

- dase inhibitor apocynin has potential prophylactic effects on melamine-related nephrolithiasis in vitro and in vivo[J]. *Mol Cell Biochem*, 2015, 399(1-2):167—178.
- 32 Chandasana H, Chhonker Y S, Bala V, et al. Pharmacokinetic, bioavailability, metabolism and plasma protein binding evaluation of NADPH-oxidase inhibitor apocynin using LC-MS/MS[J]. *J Chromatogr B Analyt Technol Biomed Life Sci*, 2015, 985: 180—188.
- 33 Ciarcia R, Damiano S, Florio A, et al. The protective effect of Apocynin on Cyclosporine A-induced hypertension and nephrotoxicity in rats[J]. *J Cell Biochem*, 2015, 116(9): 1848—1856.
- 34 Zuo J, Khan A, Glenton P A, et al. Effect of NADPH oxidase inhibition on the expression of kidney injury molecule and calcium oxalate crystal deposition in hydroxy-L-proline-induced hyperoxaluria in the male Sprague-Dawley rats [J]. *Nephrol Dial Transplant*, 2011, 26(6): 1785—1796.
- 35 Selemidis S, Sobey C G, Wingler K, et al. NADPH oxidases in the vasculature: molecular features, roles in disease and pharmacological inhibition[J]. *Pharmacol Ther*, 2008, 120(3): 254—291.
- 36 Umekawa T, Byer K, Uemura H, et al. Diphenyleneiodium (DPI) reduces oxalate ion- and calcium oxalate monohydrate and brushite crystal-induced upregulation of MCP-1 in NRK 52E cells[J]. *Nephrol Dial Transplant*, 2005, 20(5):870—878.
- 37 Hong S H, Lee H J, Sohn E J, et al. Anti-nephrolithic potential of resveratrol via inhibition of ROS, MCP-1, hyaluronan and osteopontin in vitro and in vivo[J]. *Pharmacol Rep*, 2013, 65(4): 970—979.
- 38 Lee H J, Jeong S J, Park M N, et al. Gallotannin suppresses calcium oxalate crystal binding and oxalate-induced oxidative stress in renal epithelial cells[J]. *Biol Pharm Bull*, 2012, 35(4): 539—544.
- 39 Browatzki M, Larsen D, Pfeiffer C A, et al. Angiotensin II stimulates matrix metalloproteinase secretion in human vascular smooth muscle cells via nuclear factor-kappaB and activator protein 1 in a redox-sensitive manner[J]. *J Vasc Res*, 2005, 42(5): 415—423.
- 40 Cupisti A, D'Alessandro C, Samoni S, et al. Nephrolithiasis and hypertension: possible links and clinical implications[J]. *J Nephrol*, 2014, 27(5): 477—482.
- 41 Yoshioka I, Tsujihata M, Akanae W, et al. Angiotensin type-1 receptor blocker candesartan inhibits calcium oxalate crystal deposition in ethylene glycol-treated rat kidneys[J]. *Urology*, 2011, 77(4): 1007. e9—1007. e14.

(收稿日期:2015-03-31)

间质性膀胱炎/膀胱疼痛综合征的保守治疗

高志明¹ 魏大东¹ 夏海波¹

【摘要】 间质性膀胱炎(IC)/膀胱疼痛综合征(BPS)的治疗较为困难且疗效不佳。目前尚无明确病因和有效治疗方法。美国泌尿外科协会(AUA)出版了关于 IC/BPS 的诊疗指南,一线治疗包括:健康教育,自我护理,行为矫正,缓解压力和学习积极的应对技巧^[1]。患者和医师把 IC/BPS 当成慢性病对待,将会获得更为满意的结果。本文就 IC/BPS 的保守治疗和将 IC/BPS 视为慢性病治疗的益处做一综述。

【关键词】 间质性膀胱炎;保守治疗;慢性病

doi: 10.13201/j.issn.1001-1420.2015.10.026

【中图分类号】 R694.3 【文献标识码】 A

Conservative treatment of interstitial cystitis/bladder pain syndrome

GAO Zhiming WEI Dadong XIA Haibo

(Department of Urology, Affiliated Hospital of Chifeng University, Chifeng, Inner Mongolia, 024000, China)

Corresponding author: XIA Haibo, E-mail: 15998672050@163.com

Abstract The management of interstitial cystitis/bladder pain syndrome (IC/BPS) is both frustrating and difficult. The etiology is uncertain and there is no definitive treatment. The American Urological Association (AUA) provides a guideline for the diagnosis and treatment of IC/BPS. Recommended first-line treatments include patient education, self-care practices, behavior modifications, stress management, and positive coping techniques^[1]. Management of IC/BPS may be also improved if we treat this condition as a chronic disease. This article

¹ 赤峰学院附属医院(新城)泌尿外科(内蒙古赤峰,024000)
通信作者:夏海波, E-mail: 15998672050@163.com

reviews the AUA first-line treatments for IC/BPS and the benefits of treating this condition as a chronic disease.

