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蠕形螨与干眼的相关性研究

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[摘要]蠕形螨是人类常见的体表寄生虫之一,常因过度密集寄生体表而导致多种疾病产生。眼部蠕形螨感染症状多为睑板腺功能障碍、睑缘炎以及干眼等。干眼是一种常见的眼表炎症性疾病,影响全球数亿人。干眼病因较为复杂,近年研究报道表明其与蠕形螨感染关系密切。本文就蠕形螨与干眼的相关性研究进行理论探讨,旨在推动蠕形螨相关性干眼防控向纵深发展,减少蠕形螨对人体眼部的伤害,为干眼的临床诊治提供新的参考依据和新思路。

[关键词]蠕形螨;干眼;理论探讨;中医药;眼表炎症;睑板腺功能障碍;机制分析

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Correlation between Demodex and dry eye disease

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[Abstract] Demodex is a common ectoparasite of human beings, and often causes a variety of diseases due to its high densities on the body surface. The symptoms of ocular Demodex infestation are mostly meibomian gland dysfunction, blepharitis, and dry eyes. Dry eye disease is a common ocular surface inflammatory disease that affects hundreds of millions of people worldwide. The causes of dry eye disease are complicated, and recent studies have shown that this disease is closely related to Demodex infestation. Through a theoretical discussion, this paper focuses on the correlation between Demodex and dry eye disease, aiming to promote the in-depth development of the prevention and control of Demodex-related dry eye disease, and reduce the damage of Demodex to human eyes, in the hope of providing a new reference and idea for clinical diagnosis and treatment of dry eye disease.

[Keywords] Demodex; dry eye disease; theoretical discussion; Chinese medicine; ocular surface inflammation; meibomian gland dysfunction; mechanism analysis

蠕形螨(Demodex)是一类永久性体外寄生虫,主要寄生于人与哺乳动物的毛囊和皮脂腺内,目前已知种类有百余种,仅发现两种能寄生于人体体表,即毛囊蠕形螨(*Demodex folliculorum*)和皮脂蠕形

螨(*Demodex brevis*)^[1]。蠕形螨属于条件致病性寄生虫,少量蠕形螨虫体寄生体表通常不会导致疾病的发生,当蠕形螨种群数量增多或人体免疫力下降时,则可能会出现患病状态,如酒糟鼻、睑缘炎、干眼以

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及普通皮炎等^[2]。眼部蠕形螨病是由蠕形螨感染导致的一系列螨源性眼表疾病^[3],眼部蠕形螨感染较普通面部蠕形螨感染造成的危害更为严重。近年来,蠕形螨感染引起的干眼的发病率日益升高,在此背景下,国内外诸多学者投入眼部蠕形螨病的研究行列,展开了许多相关机制的研究^[4-8]。本文主要对蠕形螨与干眼的相关性研究进行理论探讨,以期为今后干眼的临床诊疗提供更广阔的思路。

1 蠕形螨与干眼的生理病理关系

蠕形螨是生活在哺乳动物皮肤上的小型外寄生虫,具有高度复杂的生物学特性,其中毛囊蠕形螨虫体较大,一般以群居方式寄居于人体眼部睫毛毛囊,易引发干眼症状;而皮脂腺蠕形螨虫体较短,喜独居,多寄居于人体眼睫毛根部皮脂腺和睑板腺深处,主要引起眼后部睑缘炎,因离体存活率极低,二者至今均未实现体外培养^[9-10]。作用于人类眼部的蠕形螨主要是毛囊蠕形螨,毛囊蠕形螨主要在夜间活动,以体表皮屑异常分泌的油脂为食,雌性蠕形螨受精后便进入毛囊中发育,经 7~8 d 成年后再至毛囊表层继续活动,其在体表的生命活动周期为 14~16 d^[11-14]。2018 年,亚洲干眼协会中国分会达成专家共识,一致认为眼部蠕形螨感染会导致干眼,其临床症状表现为睑缘发红、眼痒、眼干、眼烧灼感、异物感、畏光及分泌物增多,严重者可伴有反复睫毛脱落、视物模糊或视力下降等^[15-17]。

2 蠕形螨引起干眼的机制

干眼病变机制复杂,目前体内和体外研究皆表明炎症是干眼病变的核心^[18]。多个临床研究结果显示,蠕形螨感染导致睑板腺功能障碍可以影响泪膜的稳定性和泪液的质量,引发干眼^[9]。临床研究认为,每根睫毛毛囊检测出 5 只蠕形螨即为被蠕形螨严重侵袭,但还未有研究表明引发干眼的蠕形螨感染的最小数目,蠕形螨相关性干眼的发病机制尚未十分明确^[19]。现阶段认为蠕形螨引起干眼的机制可能主要有以下几点。

