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白内障超声乳化术对糖尿病患者角膜内皮细胞和中央角膜厚度影响*

殷秀丽 陈卓 付安安 刘冬瑞 宋凡倩 葛红岩[△]

(哈尔滨医科大学附属第一医院眼科医学院 黑龙江 哈尔滨 150001)

摘要 目的:评估糖尿病患者和非糖尿病患者在进行白内障超声乳化手术后,角膜内皮细胞和中央角膜厚度变化。**方法:**观察于我院行白内障超声乳化吸出联合人工晶状体植入术的年龄相关性白内障患者各 100 例(100 眼),于术前 1 天、术后 1 周、1 个月、3 个月、6 个月和 1 年随访记录其角膜内皮细胞密度(endothelial cell density, ECD)、六角形细胞百分比(percentage of hexagonal cells, PHC)、变异系数(coefficient of variation, CV)和中央角膜厚度(central corneal thickness, CCT)等指标,并对结果进行统计学分析。**结果:**非糖尿病组在术前各指标无明显差异($P>0.05$),术后 1 年 ECD, PHC 在两组均下降, CV 升高($P<0.05$), CCT 出现明显波动,糖尿病组在术后一周达到峰值。ECD, CV 和 PHC 在术后各时间点出现明显的组间差异($P<0.05$)。**结论:**白内障超声乳化术后远期内,糖尿病组的角膜内皮细胞和中央角膜厚度较非糖尿病组发生显著变化。

关键词:超声乳化手术;糖尿病;内皮细胞密度;中央角膜厚度

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Corneal Endothelial Cells and Central Corneal Thickness after Phacoemulsification Surgery in Diabetic Cataract Patients*

YIN Xiu-li, CHEN Zhuo, FU An-an, LIU Dong-rui, SONG Fan-qian, GE Hong-yan[△]

(Department of ophthalmology, The First Affiliated Hospital of Harbin, Harbin, Heilongjiang, 150001, China)

ABSTRACT Objective: Here we intended to investigate the changes in corneal endothelial cells and central corneal thickness after phacoemulsification surgery on the eyes of diabetic and non-diabetic cataract patients. **Methods:** A total of 200 cataract patients who were scheduled for phacoemulsification surgery and intraocular lens implantation were recruited and divided into 2 categories (100 hundred eyes each group). Changes in endothelial cell density (ECD), coefficient of variation (CV), percentage of hexagonal cells (PHC), central corneal thickness (CCT) were all recorded at preoperative day 1 and postoperative 1 week, 1 month, 3 months, 6 months and 1 year. **Results:** None of the recorded variables showed any difference between the nondiabetic and diabetic groups before surgery ($P>0.05$). During the postoperative 1 year, ECD and PHC decreased in both groups (all $P<0.05$) while CV increased, whereas CCT and fluctuated in both groups significantly (both $P<0.05$), with the peaks at postoperative 1 week in the diabetic group. The groups differed significantly in ECD, CV and PHC at each time point postoperatively (all $P<0.05$). **Conclusions:** The diabetic group had more changes in a long time in corneal endothelial cells and central corneal thickness than the nondiabetic group postoperatively.

Key words: Phacoemulsification; Diabetes mellitus; Endothelial cells; Central corneal thickness

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前言

角膜内皮细胞通过屏障功能和 Na^+/K^+ ATP 酶的主动液泵功能维持角膜厚度及透明性^[1]。成人角膜内皮损伤后不能再生,损伤区域由邻近细胞扩展、移行覆盖。如果内皮细胞损害超过一定限度,则会发生角膜内皮失代偿。角膜厚度是反映内皮功能的一个重要指标。多形性的角膜内皮细胞更容易受到手术损伤^[2],有研究证实,糖尿病可以改变角膜内皮细胞的结构、功能和厚度。本研究所选定的糖尿病患者为 2 型糖尿病,且无糖尿