Key words interstitial cystitis; conservative treatment; chronic disease

间质性膀胱炎(interstitial cystitis, IC)/膀胱疼痛综合征(bladder pain syndrome, BPS)是一种以膀胱区疼痛、尿频、尿急为主要症状的慢性膀胱疾病,其严重影响患者生活质量,包括夜尿增多、性能力下降、抑郁和精神紧张^[2]。有研究显示,精神压力增加膀胱疼痛和尿急症状加剧^[3]。该研究还称,70%的 IC/BPS 患者其家庭关系和责任在疾病发生发展中起到了负面的作用。84%的 IC/BPS 患者发病与职业因素有关^[4]。目前口服药物治疗疗效不佳,临床上以膀胱水扩张及膀胱内注射治疗效果尚可,但疗效持续时间短,手术并发症较多^[5]。美国每例 IC/BPS 患者每年药物治疗费用约 11 000 美元^[6]。

与关节炎、糖尿病及心脏病类似,IC/BPS 是一种持续时间较长,可以被控制但不能被治愈的慢性病^[7,8]。是较为普遍、治疗昂贵的健康问题,但也是可以预防并有效控制的。2005 年,约 1.33 亿美国人(超过一半人口)至少患有一种慢性病^[9]。慢性病是美国人口致死致残的主要原因,70%的死亡人口其死因是慢性病^[9]。除了折磨病患,慢性病也给社会带来了巨大经济负担,约 3/4 医疗费用用于慢性病^[10]。随着人口老龄化的发展,慢性病发病率逐年上升。大量的时间和金钱用于慢性病的研究、教育和其医药发展。

AUA2011 版 IC/BPS 诊疗指南指出,IC/BP 治疗应循序渐进,首先保守治疗^[11]。所有患者均应接受一线治疗,包括健康教育,自我护理,行为矫正,缓解压力和学习积极的应对技巧。

1 健康教育

告知患者正常膀胱功能,教授其对抗危险因素的方法。目前尚无有效的单一治疗方法,众多控制临床症状的治疗方案(包括联合治疗)需实验证实其疗效^[11]。目前多数 IC/BPS 患者对该病了解不多,生活质量较低^[12]。IC/BPS 患者在不同社会环境下其症状不同,所以须强调个体化健康教育的重要性。健康教育的第一步就是告知患者 IC/BPS 是由不明原因引起的膀胱慢性病或膀胱相关的盆腔疼痛综合征。膀胱的功能是储存尿液,并在条件允许的情况下周期性的排出尿液。IC/BPS 使膀胱产生频发的强烈尿意,表现为尿频、尿急。盆腔疼痛症状表现为从不适到剧烈疼痛,可发生在膀胱、尿道、外阴、阴道、阴茎、直肠、会阴及腰背部^[13]。所有患者均需初诊评估,针对首要问题,进行健康教育,并给出建议和提供帮助。

通常液体摄入增多,尿频症状加重,IC/BPS 患者理应限制液体摄入以减轻尿频症状和盆腔不适。

然而,充足且持续的液体摄入可降低尿液中刺激物质和毒素浓度。尿液冲洗膀胱可缓解下尿路刺激症状。充分的水合作用可减轻便秘,进而减轻便秘造成的 IC/BPS 症状加重。Fall 等^[14]关于 IC/BPS 治疗的循证医学综述指出了 IC/BPS 药物治疗方法。患者需知尚无单一疗法可以治疗 IC/BPS,需实验性应用联合疗法控制 IC/BPS 临床症状^[15,16]。医生和患者根据症状,共同商议治疗方案。

2 自我护理

患者需知特殊习惯可能改善或加重 IC/BPS 症状^[15]。这些方法通常无害且简便易行。在耻骨上或会阴区应用热敷或冰敷的方式可减轻或解除 IC/BPS 不适症状。限制摄入咖啡、柑橘制品、巧克力、酒精饮料和辛辣食物是普遍应用于 IC/BPS 患者的自我护理策略^[17]。可用排除饮食法帮助确定哪种食物或水果对患者有帮助。

