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自体血清联合玻璃酸钠治疗白内障术后干眼症患者的效果*

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摘要 目的:研究自体血清联合玻璃酸钠治疗白内障术后干眼症患者的临床效果。**方法:**选择 2015 年 1 月~2018 年 12 月我院收治的 186 例白内障术后干眼症患者,随机分为观察组以及对照组,每组各 83 例。对照组采用玻璃酸钠滴眼液治疗,观察组联合采用自体血清滴眼液治疗。连续给药 4 w 后,比较两组的治疗有效率,治疗前后的泪膜破裂试验和泪液分泌试验结果,泪液坏死因子(TNF)- α 、白介素(IL)-6 以及高敏 C-反应蛋白(hs-CRP)水平的改变情况。**结果:**治疗后,观察组的有效率为 95.18%(79/83),明显高于对照组[79.52%(66/83)]($P<0.05$)。两组治疗后的泪膜破裂试验和泪液分泌试验结果均较治疗前明显改善($P<0.05$),且观察组的泪膜破裂试验和泪液分泌试验的改善程度明显优于对照组($P<0.05$);两组治疗后的泪液 hs-CRP、TNF- α 和 IL-6 水平均较治疗前明显降低,且观察组更少指标明显低于对照组($P<0.05$)。**结论:**自体血清联合玻璃酸钠对白内障术后干眼症患者的临床效果明显优于单用玻璃酸钠滴眼液,其可更有效增加泪膜的稳定性,减轻角膜损伤,减少泪液分泌,这可能与下调患者泪液中 hs-CRP、TNF- α 和 IL-6 水平有关。

关键词:自体血清;玻璃酸钠;白内障手术;干眼症;炎症反应

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Effect of Autologous Serum Combined with Sodium Hyaluronate on the Xeroma after Cataract Surgery*

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ABSTRACT Objective: To investigate the effect of autologous serum combined with sodium hyaluronate on the xeroma after cataract surgery. **Methods:** 186 cases of patients with xeroma after cataract surgery who were treated in our hospital from January 2015 to December 2018 were selected and randomly divided into two groups. The control group was treated with sodium hyaluronate eye drops, while the observation group was treated with autologous serum eye drops. After 4 weeks of continuous administration, the therapeutic efficacy, tear film rupture test and tear secretion test before and after treatment, changes of tear necrosis factor (TNF)- α , interleukin (IL)-6 and high sensitivity C-reactive protein (hs-CRP) levels were compared between the two groups. **Results:** After treatment, the effective rate of observation group was 95.18% (79/83), which was significantly higher than that of the control group [79.52% (66/83)] ($P<0.05$). The results of tear film rupture test and tear secretion test in the two groups were significantly improved after treatment ($P<0.05$), and the improvement of tear film rupture test and tear secretion test in the observation group was significantly better than that in the control group ($P<0.05$); the levels of hs-CRP, TNF- α and IL-6 in the tear of both groups after treatment were significantly lower than those before treatment, and fewer indexes in the observation group were significantly lower than those in the control group ($P<0.05$). **Conclusion:** Autologous serum combined with sodium hyaluronate on xeroma after cataract surgery is more effective than sodium hyaluronate eye drops alone. It can more effectively increase the stability of tear film, reduce the corneal injury and tear secretion, which may be related to the down-regulation of hs-CRP, TNF- α and IL-6 levels in the tear.

Key words: Autologous serum; Sodium hyaluronate; Cataract surgery; Xeroma; Inflammatory response

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前言

近年来,随着白内障手术的增多,手机、电脑等高科技视

频产品使用的普及而引发的不科学用眼,滥用抗生素眼液,人们工作和生活节奏的加快,空气质量下降,准分子激光手术的日益广泛使用,干眼症的发生率逐年升高^[1,2]。白内障术后干眼症

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是较为常见的一种眼表炎症性疾病,能使泪液的量或质发生异常。相关统计研究显示白内障术后干眼症的发病率高达 20%^[3],其发生机制与术中机械性损伤以及手术应激等导致细胞凋亡及眼表神经感觉异常相关。干眼症会导致视觉障碍、眼部不适以及泪膜不稳定,并且伴有眼表炎症极泪膜渗透性增加,轻度会影响日常的工作与生活,病情严重者会造成眼表组织干燥,对其视功能造成严重的危害^[4-6]。

目前,临床在干眼症治疗方面依旧处于初级阶段,主要采取人工泪液替代疗法,但效果并不理想。自体血清作为一种生理性的泪液补充液,可以发挥润滑以及营养眼表的双重效果,而且具有天然和不易致敏的优点。本研究将玻璃酸钠滴眼液与自体血清联合用于治疗白内障术后干眼症,以期白内障术后干眼症患者提供一种更为有效的治疗方法。

