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曲安奈德对年龄相关性白内障患者房水 TNF- α 、IL-1 β 、IL-6 的影响*

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摘要 目的:探讨曲安奈德对年龄相关性白内障术后患者房水肿瘤坏死因子(TNF)- α 、白介素(IL)-1 β 、IL-6 水平的影响。**方法:**选择 2014 年 6 月至 2016 年 6 月我院接诊的 92 例年龄相关性白内障患者,通过随机数表法分为观察组(n=46)和对照组(n=46),均择期行白内障超声乳化吸除联合人工晶状体植入术。观察组在人工晶状体植入后,在前房内注射曲安奈德,对照组注射复方平衡盐液,术后 24 h,使用普拉洛芬滴眼液,连续用药 1 个月。比较两组手术前、手术后 7d 后眼压、角膜内皮细胞计数、裸眼视力、最佳矫正视力、眼部体征积分、炎症因子的变化,手术后 1d、手术后 7d 时前房反应及不良反应的发生情况。**结果:**两组手术前后眼压、角膜内皮细胞计数均未发生明显变化($P>0.05$);手术后,两组裸眼视力、最佳矫正视力、眼部体征积分均较治疗前明显改善($P<0.05$),观察组裸眼视力、最佳矫正视力、眼部体征积分明显优于对照组($P<0.05$);与手术前相比,两组房水中 TNF- α 、IL-1 β 、IL-6 水平均显著降低($P<0.05$),观察组房水 TNF- α 、IL-1 β 、IL-6 水平均明显低于对照组($P<0.05$);观察组在手术后 1d、7d 时前房反应 1 级比例均高于对照组,前房反应 3 级、4 级比例均比对照组低($P<0.05$);观察组不良反应总发生率明显低于对照组($P<0.05$)。**结论:**曲安奈德用于年龄相关性白内障患者术后患者的效果显著,其可有效缓解术后前葡萄膜炎,减少并发症,促进术后视力恢复,其机制可能与抑制房水中 TNF- α 、IL-1 β 、IL-6 的表达相关。

关键词:年龄相关性白内障;曲安奈德;普拉洛芬滴眼液;前葡萄膜炎;炎症因子

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Effect of Triamcinolone Acetonide on TNF- α , IL-1 β and IL-6 Levels in the Aqueous Fluid of Patients with Age-related Cataract*

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ABSTRACT Objective: To study the effect of triamcinolone acetonide on the tumor necrosis factor (TNF)- α , interleukin (IL)-1 β and IL-6 levels in the aqueous fluid of patients after age-related cataract surgery. **Methods:** 92 patients with age-related cataract who were treated from June 2014 to June 2016 in our hospital were selected and divided into the observation group (n=46) and the control group (n=46) according to the random number table. All the patients underwent phacoemulsification combined with intraocular lens implantation. The observation group was injected with triamcinolone acetonide in the anterior chamber after IOL implantation, the control group was injected with compound balanced salt solution, at 24h postoperation, pranoprofen Eye Drops was used, continuous medication was treated for 1 months. The changes of intraocular pressure, corneal endothelial cell count, uncorrected visual acuity, best corrected visual acuity, ocular signs and inflammatory factors were compared between the two groups before and at 7 days after operation, the anterior chamber reaction at 1 day and 7 days postoperation and the incidence of adverse reactions were compared between two groups. **Results:** There was no significant change in the intraocular pressure and corneal endothelial cell count before and after operation between the two groups ($P>0.05$); after operation, the uncorrected visual acuity, best corrected visual acuity and ocular signs score of both groups were significantly improved($P<0.05$), the uncorrected visual acuity, the best corrected visual acuity and the integral of ocular signs of observation group were significantly better than those of the control group ($P<0.05$); compared with preoperation, the TNF- α , IL-1 β and IL-6 levels in the aqueous fluid were significantly decreased ($P<0.05$), the levels of TNF- α , IL-1 β and IL-6 in the aqueous fluid of observation group were significantly lower than those of the control group ($P<0.05$); the anterior chamber reaction of observation group at 1 day and 7 days after the operation were higher than those of the control group at 1 grade the 3 and the 4 grade of the anterior chamber reaction were lower than those of the control group ($P<0.05$); the incidence of adverse reactions in the observation group was significantly lower than that of the control group($P<0.05$). **Conclusion:** Triamcinolone acetonide anterior chamber injection is effective for age-related cataract patients after surgery, which can effectively alleviate the postoperative anterior uveitis, reduce the complications and promote the postoperative visual recovery, which may be related to the inhibition of the expressions of TNF- α , IL-1 β and IL-6 in the aqueous fluid.

