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术后早期散瞳对 DR 合并白内障患者眼部血流动力学的影响 及散瞳后瞳孔直径达标的因素分析 *

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摘要 目的:探讨术后早期散瞳对糖尿病视网膜病变(DR)合并白内障患者眼部血流动力学的影响,分析影响散瞳后瞳孔直径达标的相关因素。**方法:**选择2018年1月至2022年1月河北北方学院附属第一医院收治的150例行白内障手术治疗的DR合并白内障患者,将患者按随机数字表法分为对照组和观察组,两组术后均给予复方托吡卡胺滴眼液散瞳,对照组于术后7d、14d各散瞳1次,观察组给予早期散瞳治疗,即术后次日开始每日散瞳1次。比较两组术后眼部血流动力学变化。根据术后第14d散瞳后瞳孔直径是否达标分为达标组(瞳孔直径 ≥ 5 mm)和未达标组(瞳孔直径 < 5 mm),收集患者临床资料,采用多因素Logistic回归分析影响散瞳后瞳孔直径达标的因素。**结果:**观察组术后14d视网膜中央动脉、睫状后短动脉舒张末期血流速度(EDV)、收缩期速度峰值(PSV)较术后7d增加($P < 0.05$),阻力指数(RI)较术后7d降低($P < 0.05$),且术后7d、14d视网膜中央动脉、睫状后短动脉EDV、PSV高于对照组($P < 0.05$),RI低于对照组($P < 0.05$)。观察组术后14d散瞳时间较术后7d缩短($P < 0.05$),散瞳后瞳孔直径较术后7d增大($P < 0.05$),且观察组术后7d、14d散瞳时间短于对照组($P < 0.05$),散瞳后瞳孔直径大于对照组($P < 0.05$)。糖尿病病程 > 10 年、DR增殖期是影响散瞳后瞳孔直径达标的危险因素($P < 0.05$),术后早期散瞳治疗是其保护因素($P < 0.05$)。**结论:**DR合并白内障患者经白内障术后早期散瞳治疗可缩短散瞳时间,改善眼部血流动力学,增加散瞳后瞳孔直径。糖尿病病程、DR严重程度、术后散瞳时机是散瞳后瞳孔直径达标的影响因素。

关键词:糖尿病视网膜病变;白内障;血流动力学;散瞳;瞳孔直径

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Effect of Early Pupil Dilation after Surgery on Ocular Hemodynamics in Patients with Diabetic Retinopathy Complicated with Cataract and Analysis of Correlative Factors of Affecting Pupil Diameter Up to Standard after Dilation*

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ABSTRACT Objective: To explore the effect of early pupil dilation after surgery on ocular hemodynamics in patients with diabetic retinopathy (DR) complicated with cataract, and to analyze the related factors affecting pupil diameter up to standard after dilation. **Methods:** 150 patients with DR complicated with cataract who were treated in cataract surgery in The First Affiliated Hospital of Hebei North University from January 2018 to January 2022 were selected, the patients were evenly divided into control group and observation group by random number table method, two groups were given compound topicalamide eye drops to dilate pupil after surgery, pupils were dilated once on 7d, and 14d after surgery in the control group, early pupil which began to dilate pupil once a day on the next day after surgery were dilated in the observation group. The changes and differences of ocular after surgery hemodynamics between the two groups were compared. According to whether the pupil diameter reaches the standard after pupil dilation on the 14th day after operation, the patients were divided into the standard group (pupil diameter ≥ 5 mm) and the non-standard group (pupil diameter < 5 mm), clinical data of patients were collected, multivariate Logistic regression was used to analyze the factors affecting whether the pupil diameter reached the standard after pupil dilation. **Results:** The central retinal artery, short posterior ciliary artery end diastolic flow velocity (EDV) and peak systolic velocity (PSV) of the observation group increased 14 d after surgery compared with 7d after surgery ($P < 0.05$), resistance index decreased compared with 7 d after operation ($P < 0.05$), EDV and PSV of central retinal artery and short posterior ciliary artery were higher than those of control group at 7 d and 14 d after surgery ($P < 0.05$), RI was lower than that of control group ($P < 0.05$). The pupil dilation time of observation group on 14 d after surgery was shorter than that on 7 d after surgery ($P < 0.05$), the pupil diameter after pupil dilation increased compared with 7 d after operation ($P < 0.05$), the pupil dilation time of the observation group was shorter than that of the control

