

doi: 10.3978/j.issn.1000-4432.2021.09.01

View this article at: <https://dx.doi.org/10.3978/j.issn.1000-4432.2021.09.01>

## 热敷治疗睑板腺功能障碍的研究进展

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**[摘要]** 睑板腺功能障碍(meibomian gland dysfunction, MGD)是眼科常见疾病, 是蒸发过强型干眼的主要原因。基于人群流行病学的调查显示: MGD亚洲的发病率为46.2%~69.3%。目前, MGD治疗的方式包括眼睑清洁、热敷、睑板腺按摩、人工泪液、抗生素等, 其中热敷为常用的家庭治疗方法。由于不同的热敷方式、温度、时间、频次及依从性, 导致应用热敷治疗MGD到目前为止还没有统一标准。另外, 热敷的不良反应如视物模糊、皮肤烫伤等, 也没有引起临床足够重视。因此, 为提高热敷的临床疗效及减少其不良反应, 未来进行热敷的规范化指导或治疗很有必要。

**[关键词]** 睑板腺功能障碍; 热敷; 眼睑温度; 烫伤

## Research progress of warm compresses in the treatment of meibomian gland dysfunction

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**Abstract** Meibomian gland dysfunction (MGD) is a common ophthalmic disease, which is the main cause of evaporative dry eye. Population-based studies have suggested that the prevalence of MGD is high in Asia, with a reported incidence of 46.2% to 69.3%. Current modalities of MGD treatment include lid hygiene, warm compresses, massage, artificial lubricants, systemic and topical antibiotics, etc., among which warm compress is a common at-home treatment. Due to different eyelid warming methods, temperature, durations of heat application, frequency and compliance, there is no uniform standard for the application of warm compress to the treatment of MGD. In addition, adverse events of warm compress, such as blurred vision and thermal damage, have not attracted enough attention in clinical practice. Therefore, in order to improve the clinical efficacy of warm compress and

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收稿日期 (Date of reception): 2021-04-04

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基金项目 (Foundation item): 上海市卫计委卫生行业临床研究专项青年项目 (20194Y0246); 上海中医药大学附属龙华医院青年医师人才培养计划项目 (RC-2020-01-08)。This work was supported by Shanghai Municipal Health Commission (20194Y0246), and the Young Talent Program of Longhua Hospital Shanghai University of Traditional Chinese Medicine (RC-2020-01-08), China.

reduce its adverse events, it is necessary to conduct standardized guidance or treatment of warm compress in the future. Based on the above considerations, this article will briefly review the application of warm compress to the treatment of MGD.

**Keywords** meibomian gland dysfunction; warm compress; eyelid temperature; thermal damage

睑板腺功能障碍(meibomian gland dysfunction, MGD)是一种慢性、弥漫性的睑板腺异常, 通常以睑板腺终末导管的阻塞和/或睑板腺分泌物质或量的改变为特征, 常引起眼部刺激症状、泪膜异常、眼表炎症及损伤等病变<sup>[1]</sup>。这一概念最早由Korb和Henriquez<sup>[2]</sup>提出, 被用于描述睑板腺功能异常。MGD发病的核心机制是睑板腺脂质黏稠度增加和导管上皮的过度角化<sup>[3]</sup>。目前, MGD被认为是脂质性泪液缺乏的最常见原因之一<sup>[4-6]</sup>, 导致泪液不稳定和泪液破裂时间明显缩短, 临床主要表现为眼红、流泪、烧灼感、异物感、干燥感、刺激感、痒、视疲劳、视力波动等症状。

以人群为基础的流行病学调查研究<sup>[7-10]</sup>表明: 亚洲的MGD患病率为46.2%~69.3%。在美国和欧洲进行的一项多中心研究<sup>[5]</sup>发现: 超过80%的干眼患者有MGD。MGD的患病率随年龄增长而增加<sup>[8,11-12]</sup>, 另外青少年MGD也引起了很多学者的关注<sup>[13-15]</sup>。随着电脑、平板、智能手机等视频终端(video display terminal, VDT)在工作生活中的广泛使用, MGD在VDT工人中的患病率也很高(74.3%), 且可加重VDT干眼的严重程度<sup>[16-17]</sup>。此外, 异维甲酸是一种在过去几十年彻底改变了皮肤科治疗严重痤疮方法的药物<sup>[18]</sup>。但是, 这种化合物是许多眼周抗衰老化妆品的关键成分, 长期使用可导致睑缘结膜炎、睑板腺分泌物异常、睑板腺萎缩、泪膜破裂时间(break-up time, BUT)降低、泪膜渗透压增加以及干眼<sup>[19-20]</sup>。