1 资料与方法

1.1 一般资料

选择 2015 年 1 月~2018 年 12 月我院收治的白内障术后干眼症患者 186 例,纳入标准:顺利完成白内障超声乳化手术,签署知情同意书。排除标准:年龄 ≥ 80 岁或者 ≤ 18 岁,先天性无泪腺、无泪症以及神经障碍患者,哺乳期和妊娠期女性,在本研究的过程中使用抗胆碱药物、全身性抗组胺药物或者其他干扰治疗效果的眼科药物,合并有影响泪液分泌的全身性疾病患者,有泪道疾病史患者。用抽签法随机将所有患者分为两组。观察组 83 例,男 45 例,女 38 例;年龄 20~78 岁,平均 (49.53 ± 16.19) 岁;病程 2 个月~4 年,平均 (14.32 ± 2.79) 年;身高 149~187 cm,平均 (168.32 ± 10.41) cm;体质量 42~93 kg,平均 (59.34 ± 11.26) kg。对照组 83 例,男 44 例,女 39 例;年龄 20~78 岁,平均 (48.76 ± 15.42) 岁;病程 2 个月~4 年,平均 (14.57 ± 2.36) 年;身高 149~187 cm,平均 (168.42 ± 10.35) cm;体质量 42~93 kg,平均 (59.79 ± 11.64) kg。两组的基线资料比较差异均无统计学意义($P>0.05$),具有可比性。

1.2 治疗方法

对照组:给予玻璃酸钠滴眼液(批号:国药准字 H20040352,生产厂家:珠海联邦制药股份有限公司中山分公司,规格:7 mL:7 mg)进行治疗,每次 1 滴,每天给药 3 次,连续

给药 4 w。

观察组:①自体血清的制备方法如下:空腹抽取 20 mL 肘部的静脉血,按照每分钟的 3 000 r 的速度进行 15 min 的离心,然后使用无菌针管将上层血清抽取出来,按照左氧氟沙星眼药水与自体血清 4:1 的比例进行稀释,即可完成配置。②给药方法如下:直接将配置好的自体血清滴于患眼,每次 1~2 滴,每 4 h 滴眼 1 次,连续给药 4 w。玻璃酸钠滴眼液的给药方法与对照组相同。

1.3 观察指标

比较两组的治疗效果,评估标准:①治愈:泪液分泌实验检查结果大于 10 mm/5 min,患者的干眼症状基本消失;②显效:泪液分泌实验检查结果为 5~10 mm/5 min,患者的干眼症状得到显著的缓解;③有效:泪液分泌实验检查结果小于 5 mm/5 min,患者的干眼症状有所缓解;④无效:未达到上述的有效标准患者。

分别于治疗前后进行泪膜破裂试验和泪液分泌试验。泪膜破裂试验方法如下:将消毒滤纸折弯后夹持在患者下睑外结膜囊内,指导患者轻闭双眼 5 min 后,检查滤纸条被患者泪液浸湿的长度。泪液分泌试验方法如下:于患者的结膜囊内滴入 1 滴荧光素钠溶液,指导患者瞬目数次后再平视前方,检查从瞬目后睁眼到角膜产生第 1 个干燥斑所需要的时间。

两组在治疗前后均分离泪液,观察两组泪液中肿瘤坏死因子(TNF)- α 、白介素(IL)-6 以及高敏 C-反应蛋白(hs-CRP)的改变情况,其中,hs-CRP 水平采用免疫比浊法检测,TNF- α 和 IL-6 水平采用 ELISA 双抗体夹心法检测,试剂盒均购自上海邦奕生物科技有限公司。

1.4 统计学分析

采用 SPSS21.0 软件进行统计学分析,计量资料以 $\bar{x} \pm s$ 表示,组间对比用 t 检验,组间率的比较用 χ^2 检验, $P<0.05$ 为差异有统计学意义。

2 结果

2.1 两组临床疗效的对比

治疗后,观察组的有效率为 95.18%,明显高于对照组($P<0.05$)。

表 1 两组临床疗效比较[例(%)]

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

Groups	N	Cure	Obviously effective	Effective	No effect	Effective rate
Observation group	83	32 (38.55)	27 (32.53)	20 (24.10)	4 (4.82)	95.18*
Control group	83	26 (31.32)	24 (28.91)	16 (19.28)	17 (20.48)	79.52

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

2.2 两组治疗前后泪膜破裂试验和泪液分泌试验结果比较

治疗后,两组泪膜破裂试验和泪液分泌试验结果均得到明显的改善($P<0.05$),且观察组泪膜破裂试验和泪液分泌试验结果的改善更明显($P<0.05$)。

2.3 两组治疗前后泪液 hs-CRP、TNF- α 和 IL-6 水平的比较

两组治疗后的泪液 hs-CRP、TNF- α 和 IL-6 水平均较治疗前明显降低,且观察组泪液 hs-CRP、TNF- α 和 IL-6 水平较对照

组降低更为明显($P<0.05$)。

3 讨论

干眼症又称为干燥性角结膜炎、角结膜干燥症、干燥性角膜结膜炎,是指因泪液的蒸发量过多或泪液的分泌量减少等因素而导致泪膜不稳定和眼表受损,伴有眼部不适症状^[7-9]。干眼症患者主要表现为眼干涩不适、刺痛、烧灼感、畏光、磨砂感和