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group on the 7d and 14d after operation ($P<0.05$), and the pupil diameter after pupil dilation was larger than that of the control group ($P<0.05$). The duration of diabetes > 10 years and the DR proliferative period were the risk factors affecting pupil diameter after pupil dilation ($P<0.05$), and early postoperative dilation was a protective factor ($P<0.05$). **Conclusion:** In patients with cataract complicated with DR, early postoperative dilation can shorten the duration of pupil dilation of pupil, improve ocular hemodynamics, and increase pupil diameter after pupil dilation. The duration of diabetes, the severity of diabetic retinopathy and the timing of dilate pupils after surgery are the influencing factors of pupil diameter after pupil dilation.

Key words: Diabetic retinopathy; Cataract; Hemodynamics; Pupil dilation; Pupil diameter

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前言

糖尿病视网膜病变(DR)是糖尿病最常见的微血管并发症,其发生与遗传、糖尿病病程、血糖控制不佳有关,被认为是糖尿病患者发生大血管并发症的独立预测因子^[1,2]。除DR外,糖尿病往往增加其它眼部并发症,加重视力下降,其中白内障与DR往往同时存在^[3],需要接受手术治疗。眼底病变诊治需要充分散瞳以获得理想的视野,便于对疾病进行观察^[4,5],但是白内障术后往往出现散瞳困难^[6]。复方托吡卡胺滴眼液是一种短效的抗胆碱能药物,在滴注后15~20分钟内开始起效,作用可持续4~6小时^[7]。DR合并白内障患者通常于术后第7、14 d进行散瞳治疗,但是散瞳效果较差,本研究拟术后早期进行散瞳,观察其对DR合并白内障患者瞳孔直径、眼部血流动力学的影响,并在此基础上分析影响散瞳后瞳孔直径达标的因素,以期为临床散瞳治疗时机的选择和瞳孔管理提供参考。

1 资料与方法

1.1 临床资料

选择2018年1月至2022年1月河北北方学院附属第一医院收治的150例经白内障手术治疗的DR合并白内障患者,纳入标准:^①符合《我国糖尿病视网膜病变临床诊疗指南(2014年)》中DR的诊断标准^[8];^②裂隙灯显微镜、超声等检查确认存在晶状体混浊,经临床诊断为白内障^[9],符合超声乳化白内障手术指征;^③年龄18周岁以上。排除标准:^④合并青光眼、屈光不正、眼外伤、眼科手术史;^⑤服用利尿剂、血管紧张素转换酶抑制剂等影响眼部血流动力学的药物;^⑥合并高血压和目前吸烟者;^⑦对本研究药物过敏者。采用随机数字表法将患者分为两组,每组各75例。对照组:男49例,女26例,年龄51~74岁,平均(62.02 ± 10.15)岁,糖尿病病程6~15年,平均(9.45 ± 3.07)年,手术时间12~30 min,平均(20.12 ± 4.53)min,术后散瞳前瞳孔直径3~7 mm,平均(4.92 ± 1.03)mm,糖化血红蛋白5~7%,平均(6.15 ± 0.63)%。观察组:男45例,女30例,年龄52~75岁,平均(62.74 ± 10.38)岁,糖尿病病程7~17年,平均(9.62 ± 3.11)年,手术时间11~28 min,平均(20.41 ± 4.09)min,术后散瞳前瞳孔直径3~7 mm,平均(4.98 ± 1.05)mm,糖化血红蛋白5~7%,平均(6.21 ± 0.72)%。上述基线资料比较无统计学差异($P>0.05$),均衡可比。两组患者知情同意签署同意书,本研究已经获得河北北方学院附属第一医院伦理委员会批准。

