

• 临床研究 •

0.05%环孢素A与0.1%他克莫司滴眼液治疗干燥综合征相关重度干眼的疗效研究

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[摘要] 目的:探讨0.05%环孢素A与0.1%他克莫司滴眼液治疗干燥综合征相关重度干眼的临床效果。方法:连续纳入2021年10月—2023年11月南京医科大学附属无锡人民医院眼科经治的干燥综合征相关重度干眼患者56例112眼,依据随机对照表法将患者分为他克莫司组($n=28$,56眼)及环孢素A组($n=28$,56眼)。他克莫司组接受0.1%他克莫司滴眼,2次/d;环孢素A组接受0.05%环孢素A滴眼,4次/d;两组患者均规范治疗8周。治疗前后随访两组患者标准干眼症状(standard patient evaluation of eye dryness, SPEED)评分、泪膜破裂时间(touch tear film break-up time, TBUT)、泪液分泌试验(Schirmer I test, SI_t)、角膜荧光素钠染色(corneal fluorescein staining, CFS)评分等。结果:两组患者临床一般资料、治疗前SPEED评分、TBUT差异无统计学意义。与同组治疗前相比,两组患者治疗后SPEED评分及TBUT改善;此外,他克莫司组较环孢素A组TBUT时间改善更显著,而环孢素A组较他克莫司组SPEED评分改善程度更优;两组患者治疗前CFS评分、SI_t值差异无统计学意义;与同组治疗前相比,两组患者治疗后CFS评分及SI_t均有改善,两组CFS评分改善程度相似,但环孢素A组SI_t改善程度更显著。两组患者治疗前睑板腺形态及脂质层厚度间差异无统计学意义;与同组治疗前相比,两组患者治疗后睑板腺形态及脂质层厚度均有改善,其中他克莫司组睑板腺形态及脂质层厚度改善程度更显著。部分患者在使用两种药物后出现短暂的刺激症状,其刺激症状均在用药后20 min内缓解。结论:0.1%他克莫司及0.05%环孢素A在干燥综合征相关重度干眼中均取得较好疗效,其中0.05%环孢素A在改善患者舒适度、降低干眼症状等方面应用优势更加明显,而0.1%他克莫司在改善睑板腺形态及脂质层厚度方面效果更显著。

[关键词] 环孢素A;他克莫司;干燥综合征;重度干眼;疗效

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Efficacy of 0.05% cyclosporine A and 0.1% tacrolimus eye drops in the treatment of severe dry eye associated with Sjögren's syndrome

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[Abstract] **Objective:** To investigate the clinical effect of 0.05% cyclosporine A and 0.1% tacrolimus eye drops in the treatment of severe dry eye associated with Sjögren's syndrome. **Methods:** Fifty-six patients (112 eyes) with severe dry eye related to Sjögren's syndrome, treated at the Department of Ophthalmology, Wuxi People's Hospital Affiliated to Nanjing Medical University from October 2021 to November 2023, were enrolled. Patients were randomly divided into the tacrolimus group ($n=28$, 56 eyes) and the cyclosporine A group ($n=28$, 56 eyes) using a random control table. The tacrolimus group received 0.1% tacrolimus eye drops twice daily, while the cyclosporine A group received 0.05% cyclosporine A eye drops four times daily. Both groups underwent standard treatment for 8 weeks. Follow-up assessments included the Standard patient evaluation of eye dryness (SPEED), touch tear film break-up time (TBUT), Schirmer I test (SI_t), corneal fluorescein staining (CFS) score before and after treatment. **Results:** There were no significant differences in baseline clinical data, pre-treatment SPEED scores, and TBUT between the two groups. Compared to pre-treatment, SPEED score and TBUT were improved in both groups after treatment. The tacrolimus group showed a more significant improvement in

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TBUT, whereas the Cyclosporine A group demonstrated a better improvement in SPEED scores. There were no significant differences between the two groups before treatment in CFS score and SIt index. Both groups showed improvement in CFS scores and SIt post-treatment, with similar improvement levels in CFS scores but a more significant improvement in SIt in the Cyclosporine A group. There were no significant differences in the morphology of meibomian gland and lipid layer thickness between the two groups before treatment. Post-treatment, both groups showed improvement in these parameters, with the tacrolimus group exhibiting more significant improvements. Some patients experienced transient irritation symptoms after using the two eye drops, and their irritation symptoms were relieved within 20 minutes after medication. **Conclusion:** Both 0.1% tacrolimus and 0.05% cyclosporine A have good therapeutic effects in severe dry eye associated with Sjögren's syndrome, of which 0.05% cyclosporine A has more obvious advantages in improving patient comfort and reducing dry eye symptoms, while 0.1% tacrolimus has better effects in improving meibomian gland morphology and lipid layer thickness.

