

I型变态反应疾病中特异性IgE变应原引起的单一致敏和多重致敏的变应原分布特征研究*

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摘要:目的 研究I型变态反应疾病中特异性IgE(sIgE)变应原在单一致敏和多重致敏中的分布特征。方法 选取2014年10月~2017年9月徐州市医学科学研究所确诊的I型变态反应疾病患者767例作为研究对象,免疫印迹法检测患者血清中19种变应原sIgE,分析单一致敏和多重致敏比例、sIgE变应原在单一致敏和多重致敏中的阳性率及分布。结果 sIgE变应原引起的单一致敏和多重致敏分别为414例(53.98%)和353例(46.02%),户尘螨和混合霉菌在单一致敏和多重致敏中的分布接近(49.0% vs 51.0%和43.4% vs 56.6%),并且在不同数量变应原致敏的多重致敏中阳性率相对稳定,其他17种变应原75%~100%分布在多重致敏中,阳性率随致敏变应原种类增加而增高。单一致敏中最主要变应原为户尘螨(64.8%)和混合霉菌(19.0%),其次是牛奶(3.9%)和蟑螂(2.2%)。多重致敏中各变应原阳性率均高于单一致敏,差异均有统计学意义($\chi^2=5.598\sim137.2$,均 $P<0.05$),在种属相近的变应原之间呈现出高度一致的阳性现象。结论 I型变态反应疾病中单一致敏和多重致敏的sIgE变应原分布有显著差异,多重致敏中可能存在广泛的交叉致敏。

关键词:变应原;单一致敏;多重致敏;交叉致敏

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Study on the Allergens Distributional Characteristic of Monosensitization and Polysensitization Induced by Specific IgE Allergens in I Type Hypersensitivity Disease

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Abstract: Objective To study the specific IgE (sIgE) allergens distributional characteristic of monosensitization and polysensitization in I type hypersensitivity disease. **Methods** Subjects included 767 patients with I type hypersensitivity disease clinically diagnosed in Xuzhou Institute of Medical Sciences from Oct 2014 to Sept 2017. Immunoblotting was used to detect 19 kinds of allergen-specific IgE. Analysed the proportion of monosensitization and polysensitization, positive rates and distributional characteristic of sIgE allergens in monosensitization patients and polysensitization patients. **Results** In patients with sIgE positive response, monosensitization and polysensitization were 414 (53.98)% and 353 (46.02)%, respectively. The distributions of house dust mite and mixed mold in monosensitization /polysensitization were small differences: 49.0% vs 51.0% and 43.4% vs 56.6%. Their positive rates were relatively stable in polysensitization with different numbers of allergens, but the others 75%~100% distributed in the polysensitizations, and there positive rates were increased trend with the increased allergen species. The main allergens of monosensitizations were house dust mite (64.8%) and mixed mold (19.0%), followed by milk (3.9%) and cockroach (2.2%). The positive rate of each sIgE allergen in polysensitizations was higher than that in monosensitizations, and the differences were all statistically significant ($\chi^2=5.598\sim137.2$, all $P<0.05$), what's more, high multiple positive phenomena was observed among similar species allergens in polysensitization patients. **Conclusion** The distributions of allergens were significant differences between monosensitization and polysensitization in I type hypersensitivity disease, and there may be extensive cross-sensitizations in polysensitization.

Keywords: allergen; monosensitization; polysensitization; cross-sensitization

随着生活水平的提高和生活方式的改变,变态反应性疾病的发生率明显升高,I型变态反应疾病在临床上最常见,患者既可表现为单一致敏(对一

种变应原过敏),还可表现为多重致敏(对两种及以上变应原过敏)。研究发现,多重致敏与多重病症和疾病的严重程度相关^[1]。多重致敏不但会增加

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患者发病机会,也为疾病的防治带来困难。目前国内外对引起I型变态反应疾病的变应原种类主要是从总体上研究,对于I型变态反应疾病中单一致敏和多重致敏的变应原种类和特征还不清楚。本文主要分析I型变态反应疾病中19种sIgE变应原在单一致敏和多重致敏中的阳性率及分布特征,为疾病的防治提供依据。