1.2 术后散瞳治疗

观察组给予早期散瞳治疗,即术后次日开始给予复方托吡

卡胺滴眼液(邯郸康业制药有限公司,规格5mL/瓶,批号:国药准字H20044926)散瞳,每日早上8时左右于光照充足的室内进行,患者坐位抬头,操作者用食指和拇指轻轻分开患者上下眼睑,于下脸结膜囊内滴入1~2滴复方托吡卡胺滴眼液,隔5 min后再滴1~2滴,共滴3~5次,直至瞳孔对光反射消失。对照组于术后第7、14 d散瞳,药物以及滴眼方法同观察组。

1.3 观察指标

1.3.1 眼部血流动力学检测 两组术后第7、14 d散瞳结束后进行眼部超声检查,测量视网膜中央动脉和睫状后短动脉血流动力学,超声仪器采用DC-N3S彩色多普勒超声诊断仪(购自深圳迈瑞生物医疗电子股份有限公司),探头频率6~15 MHZ。患者仰卧闭双眼,探头置于上睑处,获得眼球后三角区视神经影像,频谱多普勒技术测量暗区内视网膜中央动脉、睫状后短动脉的舒张末期血流速度(EDV)、收缩期速度峰值(PSV)、阻力指数(RI)。

1.3.2 瞳孔直径、散瞳时间以及散瞳后瞳孔直径达标的标准 两组术后第7、14 d在光照充足的室内于瞳孔对光反消失后用直尺测量瞳孔直径,记录散瞳时间(第一次滴眼至瞳孔对光反消失的时间)。以术后第14 d散瞳后瞳孔直径 ≥ 5 mm为达标,散瞳后瞳孔直径 <5 mm为未达标^[10],根据散瞳后瞳孔直径是否达标分为达标组(120例)和未达标组(30例)。

1.4 临床资料收集

收集患者年龄、性别、糖尿病病程、DR严重程度(增殖期与非增殖期)、术后散瞳时机(早期与非早期)、糖化血红蛋白水平。

1.5 统计学分析

应用统计学软件SPSS 25.0录入和分析数据,经Kolmogorov-Smirnov法检验,本研究中计量资料均符合正态分布,以($\bar{x}\pm s$)表示,采用配对或成组t检验。计数资料以例(%)表示,采用 χ^2 检验。采用多因素Logistic回归模型分析影响散瞳后瞳孔直径是否达标的因素。检验水准 $\alpha=0.05$ 。

2 结果

2.1 两组术后眼部血流动力学参数比较

观察组术后14 d视网膜中央动脉、睫状后短动脉EDV、PSV较术后7 d增加($P<0.05$),RI较术后7 d降低($P<0.05$),对照组术后14 d视网膜中央动脉、睫状后短动脉EDV、PSV上升,RI下降,但是与术后7 d比较无差异($P>0.05$);观察组术后7 d、14 d视网膜中央动脉、睫状后短动脉EDV、PSV高于对照组($P<0.05$),RI低于对照组($P<0.05$),见表1。

表 1 两组术后眼部血流动力学参数差异($\bar{x} \pm s$)
Table 1 Differences in ocular hemodynamic parameters between the two groups after surgery ($\bar{x} \pm s$)

Blood vessels	Hemodynamic indexs	Groups			
		Observation group(n=75)		Control group(n=75)	
		7 d after surgery	14 d after surgery	7 d after surgery	14 d after surgery
Central retinal artery	EDV(cm/s)	4.18±0.51°	4.71±0.36°	2.65±0.35	2.71±0.29
	PSV(cm/s)	13.95±4.11°	15.02±4.56°	10.02±3.26	10.12±2.03
	RI	0.70±0.09°	0.67±0.06°	0.74±0.07	0.72±0.08
Short posterior ciliary artery	EDV(cm/s)	6.02±0.42°	7.85±0.63°	4.82±0.23	4.84±0.30
	PSV(cm/s)	18.02±4.16°	19.54±4.28°	16.32±3.26	16.35±3.07
	RI	0.67±0.13°	0.60±0.10°	0.70±0.12	0.68±0.15

Note: Compared with control group on the same day ° $P<0.05$. Compared with the same group at 7 d after surgery, ° $P<0.05$.