[Key words] cyclosporine A; tacrolimus; Sjögren's syndrome; severe dry eye; curative effect

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干燥综合征作为自身免疫性疾病引起泪腺和唾液腺受累、分泌功能障碍,导致患者出现眼部和口腔干燥等症状,进而引起干眼等临床症状,可分为轻度、中度及重度^[1-2]。学者认为,干燥综合征患者多存在泪膜渗透压升高及眼表炎症,导致患者出现干燥感、烧灼感及异物感,甚至影响患者视力^[3-4]。临床上对于干燥综合征引起的重度干眼,除了全身治疗外,还需要针对眼部进行局部治疗,分为药物治疗及手术治疗,一线治疗药物包括人工泪液、眼用凝胶^[5];在此基础上学者尝试加用局部抗炎治疗如糖皮质激素及钙调磷酸酶抑制剂等,能够有效控制局部炎症、缓解干眼症状、提高治疗效果^[6]。近年来,钙调磷酸酶抑制剂如环孢素A被广泛应用于干燥综合征所引起的干眼患者,但并非所有患者均有治疗获益^[7]。随着研究深入,学者发现,与0.05%环孢素A治疗组相比,0.1%他克莫司也能够有效抑制机体炎症反应,改善了自身免疫炎症介导的眼表干眼指标,提高患者舒适度^[8],为部分环孢素A治疗无效的干眼患者提供了新的治疗思路。本研究分析0.05%环孢素A及0.1%他克莫司在干燥综合征相关重度干眼患者治疗中的临床效果,以期为此类患者的诊治提供新的临床方案。

1 对象和方法

1.1 对象

连续纳入2021年9月—2023年11月南京医科大学附属无锡人民医院眼科收治的干燥综合征相关重度干眼患者56例112眼,依据随机对照表法将患者分为他克莫司组($n=28$, 56眼)及环孢素A组($n=28$, 56眼)。他克莫司组男4例,女24例,年龄

(58.49 ± 5.82)岁(43~79岁);环孢素A组男5例,女23例,年龄(57.67 ± 5.16)岁(51~74岁)。纳入标准:①患者均为原发性干燥综合征;②患者临床表现符合《中国干眼专家共识:定义与分类(2023年)》重度干眼^[9];③患者对本研究知情同意。排除标准:①既往3个月内接受过眼科手术或存在眼部外伤史;②合并青光眼、糖尿病视网膜病变等其他继发或原发眼部疾病;③入组前3个月患眼接受过局部免疫抑制剂和(或)糖皮质激素治疗;④合并其他自身免疫性疾病;⑤对他克莫司或环孢素A治疗不耐受;⑥治疗过程中未规律用药或失访;⑦其他不适宜入组者。

本研究通过南京医科大学附属无锡人民医院医学伦理委员会审核批准(批件号:2021LLPJ-038),所有患者入组前均获得充分知情同意。

1.2 方法

1.2.1 治疗方案

两组患者入组后均给予常规治疗,包括全身治疗及局部用药,全身治疗包括口服醋酸泼尼松、硫酸羟氯喹等,局部用药包括0.3%玻璃酸钠滴眼液(日本参天制药株式会社)、0.1%氟米龙滴眼液(日本参天制药株式会社);在常规治疗基础上,他克莫司组患者接受0.1%他克莫司滴眼液(日本千寿制药株式会社)2次/d,环孢素A组患者接受0.05%环孢素A滴眼液(沈阳兴齐眼药股份有限公司)4次/d,两组患者均规范治疗8周。

1.2.2 干眼症状主观评分

治疗前及治疗后通过标准干眼症状(standard patient evaluation of eye dryness, SPEED)量表进行两组患者干眼症状主观评分,该量表涵盖干涩感、异

物感、疼痛或刺激感及烧灼感或流泪4个方面,总分介于0~12分,总分越高提示干眼症状越重^[10]。所有问卷由研究者指导后患者自行完成,共收集56份问卷。

1.2.3 泪膜破裂时间(touch tear film break-up time, TBUT)测定

治疗前及治疗后两组患者均接受TBUT测定,通过荧光素钠染色试纸轻触患者下眼睑结膜囊,嘱患者瞬目3次后置于裂隙灯显微镜下观察最后1次瞬目至泪膜出现首个黑斑的时间,为泪膜破裂时间;每眼均测量3次,取平均值。

1.2.4 角膜荧光素钠染色(corneal fluorescein staining, CFS)评分

将TBUT测定后的CFS试纸置于裂隙灯显微镜下评估患者角膜染色点数(每眼角膜均分为5个象限),评分细则如下:①0分为无染色;②1分为镜下可见1~30个染色点;③2分为镜下可见30个染色点但均为独立分布;④3分为镜下可见角膜病变融合、丝状物附着甚至角膜溃疡等,最终评分为5个象限分之之和^[11]。

1.2.5 基础泪液分泌实验(Schirmer I test, SIt)

在安静环境下进行SIt,于患眼下结膜囊中外1/3交界处放置干燥荧光素钠染色试纸,嘱患者闭眼,保持持续闭眼约5 min后取下试纸,测量试纸湿润长度(mm)和试纸上泪液浸湿长度(mm)。