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前言

年龄相关性白内障又被称作是老年性白内障,即随着年龄的增长,患病率也随之增加,在 50 岁以上的中老年人群中较为多见,其发病和老年代谢缓慢出现退行性变存在着密切的关系^[1,2]。目前,临床上对于该病主要采取超声乳化吸除联合人工晶状体植入,多数患者术后视力可得到恢复或明显改善。但是较多报道指出由于手术过程中需分离虹膜粘连,患者术后常出现前葡萄膜炎反应,炎症反应升高,继而对视力的恢复造成影响^[3,4]。普拉洛芬滴眼液是一种非甾体类抗炎药,是白内障患者术后的常用药物,但单独用药效果不尽人意^[5]。曲安奈德是种长效的糖皮质激素,在眼科术后的抗炎治疗中已普遍应用^[6]。本研究旨在探讨曲安奈德前房注射联合普拉洛芬滴眼液在年龄相关性白内障患者手术后的应用优势,并观察其对炎症因子的抑制效果,现报道如下。

1 资料与方法

1.1 一般资料

选择 2014 年 6 月至 2016 年 6 月我院接诊的年龄相关性白内障患者 92 例。纳入标准^[7]:符合年龄相关性白内障诊断标准;①择期行白内障超声乳化吸除联合人工晶状体植入术;②年龄≥60 岁;③对此次研究知情同意。排除标准^[8]:①存在玻璃体浑浊、视网膜脱离等;②手术禁忌症;③既往有眼部外伤手术史;④术前使用过非甾体抗炎药、糖皮质激素等;⑤对本次试验药物过敏;⑥伴有心、肝、肾等严重脏器性疾病。通过随机数表法分为 2 组。观察组男 25 例,女 21 例;年龄 60~79 岁,平均(68.94±2.06)岁;病程 1~8 年,平均(4.74±0.42)年。对照组男 22 例,女 23 例;年龄 60~78 岁,平均(68.86±2.11)岁;病程 1~9 年,平均(4.78±0.41)年。两组一般临床资料比较差异无统计学意义($P>0.05$),具有可比性。

1.2 治疗方法

观察组在人工晶状体植入后,在前房内注射曲安奈德(规格 0.1%×10 mL,厂家:昆明积大制药股份有限公司,国药准字

国药准字 H53021604),剂量 2 mg;对照组则注射复方平衡盐液。手术结束后,均给予阿米卡星(规格 0.2 g:2 mL,厂家:齐鲁制药有限公司,国药准字 H37020562)20 mg+地塞米松(规格 1 mL:5 mg,厂家:华北制药秦皇岛有效公司,国药准字 H13020090)2.5 g 的结膜下注射;并于术后 24 h,使用普拉洛芬滴眼液(规格 5 mL:5 mg,厂家:Senju Pharmaceutical Co., Ltd. Fukusaki Plant,国药准字 H20130682),4 次/d,1 滴/次;用药 3 周后,调整为 3 次/d,1 滴/次。连续用药 1 个月。

1.3 观察指标

于手术前、手术后 7 d 记录以下结果:①眼压、角膜内皮细胞计数:眼压的检测采用日本 Topcon 公司所生产的 CT.8.0 眼压计,结果取三次平均值;角膜内皮细胞计数的检测使用 Topcon 公司所生产的 SBP-2000P 仪角膜内皮显微镜检测;②裸眼视力、最佳矫正视力;③眼部体征积分:评价治疗前后异物感、畏光、角膜水肿、流泪等症状、体征,分值 0~4 分,得分越高,提示表现程度越严重;④炎症因子:抽取 0.1~0.2 mL 房水,使用酶联免疫吸附法对血清肿瘤坏死因子(TNF)- α 、白介素(IL)-1 β 、IL-6 进行检测,试剂盒购于深圳晶美生物公司;⑤前房反应,1 级:无前房闪辉,或前房闪辉症状微弱,房水中没有炎性细胞存在;2 级:前房闪辉程度中等,15 个细胞/视野左右,对于晶状体、虹膜清晰可见;3 级:前房闪辉程度明显,30 个细胞/视野左右,对于晶状体、虹膜的细节难以辨别;4 级:前房闪辉程度严重,纤维性渗出物较多。⑥不良反应。

1.4 统计学分析

采用 SPSS18.0 软件包处理数据,计量资料用均数±标准差($\bar{x}\pm s$)表示,两组间比较采用 t 检验,计数资料比较采用 χ^2 检验,以 $P<0.05$ 表示差异具有统计学意义。

