

绝经泌尿生殖综合征的非激素治疗进展

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[摘要] 绝经泌尿生殖综合征 (GSM) 是指围绝经期和绝经后女性雌激素水平显著下降, 产生外阴阴道症状、泌尿系统症状以及性生活障碍等的一类慢性进展性疾病, 随着年龄增加和绝经时间延长而加重, 严重影响中老年女性的生活质量。目前, 绝经激素治疗是最有效的疗法, 但长期应用激素替代治疗并非适合所有女性。本文将对 GSM 的非激素治疗的进展进行综述, 为临床医生提供治疗策略。

[关键词] 绝经泌尿生殖综合征; 非激素药物治疗; 激光治疗; 盆底肌肉训练

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Non-hormonal Treatment for Genitourinary Syndrome of Menopause

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[Abstract] Genitourinary syndrome of menopause (GSM) is a symptom of external genitalia, urinary system, and sexual disorders in perimenopausal and postmenopausal women. This is a chronic progressive disease which becomes increasingly with age and prolonged menopause, seriously affects the quality of life of middle-aged and elderly women. For GSM patients, menopause hormone therapy (MHT) is the most effective measure, but long-term use of MHT is not suitable for all women. This article will review the non-hormone treatment of GSM and provide treatment strategies for doctors.

[Key words] Genitourinary syndrome of menopause; Non-hormone medicine treatment; Laser therapy; Pelvic floor muscle training

绝经泌尿生殖综合征 (Genitourinary syndrome of menopause, GSM) 是由于女性卵巢功能衰竭、绝经后雌激素水平降低, 引起的女性生殖道萎缩、泌尿道症状及性功能障碍。随着全球女性寿命延长, 超过一半的绝经后女性会出现上述症状, GSM 症状随着女性年龄增加和绝经时间延长而加重, 严重影响绝经过渡期和大多数绝经后妇女的健康和生活质量^[1]。一项来自我国 31 个省份 4 063 例围绝经期和绝经后女性调查显示, 泌尿生殖系统症状是最常见的主诉^[2]。北京市某社区中老年妇女生殖健康调查显示, GSM 在老年女性中很普遍, 生殖道萎缩患病率为 34.8%, 有泌尿道症状者占 47.5%^[3]。

绝经激素治疗 (Menopause hormone therapy, MHT) 的有效性已被循证医学证实。MHT 治疗除了缓解绝经相关症状, 还可以预防绝经带来的老年退化性问题。MHT 是目前治疗 GSM 的最佳方案, 同样, GSM 也是 MHT 的最佳适应证^[4]。但长期使用激素替代治疗并非适合所有妇女, 激素治疗与肿瘤、心血管疾病、静脉血栓栓塞的关系一直处于争议状态^[5]。GSM 是一个需要终身管理的疾病, 除了局部和全身激素治疗外, 也可应用非激素治疗, 包括改变生活方式等综合治疗

和非激素药物治疗、激光治疗、盆底肌肉训练等^[6]。本文就 GSM 的非激素治疗现状和研究进展作一综述。

1 综合治疗

综合疗法的实质是绝经管理, 重点是开展对医护人员的教育和对 GSM 患者的长期管理及宣教。解决许多令人痛苦的泌尿生殖系统症状, 改善绝经后妇女的性健康和生活质量^[7]。另外, 健康的生活方式是帮助 GSM 患者改善性功能障碍的最重要方法之一^[8]。

2 非激素药物治疗

2.1 阴道保湿剂和润滑剂

对于有癌症病史、无法或不愿接受 MHT 的女性, 除生活方式改变之外, 阴道保湿剂、润滑剂和凝胶是 GSM 的一线治疗^[9]。基于透明质酸的保湿剂在健康女性和癌症患者或幸存者中都显示出有效、安全且耐受性良好的临床结果, 其强大的水结合性能提供润滑和保湿效果, 有助于维持尿路和生殖器组织的水合作用和弹性水平。可能是早期管理 GSM 相关症状的有效选择^[10]。Monurelle 生物阴道凝胶含有纯化牛初乳, 可以有效改善绝经后妇女的外阴阴道萎缩 (Vulvovaginal atrophy, VVA) 症状, 改善性功能, 缓解泌尿系统症状和提高生活质量^[11]。一种由芦荟、沙棘油、

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18 β -甘草酸、透明质酸和糖原等成分制成的新型阴道凝胶,也可以有效缓解和安全治疗 VVA,改善性功能,因为是单一局部药物,患者具有良好的依从性^[12]。值得注意的是,虽然这些非激素、非处方阴道保湿剂和润滑剂可以缓解 VVA 的症状,但它们的化学成分差异大,有些产品的 pH 值、渗透压与人体内环境不一致,或应用某些添加剂,长期使用会对身体造成有害影响^[13]。因此,选择渗透压和阴道 pH 值达到最佳平衡,并且在生理上与天然阴道分泌物最相似的产品,才是绝经后女性的最佳选择^[14]。