1 材料与方法

1.1 研究对象 2014年10月~2017年9月徐州市医学科学研究所变态反应科诊断的I型变态反应疾病患者共767例,临床上以荨麻疹、湿疹、皮炎、鼻炎、哮喘、胃肠道等症状为主,并以皮肤病患者为主要人群,男性381人,年龄1~95岁,平均年龄 31.8 ± 21.7 岁;女性386人,2岁~92岁,平均年龄 37.1 ± 17.8 岁。

1.2 试剂和仪器 变应原特异性IgE抗体检测试剂盒(免疫印迹法)及AllergyScreen™变应原定量检测系统(德国)。

1.3 方法 采取患者空腹静脉血3 ml,3 000 r/

min离心5 min分离血清,采用变应原特异性IgE抗体检测试剂盒(免疫印迹法)检测血清中19种变应原sIgE抗体(半定量)。按照试剂说明书进行操作,每个检测板都设有阳性质控,显色条带通过变应原检测系统检测,软件评估条带颜色的深浅,sIgE <0.35 IU/ml判为阴性,sIgE ≥ 0.35 IU/ml判为阳性。19种变应原包括:苜、树花粉、腰果、混合草、桑树、芒果、菠萝、户尘螨、狗毛皮屑、蟑螂、牛奶、虾、蟹、猫毛皮屑、鸡蛋、牛羊肉、贝、混合霉菌和屋尘。

1.4 统计学分析 采用SPSS16.0统计软件分析处理,两样本率的比较采用 χ^2 检验, $P<0.05$ 为差异有统计学意义。

2 结果

2.1 767例I型变态反应疾病中单一致敏和多重致敏分布 见表1。在767例变应原sIgE呈现阳性反应的的患者中,单一致敏和多重致敏分别为414例(45%)和353例(46%),多重致敏中变应原数量最多可达到14种。

表1

767例sIgE变应原阳性患者的分布

项 目	单一致敏(n=414)	多重致敏(n=353)										合计
变应原数量	1	2	3	4	5	6	7	8	9	10~14		
患者例数	414	163	74	41	32	14	10	10	5	4		767
百分比(%)	53.98	21.25	9.65	5.35	4.17	1.83	1.30	1.30	0.65	0.52		100

2.2 19种sIgE变应原在单一致敏和多重致敏中的分布及阳性率 767例变应原sIgE阳性患者中,总阳性率较高的为户尘螨(71.3%)、混合霉菌(22.8%)、屋尘(14.8%)、狗毛皮屑(14.5%)、蟑螂(13.8%)、牛奶(9.5%)和虾(9.4%),阳性率较低的为菠萝(1.4%)和贝(1.0%),但是变应原在单一致敏和多重致敏中的分布存在很大差异:户尘螨和混合霉菌在单一致敏和多重致敏中分布接近,户尘螨为49.0% vs 51.0%,混合霉菌为43.4% vs

56.6%,其余17种变应原75%~100%分布在多重致敏中。各变应原在单一致敏和多重致敏中的阳性率见图1A,1B,单一致敏最主要变应原为户尘螨(64.8%)、混合霉菌(19.0%),两者占单一致敏总数的83.8%,其次是牛奶(3.9%)和蟑螂(2.2%),其他变应原阳性率均很低,多重致敏中各变应原阳性率均高于单一致敏,差异均有统计学意义($\chi^2=5.598\sim 137.2$,均 $P<0.05$)。