目前治疗MGD的主要方法有物理治疗(清洁、热敷、按摩)、人工泪液、全身和局部抗生素、局部抗炎治疗(如非甾体类抗炎药、糖皮质激素、环孢素A、他克莫司、生物制剂等)、手术治疗、调整饮食习惯、改变环境及心理管理等<sup>[17,21-22]</sup>。其中, 物理治疗为MGD的基础治疗, 能有效地疏通由导管上皮过度增生角化和睑脂浓缩固化阻塞的睑板腺腺管, 排出淤积的异常分泌物, 促进正常功能的脂质排出, 增加泪膜的稳定性<sup>[23]</sup>。

## 1 热敷的原理及机制

睑板腺是人体最大的皮脂腺, 其与睑缘垂直并互相平行排列于上、下睑板内。正常的上睑板腺细长, 有25~40个; 下睑板腺粗短, 有20~30个<sup>[3,24-25]</sup>。1条正常的睑板腺由多个全浆分泌腺泡和1条中心导管组成, 中心导管的终末部分与睑缘上皮汇合, 形成圆形睑板腺开口, 后者大部分情况下按一定间隔排列于皮肤黏膜交界线(mucocutaneous junction, MCJ)的前方<sup>[3,24-25]</sup>。睑脂是一种清亮、透明、稀薄的类脂质, 在全浆分泌腺泡内合成后由中心导管传输, 经睑板腺开口排出, 主要由蜡酯、胆固醇酯、磷酸、三酰甘油、游离脂肪酸等构成<sup>[3,24-25]</sup>。到目前为止, 对于睑脂分泌的时间特征(活动周期)还不太清楚, 可能每个腺体都有分泌睑脂的活动期, 然后处于静止期, 后续其他腺体依次发挥作用<sup>[3,24-25]</sup>。

阻塞性MGD的特征是腺体结构异常及脂质黏稠度改变<sup>[26-27]</sup>。眼睑热敷(eyelid warming or warm compress)旨在通过融化病理改变的睑脂来改善睑板腺分泌, 增加泪膜的稳定性, 为MGD的一种常规推荐治疗方法<sup>[17,21-22]</sup>。目前, 融化睑板腺排泄管内脂质分泌所需的温度和时间尚未明确<sup>[21]</sup>。研究<sup>[28-31]</sup>表明: 睑脂混合物的熔点范围为30~45℃, 反映了睑脂是一种高度复杂的脂类混合物<sup>[21,32]</sup>, 同时也意味着严重阻塞的睑板腺脂质的熔点比阻塞较少腺体脂质的熔点高<sup>[31,33-34]</sup>。由于角膜的温度与泪膜脂质层中脂质的温度接近<sup>[35]</sup>, 但比体温或睑缘的温度低<sup>[36]</sup>, 因此脂质混合物的熔点范围将会影响其在泪膜脂质层中的稳定性。

从分子生物学角度来看, 有学者<sup>[37-38]</sup>对MGD患者的睑脂成分进行分析, 结果显示: 三酰甘油和胆固醇显著降低, 单不饱和和脂肪酸的数量减少, 特别是油酸, 其中非极性不饱和脂肪酸的降低会增加它们的熔点, 导致中央导管内的睑脂黏稠增厚。Foulks等<sup>[39]</sup>通过红外光谱研究表明: 脂质顺序在MGD中发生了改变, 且相变温度较高。

McCulley等<sup>[40]</sup>认为:含有不同组成的睑脂具有不同的熔点;MGD可使脂质向较高熔点转变,产生停滞和动态性较差的泪膜;正常人及阻塞性MGD患者的睑脂分别在32℃、35℃时开始融化。此外,Murakami等<sup>[41]</sup>通过研究认为:将单个睑板腺体加热到40℃的温度可能是最佳的热敷疗法。这里的40℃指的是睑结膜和腺体的温度,而不是治疗装置接触面上的温度或眼睑外部皮肤的温度<sup>[41]</sup>。

此外,需要说明的是,对于MGD的热敷治疗,目前主要研究的是热敷后泪膜稳定性(即BUT)及脂质层厚度,而对于热敷后腺体的再通比例则研究较少<sup>[17,21-22]</sup>。其原因可能为:1)热敷前睑板腺的按压评估可能会对热敷后腺体的再通评估有影响;2)睑板腺具有活动周期,分泌睑脂后部分腺体可能会处于静止期,这可能会导致腺体的再通判断困难;3)按压睑板腺的位置、方式、力的大小等标准不好确定及临床应用不方便。