2 结果

2.1 两组手术前后眼压、角膜内皮细胞计数的比较

两组手术前后眼压、角膜内皮细胞计数均未发生明显变化($P>0.05$),见表 1。

表 1 两组手术前后眼压、角膜内皮细胞计数比较($\bar{x}\pm s$)

Table 1 Comparison of the intraocular pressure and corneal endothelial cell count between two groups before and after operation($\bar{x}\pm s$)

Groups	n	Time	Intraocular pressure(mmHg)	Corneal endothelial cell count(number/mm ²)
Observation group	46	Before operation	14.48±1.89	2785.34±184.32
		After operation	14.42±1.75**	2748.19±172.38
Control group	46	Before operation	14.51±1.85	2776.33±185.93
		After operation	14.45±1.76*	2756.42±171.92

2.2 两组手术前后裸眼视力、最佳矫正视力比较

手术前,两组裸眼视力、最佳矫正视力比较差异无统计学意义($P>0.05$);手术后,两组裸眼视力、最佳矫正视力均较术前明显改善($P<0.05$),观察组裸眼视力、最佳矫正视力明显优

于对照组($P<0.05$),见表 2。

2.3 两组手术前后眼部体征积分比较

两组手术前眼部体征积分比较差异无统计学意义($P>0.05$);和手术前比较,两组手术后眼部体征积分均显著降低

($P < 0.05$), 且观察组眼部体征积分明显低于对照组($P < 0.05$), 见表 3。

表 2 两组手术前后裸眼视力、最佳矫正视力比较($\bar{x} \pm s$)Table 2 Comparison of the uncorrected visual acuity and best corrected visual acuity between two groups before and after operation($\bar{x} \pm s$)

Groups	n	Time	Uncorrected visual acuity	Best corrected visual acuity
Observation group	46	Before operation	0.15± 0.04	0.22± 0.03
		After operation	0.62± 0.06* [#]	0.71± 0.07* [#]
Control group	46	Before operation	0.14± 0.04	0.23± 0.03
		After operation	0.41± 0.05*	0.52± 0.05*

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

表 3 两组手术前后眼部体征积分的比较($\bar{x} \pm s$, 分)Table 3 Comparison of the ocular signs score between two groups before and after operation ($\bar{x} \pm s$, scores)

Groups	n	Time	Ocular signs score
Observation group	46	Before the operation	1.94± 0.24*
		After the operation	0.75± 0.13 [#]
Control group	46	Before the operation	1.96± 0.22*
		After the operation	1.23± 0.17

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

2.4 两组手术前后房水中炎症因子水平的比较

β 、IL-6 水平均显著降低 ($P < 0.05$), 且观察组房水中 TNF- α 、

手术前, 两组房水中 TNF- α 、IL-1 β 、IL-6 水平比较差异无 IL-1 β 、IL-6 均明显比对照组低($P < 0.05$), 见表 4。

统计学意义($P > 0.05$); 较手术前比较, 两组房水中 TNF- α 、IL-1

表 4 两组手术前后房水中炎症因子水平的比较($\bar{x} \pm s$, ng/mL)Table 4 Comparison of the inflammatory factors levels in the real water between two groups before and after operation ($\bar{x} \pm s$, ng/mL)

Groups	n	Time	TNF- α	IL-1 β	IL-6
Observation group	46	Before the operation	57.43± 9.32	54.12± 7.15	67.45± 11.23
		After the operation	23.28± 3.54* [#]	27.84± 3.12* [#]	35.62± 5.31* [#]
Control group	46	Before the operation	57.49± 9.28	54.08± 7.16	67.52± 11.20
		After the operation	35.62± 4.67*	36.73± 4.50*	48.34± 6.54*

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

2.5 两组术后前房反应比较

组, 前房反应 3 级、4 级比例均比对照组低($P < 0.05$), 见表 5。

观察组在手术后 1d、7d 时前房反应 1 级比例均高于对照

表 5 两组术后前房反应的比较(例, %)

Table 5 Comparison of the anterior chamber reaction between two groups after operation(n, %)

Groups	n	Time	1 grade	2 grade	3 grade	4 grade
Observation group	46	After the operation 1d	26(56.52)*	13(28.26)	6(13.04)*	1(2.17)*
		After the operation 7d	34(73.91)*	9(19.56)	3(6.52)*	0(0.00)*
Control group	46	After the operation 1d	10(21.74)	12(26.09)	15(32.61)	9(19.56)
		After the operation 7d	18(39.13)	11(23.91)	10(21.74)	7(15.22)