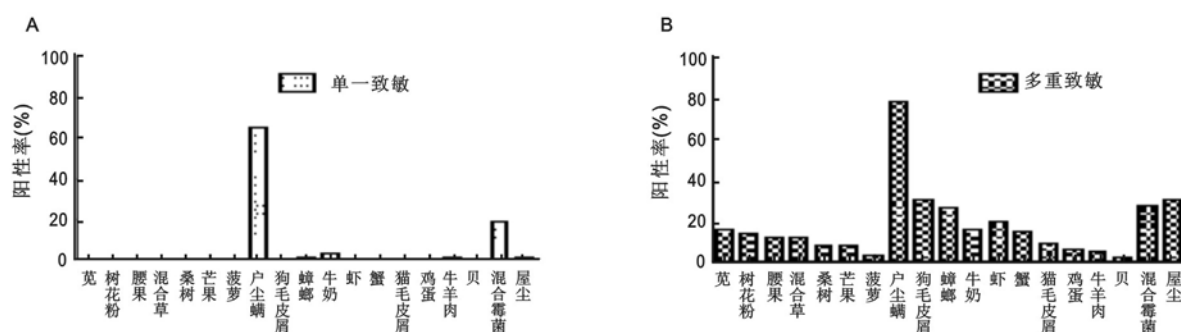


图1 19种sIgE变应原在单一致敏和多重致敏患者中的阳性率

2.3 19种sIgE变应原在不同多重致敏中分布特征 在2~14种变应原致敏的多重致敏疾病中,户

尘螨阳性率始终较高(75.5%~100%),混合霉菌阳性率在2~8种变应原致敏疾病中稳定在17.1%~33.4%之间,在9种及以上致敏疾病中未见阳性,其它17种变应原阳性率有随变应原致敏种类增多而增加的趋势,见图2A~2C。值得注意的是,户尘螨、狗毛皮屑、蟑螂、牛奶、虾等动物源性

变应原之间呈现出频率较高的同时阳性现象,苜、芒果、树花粉、混合草等植物源性变应原在2~5种变应原致敏疾病中阳性率较低1%~22%,在6种以上变应原致敏的多重致敏中阳性率显著增高14%~100%,并呈现出高频率的同时阳性现象。

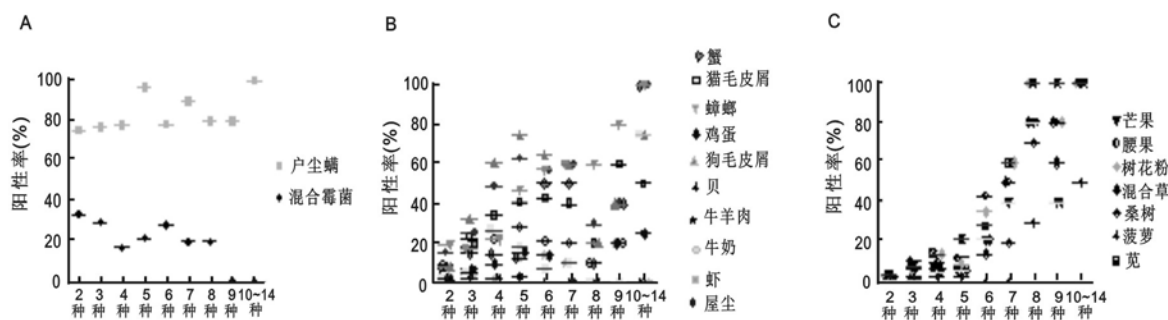


图2 19种sIgE变应原在不同多重致敏中阳性率

3 讨论 I型变态反应性疾病是指已致敏的机体再次接触或食入相同变应原后在数分钟内所发生的以IgE介导的疾病,主要表现为皮肤症状、呼吸道症状、胃肠道症状等,随着发作次数的增加,患者可伴多重病症。确定变应原,避免接触变应原和采用脱敏治疗是疾病的有效防治方法。在我们研究的767例I型变态反应性疾病患者中,多重致敏占46%,多重致敏在不同病种中和不同病程中存在着差异^[1,2]。在检测的19种sIgE变应原中,户尘螨和混合霉菌的高阳性率及其在单一致敏和多重致敏中的分布特征,提示户尘螨和混合霉菌是引起本地区过敏的主要变应原,两者共同引起的致敏为共致敏(Co-sensitization),共致敏为同时存在可以结合到变应原的不同的IgE,这些变应原不需要共同的结构特征。其他17种变应原75%~100%分布在多重致敏中,种属相近的变应原之间呈现出的高频率的同时阳性现象,均提示多重致敏中不但存在共致敏,更可能存在广泛的交叉致敏(Cross-sensitization),即相同的IgE结合到具有共同结构特征的不同变应原上引起的致敏。交叉反应经常发生在种属相近的变应原分子或不同种属有相似功能的非常保守的分子,属于同一蛋白家族。螨虫是变态反应疾病的最主要变应原^[2,3],也是最早研究的变应原,原肌球蛋白、精氨酸酶等被鉴定出是户尘螨参与虾、昆虫等其他无脊椎动物起交叉反应的主要变应原^[4,5],文献还报道,植物源性变应原之间的交叉反应碳水化合物决定簇(cross-reactive carbohydrate determinants, CCDs)能诱导产生高交叉反应IgE^[6,7],这与我们发现的植物源性变应原多出现在6种以上的多重致敏中可能有一定关系。免