## 2 热敷的分类

很多临床研究<sup>[41-52]</sup>已证明热敷治疗MGD是安全、有效的。其中,Ishida等<sup>[42]</sup>通过研究发现:佩戴保暖眼罩(整夜)持续2周可改善单纯性MGD患者的眼表状态和泪液功能。Goto等<sup>[43]</sup>报道了在使用红外线加热眼罩(每天2次,每次5 min)治疗阻塞性MGD 2周后,患者的眼部不适症状、泪膜稳定性、眼表上皮损伤以及睑板腺孔阻塞均得到了改善。Mori等<sup>[44]</sup>使用一次性化学发热眼罩(每天1次,每次5 min)热敷眼睑2周后,发现MGD患者的干眼症状、泪膜稳定性也都得到了改善。另有一些学者<sup>[45-46]</sup>使用湿热空气装置治疗MGD,发现其可以减轻患者的眼部不适症状及增加泪膜脂质层厚度。

眼睑热敷的应用,无论是否加湿,在MGD治疗中均得到了广泛的研究<sup>[41-52]</sup>。其中,Murakami等<sup>[41]</sup>测试了8种的接触式和非接触式眼睑热敷(干热、湿热及化学活化干热)方法,发现大多数方法都能在第1分钟内将外上睑表面温度提高到40℃以上,其中湿热毛巾捆绑法是唯一能将所有3个眼睑表面(外上睑、外下睑和内下睑)的温度升高到40℃或以上的热敷方法。该研究结果表明:湿热热敷的效果优于干热敷,这可能与热量传递的不同物理属性有关。然而,Arita等<sup>[52]</sup>评估了5种市

面上可买到的眼睑加热装置(2种干热和3种湿热)对10名MGD患者和10名健康志愿者眼部温度、泪膜功能及睑板腺功能的影响,发现用非湿润装置热敷眼睑可以改善正常人的泪膜功能,并可能对MGD患者的泪膜和睑板腺功能产生有益的影响。该研究<sup>[52]</sup>结果还表明:热毛巾等热敷方法会引起眼睑皮肤表面“湿润”,导致蒸发冷却,从而限制了眼睑加热的效果。以上不同的观察结果表明,与干热敷相比,湿热热敷对眼睑的加热效果仍存在争议。

目前,新型热敷方式也被用于临床,比如Lipiflow热脉动治疗仪(TearScience, Morrisville, NC, USA)、强脉冲光(intense pulsed light, IPL)等<sup>[53-58]</sup>。其中,Lipiflow热脉动治疗仪从根本上不同于其他热疗法,因为它结合了热敷(42.5℃)与挤压按摩,单次12 min的治疗可以持续改善MGD的睑板腺功能及减少干眼症状,效果甚至可达12个月<sup>[53-55]</sup>。近来,IPL被用于MGD的治疗,取得了令人满意的疗效<sup>[57-59]</sup>,但具体作用机制尚不明确,可能与热敷、杀灭微生物和抗炎等作用有关<sup>[59-62]</sup>。尽管IPL的应用会导致皮肤温度的升高、表皮下中大血管(>150 μm)内部的瞬时温度可能超过80℃<sup>[63]</sup>,但由于医用超声耦合剂或导电凝胶的使用,故很难测量IPL治疗期间眼睑皮肤的温度<sup>[60]</sup>,比如Craig等<sup>[56]</sup>发现在使用IPL治疗后即刻的皮肤温度增加小于1℃。

另外,对于较为经济的热敷方式——湿热毛巾,有学者也对其进行了相关研究<sup>[64-65]</sup>。其中,Blackie等<sup>[64]</sup>发表了一项关于优化热敷的治疗方案,建议在热敷毛巾和眼睑之间保持最佳接触的情况下,使用45℃的折叠毛巾热敷至少4 min,每2 min更换1次微波炉已预热到45℃的毛巾,以保证下眼睑面的温度可达到40℃。另外,对于中度至重度阻塞性MGD,热敷治疗至少需要10 min,而对于严重阻塞性MGD,可能需要15~20 min,因为睑脂在温度升高的一段时间后才开始融化<sup>[64]</sup>。Olson等<sup>[65]</sup>研究发现:用40℃热毛巾敷于眼睑皮肤5 min,可使阻塞性MGD患者的泪膜脂质层厚度增加80%以上,15 min后又增加20%,并认为泪膜脂质层厚度的增加与症状评分的降低显著相关。由于热敷的温度随时间变化而变化<sup>[41]</sup>,为了达到有效的热敷温度则需要频繁更换热敷毛巾,劳动强度较大,因此这种经济的方法比较适合MGD的家庭治疗。

