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普拉洛芬滴眼液治疗2型糖尿病合并干眼症的临床疗效*

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摘要 目的:探讨普拉洛芬滴眼液治疗2型糖尿病合并干眼症的临床疗效。**方法**:选取我院收治的2型糖尿病合并干眼症患者70例,随机分为对照组和实验组,每组35例。对照组患者采用人工泪液滴眼治疗,实验组患者在对照组基础上采用普拉洛芬滴眼液治疗。观察并比较治疗前后两组患者泪膜破裂时间、基础泪液分泌量、角膜荧光染色阳性率及临床疗效。**结果**:实验组总有效率高于对照组(P<0.05);与治疗前相比,两组患者泪膜破裂时间延长、基础泪液分泌量及泪液中的溶菌酶、EGF及LF水平明显升高(P<0.05),角膜荧光染色阳性反应发生率降低(P<0.05);治疗后与对照组相比,实验组患者泪膜破裂时间较长、基础泪液分泌量较高,溶菌酶、EGF及LF水平较高(P＜0.05),角膜荧光染色阳性反应发生率较低(P<0.05)。**结论**:普拉洛芬滴眼液对2型糖尿病并发干眼症患者的治疗临床疗效良好,推测其机制与泪膜破裂时间的延长、基础泪液分泌量增加及溶菌酶、EGF及LF水平的升高有关。

关键词:干眼症;2型糖尿病;普拉洛芬

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Effect of Pranoprofen in Patients with Type 2 Diabetes and Xerophthalmia*

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ABSTRACT Objective: To investigate the effect of pranoprofen in patients with type 2 diabetes and xerophthalmia. **Methods:** 70 patients with Type 2 diabetes and xerophthalmia who were treated in our hospital were selected and randomly divided into the control group and the experiment group, with 35 cases in each group. The patients in the control group were treated with artificial tears eye drops, while the patients in the experiment group were treated with pranoprofen on the basis of the control group. Then the tear break-up time, schirmer, corneal fluorescein staining positive rate and clinical efficacy were observed and compared between two groups before and after treatment. **Results:** Compared with the control group, the clinical efficacy rate in the experiment group was higher (P<0.05). Compared with before treatment, the tear break-up time prolonged, basic tear secretion, tear lysozyme, and the levels of EGF and LF were higher in the two groups after treatment, while the positive reaction rate of corneal fluorescence staining were lower (P<0.05). Compared with the control group after treatment, the tear break-up time prolonged, basic tear secretion, tear lysozyme, and the levels of EGF and LF in the experiment group were higher, while the positive reaction rate of corneal fluorescence staining was lower (P<0.05). **Conclusion:** Pranoprofen eyedrops has better clinical efficacy on the treatment of type 2 diabetes mellitus and xerophthalmia. It is speculated that the mechanism and tear break-up time prolonged, basal tear secretion increase and lysozyme, epidermal growth factor (EGF) and LF increased.

Key words: Xerophthalmia; Type 2 diabetes; Pranoprofen

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前言

干眼症又称角结膜干燥症(keratoconjunctivitis sicca),是由多种原因导致的泪膜稳定性下降、角结膜干燥并伴有炎症反应的眼部疾病[1],临床以眼干、眼涩、眼部异物感、视力疲劳和眼部痒痛为主要症状[2]。干眼症多由于水液层、油脂层以及粘蛋白层泪液分泌分泌异常、泪液蒸发过多和泪膜分布不均诱发[3]。流行病学调查显示,干眼症发病率17%～33%,而2型糖尿病患者干眼症的发病率可高达60%以上[4]。人工泪液作为干眼症的传统疗法广泛应用于临床中,pH值、渗透压和蕴含的生物活性成分与泪液基本一致,能有效修复眼角结膜上皮细胞,提高修复能力,缩短修复时间,同时促进眼表水分代谢的正常化[5]。但人工泪液中所含有的玻璃酸钠等成分可引起自然泪液的稀释,破坏泪膜,加重眼部刺激,引起炎症反应。普拉洛芬滴眼液是一种通过抑制前列腺素的生长来实现抗炎抗过敏作用的一类非甾体类抗炎药,可有效缓解眼部不适,同时对过敏性结膜炎、急性结膜炎及持续性结膜炎等炎症反应均有良好效果[6]。本实验通过观察治疗前后患者泪膜破裂时间、基础泪液分泌量、角膜荧

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光染色阳性率及临床疗效的变化，探讨普拉洛芬滴眼液对 2 型糖尿病干眼症患者的疗效及机制。

1 资料与方法

1.1 临床资料

共收集我院 2013 年 9 月～2015 年 5 月收治的干眼症合并 2 型糖尿病患者 70 例，随机分为对照组和实验组，每组 35 例。患者年龄为 17～69 岁，年龄(37.03± 5.57)岁，男 38 例，女 37 例，其中对照组平均年龄为(37.34± 5.27)岁；实验组平均年龄(36.28± 5.68)岁，两组性别比例以及平均年龄、等临床资料选择无偏倚性，差异无统计学意义(P＞0.05)。

