世界华人消化杂志®
wcjd@wjgnet.com
世界华人消化杂志 2012年2月18日; 20(5): 389-393
ISSN 1009-3079 (print) ISSN 2219-2859 (online)

文献综述 REVIEW

食物敏感与肠易激综合征研究进展

唐吟菡, 许树长, 吴 萍

唐吟菡, 许树长, 上海同济大学附属同济医院消化科 上海市 200065
吴萍, 上海同济大学附属同济医院营养科 上海市 200065
唐吟菡, 在读硕士, 主要从事食物与肠易激综合征关系的研究.
作者贡献分布: 本文综述由唐吟菡完成; 许树长与吴萍审校.
通讯作者: 许树长, 主任医师, 200065, 上海市, 上海同济大学附属同济医院消化科. xschang@163.com
收稿日期: 2011-10-29 修回日期: 2011-11-15
接受日期: 2011-11-25 在线出版日期: 2012-02-18

Irritable bowel syndrome and food allergy

Yin-Han Tang, Shu-Chang Xu, Ping Wu

Yin-Han Tang, Shu-Chang Xu, Department of Gastroenterology, Tongji Hospital, Tongji University School of Medicine, Shanghai 200065, China
Ping Wu, Department of Nutriology, Tongji Hospital, Tongji University School of Medicine, Shanghai 200065, China
Correspondence to: Shu-Chang Xu, Chief Physician, Department of Gastroenterology, Tongji Hospital, Tongji University School of Medicine, Shanghai 200065, China. xschang@163.com
Received: 2011-10-29 Revised: 2011-11-15
Accepted: 2011-11-25 Published online: 2012-02-18

Abstract
Irritable bowel syndrome (IBS) is a kind of functional gastrointestinal disease characterized by abdominal pain or discomfort associated with changes in bowel habits. The alternating symptoms of IBS seriously affect the patients' quality of life. Some studies have found that food could cause or aggravate the symptoms of IBS possibly by inducing food allergy and food intolerance. However, the specific mechanisms have not been established yet. Currently there are "bacterial 'toxin' hypothesis", "immune or inflammatory response hypothesis" and "physical or chemical irritation hypothesis" explaining the role of food in the pathogenesis of IBS. It has been known that food factors play a very important role in the pathogenesis of IBS. This article reviews food allergy and the possible mechanisms, diagnosis and treatment of IBS caused by food.

Key Words: Irritable bowel syndrome; Food allergy; Food intolerance; Food-specific IgG

Tang YH, Xu SC, Wu P. Irritable bowel syndrome and food allergy. Shijie Huaren Xiaohua Zazhi 2012; 20(5): 389-393

摘要
肠易激综合征(irritable bowel syndrome, IBS)是一种以腹痛或腹部不适伴排便习惯改变为特征的功能性胃肠病, 其症状反复, 严重地影响了患者的生活质量. 研究发现, 食物可引发或加重IBS患者的症状, 其实质即食物过敏和食物不耐受, 但具体的发病机制尚未得到肯定, 目前包括细菌"代谢'毒物'假说"、"免疫或炎症反应假说"、"物理或化学刺激假说"等. 因此食物因素在IBS发病中的作用越来越受到重视, 成为当前研究IBS病因的热点之一, 本文将对食物敏感及食物引发IBS的可能机制、检测方法及干预措施的研究进展作一综述.

关键词: 肠易激综合征; 食物敏感; 食物不耐受; 食物特异性IgG

唐吟菡, 许树长, 吴萍. 食物敏感与肠易激综合征研究进展. 世界华人消化杂志 2012; 20(5): 389-393
http://www.wjgnet.com/1009-3079/20/389.asp

0 引言
肠易激综合征(irritable bowel syndrome, IBS)是一种以腹痛或腹部不适伴排便习惯改变为特征的功能性胃肠病, 须经检查排除可引起这些症状的器质性疾病[1,2]. 本病是最常见的一种功能性肠道疾病, 据报道其在亚洲国家的患病率已由2.9%增至15.6%[3]. IBS症状反复, 严重地影响了患者的生活质量. 研究发现, 食物可引发或加重IBS患者的症状[3], 因此食物因素在IBS发病中的作用越来越受到重视, 成为当前研究IBS病因的热点之一[4]. 本文将对食物敏感及食物引发IBS的机制、检测及干预的研究进展作一综述.