2.1 蠕形螨的机械性损害

蠕形螨体内无排泄器官,卵过度繁殖堆积于睫毛根部引起卵泡扩张,而虫体分泌物堆积于眼部皮肤,其中上皮细胞和角蛋白会沉积形成圆柱形鳞屑。研究发现,圆柱形鳞屑中的螨脂肪酶和蛋白酶的酶促反应会导致眼表炎症,引发眼部干涩、瘙痒、异物

感、视物模糊等症状^[20-21]。Cheng 等^[22]对 119 名具有干眼症状的患者进行了一项横断面研究,根据蠕形螨与干眼眼部表面参数间的关联,发现感染蠕形螨的个体伴有更严重的眼睑异常和干眼症状。

2.2 蠕形螨的载体作用

蠕形螨可直接作为病原微生物的载体,其虫体出入毛囊和皮脂腺时会携带某些致病微生物进入睑板腺导致继发性感染,常见包括葡萄球菌和链球菌。这些病原微生物进入眼部会使脂质泪膜发生改变,引起泪液过度蒸发和泪膜稳定性降低,最终导致干眼^[23]。PONDELIS 教授将 57 名干眼患者与非干眼患者进行对比研究,研究结果显示干眼患者眼表寄生的蠕形螨密度远远高出非干眼患者眼表寄生的蠕形螨密度^[24]。

2.3 宿主免疫力下降

正常人体体表皆可检测出微量蠕形螨寄生,蠕形螨寄居宿主体表而生存,宿主免疫力下降时,蠕形螨会乘机大量繁殖,当虫体数量达到临界点,寄居在睫毛毛囊内的蠕形螨会导致血管扩张、睫毛脆弱和周围毛囊过度扩张,引发宿主的免疫反应及炎症。目前,已有研究表明感冒、糖尿病、癌症放化疗、免疫缺陷患者中蠕形螨侵袭更严重^[25]。JACOBI 等^[26]对 73 例轻度至重度干眼患者的睫毛蠕形螨情况进行研究,发现 43.8% 的患者眼睑边缘睫毛根部含有蠕形螨,且蠕形螨数量与年龄呈正相关性,随着年龄增长,蠕形螨数量不断增加,干眼症状也不断加重。

总之,蠕形螨虫体摄食及交配等活动产生机械性刺激和分泌物、代谢产物的化学刺激,以及虫体出入毛囊、皮脂腺时携带某些致病微生物进入人体引起泪液过度蒸发、泪膜稳定性降低,最终导致周围眼组织的炎症,这是引起蠕形螨性干眼的主要原因^[27]。越来越多的研究发现,迁延不愈的干眼患者眼眼中存在着大量蠕形螨寄居,在除螨治疗后,干眼症状得到明显改善,这从侧面验证了眼部蠕形螨具有干眼致病性的可能,眼部感染蠕形螨会直接导致或加重干眼的发生^[28-32]。

3 蠕形螨相关性干眼的治疗

目前,蠕形螨相关性干眼治疗缺乏特效药,治疗措施主要有化学药物、植物提取物及物理疗法等。蠕形螨相关性干眼病程较长,停药后易复发,要注意早发现、早诊断、早治疗,同步治疗,避免相互扩散,以减少复发^[33]。

3.1 化学药物

氯菊酯(permethrin)是一类广谱杀虫剂,对多种寄生虫具有灭活作用。多项实验研究发现氯菊酯在治疗蠕形螨感染性眼病上具有良好的体外除螨效果^[34-35]。HECHT等^[36]用5%氯菊酯乳霜治疗眼部蠕形螨患者6个月后发现患者眼部螨虫数量明显减少,眼干、眼痒及眼烧灼感等伴随症状好转,且无不良反应。临床上常协同使用玻璃酸钠滴眼液以缓解眼睛干涩症状,效果良好^[37]。

3.2 植物提取物

蠕形螨相关性干眼的治疗多以局部药物杀螨为主,植物中提取的精油及其成分毒性低、易降解且不易产生耐药,被认为是新型杀螨剂。茶树油(tea tree oil, TTO)已经被证实可以有效杀除螨虫,是具有杀螨作用的眼部局部药物^[38]。TTO在临床上常被制成便携的茶树油眼贴及眼睑清洁湿巾使用。JACOBI等团队使用TTO提取物治疗蠕形螨眼病4周后,发现蠕形螨虫体数量减少将近一半,同时眼表疾病指数(ocular surface disease index, OSDI)降低至12~22分^[39]。艾丽珍等研究了不同浓度茶树精油对蠕形螨眼病的治疗效果,结果表明15%的茶树精油为治疗蠕形螨眼病的最佳浓度,肯定了茶树精油治疗蠕形螨眼病的潜力^[40]。蓖麻油是公认的抗炎剂,同时还具有抗氧化、促进伤口愈合和血管收缩的特性。研究表明,蓖麻油局部应用于眼表可以增加泪膜层厚度,改善蠕形螨引起的眼部炎症和干眼症状^[41-42]。