疫疗法是治疗变态反应性疾病的有效方法。目前,针对多重致敏的免疫疗法,欧洲使用一种或两种临床相关变应原,美国使用所有临床相关变应原^[8],国内邢琼波等^[9]报道,舌下含服粉尘螨滴剂对单一致敏和多重致敏的变应性鼻炎伴哮喘具有相似疗效,并且疗效显著。交叉致敏现象的存在是否提示对于多重致敏疾病的治疗不需要采用多种相关变应原的免疫疗法?这还需要更多的数据支持。

总之,我们研究的结果显示,I型变态反应性疾病中sIgE变应原在单一致敏和多重致敏的分布差异显著,多重致敏即可能是两种以上变应原的共致敏引起,更多的可能是交叉致敏引起。

参考文献:

- [1] Ha EK, Baek JH, Lee SY, et al. Association of polysensitization, multimorbidity, and allergy severity: a cross-sectional study of school children[J]. *Int Arch Allergy Immunol*, 2017, 171(3/4): 251-360.
- [2] 马燕, 方平, 刘业海, 等. 安徽省合肥地区过敏性鼻炎、哮喘的过敏原分布及临床意义[J]. *安徽医科大学学报*, 2013, 48(10): 1249-1251.
Ma Y, Fang P, Liu YH, et al. Allergens distribution and clinical significance with allergic rhinitis and asthma in Hefei of Anhui Province[J]. *Acta Universitatis Medicinalis Anhui*, 2013, 48(10): 1249-1251.
- [3] 赵秋剑, 王登峰. 支气管哮喘患者变应原检测及免疫分子研究[J]. *现代检验医学杂志*, 2014, 29(6): 96-98.
Zhao QJ, Wang DF. Study on allergen detection and immune molecules in the patients with bronchial asthma[J]. *J Mod Lab Med*, 2014, 29(6): 96-98.
- [4] Verhoeckx KC, van Broekhoven S, den Hartog-Jager CF, et al. House dust mite (Derp 10) and crustacean

- allergic patients may react to food containing Yellow mealworm proteins[J]. Food Chem Toxicol, 2014, 65(2):364-373.
- [5] Popescu FD. Cross-reactivity between aeroallergens and food allergens[J]. World J Methodol, 2015, 5(2):31-50.
- [6] Bohle B. The impact of pollen-related food allergens on pollen allergy[J]. Allergy, 2007, 62(1):3-10.
- [7] Skypala IJ, Bull S, Deegan K, et al. The prevalence of PFS and prevalence and characteristics of reported food allergy; a survey of UK adults aged 18~75 incorporating a validated PFS diagnostic questionnaire[J]. Clin Exp Allergy, 2013, 43(8):928-940.
- [8] Damask C. Immunotherapy: Treating with fewer allergens? [J]. Otolaryngol Clin North Am, 2017, 50(6):1153-1165.
- [9] 邢琼波, 陈实, 陈冰, 等. 舌下含服粉尘螨滴剂治疗儿童单一致敏和多重致敏变应原鼻炎伴哮喘的疗效评估[J]. 临床耳鼻咽喉头颈外科杂志, 2017, 31(3):204-208.
- Xing QB, Chen S, Chen B, et al. Efficacy of sublingual immunotherapy with dermatophagoides farinae drops in monosensitized and polysensitized children with allergic rhinitis and asthma[J]. J Clin Otorhinolaryngology Head Neck Surg(China), 2017, 31(3):204-208.

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(上接99页)T2DM患者胰岛素抵抗、血脂紊乱和炎症反应的相互关系,进一步阐明胰岛素抵抗和血管并发症的发病机制,为T2DM血管病变的预防和治疗提供新的思路。

参考文献:

- [1] 王丹,王养维,李辉,等. 2型糖尿病患者动脉粥样硬化病变与血清CTRP3和CTRP9水平的相关性研究[J]. 现代检验医学杂志, 2015, 30(6):20-24.
- Wang D, Wang YW, Li H, et al. Correlation research on atherosclerotic lesions with serum CTRP3, CTRP9 levels in patients with type 2 diabetes[J]. Journal of Modern Laboratory Medicine, 2015, 30(6):20-24.
- [2] Thielens NM, Tedesco F, Bohison SS, et al. C1q: A fresh look upon an old molecule[J]. Molecular Immunology, 2017, 89(9):73-83.
- [3] 刘阁,逢越,刘欣,等. C1q蛋白家族的结构、分布、分类和功能[J]. 遗传, 2013, 35(9):1072-1080.
- Liu G, Pang Y, Liu X, et al. Structure, distribution, classification and function of C1q protein family: a review[J]. Heredity, 2013, 35(9):1072-1080.
- [4] Milder FJ, Gomes L, Schouten A, et al. Factor B structure provides insights into activation of the central protease of the complement system[J]. Nature Structural & Molecular Biology, 2007, 14(3):224-228.
- [5] Tesch GH. Diabetic nephropathy is this an immune disorder? [J]. Clinical Science (Lond), 2017, 131(16):2183-2199.
- [6] Chhablani J, Sharma A, Goud A, et al. Neurodegeneration in type 2 diabetes: evidence from spectral-domain optical coherence tomography[J]. Invest Ophthalmol Vis Sci, 2015, 56(11):6333-6338.
- [7] 喻亚兰,谭茜,罗艺,等. 血清补体C1q与2型糖尿病患者血脂紊乱及胰岛素抵抗的相关性研究[J]. 检验医学与临床, 2017, 14(15):2167-2169.
- Yu YL, Tan Q, Luo Y, et al. The correlation for C1q and T2DM with dyslipidemia and insulin resistance[J]. Laboratory Medicine and Clinic, 2017, 14(15):2167-2169.
- [8] 贾丹丹,闫朝丽,王铭婕. 胰岛素抵抗与补体系统的相关研究进展[J]. 内蒙古医科大学学报, 2016, 38(2):151-155.
- Jia DD, Yan CL, Wang MJ. The research progress of insulin resistance and complement system[J]. Journal of Inner Mongolia Medical University, 2016, 38(2):151-155.
- [9] Nakatsuji H, Kishida K, Kobayashi H, et al. Correlation of circulating C1q and C1q-binding adiponectin concentrations with aging in males; a preliminary report[J]. Diabetol Metab Syndr, 2013, 5(1):3-5.
- [10] Hirata A, Kishida K, Nakatsuji H, et al. High serum C1q-adiponectin/total adiponectin ratio correlates with coronary artery disease in Japanese type 2 diabetics[J]. Metabolism, 2013, 62(4):578-585.
- [11] Kishida K, Nakagawa Y, Kobayashi H, et al. High serum C1q-binding adiponectin levels in male patients with acute coronary syndrome[J]. Cardiovasc Diabetol, 2014, 13:9.
- [12] 丁梦蕾,范列英. 补体C1q与疾病发生发展相关性研究的新进展[J]. 中华检验医学杂志, 2015, 38(9):642-645.
- Ding ML, Fan LY. Recent advances in research of cofactor C1q related diseases[J]. Chinese Journal of Laboratory Medicine, 2015, 38(9):642-645.
- [13] 黄山,洪燕英,张雅然. 肾组织补体C1q沉积水平在糖尿病肾病的临床应用价值研究[J]. 标记免疫分析与临床, 2017, 24(9):979-981.
- Huang S, Hong YY, Zhang YR. Clinical study between the complement C1q levels in kidney tissues and diagnosis of diabetic nephropathy[J]. Labeled Immunoassays and Clinical Medicine, 2014, 24(9):979-981.
- [14] 陈兵华,王峰,邬丽娜,等. 强直性脊柱炎患者血清补体B因子及免疫球蛋白测定的临床意义[J]. 医学研究杂志, 2015, 44(10):135-137.
- Chen BH, Wang F, Wu LN, et al. Clinical value of detecting serum complement factor B and immunoglobulin in patients with ankylosing spondylitis[J]. Journal of Medical Research, 2015, 44(10):135-137.
- [15] 宋令雄,张燕,张明威,等. 儿童原发性肾病综合征患者血清补体C1q水平变化及其临床意义[J]. 现代检验医学杂志, 2017, 32(4):1-5.
- Song LX, Zhang Y, Zhang MW, et al. Study on serum levels of C1q and their clinical significance in children with nephritic syndrome [J]. Journal of Modern Laboratory Medicine, 2017, 32(4):1-5.

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