1 概述
近年来, 食物在IBS发病中的作用逐渐受到人们的关注. 国内外多项科学实验[5-7]研究结果提示

■背景资料
肠易激综合征是最常见的一种功能性肠道疾病, 近年来在亚洲国家的患病率逐渐升高. 其症状反复, 且由食物引发者不易诊断, 造成治疗上的困难, 严重地影响了患者的生活质量.

■同行评议者
白爱平, 副教授, 江西省南昌大学第一附属医院消化病研究所

■研发前沿
食物因素在IBS患病中的作用越来越受到重视. 但食物引发IBS具体的分子机制仍未得到肯定, 还有待进一步研究, 该问题也成为目前研究IBS病因的热点之一; 在诊断上, 尚无公认、客观的诊断方法; 在治疗上, 讲究个体化, 目前也无特效的治疗药物.

食物敏感是IBS发病的一个重要因素, 充分证实了IBS是患者食用了特定的食物所引起的症状, 食物敏感在IBS发病中具有重要的作用. 在IBS患者中, 20%-67%的患者存在食物敏感现象, 普遍高于其在普通人群中所占的比例(5%-45%)[8]. 食物诱发或加重IBS患者症状的实质系食物过敏和食物不耐受. 食物过敏(food allergy, FA)是指由于某种食物或食品添加剂等引起的IgE或非IgE介导的免疫反应, 从而导致消化系统内或全身性的变态反应. IgE介导的食物变态反应临床症状出现较快, 可在进食后几分钟到1-2 h.

食物不耐受(food intolerance, FI)是指当机体缺乏一些消化酶而无法完全消化利用某种食物或所含的成分时, 未被完全消化的蛋白便以多肽等大分子形式透过肠道进入血液或淋巴液中, 成为可被机体免疫系统识别的抗原, 刺激机体产生食物特异性IgG抗体, 导致机体对进入人体内的某种或多种食物产生过度保护性免疫反应[9]. 这种IgG抗体介导的迟发型变态反应常由多种食物引起, 一般在摄入不耐受食物24 h至几天后发作, 在食物引发的IBS中占主要地位. 食物不耐受不但可诱发腹泻或便秘等IBS症状, 还可引起所有组织(包括血管)发生炎症反应, 并表现为胃肠道以外各系统的症状与疾病[10-12].

2 食物引发IBS的可能机制

IBS可由内脏高敏感、肠动力异常、基因易感性、肠黏膜屏障、感染及免疫、精神心理因素等多种机制引起[13], 食物引发IBS的可能机制包括以下不同假说.

2.1 代谢“毒物”假说 细菌代谢“毒物”假说[14]提出: 食用不耐受食物可使肠道菌群产生一系列糖的无氧酵解代谢物, 包括酒精、二醇(如丁烷)、酮类、酸、醛类(如丙酮醛)[15,16], 这些代谢物未能被小肠所吸收, 他们通过影响肠道菌群的钙信号转导, 并对其基因的表达和生长产生影响, 同时还对神经元、骨骼、心肌细胞、肥大细胞、免疫细胞和一些其他类型细胞产生影响, 致使肠道内菌群的平衡发生了改变, 生成代谢毒物, 从而产生了IBS及与食物不耐受相关的各系统症状. 以下4方面的证据支持了细菌代谢“毒物”假说: (1)肠道菌群能产生丙酮醛等一系列糖的无氧酵解代谢物, 因其含有合成和降解这些代谢物的酶[17]; (2)有相当多的证据表明这些代谢物会影响细菌基因的生长和表达[17,18]; (3)在人类血浆中可检测到这些代谢毒物; (4)这些代谢毒物亦可影响人体细胞的生理活动[19,20]. 然而, 丙酮醛及其他代谢毒物影响细菌并导致肠易激综合征及食物不耐受的一系列症状的分子机制仍有待进一步研究[14].