1.2.6 两组患者睑板腺形态及脂质层厚度

治疗前及治疗后由培训合格的专科医生分别评估2组患者睑板腺形态及脂质层厚度^[12]。①睑板腺形态:裂隙灯显微镜下观察患者睑板腺形态,异常形态包括睑缘充血、睑缘不规则或增厚、睑板腺口堵塞及灰线移位,每项记1分,总分4分;②脂质层厚度:应用眼表干涉仪(型号:Keratograph 5M, OCULUS Optikgeräte GmbH组,德国)测量脂质层厚

度并记录。通过结构清晰度和色彩丰富度将脂质层厚度分为薄、中度及厚3级,分别记0、1、2分。薄的脂质层结构较模糊,颜色灰暗,正常的脂质层结构清晰、色彩丰富,而厚的脂质层结构高度清晰,色彩极为丰富。上述两指标均由2名专科医生独立测量,评估一致性,如一致性较低则重复测量,并取平均值。

1.2.7 不良反应观察

本研究随访至用药结束后3 d,随访时通过询问患者用药后出现的不良反应如灼烧感、结膜充血、溢泪、刺痛、异物感、瘙痒、短暂视物模糊等进行调查^[13]。根据患者的主观感受、是否影响治疗进程及对患者的健康所造成的客观后果,不良反应分为轻度:患者可忍受,不影响治疗进程,不需特别处理,对患者康复无影响;中度:患者难以忍受,需要撤药或作特殊处理,对患者康复有直接影响;重度:危及患者生命,致残或致死,需立即停药并紧急处理。

1.3 统计学方法

本研究所有数据均通过SPSS 25.0统计学软件分析,其中计数资料以频数(百分率)表示,组间比较采用卡方检验;计量资料符合正态分布,以均数±标准差($\bar{x} \pm s$)表示,组间比较采用 t 检验。 $P < 0.05$ 为差异存在统计学意义。

2 结果

2.1 两组患者临床一般资料比较

两组患者临床一般资料年龄、性别、双眼视力、病程长短差异均无统计学意义(P 均 >0.05 ,表1)。

2.2 两组患者干眼症状、TBUT比较

两组患者治疗前SPEED评分及TBUT差异无统计学意义(P 均 >0.05);与同组治疗前相比,两组患者治疗后SPEED评分及TBUT时间均有改善(P 均 <0.001);组间比较,他克莫司组TBUT时间改善更优,而环孢素A组SPEED评分改善程度更优(表2)。

表1 患者临床一般资料
Table 1 Baseline characteristics of patients

Variable	Tacrolimus group($n=28$)	Cyclosporine A group($n=28$)	t	P
Age(years, $\bar{x} \pm s$)	58.49 \pm 5.82	57.67 \pm 5.16	0.667	0.507
Sex[$n(\%)$]			0.718	0.832
Male	4(14.29)	5(17.86)		
Female	24(85.71)	23(82.14)		
Vision($\bar{x} \pm s$)				
Left eye	0.98 \pm 0.13	0.93 \pm 0.11	1.857	0.067
Right eye	1.02 \pm 0.20	0.99 \pm 0.15	0.759	0.450
Course of disease(months, $\bar{x} \pm s$)	7.84 \pm 1.25	8.09 \pm 2.26	0.612	0.542

表2 治疗前后干眼症状评分、TBUT对比

Table 2 Comparison of scores of symptoms and TBUT before and after treatment ($\bar{x} \pm s$)

Variable	Tacrolimus (n=28)	Cyclosporine A(n=28)	t	P
SPEED score				
Before treatment	8.50 ± 2.17	9.03 ± 2.29	1.063	0.291
After treatment	6.84 ± 1.93	4.47 ± 1.05	6.822	<0.001
TBUT(s)				
Before treatment	2.11 ± 0.65	2.03 ± 0.74	0.514	0.609
After treatment	3.95 ± 0.52	3.04 ± 0.83	5.876	<0.001

2.3 两组患者CFS、SIt比较

两组患者治疗前CFS、SIt差异无统计学意义(P均>0.05);与同组治疗前相比,两组患者治疗后CFS及SIt均有改善(P均<0.01);组间比较,两组CFS改善程度相似,但环孢素A组SIt改善程度更优(表3)。

2.4 两组患者睑板腺形态及脂质层厚度比较

两组患者治疗前睑板腺形态及脂质层厚度差异无统计学意义(P均>0.05);与同组治疗前相比,两组患者治疗后睑板腺形态及脂质层厚度均有改善(图1、2);组间比较,他克莫司组睑板腺形态及脂质层厚度改善程度更优(表4)。

2.5 不良反应

在他克莫司组28例患者中,15例患者(53.6%)