3 行为矫正

行为矫正治疗以放松盆底肌为目的,具体方法有:抱紧双腿使膝盖紧贴胸部、伸展双腿平躺和蹲伏等。Carrico 等^[18]让 IC/BPS 患者观看意象引导视频,集中精力放松膀胱、松弛盆底肌,IC/BPS 症状好转。以尿频为主的患者,应行尿流动力学检查。对于存在膀胱过度活动的患者,嘱其记录排尿日记,控制液体摄入,坚持盆底肌锻炼,以延长排尿间隔^[19,20]。由于刺激物质刺激所致的尿频需增加液体摄入,一些行为亦可加重 IC/BPS 症状,如盆底肌锻炼、性交和穿紧身衣等。用于治疗 IC/BPS 的非处方药物,目前尚无充分的随机对照实验及安慰剂对照实验。有研究称,应用生物类黄酮槲皮素的大部分 IC/BPS 患者症状得到缓解^[21]。甘油磷酸钙可降低食物中的可滴定酸,防止食物引起 IC/BPS 症状发作^[22]。盐酸非那吡啶可短期控制 IC/BPS 症状^[16]。

4 缓解压力

精神压力是 IC/BPS 临床症状的显著危险因素^[23]。缓解压力可以减轻临床症状和预防临床症状发作。较高的精神压力水平与 IC/BPS 患者尿急、盆腔疼痛症状明显相关^[24]。缓解压力的方法众多,例如锻炼、沐浴、沉思、缩短工作时间、创建无压力环境及亲友帮助其降低精神压力等^[20,25]。

5 学习积极的应对技巧

应鼓励患者学习积极的应对技巧,以积极的态度面对并做出调整,提高生活质量^[23]。对疾病过分担忧,被当前状况所困扰的患者,消极对待,认为该病无药可治,不能忍受现状,抑郁,对疼痛过分敏感及社交能力低下,对治疗非常不利^[26]。绝望的

IC/BPS 患者其抑郁时间延长,疼痛级别也相对较高^[26]。相反,乐观的患者显示出了较强的调节能力^[27]。

寻找社会情感支持是 IC/BPS 患者积极的应对策略^[28]。包括来自配偶、家人、朋友、IC/BPS 支援团体及卫生领域专业人员的支持。寻找社会情感帮助的 IC/BPS 患者,特别是在 IC/BPS 发作期,效果显著^[29]。向他人寻求帮助的 IC/BPS 患者,孤独感降低,控制感增强,较少继发抑郁症^[27]。Check 等^[26]报道称,IC/BPS 患者消极对待、绝望、拒绝接受社会支持,其症状严重程度相对较高。寻找社会帮助可使 IC/BPS 患者心理健康,降低不适程度,以此获得更好的生活质量。这些发现与其他慢性病研究完全一致。正如 Nordling 等^[30]的报道中讲述“降低患者精神压力是应对 IC/BPS 的重要方法”。

6 将 IC/BPS 当成慢性病治疗

相比于 IC/BPS 的预防,目前 AUA 关于 IC/BPS 的指南仍然更注重其治疗。我们要考虑到社会因素和环境因素,让 IC/BPS 患者充分认识其病因,以便更好的治疗和预防。历史证明,社会问题深刻地影响社会健康。良好的生活条件、干净的生活环境、安全的工作环境、适当的营养摄入和卫生保健是一个民族健康的关键因素。社会压力、家庭环境、社会支持均可加重或减轻慢性病症状。我们应将 IC/BPS 放在当前医疗环境、社会环境和自然环境的大前提下讨论分析。

Takahashi^[31]报道当前医生都忙于解决 IC/BPS 的急性症状,未重视调查其病因及恶化因素,也未研究其预防方法。以往的医疗实践更重视患者发病后的对症治疗,而不是重视环境因素、社会因素及其病因。

自身免疫是 IC/BPS 的一个重要原因。像其他自身免疫病一样,IC/BPS 患者女性多于男性。发病率逐年增长^[32~34]。这说明环境因素在起作用,基因在这么短的时间内不会有变。在自身免疫启动的过程中,环境暴露为其触点^[35]。Yamada^[36]报道 80% 的 IC/BPS 患者患有过敏性疾病。过敏均由环境暴露引起,如霉菌、花粉及不断增加的工业化工产品。Shorter 等^[17]报道 90% 的 IC/BPS 患者发病与进食特殊食品有关。生活方式的转变,人们更多的食用加工过的食品。若 IC/BPS 确实为自身免疫性疾病,明确引发或加重其症状的环境因素对其治疗和预防至关重要。医生在治疗 IC/BPS 患者时需采取不同治疗方法,须视 IC/BPS 为慢性病,寻求一个长期的医疗保健计划。医生须视自己为“保健医生”而不是内科医生或外科医生。