2.2 免疫或炎症反应假说 迷走神经传入通路广泛分布于肠道中, 不仅调节着胃肠道的分泌和蠕动, 还参与传导和调控与IBS相关的内脏感觉. 临床数据表明, 迷走神经功能紊乱可见于一部分IBS患者[21]. 同时, IBS患者的肠道黏膜, 尤其是近端肠神经中, 可发现肥大细胞及其所释放的介质数量明显增多[22]. 肠腔内的化学或机械刺激可诱使黏膜肠嗜铬细胞和免疫细胞释放5-羟色胺(5-HT)[23]. 5-HT是重要的神经递质, 通过激活神经元上的特异性受体, 参与肠道的运动和分泌反射及大脑的疼痛调节[24]. 迷走神经传入通路上的5-HT3受体可调控内脏感觉[25], 5-HT3受体拮抗剂能有效缓解腹泻型IBS患者的上腹疼痛症状[26,27]. Chen等[28]通过研究提出了免疫或炎症反应假说: 在食物过敏原刺激肠道的早期阶段, 5-HT(主要由黏膜肥大细胞分泌)水平的升高可通过激活迷走神经通路上的5-HT3受体, 并上调其亚基的表达, 降低了迷走神经的镇痛能力. 然而, 过高的5-HT水平触发了兴奋性毒性, 可损伤迷走神经的调控能力, 最终导致了内脏的高度敏感[29-32]. 同时, 过敏原亦可改变胃排空、肠道渗透压及提高胃肠道激素水平, 这些反应均可引起内脏感觉的异常. 该假说阐明了IBS患者迷走神经功能紊乱的机制, 但并不能排除肥大细胞释放的其他具有生物活性介质的作用. 另外, 脊髓传入通路和5-HT3受体在慢性阶段对内脏感觉的作用, 及其与IBS的关系仍需进一步研究.

2.3 物理或化学刺激假说 食物在进入胃肠道后, 应当被消化至氨基酸、甘油和单糖水平, 这样才能完全转化为能量提供人体所需. 然而, 不耐受食物因缺乏相应的酶而无法被机体完全消化和吸收时, 以多肽或其他分子的形式进入肠道, 成为可被机体免疫系统识别的抗原, 刺激机体产生食物特异性IgG抗体, 与食物抗原形成免疫复合物(immune complex, IC), 刺激了肠道黏膜, 导致肠蠕动增加、肠黏膜渗透压增高、功能紊乱, 引起肠道分泌和运动的异常, 导致一系列腹痛、腹泻等IBS症状[8,33,34].

3 食物引发IBS的诊断

3.1 IBS的诊断 诊断IBS须结合病史、临床症状等, 目前普遍参考RomeIII标准, 同时应警惕报

警症状[35-37](年龄>45岁, 便血, 不明原因的体质量下降, 夜间症状, 发热, 可触及腹部肿块, 腹水, 有结直肠肿瘤家族史, 贫血)以排除器质性病变. Rome Ⅲ标准: 最近3 mo内, 每个月至少有3 d出现反复发作的腹痛或不适症状, 并具有下列中的2项及以上: (1)排便后症状缓解; (2)伴随排便频率的改变; (3)伴随粪便性状的改变[38-41]. 分型: 便秘型(C-irritable bowel syndrome, IBS-C); 腹泻型(diarrhea-predominant irritable bowel syndrome, IBS-D); 混合型(IBS-M); 未定型(IBS-A).

3.2 食物敏感的诊断 首先, 询问患者的饮食情况, 如是否经常食用辛辣食物、咖啡、浓茶、酒精等刺激性食物, 另外, 患者的过敏史及是否患有其他过敏性疾病对诊断食物不耐受亦有一定的帮助. 检测血清食物特异性IgG可帮助诊断食物不耐受[42-45]. 目前多采用14种常见食物特异性IgG抗体检测, 使用酶联免疫吸附法, 可以判断患者是否存在食物不耐受以及不耐受食物的种类, 是一种快速、有效的检测方法. 另有研究表明某些食物抗原皮肤划痕试验阳性率较高[46], 也可作为诊断食物不耐受的一项客观依据. 另外, 氢呼气试验、粪便化验等检测可帮助判断是否存在消化吸收不良. 发生食物不耐受的患者可同时对多种食物产生不耐受现象, 而不同人对于同一种食物不耐受时所表现的症状也不尽相同, 多方面的原因均造成了诊断上的困难, 因此, 目前尚无公认的、客观的诊断方法.

