin prick tests (SPTs), serum-specific immunoglobulin E (IgE) tests using the radioallergosorbent test (RAST), oral food challenge, and elimination diets ^{2,5,28}. According to previous reports, a positive SPT does not necessarily prove a FA is clinically relevant ²⁹. Thus, the specificity of the SPT for the outcome of oral food challenges is limited. Studies by Bernstein and Chafen concluded that both serum IgE tests and SPT are sensitive and have similar diagnostic properties. ^{30,31} In our study too more than 50% of the participants in both the groups had correct knowledge that SPT and RAST are not the sufficient tools/biomarkers to diagnose FA, but no statistically significant difference was observed between the responses of GPs and homeopaths. The limitation of the study was inability to enroll participants from all the corners of the city and only volunteers participated in the study, though we tried to involve as many participants as possible. The mechanisms of FA are complex and multifactorial. Few experimental medications promised to change the field of FA dramatically, but none of these treatments are currently available. Frequent incidence of anaphylaxis in FA patients is constantly increasing. Present study concludes that overall knowledge of FA among GPs and homeopaths was comparable with strengths and weakness in each domain. GPs had more precise knowledge than homeopaths, particularly regarding the treatment schedule, in case of anaphylaxis, which in turn reflects the differences in attitude and approach among the groups. Thus, with the recent increase in FA and threat posed by food induced anaphylaxis, it is important for health care providers and doctors to be educated about the diagnosis and treatment of this condition.

Acknowledgements

I am thankful to all the participants (GPs and homeopaths) and staff who co-operated in this study. I am also thankful to National Institute of Nutrition (ICMR) for providing intramural financial support. Conflict of Interest: There is no conflict of interest.

REFERENCES

1. Venter C, Arshad SH. Epidemiology of FA. *PediatrClin North Am.* 2011;58:327-49.
2. Moore LE, Stewart PH, deShazo RD. FA: What We Know Now. *Am J MedSci.* 2017 Apr;353(4):353-366.
3. Tang ML, Mullins RJ. FA: is prevalence increasing? *Intern Med J.* 2017 Mar;47(3):256-261.
4. Mullins RJ, Wainstein BK, Barnes EH, Liew WK, Campbell DE. Increases in anaphylaxis fatalities in Australia from 1997 to 2013.
5. Mahesh PA, Wong GW, Ogorodova L, Potts J, Leung TF, Fedorova O, Holla AD, Fernandez-Rivas M, Clare Mills EN, Kummeling I, Versteeg SA, van Ree R, Yazdanbakhsh M, Burney P. Prevalence of food sensitization and probable FA among adults in India: the europeval INCO study. *Allergy.* 2016 Jul;71(7):1010-9.
6. Chafen JJ, Newberry S, Riedl M, Bravata DM, Maglione M, Suttrop M, et al. RAND Corporation. Prevalence, natural history, diagnosis, and treatment of FA: a systematic review of the evidence. RAND working paper, prepared for the National Institute of Allergy and Infectious Diseases. Santa Monica (CA): RAND Corporation; 2010.
7. Parlaman JP, Oron AP, Uspal NG, deJong KN, Tieder JS. Emergency and Hospital Care for Food-Related Anaphylaxis in children. *HospPediatr.* 2016 May;6(5):269-74.
8. Lack G. Clinical practice. FA. *N Engl J Med.* 2008;359:1252---60.
9. Gupta RS, Springston EE, Kim JS, Smith B, Pongracic JA, Wang X, et al. FA knowledge, attitudes, and beliefs of primary care physicians. *Pediatrics.* 2010;125:126---32
10. Erkoçoğlu M, Civelek E, Azkur D, Özcan C, Öztürk K, Kaya A, Metin A, KocabaşCN. Knowledge and attitudes of primary care physicians regarding FA and anaphylaxis in Turkey. *AllergoImmunopathol (Madr).* 2013 Sep-Oct;41(5):292-7.
11. Van Wassenhoven M. Clinical verification in homeopathy and allergic conditions. *Homeopathy.* 2013 Jan;102(1):54-8.
12. Longo G, Berti I, Burks AW, Krauss B, Barbi E. IgE-mediated FA in children. *The Lancet.* 2013 Nov 22;382(9905):1656-64.
13. Abahussin AA, Albarrak AI. Vaccination