通过学习 IC/BPS 相关知识,让患者知道他们不是唯一一个有此症状的人,他们正经历一个已被

熟知、对生命没有威胁的疾病。医生需告知患者使 IC/BPS 症状加剧的社会因素和环境因素,同时施用药物治疗及社会治疗。IC/BPS 标准治疗包括饮食建议、胃肠功能调节、性生活建议及松弛身心。医生的建议和支持加上患者生活方式的改变,可使患者生活质量得到显著提升。

AUA 关于 IC/BPS 的诊疗指南确定了一个治疗策略,所有患者均应接受一线治疗,包括健康教育、自我护理、行为矫正、缓解压力和学习积极的应对技巧。在照顾 IC/BPS 患者方面,医生需更进一步,治疗策略需包括将 IC/BPS 当做慢性病治疗,认识该病的所有组成部分,鉴别使其发作或加剧的社会因素和环境因素;提供社会治疗和临床治疗两种治疗方式。将 IC/BPS 治疗当作卫生保健对待,而不只是临床治疗,这将是 IC/BPS 患者的最优优化治疗方案。

[参考文献]

- 1 Hanno P M, Burks D A, Clemens J Q, et al. AUA guideline for the diagnosis and treatment of interstitial cystitis/bladder pain syndrome[J]. J Urol, 2011, 185 (6): 2162—2170.
- 2 朱绪辉,杜鹏,善辉,等. 阿米替林联合透明质酸钠治疗膀胱疼痛综合征/间质性膀胱炎的临床研究(附 58 例报告)[J]. 临床泌尿外科杂志, 2012, 27(2): 117—120, 123.
- 3 Nickel J C, Tripp D A, Pontari M, et al. Psychosocial phenotyping in women with interstitial cystitis/painful bladder syndrome: a case control study[J]. J Urol, 2010, 183(1): 167—172.
- 4 Lai H H. Clinical trials: Placebo effects in interstitial cystitis/bladder pain syndrome[J]. Nat Rev Urol, 2014, 11(9): 494—495.
- 5 Gülpınar O, Kayış A, Süer E, et al. Clinical comparison of intravesical hyaluronic acid and hyaluronic acid-chondroitin sulphate therapy for patients with bladder pain syndrome/interstitial cystitis[J]. Can Urol Assoc J, 2014, 8(9-10): E610—E614.
- 6 Robinson R, Montejano L, Ruiz K, et al. The economic burden of interstitial cystitis and painful bladder syndrome[J]. J Urol, 2011, 185(4 Suppl): e129.
- 7 Fiehn O, Kim J. Metabolomics insights into pathophysiological mechanisms of interstitial cystitis[J]. Int Neurourol J, 2014, 18(3): 106—114.
- 8 Diniz S, Dinis P, Cruz F, et al. Bladder pain syndrome/interstitial cystitis: present and future treatment perspectives[J]. Minerva Urol Nefrol, 2013, 65(4): 263—276.
- 9 Fall M, Peeker R. Methods and incentives for the early diagnosis of bladder pain syndrome/interstitial cystitis [J]. Expert Opin Med Diagn, 2013, 7(1): 17—24.
- 10 Vas L, Pattanik M, Titarmore V. Treatment of interstitial cystitis/painful bladder syndrome as a neuropath-