4 食物引发IBS的干预

4.1 饮食治疗 了解饮食习惯, 科学地调整饮食结构有利于症状的改善[3,47]. 患者可通过记录每天的饮食内容以及根据食物特异性IgG抗体的检测结果来明确不耐受食物的种类, 将其从饮食中剔除, 可从一定程度上改善肠道症状[43,48,49].

4.2 药物治疗 肥大细胞稳定剂通过肥大细胞的脱颗粒过程, 使其释放的生物介质减少, 作用于肠道神经元的作用减弱, 从而能预防IgG阳性食物引起的IBS症状[50]. 有多项研究表明, 益生菌能改善IBS患者的临床症状, 提高生活质量[51-57]. 但IBS有不同的亚型, 菌群失调的种类也不同[58], 因此, 各种益生菌制剂的疗效不尽相同, 并可能存在安慰剂效应[59], 故益生菌对IBS疗效的证据仍需进一步深入[60]. 另外, 根据患者的具体症状可联合应用解痉、止泻、导泻、促动力的药物进行个体化治疗. 但在用药过程中需注意药物的疗效及不良反应, 如导泻剂可缓解便秘型IBS患者的便秘症状但同时可能引起腹痛等不良反应, 止泻药物能控制腹泻症状但没有能改善腹痛、腹胀等症状的证据[3]. 最近研究表明, 小剂量应用抗抑郁药物(如三环类抗抑郁剂和5-HT再摄取抑制剂)亦可有效治疗伴或不伴精神疾病诊断的IBS患者[3,61-66].

5 结论

随着人们对IBS研究的深入, 食物因素越来越受到广泛的关注. 虽然目前已明确了食物敏感对IBS的作用, 但对其产生的分子机制仍未得到肯定; 而在诊断上, 食物抗原的种类、检出率等方面仍有局限性; 在治疗上, 讲究个体化, 目前也无特效的治疗药物. 但若在现有基础上进一步深入研究, 相信在不久的将来, 食物引发的IBS患者定能得到有效的治疗, 以达到缓解症状、改善生活质量的目的[67-70].

■应用要点

此文可以帮助研究者在现有基础上对食物引发IBS的分子机制进行进一步的深入研究. 另外, 根据目前的方法辅助诊断食物不耐受, 并有待普及更准确、简便的检测方法; 在饮食治疗的同时, 注意药物副反应, 选择最合理的治疗方法.

6 参考文献

1 Jiang X, Locke GR, Choung RS, Zinsmeister AR, Schleck CD, Talley NJ. Prevalence and risk factors for abdominal bloating and visible distention: a population-based study. *Gut* 2008; 57: 756-763

2 Tuteja AK, Talley NJ, Joos SK, Tolman KG, Hickam DH. Abdominal bloating in employed adults: prevalence, risk factors, and association with other bowel disorders. *Am J Gastroenterol* 2008; 103: 1241-1248

3 Gwee KA, Bak YT, Ghoshal UC, Gonlachanvit S, Lee OY, Fock KM, Chua AS, Lu CL, Goh KL, Kositchaiwat C, Makharia G, Park HJ, Chang FY, Fukudo S, Choi MG, Bhatia S, Ke M, Hou X, Hongo M. Asian consensus on irritable bowel syndrome. *J Gastroenterol Hepatol* 2010; 25: 1189-1205