2.2 两组散瞳时间、散瞳后瞳孔直径比较

观察组术后 14 d 散瞳时间较术后 7 d 缩短 ($P<0.05$), 散瞳后瞳孔直径较术后 7 d 增大 ($P<0.05$), 对照组术后 14 d 散

瞳时间、散瞳后瞳孔直径与术后 7 d 比较无统计学差异 ($P>0.05$); 观察组术后 7 d、14 d 散瞳时间短于对照组 ($P<0.05$), 散瞳后瞳孔直径大于对照组 ($P<0.05$), 见表 2。

表 2 两组散瞳时间、散瞳后瞳孔直径差异($\bar{x} \pm s$)
Table 2 Differences of pupil dilation time and pupil diameter after dilation between the two groups ($\bar{x} \pm s$)

Groups	Time	Pupil dilation time(min)	Pupil diameter after dilation(mm)
Observation group (75 cases)	7 d after surgery	25.02±4.16°	5.89±1.41°
	14 d after surgery	23.05±3.11°	6.78±1.62°
Control group(75 cases)	7 d after surgery	28.15±5.31	5.21±1.32
	14 d after surgery	27.81±4.09	5.23±1.55

Note: Compared with control group on the same day ° $P<0.05$. Compared with the same group at 7d after surgery, ° $P<0.05$.

2.3 影响散瞳后瞳孔直径达标的单因素分析

两组散瞳后共达标 120 例,未达标 30 例。达标组糖尿病病程>10 年、DR 增殖期比例低于未达标组 ($P<0.05$),术后早期散瞳比例高于未达标组 ($P<0.05$),两组年龄、性别、糖化血红蛋白比较差异无统计学意义 ($P>0.05$),见表 3。

2.4 影响散瞳后瞳孔直径达标的多因素分析

选取表 3 中比较差异有统计意义的因素进行多因素 Logistic 分析。以糖尿病病程(赋值:0=≤10 年,1=>10 年)、DR 严重程度(赋值:0= 非增殖期,1= 增殖期)、术后散瞳时机(赋值:0= 术后非早期散瞳,1= 术后早期散瞳)为自变量,散瞳后瞳孔直径是否达标为因变量(赋值:0= 是,1= 否),最终结果显示糖尿病病程>10 年、DR 增殖期是影响散瞳后瞳孔直径达标的危险因素,术后早期散瞳是保护因素 ($P<0.05$)。见表 4。

3 讨论

DR 是一种微血管疾病,其特征是毛细血管脱落导致的视网膜缺血和血管重塑,并引起血流速度减慢和血管阻力增加^[10]。白内障手术后需要及时进行眼底检查^[11,12],必要时需要补充光凝手术治疗,并进行散瞳治疗以获得理想的瞳孔直径为眼底激光治疗提供保障^[13]。但是糖尿病患者往往散瞳效果不佳,小瞳孔给白内障手术以及术后眼底检查带来了巨大挑战^[14]。复方托吡卡胺滴眼液是临床常用的散瞳治疗药物,有助于快速散瞳验

光检查^[15,16]和眼底检查,但是何时散瞳的效果更佳尚不明确,因此有必要分析影响 DR 合并白内障患者术后散瞳后瞳孔直径的影响因素,为临床术后散瞳治疗提供理论依据。

本研究结果显示观察组术后 14 d 视网膜中央动脉、睫状后短动脉血流速度较术后 7 d 加快,阻力较术后 7 d 降低,而对照组视网膜中央动脉、睫状后短动脉血流速度减慢,阻力增高,说明术后次日每日一次散瞳可有效地改善眼部局部血流动力学和微循环。分析原因为复方托吡卡胺滴眼液中含去氧肾上腺素可加快血液流动,并降低血管阻力^[17,18],观察组每日应用复方托吡卡胺滴眼液散瞳可能产生累积效应,可更好地改善眼部血流动力学。而对照组术后散瞳治疗次数有限,因此导致散瞳效果不佳,眼部血流动力学改善不明显。