视疲劳等。大多数患者由于症状不严重而极易被忽视,但是眼睛长时间处于干涩状态,会对眼球造成不可恢复的伤害,患者的角膜结膜上皮干燥,甚至出现纤维形成以及干燥斑等,引发眼部感染及结膜炎,病情严重时能导致失明,因此应引起广泛的重视^[10-13]。白内障患者术前的基础疾病或手术操作能通过不

同的作用途径对泪液的质或量造成影响,泪液成分的改变以及泪液量的减少会刺激泪液分泌神经,易引发异物感、眼干、烧灼和视物模糊等不良症状。而且手术会对患者自身的免疫功能造成影响,活化 T 细胞并释放炎症细胞因子,从而促进眼表炎症的发生^[14-17]。

表 2 两组治疗前后的泪膜破裂试验和泪液分泌试验结果比较($\bar{x} \pm s$)

Table 2 Comparison of the tear film rupture test and tear secretion test between the two groups before and after treatment ($\bar{x} \pm s$)

Groups	n		Tear film rupture test(mm)	Schirmer test(s)
Observation group	83	Before treatment	5.29± 1.34	3.44± 1.19
		After treatment	8.03± 1.57* [#]	7.24± 1.38* [#]
Control group	83	Before treatment	5.27± 1.45	3.43± 1.16
		After treatment	6.72± 1.43 [#]	5.16± 1.49 [#]

Note: Compared with the control group, * $P < 0.05$; compared with before treatment, [#] $P < 0.05$.

表 3 两组治疗前后泪液 hs-CRP、TNF- α 和 IL-6 水平的对比($\bar{x} \pm s$)

Table 3 Comparison of tear levels of hs-CRP, TNF- α and IL-6 between two groups before and after treatment($\bar{x} \pm s$)

Groups	n		hs-CRP(mg/L)	TNF- α (pg/mL)	IL-6(pg/mL)
Observation group	83	Before treatment	46.35 ± 4.27	24.32 ± 1.72	182.31 ± 13.49
		After treatment	13.82 ± 2.64* [#]	12.43 ± 1.32* [#]	58.32 ± 10.24* [#]
Control group	83	Before treatment	47.18 ± 3.36	24.63 ± 2.19	181.74 ± 12.45
		After treatment	23.27 ± 1.65 [#]	17.93 ± 1.45 [#]	95.43 ± 11.27 [#]

Note: Compared with the control group, * $P < 0.05$; compared with before treatment, [#] $P < 0.05$.

玻璃酸钠能有效保护角膜内皮细胞,具有较好的保湿效果。干眼症的发生主要是由于泪膜上皮角膜受到损伤而造成,但是玻璃酸钠主要功效为润滑,对角膜的修补作用较差。自体血清的生化特性与正常的泪液极为相似,不仅可以有效润滑眼表,还对眼表具有营养功能,且不会产生过敏排斥反应;其包含的生物活性成分,如上皮生长因子以及维生素 A 等,可使眼表上皮细胞成熟、分化和增殖速度加快;而含有的多种抗菌因子,如:补体以及溶菌酶等,能有效增加受损眼表抗感染能力及抑制细菌效果;此外,血清中还包含白蛋白以及球蛋白等,可以营养、润滑和保护角膜,并可防止重要细胞因子发生分解,改善泪膜状态,明显抑制干眼症病理进程,达到改善患者视觉质量,缓解其眼部不适的临床治疗目的^[18-21]。本研究结果显示玻璃酸钠滴眼液以及自体血清联合使用能发挥协同作用,提高白内障术后干眼症的疗效,可以有效缓解患者眼部的炎症,减轻角膜损伤程度,从而促进泪膜稳定以及角膜愈合,效果明显优于单独使用玻璃酸钠。

有研究表明干眼症的发生与 T 淋巴细胞所介导的炎症反应呈密切的相关性,炎症反应在各种干眼症的疾病发展过程中均发挥着重要的调节作用^[22-24]。TNF- α 是机体中一种重要的免疫性炎症因子,也是干眼症患者泪液中的一种主要的炎症细胞因子^[25-28]。hs-CRP 作为一种典型的炎症标志物,其水平的升高表明机体出现了炎症反应。hs-CRP 能激活机体中的补体功能,增强吞噬细胞的作用,强化吞噬细胞在体内的清理作用,发挥清除病原微生物以及保护机体组织的目的^[29,30]。IL-6 主要由机体中活化的巨噬细胞分泌,是 TNF- α 等炎症细胞因子的强力

诱导产物^[31,32]。本研究中,观察组治疗后泪液 hs-CRP、TNF- α 和 IL-6 水平降低较对照组更为明显,表明自体血清联合玻璃酸钠发挥对白内障术后干眼症患者的疗效可能与下调患者泪液中 hs-CRP、TNF- α 和 IL-6 水平相关。

综上所述,自体血清联合玻璃酸钠对白内障术后干眼症患者的临床效果明显优于单用玻璃酸钠滴眼液治,其可更有效增加泪膜的稳定性,减轻角膜损伤,减少泪液分泌,这可能与下调患者泪液中 hs-CRP、TNF- α 和 IL-6 水平有关。

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