4 谢志贤, 刘倩. 食物不耐受与相关性疾病. 中华内科杂志 2006; 45: 150-151

5 Gremse DA. Alternative approach to IBS and migraine is winning over providers. *Dis Manag Advis* 2004; 10: 6-10, 1

6 Dainese R, Patoureaux S, Vivinus MH, Saint Paul MC, Nano JL, Bernard A, Lannelli A, Hébuterne X, Neunlist M, Piche T. W1695 Influence of Gastrointestinal Food Allergy On Colonic Immune Activation and Barrier Integrity in the Irritable Bowel Syndrome. *Gastroenterology* 2009; 136: A719-A719

7 陈云峰, 张炜, 王德旭, 周忠明, 毕仕强. 肠易激综合征与食物过敏关系的研究. 中华消化杂志 2008; 28: 850-851

8 Eswaran S, Tack J, Chey WD. Food: the forgotten factor in the irritable bowel syndrome. *Gastroenterol Clin North Am* 2011; 40: 141-162

9 戴夫, 甘惠中, 彭琼, 夏云玲. 剔除特异性IgG阳性食物治疗腹泻型肠易激综合征效果观察. 安徽医药 2011; 15: 590-592

10 Matthews SB, Campbell AK. When sugar is not so sweet. *Lancet* 2000; 355: 1330

11 Matthews SB, Waud JP, Roberts AG, Campbell AK. Systemic lactose intolerance: a new perspective on an old problem. *Postgrad Med J* 2005; 81: 167-173

12 Waud JP, Matthews SB, Campbell AK. Measurement of breath hydrogen and methane, together

■同行评价
食物与IBS发病关系密切，但具体的机制尚不十分明了. 该文对食物敏感及食物引发IBS的机制、检测及干预的研究进展进行了综述，论据较充分，结论可靠.