瞳孔直径变化由虹膜括约肌和虹膜扩张肌控制,分别收缩和扩张瞳孔,同时还受动眼神经的副交感神经和瞳孔开大肌的交感神经支配^[19]。复方托吡卡胺滴眼液由托吡卡胺和去氧肾上腺素组成,托吡卡胺可阻断 M 胆碱受体引起瞳孔括约肌舒张,M 胆碱受体可兴奋肾上腺素α受体引起瞳孔开大肌收缩,达到散瞳的目的^[20,21]。本研究观察组术后 7、14 d 散瞳时间短于对照组,瞳孔直径大于对照组,且术后次日后每日一次散瞳是影响散瞳后瞳孔直径达标的保护因素,表明术后每日散瞳治疗可产生更好的散瞳效果,并缩短散瞳时间,分析原因为早期散瞳治疗能更有效地促使眼部血液循环,促使受损瞳孔括约肌和虹膜

扩张肌及其支配神经恢复。

表 3 影响散瞳后瞳孔直径达标的单因素分析

Table 3 The effect of univariate factor analysis on whether the pupil diameter reaches the standard after pupil dilation

Groups	Standard group (n=120)	Non-standard group (n=30)	χ^2 value	P value
Age [n(%)]				
≥60 years old	77(64.17)	19(63.33)	0.007	0.932
<60 years old	43(35.83)	11(36.67)		
Gender [n(%)]				
male	76(63.33)	18(60.00)	0.114	0.736
female	44(36.67)	12(40.00)		
Duration of diabetes [n(%)]				
<5 years	60(50.00)	6(20.00)		
5~10 years	24(20.00)	7(23.33)	12.134	0.002
>10 years	36(30.00)	17(56.67)		
Severity of DR [n(%)]				
Proliferative period	45(37.50)	21(70.00)	10.215	0.001
Non-proliferative period	75(62.50)	9(30.00)		
Glycosylated hemoglobin level (%)	6.19±0.67	6.14±0.70	0.362	0.718
Timing of dilate pupils after surgery [n(%)]				
Early stage	75(62.50)	0(0.00)	37.500	0.000
Non-early stage	45(37.50)	30(100.00)		

表 4 影响散瞳后瞳孔直径达标的多因素分析

Table 4 The effect of multivariate factor analysis on the pupil diameter reaches the standard after pupil dilation

Factors	β	SE	Wald χ^2	OR(95%CI)	P value
Constant term	0.592	0.169	12.271	-	0.000
Duration of diabetes>10 years	0.495	0.124	15.936	1.640(1.287~2.092)	0.000
proliferative period of diabetic retinopathy	0.632	0.217	8.482	1.881(1.230~2.879)	0.016
Timing of dilate pupils after surgery	-0.695	0.236	8.673	0.403(0.262~0.682)	0.012

本研究回归分析结果显示糖尿病病程>10年、DR 增殖期是影响散瞳后瞳孔直径达标的危险因素。研究显示糖尿病患者对药物散瞳反应比非糖尿病患者差,DR 患者小瞳孔的患病率高于非 DR 患者^[22]。随着糖尿病病程延长,胰岛功能逐渐衰退,血糖控制困难,在高糖环境中糖基化终产物(AGEs)产生不断增加,AGEs 在虹膜组织、瞳孔括约肌、虹膜扩张肌等组织中积聚,通过结合胶原蛋白改变组织的结构完整性,并与 AGEs 受体结合上调炎症反应^[23,24],导致组织弹性降低,散瞳困难^[25]。现有报道显示白内障术后瞳孔缩小与糖尿病患者前房炎症反应有关^[26],已知在 DR 发病过程中多种炎症介质表达上调,引起视网膜损伤和视网膜中神经元细胞凋亡,并促使基底膜降解、内皮细胞迁移和增殖以及新生血管生成^[27,28],且随着 DR 病情的加重炎症反应加剧,增殖期 DR 泪液中白细胞介素-6 水平

高于非增殖期 DR^[29],提示增殖期 DR 炎症反应明显,因此散瞳后易发生瞳孔直径不达标现象。

综上,术后次日每日一次散瞳可改善 DR 合并白内障患者眼部血流动力学,缩短散瞳时间,增加瞳孔直径。糖尿病病程>10年、DR 增殖期是影响散瞳后瞳孔直径达标的危险因素,术后次日每日一次散瞳是保护因素。本研究收集临床资料有限,样本例数偏少,散瞳后瞳孔直径的影响因素仍需增加样本量,进一步的临床研究以证实。

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