### 3 热敷的治疗周期及间隔

目前, 对于热敷治疗MGD的时间、频次及治疗周期还没有统一标准。2011年睑板腺功能障碍国际研讨会<sup>[17]</sup>建议: MGD(stage 2)患者先进行眼睑清洁, 热敷(至少4 min, 每天1~2次), 然后行睑板腺按摩。我国睑板腺功能障碍诊断与治疗专家共识建议<sup>[22]</sup>, 每次热敷持续5~10 min, 温度维持在40℃左右, 每天1~2次, 连续1个月; 然后改为隔天1次, 连续1个月; 对于重度MGD患者可延长热敷疗程。

### 4 热敷的注意事项

眼睑热敷会导致短暂的视物模糊, 可能的原因是接触性热敷通过眼睑对角膜施加了轻微的压力而引起角膜变形<sup>[66]</sup>。若此时配合不恰当的睑板腺按摩, 可能会加重角膜变形及增加眼压, 进而加重视物模糊<sup>[67-68]</sup>, 所以不建议对圆锥角膜或有圆锥角膜发生风险的患者、高度近视患者、青光眼患者进行接触式热敷或/和睑板腺按摩治疗<sup>[69-70]</sup>。另外, 过敏性结膜炎和接触性皮炎热敷会加重炎症及过敏反应。

热敷时应避免温度过高, 因为高温不仅会烫伤眼睑皮肤, 而且还有损伤晶体的风险<sup>[64,67,71-75]</sup>。Moritz等<sup>[73]</sup>通过研究发现: 将人体皮肤加热到44℃的温度持续5 h仅导致2名受试者的皮肤出现轻度充血。Blackie等<sup>[64,67]</sup>使用45℃的毛巾治疗MGD, 持续30 min, 未发现有眼睑烫伤的报告。我国学者凌峭等<sup>[74]</sup>认为: 接触70℃的温度持续1 min、60℃的温度持续5 min, 皮肤可能会被烫伤。以上研究提示不要将眼睑皮肤温度加热至45℃以上, 以避免烫伤。幸运的是, 患者的疼痛反应是一种保护措施, 它可以防止过热损伤眼睑皮肤<sup>[76]</sup>。此外, 对于儿童、青少年MGD的热敷治疗相关文献报道较少, 临床应用需谨防烫伤。

需要强调的是, 眼局部冷敷适用于睑缘炎或眼表炎症较重的患者, 表现为分泌物多、结膜充血、睑缘红肿。常用的方法是用凉毛巾或包有冰块的毛巾冷敷眼睑, 温度在10℃左右, 一般持续5~10 min, 待睑缘炎性反应消退后可改为热敷<sup>[22]</sup>。

### 5 存在的困难及展望

热敷在MGD治疗中发挥重要作用, 常常需配合睑板腺按摩治疗, 是一种常规推荐但没有标准规范的治疗方法, 主要是由患者不同的热敷方式、温度、时间、频次和不同的依从性引起的<sup>[17]</sup>。因此, 为提高热敷的临床疗效, 眼科医生有必要指导患者的行为和监督患者的依从性。另外, 进一步的大样本、多中心、随机对照研究以调查热敷治疗正常人和MGD患者主观和客观结果变化是很有必要的。

### 6 结语

笔者建议热敷温度应为40~45℃, 时间为5~15 min, 频次为每天1~2次, 具体治疗周期则依据病情轻重程度。目前, 在众多热敷方法中, 湿热毛巾捆绑法仍是最为经济有效的一种传统热敷方法, 尽管劳动强度大及患者依从性差, 而新型热敷方法也逐渐受到临床医生的关注, 疗效显著, 但价格昂贵。最后, 需要注意的是, 特殊人群及眼表炎症明显时不宜应用热敷治疗。

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**本文引用:** 王大虎, 梁晓江, 刘新泉. 热敷治疗睑板腺功能障碍的研究进展[J]. *眼科学报*, 2021, 36(11): 935-941. doi: 10.3978/j.issn.1000-4432.2021.09.01

**Cite this article as:** WANG Dahu, LIANG Xiaojiang, LIU Xinquan. Research progress of warm compresses in the treatment of meibomian gland dysfunction[J]. *Yan Ke Xue Bao*, 2021, 36(11): 935-941. doi: 10.3978/j.issn.1000-4432.2021.09.01