表3 两组患者治疗前后CFS评分及SIt比较

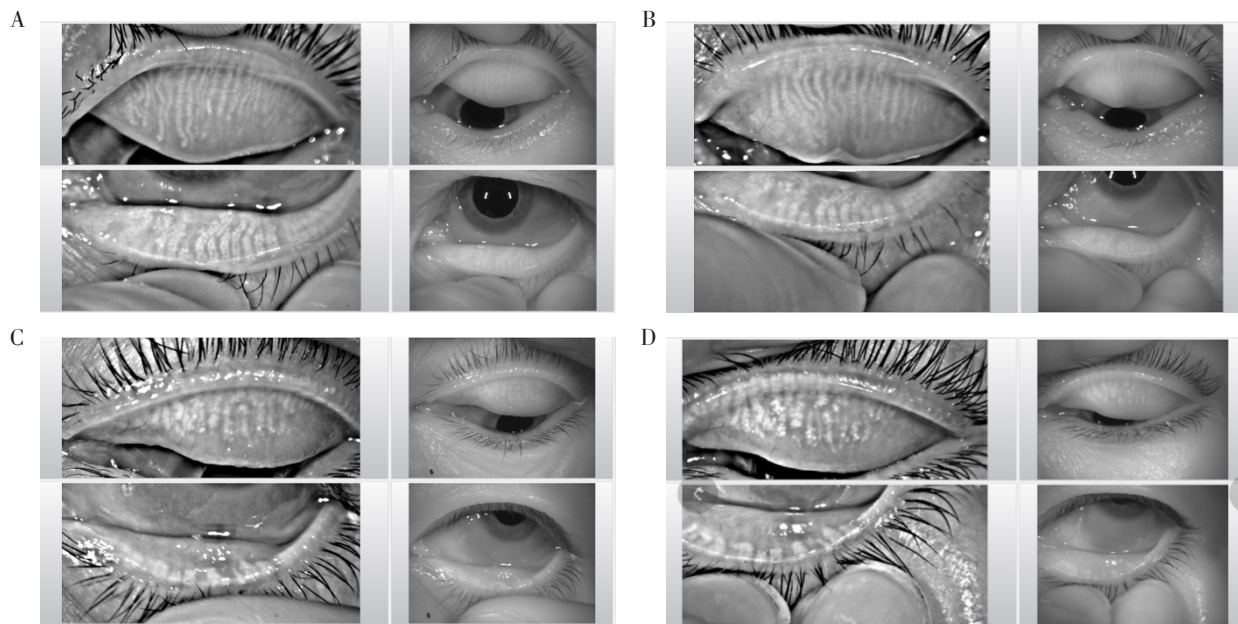
Table 3 Comparison of corneal fluorescein staining and SIt before and after treatment in the two groups of patients ($\bar{x} \pm s$)

Variable	Tacrolimus (n=28)	Cyclosporine A(n=28)	t	P
FL(scores)				
Before treatment	8.49 ± 2.01	7.86 ± 2.04	1.359	0.178
After treatment	4.33 ± 1.14	5.06 ± 1.22	2.765	0.007
SIt(mm/5 min)				
Before treatment	3.48 ± 1.02	4.17 ± 1.26	2.692	0.009
After treatment	8.23 ± 2.15	10.52 ± 2.39	4.021	0.001

滴用他克莫司滴眼液后出现刺激症状,其中9例疼痛或刺痛感(32.1%),6例为灼烧感(21.4%)。在环孢素A组28例患者中,12例患者(42.9%)滴用环孢素A滴眼液后出现刺激症状,其中8例为疼痛或刺痛感(32.1%),4例为灼烧感(17.9%)。所有出现刺激症状的患者均为轻度不良反应,其刺激症状均在用药后20 min内缓解。

3 讨论

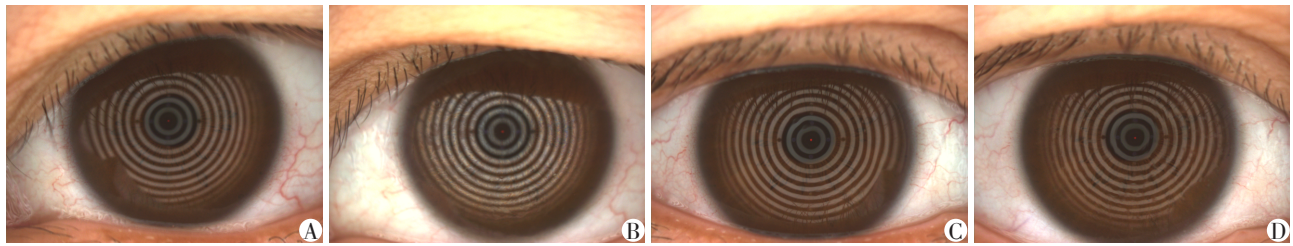
干燥综合征多发于中老年女性,病理机制为自身免疫介导的淋巴细胞浸润,临床常见外分泌腺功能损伤及障碍,其中干眼症状较为常见,与泪腺分



A: Morphology of meibomian gland in cyclosporine A group before treatment. B: Morphology of meibomian gland improved in cyclosporine A group after treatment. C: Morphology of meibomian gland in tacrolimus group before treatment. D: Morphology of meibomian gland improved in tacrolimus group after treatment.