with lactase genotype, defines the current best practice for investigation of lactose sensitivity. *Ann Clin Biochem* 2008; 45: 50-58
13 罗小雨, 钟良. 肠易激综合征发病机制的研究进展. 国际消化病杂志 2010; 30: 321-324
14 Campbell AK, Matthews SB, Vassel N, Cox CD, Naseem R, Chaichi J, Holland IB, Green J, Wann KT. Bacterial metabolic 'toxins': a new mechanism for lactose and food intolerance, and irritable bowel syndrome. *Toxicology* 2010; 278: 268-276
15 Campbell AK, Waud JP, Matthews SB. The molecular basis of lactose intolerance. *Sci Prog* 2005; 88: 157-202
16 Campbell AK, Waud JP, Matthews SB. The molecular basis of lactose intolerance. *Sci Prog* 2009; 92: 241-287
17 Ward RA, McLeish KR. Methylglyoxal: a stimulus to neutrophil oxygen radical production in chronic renal failure? *Nephrol Dial Transplant* 2004; 19: 1702-1707
18 Jia X, Olson DJ, Ross AR, Wu L. Structural and functional changes in human insulin induced by methylglyoxal. *FASEB J* 2006; 20: 1555-1557
19 Riboulet-Chavey A, Pierron A, Durand I, Murdaca J, Giudicelli J, Van Obberghen E. Methylglyoxal impairs the insulin signaling pathways independently of the formation of intracellular reactive oxygen species. *Diabetes* 2006; 55: 1289-1299
20 Guo Q, Mori T, Jiang Y, Hu C, Osaki Y, Yoneki Y, Sun Y, Hosoya T, Kawamata A, Ogawa S, Nakayama M, Miyata T, Ito S. Methylglyoxal contributes to the development of insulin resistance and salt sensitivity in Sprague-Dawley rats. *J Hypertens* 2009; 27: 1664-1671
21 Spaziani R, Bayati A, Redmond K, Bajaj H, Mazzadi S, Bienenstock J, Collins SM, Kamath MV. Vagal dysfunction in irritable bowel syndrome assessed by rectal distension and baroreceptor sensitivity. *Neurogastroenterol Motil* 2008; 20: 336-342
22 Kalliomäki MA. Food allergy and irritable bowel syndrome. *Curr Opin Gastroenterol* 2005; 21: 708-711
23 Spiller R. Serotonin and GI clinical disorders. *Neuropharmacology* 2008; 55: 1072-1080
24 Greenwood-van Meerveld B. Importance of 5-hydroxytryptamine receptors on intestinal afferents in the regulation of visceral sensitivity. *Neurogastroenterol Motil* 2007; 19 Suppl 2: 13-18
25 Bradesi S, Lao L, McLean PG, Winchester WJ, Lee K, Hicks GA, Mayer EA. Dual role of 5-HT3 receptors in a rat model of delayed stress-induced visceral hyperalgesia. *Pain* 2007; 130: 56-65
26 Matsueda K, Harasawa S, Hongo M, Hiwatashi N, Sasaki D. A phase II trial of the novel serotonin type 3 receptor antagonist ramosetron in Japanese male and female patients with diarrhea-predominant irritable bowel syndrome. *Digestion* 2008; 77: 225-235
27 Andresen V, Montori VM, Keller J, West CP, Layer P, Camilleri M. Effects of 5-hydroxytryptamine (serotonin) type 3 antagonists on symptom relief and constipation in nonconstipated irritable bowel syndrome: a systematic review and meta-analysis of randomized controlled trials. *Clin Gastroenterol Hepatol* 2008; 6: 545-555
28 Chen S, Li J, Zhang L, Dong X, Gao W, Mo J, Chen H, Xiao S, Li Y. 5-HT 3 receptors mediate the time-dependent vagal afferent modulation of nociception during chronic food allergen-sensitized visceral hyperalgesia in rats. *Neurogastroenterol Motil* 2009; 21: 1222-e113