- adherence: Review and proposed model. *J Infect Public Health*. 2016 Sep 19.
14. Shimizu m, imai t, yamazaki s, yagawa a, miyazawa t, nakamura t, hojon,ishikawa r, kamiya t, itahashi k. [safety of influenza vaccination in children with severe allergy to hen's eggs: a prospective case series study]. *Arerugi*. 2016 mar;65(2):128-33.
 15. Kansu A, Yüce A, Dalgıç B, Şekerel BE, Çullu-Çokuğraş F, Çokuğraş H. Consensus statement on diagnosis, treatment and follow-up of cow's milk protein allergy among infants and children in Turkey. *Turk J Pediatr*. 2016;58(1):1-11.
 16. Errázuriz G, Lucero Y, Ceresa S, Gonzalez M, Rossel M, Vives A. [Clinical characteristics and management of infants less than 1-year-old suspected with allergy to cow's milk protein]. *Rev Chil Pediatr*. 2016 Nov - Dec;87(6):449-454.
 17. Osborn DA, Sinn JK, Jones LJ. Infant formulas containing hydrolysed protein for prevention of allergic disease and FA. *Cochrane Database Syst Rev*. 2017 Mar 15;3:CD003664.
 18. Fewtrell M, Bronsky J, Campoy C, Domellöf M, Embleton N, FidlerMis N, Hojsak I, Hulst JM, Indrio F, Lapillonne A, Molgaard C. Complementary Feeding: A Position Paper by the European Society for Paediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) Committee on Nutrition. *J Pediatr Gastroenterol Nutr*. 2017 Jan;64(1):119-132.
 19. Swain A, Soutter V, Loblay R 2011, *RPAH Elimination Diet Handbook*. Sydney: Allergy Unit, Royal Prince Alfred Hospital.
 20. Martín-Muñoz MF, Pineda F, GarcíaParrado G, Guillén D, Rivero D, Belyer T, Quirce S. FA in breastfeeding babies. Hidden allergens in human milk. *Eur Ann Allergy Clin Immunol*. 2016 Jul;48(4):123-8.
 21. Jain R, Watson U, Saini DK. ERK activated by Histamine H1 receptor is anti-proliferative through spatial restriction in the cytosol. *Eur J Cell Biol*. 2016 Dec;95(12):623-634.
 22. White MV, Hogue SL, Odom D, Cooney D, Bartsch J, Goss D, Hollis K, Herrem C, Silvia S. Anaphylaxis in Schools: Results of the EPIPEN4SCHOOLS Survey Combined Analysis. *Pediatr Allergy Immunol Pulmonol*. 2016 Sep 1;29(3):149-154.
 23. Campbell RL, Bellolio MF, Knutson BD, Bellamkonda VR, Fedko MG, Nestler DM, Hess EP. Epinephrine in anaphylaxis: higher risk of cardiovascular complications and overdose after administration of intravenous bolus epinephrine compared with intramuscular epinephrine. *J Allergy Clin Immunol Pract*. 2015 Jan-Feb;3(1):76-80.
 24. Bewick DC, Wright NB, Pumphrey RS, Arkwright PD. Anatomic and anthropometric determinants of intramuscular versus subcutaneous administration in children with epinephrine autoinjectors. *J Allergy Clin Immunol Pract*. 2013 Nov-Dec;1(6):692-4.
 25. Lieberman PL. Recognition and first-line treatment of anaphylaxis. *Am J Med*. 2014 Jan;127(1 Suppl):S6-11.
 26. Song TT, Lieberman P. Epinephrine in anaphylaxis: doubt no more. *Curr Opin Allergy Clin Immunol*. 2015 Aug;15(4):323-8.
 27. Fromer L. Prevention of Anaphylaxis: The Role of the Epinephrine Auto-Injector. *Am J Med*. 2016 Dec;129(12):1244-1250.
 28. Dey D, Ghosh N, Pandey N, Gupta Bhattacharya S. A hospital based survey on food allergy in the population of Kolkata, India. *Int Arch Allergy Immunol*. 2014;164(3):218-21
 29. Leśniak M, Juda M, Dyczek Ł, Czarnobilska M, Leśniak M, Czarnobilska E. [Diagnosis of FA]. *Przegl Lek*. 2016;73(4):245-9. Review.
 30. Bernstein I, Li J, Bernstein D, Hamilton R, Spector S, Tan R, et al. Allergy diagnostic testing: an updated practice parameter. *Ann Allergy Asthma Immunol*. . 2008;100(3 suppl 3):S1-S148. American Academy of Allergy, Asthma and Immunology; American College of Allergy, Asthma and Immunology.
 31. Chafen JJS, Newberry SJ, Riedl MA, Bravata DM, Maglione M, Suttorp MJ, et al. Diagnosing and managing common food allergies: a systematic review. *JAMA*. 2010;303(18):1848-56.