图1 两组患者治疗前后睑板腺形态图

Figure 1 Morphology images of meibomian gland in patients from both groups before and after treatment



A: A lipid layer with single color and thin thickness in tacrolimus group before treatment. B: A lipid layer with rich color and normal thickness in tacrolimus group after treatment. C: A lipid layer with single color and thin thickness in Cyclosporine A group before treatment. D: A lipid layer with single color and approaching normal thickness in Cyclosporine A group after treatment.

图2 治疗前后睑板腺脂质层厚度

Figure 2 Lipid layer thickness before and after treatment

表4 两组患者治疗前后睑板腺形态及脂质层厚度比较

Table 4 Comparison of morphology of meibomian gland and lipid layer thickness before and after treatment in the two groups of patients

Variable	Tacrolimus (n=28)	Cyclosporine A (n=28)	t	P
Morphology of meibomian gland(scores)				
Before treatment	2.81 ± 0.87	3.03 ± 0.74	1.218	0.227
After treatment	0.97 ± 0.22	1.58 ± 0.36	9.144	<0.001
Lipid layer thickness(scores)				
Before treatment	0.82 ± 0.36	0.86 ± 0.55	0.443	0.659
After treatment	0.89 ± 0.54	1.25 ± 0.56	4.624	<0.010

泌功能受损导致泪液量及质的双重变化后泪膜不稳定及眼表炎症有关^[2,14]。马骄等^[8]研究发现,干燥综合征相关干眼患者泪液中炎症介质,如白介素、肿瘤坏死因子等存在不同程度的表达升高,且通过有效药物治疗后患者上述炎症介质水平下降,临床症状明显好转,因此抗炎治疗已成为干眼患者局部治疗方案中必不可少的组成部分,其中钙调磷酸酶抑制剂如环孢素A及他克莫司等近年来被证实能够提高此类患者治疗效果。

环孢素A是一种选择性免疫抑制剂,可以通过抑制T淋巴细胞活化及下游细胞因子生成、阻断眼表上皮细胞凋亡标志物的表达、减少结膜上皮细胞鳞状化生以及增加结膜杯状细胞密度等途径发挥抗炎作用^[15-18]。近年来,环孢素A在中、重度干眼治疗中的研究较多,学者已明晰环孢素A的最佳作用浓度及起效时间,而他克莫司作为环孢素A类似物,通过抑制T淋巴细胞内的钙调神经磷酸酶或丝裂原活化蛋白激酶信号通路,抑制眼表细胞中的核因子- κ B通路,抑制眼表细胞凋亡等机制发挥对干眼眼表炎症的治疗作用^[19-28],其免疫抑制作用更强,能够有效发挥全身免疫抑制效果,但其在局部组织如滴眼中的临床证据较少。为进一步明确他克莫司滴眼

液在重度干眼中的治疗效果,同时分析其与环孢素A的治疗优势所在,笔者所在团队开展了本研究。

本研究发现,两组患者治疗后SPEED评分、TBUT时间、CFS评分、SIt、睑板腺形态及脂质层厚度均得到显著改善,说明0.1%他克莫司及0.05%环孢素A在干燥综合征相关重度干眼中均取得较好治疗效果,两者均可用于干燥综合征所致重度干眼患者的治疗,与既往研究结论一致^[8]。但是进一步深入分析发现,两者在相关指标改善方面不尽相同,其中0.05%环孢素A在提高患者舒适度、降低干眼症状等方面应用优势更加明显,这可能与本研究所使用的0.05%环孢素A滴眼液是纳米微乳剂型,其药物颗粒的大小仅为普通乳剂剂型的1/7,这使得药物具有较高的生物利用度,同时也具备了颗粒更为均匀、制剂更加稳定、点眼更加舒适的优势。而0.1%他克莫司在延长TBUT、改善睑板腺形态及脂质层厚度方面效果更优。在用药后的不良反应方面,本研究发现部分患者在使用这两种药物后可能会出现短暂的刺激症状,但这些症状都会在20 min内自行缓解,患者对这两种药物的不良反应表示可以耐受。但本研究只是对患者使用药物后的刺激症状进行了简单统计,未来的研究需要扩大样本量,以充分