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

2.6 两组不良反应发生情况的比较

观察组不良反应总发生率为 15.22%, 明显比对照组的 36.96%低($P < 0.05$), 见表 5。

3 讨论

年龄相关性白内障患者在实施手术后, 眼内会有部分晶状体皮质残留, 会在房水中释放形成可溶性原, 加上人工晶状体植入的异物刺激, 会破坏到眼组织中血 - 房水屏障结构, 在抗体进入眼内后, 和抗原相互结合形成复合物。当抗原抗体复合物达到一定程度, 则会诱导机体出现免疫功能紊乱, 血管通透

表 6 两组不良反应发生情况的比较(例,%)

Table 6 Comparison of the incidence of adverse reactions between two groups (n, %)

Groups	n	Cystoid macular edema	Corneal edema	Synechia	Photophobia	The total incidence rate
Observation group	46	1(2.17)	1(2.17)	2(4.35)	3(6.52)	7(15.22)*
Control group	46	3(6.52)	2(4.35)	5(10.87)	7(15.22)	17(36.96)

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

性增加,促使炎症因子的释放,形成前葡萄炎。研究表明房水中炎症因子的增加不仅加剧机体炎症反应,还可导致前房内纤维素的渗出,在人工晶状体中粘附,对术后视力恢复造成影响^[9,10]。

普拉洛芬滴眼液主要作用是抑制环加氧酶的活性,使前列腺素的合成产生阻断作用,稳定血管内皮细胞,改善血管通透性^[11]。曲安奈德作为长效水溶性糖皮质激素,可对血管内皮生长因子的产生发挥刺激作用,有利于缓解炎症反应和毛细血管的扩张,并有效抑制纤维蛋白的渗出^[12]。Mohamed TA 等^[13]报道证实曲安奈德在前房内注射后,可在眼球的靶组织中直接产生作用,并且在术后 3 周内前房中的药物浓度均保持在一个相对较高的水平。Ibraheem RF 等^[14]也指出其在改善炎症反应的同时,还可减少并发症,有利于促进视力恢复。

本研究结果显示:在术后 1d、7d 时,联合曲安奈德的患者在前房反应中 3 级、4 级的比例明显比单独用药的患者低,术后裸眼视力、最佳矫正视力、眼部体征积分改善情况更为明显,证实其在有效缓解前葡萄膜炎症状后,在促进视力恢复上具有积极意义,且联合用药不对患者眼压、角膜内皮计数造成影响。Ozge G 等^[15]研究也显示曲安奈德对角膜内皮细胞不存在毒副作用。此外,白内障术后炎症所造成的角膜水肿、黄斑囊状水肿、虹膜粘连等不良反应也会导致病情恶化,影响视力恢复^[16]。本研究结果显示:联合用药的患者术后黄斑囊状水肿、角膜水肿、虹膜粘连、畏光流泪不良反应的总发生率仅为 15.22%,而单独使用普拉洛芬滴眼液的患者高达 36.96%,提示该方式在缓解炎症反应后有利于降低术后不良反应,改善患者预后。

TNF- α 是主要由巨噬细胞及活化的单核细胞所生成的重要免疫调节因子,可增加白细胞的粘附,促使其趋化,在诱导、调节炎症反应中发挥着重要的作用,并且可刺激 IL-1 β 、IL-6 等的生成^[17,18]。IL-1 β 在细胞因子网络中是一种重要介质,在炎症反应的早期过程中即有所参与,其可刺激前列腺素的产生,对血-房水屏障造成破坏。Sabzevari A 等^[19]动物试验表明在白内障术后眼眼中存在 IL-1 β ,且其不仅作为一种炎症介质,还在后发性白内障形成中也可能有所参与。IL-6 具有多种免疫调节功能,Wang L 等^[20]研究显示 IL-6 在葡萄膜炎房水中具有较高的浓度,可对前房局部炎症程度进行有效反应。本研究结果显示联合安奈德治疗的患者在术后房水 TNF- α 、IL-1 β 、IL-6 水平较单独用药的患者更低,进一步证实曲安奈德可有效控制炎症反应,且其可在长时间内发挥效果,在缓解前房炎症反应中更具有优势。

综上所述,曲安奈德用于年龄相关性白内障患者术后患者的效果显著,其可有效缓解术后前葡萄膜炎,减少并发症,促进术后视力恢复,其机制可能与抑制房水中 TNF- α 、IL-1 β 、IL-6 的表达相关。

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