- ic pain condition[J]. *Indian J Urol*, 2014, 30(3): 350–353.
- 11 Tirlapur S A, Riordain R N, Khan K S, et al. Variations in the reporting of outcomes used in systematic reviews of treatment effectiveness research in bladder pain syndrome[J]. *Eur J Obstet Gynecol Reprod Biol*, 2014, 180: 61–67.
- 12 Rourke W, Khan S A, Ahmed K, et al. Painful bladder syndrome/interstitial cystitis: aetiology, evaluation and management[J]. *Arch Ital Urol Androl*, 2014, 86(2): 126–131.
- 13 Van der Aa F, Beckley I, de Ridder D. Polyomavirus BK—a potential new therapeutic target for painful bladder syndrome/interstitial cystitis[J]? *Med Hypotheses*, 2014, 83(3): 317–320.
- 14 Fall M, Oberpenning F, Pecker R. Treatment of bladder pain syndrome/interstitial cystitis 2008: can we make evidence-based decisions[J]? *Eur Urol*, 2008, 54(1): 65–75.
- 15 Bosch P C. Examination of the significant placebo effect in the treatment of interstitial cystitis/bladder pain syndrome[J]. *Urology*, 2014, 84(2): 321–326.
- 16 Schrepf A, O'Donnell M, Luo Y, et al. Inflammation and inflammatory control in interstitial cystitis/bladder pain syndrome: Associations with painful symptoms[J]. *Pain*, 2014, 155(9): 1755–1761.
- 17 Shorter B, Lesser M, Moldwin R M, et al. Effect of comestibles on symptoms of interstitial cystitis[J]. *J Urol*, 2007, 178(1): 145–152.
- 18 Carrico D J, Peters K M, Diokno A C. Guided imagery for women with interstitial cystitis: results of a prospective, randomized controlled pilot study[J]. *J Altern Complement Med*, 2008, 14(1): 53–60.
- 19 Gülpınar O, Haliloglu A H, Gökce M İ, et al. Instillation of Hyaluronic Acid via Electromotive Drug Administration Can Improve the Efficacy of Treatment in Patients With Interstitial Cystitis/Painful Bladder Syndrome: A Randomized Prospective Study[J]. *Korean J Urol*, 2014, 55(5): 354–359.
- 20 Chelimsky T, Chelimsky G, McCabe N P, et al. Interstitial Cystitis-Elucidation of Psychophysiologic and Autonomic Characteristics (the ICEPAC Study): design and methods[J]. *J Pain Res*, 2014, 7: 243–253.
- 21 Fiehn O, Kim J. Metabolomics insights into pathophysiological mechanisms of interstitial cystitis[J]. *Int Neurourol J*, 2014, 18(3): 106–114.
- 22 Nickel J C, Tripp D A, Pontari M, et al. Psychosocial phenotyping in women with interstitial cystitis/painful bladder syndrome: a case control study[J]. *J Urol*, 2010, 183(1): 167–172.
- 23 Tsai C F, Ouyang W C, Tsai S J, et al. Risk factors for poor sleep quality among patients with interstitial cystitis in Taiwan[J]. *Neurourol Urodyn*, 2010, 29(4): 568–572.
- 24 王超, 廖泽明, 蔡勇. 中西医结合治疗膀胱疼痛综合征/间质性膀胱炎 24 例报告[J]. *临床泌尿外科杂志*, 2013, 28(7): 550–551.
- 25 Kim J, Freeman M R. Antiproliferative factor signaling and interstitial cystitis/painful bladder syndrome[J]. *Int Neurourol J*, 2011, 15(4): 184–191.
- 26 Check J H, Cohen G, Cohen R, et al. Sympathomimetic amines effectively control pain for interstitial cystitis that had not responded to other therapies[J]. *Clin Exp Obstet Gynecol*, 2013, 40(2): 227–228.
- 27 Beckett M K, Elliott M N, Clemens J Q, et al. Consequences of interstitial cystitis/bladder pain symptoms on women's work participation and income: results from a national household sample[J]. *J Urol*, 2014, 191(1): 83–88.
- 28 Colaco M A, Evans R J. Current recommendations for bladder instillation therapy in the treatment of interstitial cystitis/bladder pain syndrome[J]. *Curr Urol Rep*, 2013, 14(5): 442–447.
- 29 Neuhaus J, Schwalenberg T. Intravesical treatments of bladder pain syndrome/interstitial cystitis[J]. *Nat Rev Urol*, 2012, 9(12): 707–720.
- 30 Nordling J, Fall M, Hanno P. Global concepts of bladder pain syndrome (interstitial cystitis)[J]. *World J Urol*, 2012, 30(4): 457–464.
- 31 Takahashi S. Editorial comment to on-and post-treatment symptom relief by repeated instillations of heparin and alkalized lidocaine in interstitial cystitis[J]. *Int J Urol*, 2013, 20(11): 1123.
- 32 Argade S, Shaw T, Su Y, et al. Tamm-Horsfall protein-associated nucleotides in patients with interstitial cystitis[J]. *BJU Int*, 2013, 111(5): 811–819.
- 33 Pinto R, Lopes T, Silva J, et al. Persistent therapeutic effect of repeated injections of onabotulinum toxin a in refractory bladder pain syndrome/interstitial cystitis[J]. *J Urol*, 2013, 189(2): 548–553.
- 34 Schmidt C W. Questions persist: environmental factors in autoimmune disease. *Environ Health Perspect*[J]. 2011, 119(6): A249–A253.
- 35 Javierre B M, Hernando H, Ballestar E. Environmental triggers and epigenetic deregulation in autoimmune disease[J]. *Discov Med*, 2011, 12(67): 535–545.
- 36 Yamada T. Significance of complications of allergic diseases in young patients with interstitial cystitis[J]. *Int J Urol*, 2003, 10 Suppl: S56–S58.

(收稿日期: 2014-11-04)