1.2 纳入标准

① 所有研究对象符合 2 型糖尿病的诊断标准，空腹血糖超过 7.0 mmol/L，餐后 2 h 血糖超过 11.0 mmol/L；② 患者符合干眼症的诊断标准，出现眼部干涩、瘙痒、异物感以及疲劳等临床表现；③ 年龄超过 16 岁。④ 排除心肝肾功能损伤、血液系统异常、类风湿性关节炎、妊娠期及哺乳期患者；⑤ 排除其他原因引起的视力疲劳、眼干眼涩及全身干燥综合征的患者；⑥ 排除有眼部手术史及过敏史患者；⑦ 排除对阿司匹林那等非甾体类抗炎药过敏的患者；⑧ 排除对本研究使用的药物具有过敏史。

1.3 方法

所有患者均进行盐酸二甲双胍片(上海北杰集团关东药业有限公司，国药准字：H20130826)1.5 mg/ 次，2 次 /d 口服。对照组所有患者均进行人工泪液(日本 SantenPharmaceuticalCoLtd，注册证号：H20080559)0.1 mL/ 次滴眼，6 次 /d 治疗；实验组在对照组基础上，给予普拉洛芬滴眼液(山东海山药业有限公司，国药准字：H20093827)0.15 mL/ 次滴眼，4 次 /d。所有患者以 14 d 为一个疗程，连续治疗 2 个疗程。

1.4 观察指标及检测方法

1.4.1 泪膜破裂时间(BUT)、基础泪液分泌量角膜荧光染色阳性率 通过裂隙灯显微镜测定泪膜稳定性，观察泪膜破裂时间；通过 schirmer 试验测定治疗前后两组患者基础泪液分泌量；采用荧光素染色试验对角膜进行荧光测试，并计算阳性反应发生率；观察记录患者临床症状的变化。

1.4.2 泪液中溶菌酶、表皮生长因子 EGF 及乳铁蛋白(LF)含量 别采用微量快速比浊法及放射免疫法检测两组患者治疗前后泪液中的溶菌酶及 EGF 的含量；酶联免疫吸附法法测定患者治疗前后 LF 含量。

1.4.3 疗效评价标准 治愈：患者眼干燥、疲劳、异物感等临床症状完全消失，schirmer 试验值超过 10 mm/5 min；显效：患者眼疲劳、烧灼感、异物感等临床症状明显缓解，schirmer 试验值超过 7 mm/5 min；有效：患者眼疲劳、烧灼感、异物感等临床症状缓解，schirmer 试验值超过 4 mm/5 min；无效：患者临床症状无改善或加重，schirmer 试验值低于 4 mm/5 min。总有效率 =(治愈患者数＋显效患者数＋有效患者数)/ 本组患者例数。

1.5 统计学分析

采用 SPSS17.0 统计软件，计量数据以均数± 标准差($\bar{x}$± s)表示，采用单因素方差分析法，实施 Turkey 检验进行组间检验、校正，P＜0.05 认为有统计学意义。

2 结果

2.1 两组患者的临床疗效比较

实验组临床疗效总有效率 (91.43%) 显著高于对照组(65.71%)，差异有统计学意义(P＜0.05)(表 1)。

表 1 两组临床疗效比较[例(%)]

Table 1 Comparison of the clinical curative effect between two groups[n(%)]

Groups	n	Cure	Excellence	Effective	Invalid	Clinical effect rate
Control group	35	5(14.29)	7(20.00)	11(41.43)	12(34.29)	23(65.71)
Experiment group	35	10(28.57)	9(25.71)	13(37.14)	3(8.57)	32(91.43)*

Note: compared with the control group, *P＜0.05.

2.2 两组患者治疗前后泪膜破裂时间、基础泪液分泌量、角膜荧光染色阳性率比较

与治疗前相比，两组患者泪膜破裂时间延长、基础泪液分泌量显著提高，角膜荧光染色阳性率降低，差异有统计学意义(P＜0.05)；与对照组相比，实验组患者泪膜破裂时间较长、基础泪液分泌量较高，角膜荧光染色阳性率降低，差异具有统计学意义(P<0.05)(表 2)。

表 2 两组患者治疗前后泪膜破裂时间、基础泪液分泌量、角膜荧光染色阳性率的比较

Table 2 Comparison of the tear break-up time, Schirmer, corneal fluorescein staining positive rate between two groups before and after treatment

Groups		Tear break-up time (min)	Schirmer (mm)	Corneal fluorescein staining positive rate (%)
Control group (n=35)	Before treatment	8.83± 1.51	5.44± 0.82	69.72± 5.54
	After treatment	10.04± 1.72*	8.35± 1.52*	28.75± 4.74*
Experiment group (n=35)	Before treatment	8.44± 1.67	5.57± 0.88	68.93± 5.78
	After treatment	12.34± 2.03*#	11.64± 2.33*#	13.37± 3.21*#

Note: Compared with before treatment,*P＜0.05; Compared with the control group after treatment, *P＜0.05.