29 Kirsch R, Riddell RH. Histopathological alterations in irritable bowel syndrome. *Mod Pathol* 2006; 19: 1638-1645
30 Bhuiyan MR, Majumder TK, Raihan AA, Roy PK, Farha N, Kamal M. Histopathological alterations in post-infectious irritable bowel syndrome in Bangladeshi population. *Mymensingh Med J* 2010; 19: 275-281
31 Spiller RC. Role of infection in irritable bowel syndrome. *J Gastroenterol* 2007; 42 Suppl 17: 41-47
32 Monsbakken KW, Vandvik PO, Farup PG. Perceived food intolerance in subjects with irritable bowel syndrome-- etiology, prevalence and consequences. *Eur J Clin Nutr* 2006; 60: 667-672
33 Shanahan F, Whorwell PJ. IgG-mediated food intolerance in irritable bowel syndrome: a real phenomenon or an epiphenomenom? *Am J Gastroenterol* 2005; 100: 1558-1559
34 曾黎明, 杨光. 食物不耐受与肠易激综合征研究进展. 国际消化病杂志 2008; 28: 289-291
35 Liebregts T, Adam B, Bredack C, Röth A, Heinzel S, Lester S, Downie-Doyle S, Smith E, Drew P, Talley NJ, Holtmann G. Immune activation in patients with irritable bowel syndrome. *Gastroenterology* 2007; 132: 913-920
36 Gwee KA, Lu CL, Ghoshal UC. Epidemiology of irritable bowel syndrome in Asia: something old, something new, something borrowed. *J Gastroenterol Hepatol* 2009; 24: 1601-1607
37 Seifert B, Rubin G, de Wit N, Lionis C, Hall N, Hungin P, Jones R, Palka M, Mendive J. The management of common gastrointestinal disorders in general practice A survey by the European Society for Primary Care Gastroenterology (ESPCG) in six European countries. *Dig Liver Dis* 2008; 40: 659-666
38 Miwa H. Prevalence of irritable bowel syndrome in Japan: Internet survey using Rome III criteria. *Patient Prefer Adherence* 2008; 2: 143-147
39 Ghoshal UC, Abraham P, Bhatt C, Choudhuri G, Bhatia SJ, Shenoy KT, Banka NH, Bose K, Bohidar NP, Chakravartty K, Shekhar NC, Desai N, Dutta U, Das G, Dutta S, Dixit VK, Goswami BD, Jain RK, Jain S, Jayanthi V, Kochhar R, Kumar A, Makharia G, Mukewar SV, Mohan Prasad VG, Mohanty A, Mohan AT, Sathyaprakash BS, Prabhakar B, Philip M, Veerraju EP, Ray G, Rai RR, Seth AK, Sachdeva A, Singh SP, Sood A, Thomas V, Tiwari S, Tandan M, Upadhyay R, Vij JC. Epidemiological and clinical profile of irritable bowel syndrome in India: report of the Indian Society of Gastroenterology Task Force. *Indian J Gastroenterol* 2008; 27: 22-28
40 Gwee KA, Hwang JE, Ho KY, Yeoh KG, Lum CF, Ang PK. In-practice predictors of response to proton pump inhibitor therapy in primary care patients with dyspepsia in an Asian population. *J Clin Gastroenterol* 2008; 42: 134-138
41 Jeong JJ, Choi MG, Cho YS, Lee SG, Oh JH, Park JM, Cho YK, Lee IS, Kim SW, Han SW, Choi KY, Chung IS. Chronic gastrointestinal symptoms and quality of life in the Korean population. *World J Gastroenterol* 2008; 14: 6388-6394
42 Zuo XL, Li YQ, Li WJ, Guo YT, Lu XF, Li JM, Desmond PV. Alterations of food antigen-specific serum immunoglobulins G and E antibodies in patients with irritable bowel syndrome and functional dyspepsia. *Clin Exp Allergy* 2007; 37: 823-830
43 Atkinson W, Sheldon TA, Shaath N, Whorwell PJ.