2.2 阴道菌群调节剂

GSM 女性雌激素分泌逐渐减少、阴道 pH 值升高,阴道微生物菌群也发生了改变,如乳酸杆菌水平降低,可影响阴道结构和功能,导致 GSM 的发生和发展^[15]。绝经后女性乳酸杆菌丰度降低并且多样性显著增高,具有低乳酸菌相对丰度的独特细菌群落状态,与 VVA 相关^[16]。乳酸菌代谢产生的乳酸为阴道提供并保持酸性环境,有助于排除其他病原微生物。使用益生菌治疗 GSM,可以增加绝经后女性生殖道乳酸杆菌丰度,保护其免受雌激素戒断引起的 GSM^[17]。乳酸菌与 GSM 呈负相关。未经系统治疗的 GSM 患者,其阴道菌群明显包括几种厌氧菌,有着严重的 GSM 症状。经治疗后,阴道微生物多样性减少,乳酸菌丰度显著增加,成为优势比例^[18]。

2.3 选择性雌激素受体调节剂

选择性雌激素受体调节剂,如他莫昔芬、雷洛昔芬等常用于缓解更年期症状,但是有发生子宫内膜癌的潜在危险。奥培米芬(Ospemifene)安全性较高,接受奥培米芬治疗的女性,基线时子宫内膜厚度为 2.1~2.3 mm,治疗后为 2.5~3.2 mm,低于公认的临床阈值 4 mm。且未观察到子宫内膜癌或增生病例,治疗长达 52 周后未观察到子宫内膜非典型增生或癌灶^[19]。奥培米芬同时有激动和拮抗雌激素受体的作用,且具有组织特异性,作为第一种用于性交困难的非激素药物,用于缓解围绝经期女性性交痛,可以改善阴道成熟指数、降低阴道 pH 值、增加润滑度^[20]。此外,使用 60 mg 的奥培米芬治疗 GSM 妇女的 II 期、III 期研究结果表明,奥培米芬对于患者的骨骼、心血管系统以及乳房的总体安全性较高^[21]。

3 激光治疗

由于 CO₂ 激光具有低能量、微创优势,除了广泛应用于皮肤科美容领域之外,近年已引入到阴道和外阴疾病的微创治疗中^[22]。点阵式 CO₂ 激光治疗用于绝经后 VVA 的治疗,简单方便,无须麻醉和镇痛,门诊即可进行操作^[23]。且近期疗效显著,能够有效改善阴道灼热、干燥、性交痛,症状的改善与阴道局部雌激素治疗相当,疗效至少持续 6~12 个月^[24]。阴道灼热、瘙痒、排尿困难评分显著降低,欲望、唤醒、性高潮、满意度显著提高^[25]。与外用雌激素相比,CO₂ 点阵激光治疗 GSM 之后,激光组阴道雌激素和孕激素受体水

平增加并维持,激光治疗的结果与外用激素黄金标准相似^[26]。一项对 1 152 例使用 CO₂ 激光治疗患者的调查表明,疗效确切,无重大不良事件^[27]。

除 CO₂ 激光外,铒激光也可以有效改善阴道干燥、痛、瘙痒、灼热等症状,且对女性性功能和性生活的总体满意度有显著改善,治疗后未发现长期并发症^[28]。

4 盆底肌肉训练

随着女性年龄增长,脊柱生理弯曲发生改变,绝经后女性脂肪再分布,出现腹型肥胖,导致盆腔支持结构退化,盆底肌力下降,对盆腔脏器的支撑作用减弱。雌激素和孕激素受体广泛存在于整个骨盆底,绝经前后雌、孕激素的下降不可避免地会影响骨盆底的功能^[29]。盆底肌肉训练是一种无副作用的低成本保守治疗,教育和鼓励患者通过自主收缩和舒张盆底肌肉群,可以有效增强盆底肌力,改善外阴阴道组织的血液流动和弹性。盆底肌肉训练不仅可以单独使用,也可与其他治疗方式联合使用,可以有效减轻 GSM 的体征和症状^[30]。对 GSM 患者进行盆底肌肉训练 12 周后利用阴道健康评估量表、萎缩症状问卷进行调查,盆底肌肉训练可显著改善 VVA/GSM 症状和体征,改善生活质量,对性功能产生积极影响^[31]。为进一步发现盆底肌肉训练改善 GSM 的作用机制,使用彩色多普勒超声,在静息时和盆底肌肉收缩后测量并比较背侧动脉的收缩期峰值速度、平均最大速度和搏动指数,发现盆底肌肉训练显著改善了两条动脉的血流参数,显著提高了宫缩后盆底肌松弛的速度。盆底肌肉训练改善了 GSM 妇女的外阴阴道组织的血流量、盆底肌肉松弛能力和外阴阴道组织弹性,从而达到治疗目的。

5 小结

GSM 是不可治愈的慢性进展性疾病,患者需要终身接受教育和管理。MHT 是目前能够全面解决绝经相关问题的方案,但因患者的依从性或存在 MHT 禁忌,应考虑使用非激素治疗方案。非激素药物治疗、激光治疗和盆底肌肉训练也可以有效改善 GSM 的症状和体征。

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