评估免疫抑制剂类眼药水的耐受性。

既往研究指出,钙调磷酸酶抑制剂能够阻断T细胞活化且通过Caspase通路促进T细胞凋亡,发挥减少炎症因子的合成及释放,抑制机体自身免疫反应,代表药物环孢素A能够有效改善患者症状,但其缺点在于起效较慢,早期多需辅以局部激素治疗,增加了青光眼及白内障等治疗并发症风险^[6,29],基于此,选择免疫抑制能力更强且起效更快的药物是临床关注热点所在。来自巴西的一项随机对照研究证实,与安慰剂相比,他克莫司能够显著改善干燥综合征相关干眼症患者眼表炎症反应及泪液稳定性,且起效快,治疗7 d后患者CFS评分即呈现显著改善现象^[30]。本研究同样发现,与环孢素A相比,他克莫司组TBUT时间改善程度更优,但两者在CFS评分改善方面表现出相似性,这可能与本研究未早期观察对比两组治疗效果有关,也可能与纳入样本量偏小有一定相关性。不可忽视的是,环孢素A在患者舒适度、降低干眼症状等方面仍有较强优势,且长期治疗两者之间效果相似,因此,临床仍需充分应用环孢素A,根据患者实验室检查选择合适的药物方案,达到个性化治疗的目的。机体炎症反应影响睑板腺形态及脂质层厚度,睑板腺形态异常导致功能障碍进而引起脂质层偏薄,使泪膜蒸发过快过强,造成蒸发过强型干眼,导致眼干、眼涩及畏光等临床症状^[31-32]。他克莫司组患者睑板腺形态及脂质层厚度改善程度更加明显,这可能得益于他克莫司具备更强的免疫抑制作用。然而,本研究未分析治疗前后泪液中炎症介质表达及局部组织中炎症细胞浸润情况,是临床局限性所在,后续仍需开展深入研究,阐明两种药物作用机制的差异性。此外,本研究样本量偏小,虽然达到了初步的对比效果,但可能会限制研究结果的普遍性和统计学的显著性,后续研究将扩大样本量以提高研究的可靠性;且随访时间较短,后续研究将延长随访时间以观察药物的长期疗效以及安全性。

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YIN Li performed research, analyzed data and wrote the manuscript. YAO Yong was responsible for research design,

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[参考文献]

- [1] 冯丹,周素芬,刘月君,等.干燥综合征不同程度干眼患者的泪腺超声表现[J].中国超声医学杂志,2023,39(6):609-612
- [2] 江婷婷,郭俊巧,王越,等.白芍总苷抑制NLRP3活化治疗干燥综合征小鼠的实验研究[J].南京医科大学学报(自然科学版),2023,43(11):1509-1514
JIANG T T, GUO J Q, WANG Y, et al. Total glucosides of paeony inhibited NLRP3 activation for treatment of mice with Sjögren's syndrome [J]. Journal of Nanjing Medical University (Natural Sciences), 2023, 43(11): 1509-1514
- [3] BJORDAL O, NORHEIM K B, RØDAHL E, et al. Primary sjögren's syndrome and the eye [J]. Surv Ophthalmol, 2020, 65(2): 119-132
- [4] MANFRÈ V, CAFARO G, RICCUCCI I, et al. One year in review 2020: comorbidities, diagnosis and treatment of primary Sjögren's syndrome [J]. Clin Exp Rheumatol, 2020, 126(4): 10-22
- [5] RAMOS-CASALS M, BRITO-ZERÓN P, BOMBARDIERI S, et al. EULAR recommendations for the management of Sjögren's syndrome with topical and systemic therapies [J]. Ann Rheum Dis, 2020, 79(1): 3-18
- [6] 罗启惠,熊洁,周青青,等.0.05%环孢素滴眼液治疗原发性干燥综合征相关干眼病的临床观察[J].重庆医学,2023,52(12):1827-1832
LUO Q H, XIONG J, ZHOU Q Q, et al. Clinical observation of topical cyclosporine 0.05 in the treatment of dry eye associated with primary Sjögren's syndrome [J]. Chongqing Medical Journal, 2023, 52(12): 1827-1832
- [7] JAIN A K, SUKHIJA J, DWEDI S, et al. Effect of topical cyclosporine on tear functions in tear-deficient dry eyes [J]. Ann Ophthalmol (Skokie), 2007, 39(1): 19-25
- [8] 马骄,申展,胡博浩,等.0.05%环孢素与0.1%他克莫司滴眼液治疗慢性oGVHD后患者眼表干眼相关指标及泪液炎症因子比较[J].中华实验眼科杂志,2023,41(10):980-984
MA J, SHEN Z, HU B H, et al. Comparison of ocular surface dry eye-related induces and tear cytokine levels in chronic ocular graft-versus-host disease patients after receiving topical treatment of 0.05% cyclosporine and 0.1% tacrolimus eye drops [J]. Chinese Journal of Ophthalmology, 2023, 41(10): 980-984
- [9] 亚洲干眼协会中国分会,海峡两岸医药卫生交流协会眼科学专业委员会眼表与泪液病学组,中国医师协会眼科医师分会眼表与干眼学组.中国干眼专家共识:定义和分类(2020年)[J].中华眼科杂志,2020,56(6):418-422