2.3 两组患者治疗前后泪液中溶菌酶、EGF 及 LF 含量比较

治疗后，两组患者泪液中溶菌酶、EGF 和 LF 水平显著增高，差异具有统计学意义（P＜0.05；与对照组相比，实验组患者溶菌酶、EGF 和 LF 水平升高，差异具有统计学意义（P＜0.05）（表 3）。

表 3 两组患者治疗前后泪液中溶菌酶、EGF 及 LF 含量的比较

Table 3 Comparison of the lysozyme, EGF and LF content in tears between two groups before and after treatment

Groups		Lysozyme（μg/mL）	EGF（ng/mL）	LF（mg/mL）
Control group（n=35）	Before treatment	8.83± 1.51	0.58± 0.12	1.02± 0.14
	After treatment	10.04± 1.72*	2.05± 0.62*	1.55± 0.34*
Experiment group（n=35）	Before treatment	8.44± 1.67	0.57± 0.18	0.93± 0.18
	After treatment	12.34± 2.03*#	4.64± 1.33*#	1.87± 0.91*#

Note: Compared with before treatment, *P＜0.05; Compared with the control group after treatment, *P＜0.05.

3 讨论

2 型糖尿病患者出现的血糖异常升高可加重血管内皮及周围神经的病变，增加干眼症的发病率[7]。干眼症能够诱发角膜炎以及角膜溃疡，加速视力下降的发生，严重者出现视觉障碍，甚至失明[8]。干眼症是由多种原因造成的泪液分泌系统失调，从而引起泪液分泌过少、泪膜结构不稳定的眼部高发疾病[10]。现代统计学显示，人工泪液是临床治疗干眼症的常用方法，可有效缓解眼干眼涩，异物感等眼部不适[9]。然而，其有效成分玻璃酸钠及羧甲基纤维素钠的长期使用可导致角结膜上皮细胞的损伤，危害眼部健康，加重干眼症的病情。研究表明[11-13]，干眼症的炎性反应是影响人工泪液治疗效果的重要因素。前列腺素是一种由花生四烯酸所合成的脂代谢产物，其水平的异常增高可引起局部炎性反应的发生[14]。有研究表明，普拉洛芬滴眼液的应用对实验性葡萄糖炎的豚鼠的抗炎治疗作用疗效明显；对家兔结膜炎及干燥性角膜炎的炎性反应治疗效果显著[15]。研究证实，普拉洛芬滴眼液在眼部抗炎、抗过敏及改善泪液分泌系统等方面疗效突出[16]。我们的研究显示，治疗后对照组相比，实验组临床总有效率较高，证实普拉洛芬滴眼液对 2 型糖尿病并发干眼症的治疗疗效好、安全性高。

泪膜破裂时间、基础泪液分泌量的测定及角膜荧光染色试验阳性反应发生率是诊断和评估干眼症发生发展的重要指标[17]。眼泪膜破裂时间是临床常用的评估泪膜稳定性的指标，基础泪液分泌量的测定为泪液分泌功能的评估提供有效依据，而角膜荧光染色阳性率则可直观法映出角膜的损伤程度[18]。本研究结果证实，治疗后患者泪膜破裂时间延长、基础泪液分泌量升高，角膜荧光染色试验阳性反应发生率降低，结果说明普拉洛芬滴眼液能有效治疗 2 型糖尿病并发干眼症。

溶菌酶是一种广泛存在于人体体液及肝肾等组织中的免疫物质，泪液中溶菌酶的含量居于体外液体首位，可由泪腺细胞分泌，干眼症的发生可导致溶菌酶浓度的降低[19]。EGF 是干眼症诊断的常用指标之一，可有效缩短修复角膜上皮细胞破损的时间，乳铁蛋白是一种由泪腺分泌的抗炎因子，LF 分泌的不足常常提示干眼症的发生。研究表明[20]，普拉洛芬滴眼液可使泪液中溶菌酶、EGF 及 LF 水平升高，有效治疗 2 型糖尿病并发干眼症所引起的血清异常。本研究发现，治疗时升高患者泪液中溶菌酶、EGF 及 LF 水平，使临床有效率提高（P＜0.05）。证实普拉洛芬滴眼液治疗 2 型糖尿病并发干眼症能有效改善血清异常，提高治疗成功率。

综上所述，普拉洛芬滴眼液能够改善 2 型糖尿病合并干眼症患者的临床症状，降低不良反应发生率，值得在临床推广应用。

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