Food elimination based on IgG antibodies in irritable bowel syndrome: a randomised controlled trial. *Gut* 2004; 53: 1459-1464
44 Zar S, Benson MJ, Kumar D. Food-specific serum IgG4 and IgE titers to common food antigens in irritable bowel syndrome. *Am J Gastroenterol* 2005; 100: 1550-1557
45 Zar S, Mincher L, Benson MJ, Kumar D. Food-specific IgG4 antibody-guided exclusion diet improves symptoms and rectal compliance in irritable bowel syndrome. *Scand J Gastroenterol* 2005; 40: 800-807
46 Jun DW, Lee OY, Yoon HJ, Lee SH, Lee HL, Choi HS, Yoon BC, Lee MH, Lee DH, Cho SH. Food intolerance and skin prick test in treated and untreated irritable bowel syndrome. *World J Gastroenterol* 2006; 12: 2382-2387
47 Morcos A, Dinan T, Quigley EM. Irritable bowel syndrome: role of food in pathogenesis and management. *J Dig Dis* 2009; 10: 237-246
48 Whorwell P, Lea R. Dietary Treatment of the Irritable Bowel Syndrome. *Curr Treat Options Gastroenterol* 2004; 7: 307-316
49 李汉华, 韩盛玺, 董巍. 肠易激综合征患者食物不耐受临床研究. 实用医院临床杂志 2008; 5: 30-31
50 杨崇美, 李延青. 色甘酸钠防治肠易激综合征患者的临床研究. 中华消化杂志 2007; 27: 566-567
51 Hoveyda N, Heneghan C, Mahtani KR, Perera R, Roberts N, Glasziou P. A systematic review and meta-analysis: probiotics in the treatment of irritable bowel syndrome. *BMC Gastroenterol* 2009; 9: 15
52 Zeng J, Li YQ, Zuo XL, Zhen YB, Yang J, Liu CH. Clinical trial: effect of active lactic acid bacteria on mucosal barrier function in patients with diarrhoea-predominant irritable bowel syndrome. *Aliment Pharmacol Ther* 2008; 28: 994-1002
53 Sinn DH, Song JH, Kim HJ, Lee JH, Son HJ, Chang DK, Kim YH, Kim JJ, Rhee JC, Rhee PL. Therapeutic effect of Lactobacillus acidophilus-SDC 2012, 2013 in patients with irritable bowel syndrome. *Dig Dis Sci* 2008; 53: 2714-2718
54 朱丽明, 柯美云, 周丽雅, 袁耀宗, 罗金燕, 候晓华, 陈雯湖. 益生菌治疗腹泻型肠易激综合征. 基础医学与临床 2008; 28: 1071-1074
55 Tsuchiya J, Barreto R, Okura R, Kawakita S, Fesce E, Marotta F. Single-blind follow-up study on the effectiveness of a symbiotic preparation in irritable bowel syndrome. *Chin J Dig Dis* 2004; 5: 169-174
56 Kim YG, Moon JT, Lee KM, Chon NR, Park H. [The effects of probiotics on symptoms of irritable bowel syndrome]. *Korean J Gastroenterol* 2006; 47: 413-419
57 McFarland LV, Dublin S. Meta-analysis of probiotics for the treatment of irritable bowel syndrome. *World J Gastroenterol* 2008; 14: 2650-2661
58 Kassinen A, Krogius-Kurikka L, Mäkivuokko H, Rinttilä T, Paulin L, Corander J, Malinen E, Apajalahti J, Palva A. The fecal microbiota of irritable bowel syndrome patients differs significantly from that of healthy subjects. *Gastroenterology* 2007; 133: 24-33
59 Williams EA, Stimpson J, Wang D, Plummer S, Garaiova I, Barker ME, Corfe BM. Clinical trial: a multistrain probiotic preparation significantly reduces symptoms of irritable bowel syndrome in a double-blind placebo-controlled study. *Aliment Pharmacol Ther* 2009; 29: 97-103
60 赵威, 柯美云. 益生菌治疗肠易激综合征的研究现状和进展. 中华消化杂志 2010; 30: 131-134
61 Ford AC, Talley NJ, Schoenfeld PS, Quigley EM, Moayyedi P. Efficacy of antidepressants and psychological therapies in irritable bowel syndrome: systematic review and meta-analysis. *Gut* 2009; 58: 367-378
62 Vahedi H, Merat S, Momtahen S, Kazzazi AS, Ghaffari N, Olfati G, Malekzadeh R. Clinical trial: the effect of amitriptyline in patients with diarrhoea-predominant irritable bowel syndrome. *Aliment Pharmacol Ther* 2008; 27: 678-684
63 Bahar RJ, Collins BS, Steinmetz B, Ament ME. Double-blind placebo-controlled trial of amitriptyline for the treatment of irritable bowel syndrome in adolescents. *J Pediatr* 2008; 152: 685-689
64 Blanchard EB, Lackner JM, Jaccard J, Rowell D, Carosella AM, Powell C, Sanders K, Krasner S, Kuhn E. The role of stress in symptom exacerbation among IBS patients. *J Psychosom Res* 2008; 64: 119-128
65 Hertig VL, Cain KC, Jarrett ME, Burr RL, Heitkemper MM. Daily stress and gastrointestinal symptoms in women with irritable bowel syndrome. *Nurs Res* 2007; 56: 399-406
66 Park HJ, Jarrett M, Cain K, Heitkemper M. Psychological distress and GI symptoms are related to severity of bloating in women with irritable bowel syndrome. *Res Nurs Health* 2008; 31: 98-107
67 Husain N, Chaudhry IB, Jafri F, Niaz SK, Tomenson B, Creed F. A population-based study of irritable bowel syndrome in a non-Western population. *Neurogastroenterol Motil* 2008; 20: 1022-1029
68 Rey E, García-Alonso MO, Moreno-Ortega M, Alvarez-Sanchez A, Diaz-Rubio M. Determinants of quality of life in irritable bowel syndrome. *J Clin Gastroenterol* 2008; 42: 1003-1009
69 Park JM, Choi MG, Kim YS, Choi CH, Choi SC, Hong SJ, Jeong JJ, Lee DH, Lee JS, Lee KJ, Son HJ, Sung IK. Quality of life of patients with irritable bowel syndrome in Korea. *Qual Life Res* 2009; 18: 435-446
70 Huang WW, Zhou FS, Bushnell DM, Diakite C, Yang XH. Cultural adaptation and application of the IBS-QOL in China: a disease-specific quality-of-life questionnaire. *Qual Life Res* 2007; 16: 991-996

编辑 曹丽鸥 电编 闫晋利