- Chinese Branch of the Asian Dry Eye Society; Ocular Surface and Tear Film Diseases Group of Ophthalmology Committee of Cross-Straits Medicine Exchange Association; Ocular Surface and Dry Eye Group of Chinese Ophthalmologist Association. Chinese expert consensus on dry eye: definition and classification (2020) [J]. Chinese Journal of Ophthalmology, 2020, 56(6): 418-422
- [10] 王江维, 刘茂雄, 洪 利, 等. 不同浓度氟米龙滴眼液治疗儿童重度混合型春季角结膜炎[J]. 国际眼科杂志, 2023, 23(12): 2092-2095
WANG J W, LIU M X, HONG L, et al. Different concentrations of fluorometholone eye drops on the treatment of children with severe mixed vernal keratoconjunctivitis [J]. International Eye Science, 2023, 23(12): 2092-2095
- [11] SHEN Z, MA J, PENG R M, et al. Biomarkers in ocular graft-versus-host disease: implications for the involvement of B cells [J]. Transplant Cell Ther, 2022, 28(11): 749. e1-749749.e7
- [12] 胡 雁, 何帆帆, 张 萍. 白内障超声乳化摘除术对睑板腺形态和功能的影响[J]. 局解手术学杂志, 2022, 31(1): 70-73
HU Y, HE F F, ZHANG P. Effect of phacoemulsification on morphology and function of meibomian gland [J]. Journal of Regional Anatomy and Operative Surgery, 2022, 31(1): 70-73
- [13] INAMOTO Y, PETRIČEK I, BURNS L, et al. Non-GVHD ocular complications after hematopoietic cell transplantation: Expert review from the Late Effects and Quality of Life Working Committee of the CIBMTR and Transplant Complications Working Party of the EBMT [J]. Bone Marrow Transplant, 2019, 54: 648-66
- [14] 胡海林, 方思捷, 崔 昌, 等. 抗SSA60、SSA52、SSB/La抗体及抗着丝点B抗体在老年性干燥综合征干眼症诊断中的意义[J]. 临床眼科杂志, 2020, 28(3): 223-227
HU H L, FANG S J, CUI Chang, et al. Significance of anti-SSA60, anti-SSA52, anti-SSB/La, anti-centromere B antibodies in the diagnosis of dry eye due to senile Sjögren's syndrome [J]. Journal of Clinical Ophthalmology, 2020, 28(3): 223-227
- [15] ANTO N P, ARYA A K, MURALEEDHARAN A, et al. Cyclophilin A associates with and regulates the activity of ZAP70 in TCR/CD3-stimulated T cells [J]. Cell Mol Life Sci, 2022, 80(1): 7
- [16] YOON H J, JIN R J, YOON H S, et al. Bacillus-derived manganese superoxide dismutase relieves ocular-surface inflammation and damage by reducing oxidative stress and apoptosis in dry eye [J]. Invest Ophthalmol Vis Sci, 2023, 64(12): 30
- [17] WIBFELD J, HERING M, TEN BOSCH N, et al. The immunosuppressive drug cyclosporin A has an immunostimulatory function in CD8⁺ T cells [J]. Eur J Immunol, 2024, 54(7): e2350825
- [18] KAWAI H, YAGYU F, TERADA A, et al. CD28 confers CD4⁺ T cells with resistance to cyclosporin A and tacrolimus but to different degrees [J]. Asian Pac J Allergy Immunol, 2024, 42(3): 298-304
- [19] CHEN X, WU J, LIN X, et al. Tacrolimus loaded cationic liposomes for dry eye treatment [J]. Front Pharmacol, 2022, 13: 838168
- [20] SPATOLA R, NADELSTEIN B, BERDOULAY A, et al. The effects of topical aqueous sirolimus on tear production in normal dogs and dogs with refractory dry eye [J]. Vet Ophthalmol, 2018, 21(3): 255-263
- [21] LI T, TANG J, WU X, et al. Evaluating the efficacy of polyglycolic acid-loading tetrandrine nanoparticles in the treatment of dry eye [J]. Ophthalmic Res, 2023, 66(1): 1148-1158
- [22] NIU W, ZHENG X, LI Z, et al. Donor and recipient polymorphisms of MAPK signaling pathway genes influence post-transplant liver function in Chinese liver transplant patients taking tacrolimus [J]. Gene, 2023, 857: 147190
- [23] WANG L, WANG X, CHEN Q, et al. MicroRNAs of extracellular vesicles derived from mesenchymal stromal cells alleviate inflammation in dry eye disease by targeting the IRAK1/TAB2/NF- κ B pathway [J]. Ocul Surf, 2023, 28: 131-140
- [24] TONG M M, JIANG Y. FK506-binding proteins and their diverse functions [J]. Curr Mol Pharmacol, 2015, 9(1): 48-65
- [25] KIM D W, LEE S H, KU S K, et al. The effects of PEP-1-FK506BP on dry eye disease in a rat model [J]. BMB Rep, 2015, 48(3): 153-158
- [26] HAN Y, GUO S, LI Y, et al. Berberine ameliorate inflammation and apoptosis *via* modulating PI3K/AKT/NF κ B and MAPK pathway on dry eye [J]. Phytomedicine, 2023, 121: 155081
- [27] CHEN C C, HUANG T M, HUANG Y J, et al. Tacrolimus regulates extracellular vesicle secretion from T cells via autophagy-lysosomal pathway [J]. Biomed Pharmacother, 2025, 182: 117765
- [28] HOSOTANI Y, YASUDA K, NAGAI M, et al. IL-33-induced keratoconjunctivitis is mediated by group 2 innate lymphoid cells in mice [J]. Allergol Int, 2023, 72(2): 324-331
- [29] JINAGAL J, GUPTA P C, PILANIA R K, et al. Systemic toxicity of topical corticosteroids [J]. Indian J Ophthalmol, 2019, 67(4): 559-561