3.3 物理疗法

3.3.1 睑板腺按摩 睑板腺是位于眼皮睑板内的大皮脂腺,位置与睑缘垂直,开口与睑缘同向。每个腺体含10~15个分泌性腺泡,腺体通过腺泡分泌脂质润滑睑缘、防止泪液外溢。蠕形螨与睑板腺联系密切,皮脂蠕形螨多寄居于睑板腺导管,虫体过度繁殖寄居及其代谢产物导致睑板腺导管阻塞及睑板腺分泌异常,引发睑板腺功能障碍(meibomian gland dysfunction, MGD)。睑板腺按摩是热敷后借助外力按摩睑板腺,排出睑板腺导管内溶解的脂质和螨虫代谢物,达到疏通睑板腺导管的作用。LIN等对38例蠕形螨导致的MGD患者展开研究,发现睑板腺按摩联合治疗比单纯药物治疗更能改善患者干眼情况^[43]。

3.3.2 强脉冲光(intense pulsed light, IPL)疗法 IPL是现代一种抑制炎症介质的光治疗技术,因对肌肤浅表损伤疾病有较好作用,被广泛应用于临床。CHENG等^[44]对25例蠕形螨眼病患者进行了回顾性研究,发

现经过IPL治疗后,患者睫毛根部螨虫数量逐渐减少,其伴随的MGD症状和干眼症状得到明显改善。有研究对47例门诊干眼患者使用IPL进行治疗后症状改善,睫毛处的鳞屑与分泌物有所减少,且无明显不良反应,证明了IPL对于蠕形螨相关性干眼具有安全有效的治疗作用^[45]。

3.3.3 中医治疗 蠕形螨相关性干眼在中医古籍中无明确记载,后世医家常将蠕形螨相关性干眼归属于“白涩症”“风沿烂眼”等范畴。胞睑属于中医五轮学说的肉轮,在脏属脾,蠕形螨相关性干眼当先从脾胃论治。现代中医各家对于该病的中医辨证分型不尽相同,目前尚无统一的蠕形螨相关性干眼的辨证标准。中医作为传统医药,除了传统的汤剂内服治疗外,还有独具特色的中医外治法。外治法在治疗眼部蠕形螨感染方面也有其独特优势。许多中药既具有杀螨作用又兼有抗菌作用,且除螨效果良好^[46]。艾叶是典型的天然抗炎杀菌中药,艾灸是传统中医外治技术,艾叶点燃后的挥发性气味可以引起蠕形螨剧烈翻滚扭动,加剧虫体死亡,达到驱螨效果^[47-48]。随着中医药学的不断发展,现代技术与中药联系日益紧密,中药超声雾化治疗技术应运而生。现代研究表明中药超声雾化治疗不仅用药量少、不良反应少,还可以有效促进局部炎症的消退、加速组织修复。临床上使用超声波将相应中药汤液雾化成极细雾状颗粒,使药物在睑缘均匀敷布,疏通睑板腺口以达到缓解眼部干涩等不适症状的效果。中药超声雾化治疗蠕形螨相关性干眼方便简练,安全且无毒副作用^[49-50]。

3.4 日常预防

未病先防,蠕形螨主要通过直接或间接接触传播,预防应当置于首位^[51]。避免直接接触蠕形螨感染者,注意个人卫生及日常生活清洁,定期换洗毛巾,晾晒被褥等贴身物品;注意居住环境卫生,保持室内适宜的温度、湿度;清淡饮食,少食肥甘厚腻;保持面部洁净,勿用手揉搓眼部;日常可局部热敷眼睑以免眼疲劳、干涩。

4 结语

人体蠕形螨是一类永久性寄生虫,其在眼部造成的感染情况日益受到眼科领域重视。目前,蠕形螨感染造成的MGD的研究报道较多,干眼与睑板腺功能障碍密切相关,但在国内外研究报道中蠕形螨感染与干眼的相关性仍涉及较少。本文仅对蠕形螨与干眼相关性研究作出综述,蠕形螨相关性干眼的

致病条件及致病机制尚未十分明确,需进一步研究以提高对蠕形螨相关性干眼的临床认识,以期为今后蠕形螨相关性干眼的预防和治疗提供可靠依据。

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