- [30] MOSCOVICI B K, HOLZCHUH R, SAKASSEGAWA - NAVES F E, et al. Treatment of Sjögren's syndrome dry eye using 0.03% tacrolimus eye drop: prospective double-blind randomized study [J]. *Cont Lens Anterior Eye*, 2015, 38(5):373-378
- [31] 梁庆丰, 杜向红, 苏远东, 等. 不同类型干眼患者泪膜脂质层厚度及其与临床特征的关系[J]. *中华实验眼科杂志*, 2018, 36(2):124-129
- LIANG Q F, DU X H, SU Y D, et al. Lipid layer thickness of tear film and its association with clinical characteristics in different types of dry eye patients[J]. *Chinese Journal of Experimental Ophthalmology*, 2018, 36(2):124-129
- [32] 亚洲干眼协会中国分会, 海峡两岸医药卫生交流协会眼科学专业委员会眼表与泪液病学组, 中国医师协会眼科医师分会眼表与干眼学组. 中国干眼专家共识: 检查和诊断(2020年)[J]. *中华眼科杂志*, 2020, 56(10):741-747
- Chinese Branch of the Asian Dry Eye Society; Ocular Surface and Tear Film Diseases Group of Ophthalmology Committee of Cross-Straits Medicine Exchange Association; Ocular Surface and Dry Eye Group of Chinese Ophthalmologist Association. Chinese expert consensus on dry eye: examination and diagnosis (2020) [J]. *Chinese Journal of Ophthalmology*, 2020, 56(10):741-747
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(上接第874页)

- review of the pathophysiology, management and prospective advances [J]. *Curr Cardiol Rev*, 2021, 17(4): e230421186875
- [17] KAJI S. Update on the therapeutic strategy of type B aortic dissection [J]. *J Atheroscler Thromb*, 2018, 25(3):203-212
- [18] KIM S H, FECHNER J. Remimazolam-current knowledge on a new intravenous benzodiazepine anesthetic agent[J]. *Korean J Anesthesiol*, 2022, 75(4):307-315
- [19] BROHAN J, GOUDRA B G. The role of GABA receptor agonists in anesthesia and sedation[J]. *CNS Drugs*, 2017, 31(10):845-856
- [20] LEE A, SHIRLEY M. Remimazolam: a review in procedural sedation[J]. *Drugs*, 2021, 81(10):1193-1201
- [21] JHUANG B J, YE H B H, HUANG Y T, et al. Efficacy and safety of remimazolam for procedural sedation: a meta-analysis of randomized controlled trials with trial sequential analysis[J]. *Front Med*, 2021, 8:641866
- [22] XU Q, WU J, SHAN W, et al. Effects of remimazolam combined with sufentanil on hemodynamics during anesthetic induction in elderly patients with mild hypertension undergoing orthopedic surgery of the lower limbs: a randomized controlled trial [J]. *BMC Anesthesiol*, 2023, 23(1):311
- [23] QIU Y, GU W, ZHAO M, et al. The hemodynamic stability of remimazolam compared with propofol in patients undergoing endoscopic submucosal dissection: a randomized trial [J]. *Front Med*, 2022, 9:938940
- [24] KO C C, HUNG K C, ILLIAS A M, et al. The use of remimazolam versus propofol for induction and maintenance of general anesthesia: a systematic review and meta-analysis [J]. *Front Pharmacol*, 2023, 14:1101728
- [25] KOTANI T, IDA M, NAITO Y, et al. Comparison of remimazolam-based and propofol-based total intravenous anesthesia on hemodynamics during anesthesia induction in patients undergoing transcatheter aortic valve replacement: a randomized controlled trial [J]. *J Anesth*, 2024, 38(3):330-338
- [26] URABE T, MIYOSHI H, NARASAKI S, et al. Characterization of intracellular calcium mobilization induced by remimazolam, a newly approved intravenous anesthetic [J]. *PLoS One*, 2022, 17(2):e0263395
- [27] URABE T, YANASE Y, MOTOIKE S, et al. Propofol induces the elevation of intracellular calcium via morphological changes in intracellular organelles, including the endoplasmic reticulum and mitochondria [J]. *Eur J Pharmacol*, 2020, 884:173303
- [28] SNEYD J R, RIGBY-JONES A E. Remimazolam for anaesthesia or sedation [J]. *Curr Opin Anaesthesiol*, 2020, 33(4):506-511
- [29] KILPATRICK G J. Remimazolam: non-clinical and clinical profile of a new sedative/anesthetic agent [J]. *Front Pharmacol*, 2021, 12:690875
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