病视网膜病变的患者。研究糖尿病患者行白内障超声乳化手术和单纯年龄相关性白内障行超声乳化手术对角膜内皮的影响,及远期愈合情况,具有十分重要的临床意义。

本研究的目的是评估糖尿病患者和非糖尿病患者在行白内障超声乳化手术后远期内,角膜内皮细胞和黄斑中心凹厚度的变化。

1 材料与方法

1.1 研究对象

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作者简介:殷秀丽(1963-),女,副主任护师,主要研究方向:白内障术后临床观察, E-mail: yx113845113914@163.com

[△] 通讯作者:葛红岩(1970-),女,硕士生导师,主任医师,主要研究方向:角膜病、白内障的发病机制及治疗,

E-mail: hongyan@hotmail.com, 电话: 13936268986

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收集 2016 年 12 月至 2018 年 02 月于我院住院行白内障超声乳化吸除联合人工晶状体植入手术的患者,依据 2 型糖尿病诊断标准将患者分为 2 组:糖尿病组和非糖尿病组。每组 100 只眼、100 人。纳入标准:糖尿病患者经内分泌科根据 WHO 标准确诊为非胰岛素依赖型糖尿病,病程为 1~10 年,术前空腹血糖均控制在 7.0 mmol/L 以内。依据 Emery 分级标准,在裂隙灯下检查晶状体,核硬度在 III~IV 级核之间者纳入本研究。排除标准:可能影响角膜内皮细胞监测的任何眼部疾病如翼状胬肉、高度近视、角膜内皮营养不良、角膜炎和圆锥角膜等。

统计年龄、性别等。通过测量糖尿病组糖化血红蛋白(HbA1c)水平和血浆葡萄糖评估糖尿病的严重程度。该研究获得我院伦理委员会的批准,所有患者在纳入之前对该研究均知情并同意。

1.2 主要指标结果

所有眼在术前第一天都进行了完善的眼科检查(基线),包括最佳矫正视力(best corrected visual acuity, BCVA)、Amsler 表、裂隙灯检查、眼内压(intraocular pressure, IOP)测量和散瞳眼底检查。视力每次都用 Snellen 视力表测量。与超声乳化术相关的角膜内皮细胞损伤用内皮细胞密度和形态进行评估。角膜内皮细胞用非接触式角膜内皮镜(Noncon Robo-CAKonan SP-9000p Tokyo, Japan)进行检测。检测指标为术前和术后 1 周,术后 1 个月、3 个月、6 个月,1 年细胞密度(ECD),以及其他的参数包括内皮细胞大小,六角形细胞百分比(PHC)、变异系数(CV)和中央角膜厚度(CCT)。

1.3 手术

1.3.1 术前准备 拟行手术的患者术前三天左眼氟沙星(可乐必妥)点眼,1 日 4 次,点 3 天。冲洗泪道,有脓者不予以纳入手术。聚维酮碘(点而康)和 0.9%的 NaCl 冲洗结膜囊。

1.3.2 手术方法 所有患者手术过程中植入相同的人工晶状体,手术由同一医生团队在无菌条件下完成。术前 30 分钟时复方托吡卡胺滴眼(美多丽,参天制药,日本)散瞳,盐酸奥布卡因滴眼液(倍诺喜,参天制药,日本)表面麻醉 3 次,采用自闭式透明角膜切口,使用 3.0 mm 穿刺刀于角膜缘内 1 mm 穿入,隧道

潜行 1.5 mm 后穿入前房。15° 尖刀在 2 点位于角膜缘内做辅助切口,前房注入粘弹剂(Healon; Advanced Medical Optics, Santa Ana, CA, USA),连续环形撕囊,直径 5.5-6.0 mm,充分水分离和分层,使皮质与核及囊分离,核能在囊袋内转动,囊袋内乳化晶状体核,乳化参数能力 40%,负压 300 mmHg,流量 24-28 mL/min,灌注瓶高度 76 cm。自动抽吸灌注器吸出残余皮质,行后囊抛光,囊袋内注入粘弹剂,植入 AMO 折叠人工晶状体于囊袋内,置换粘弹剂,切口做角膜基质水化处理。妥布霉素/地塞米松眼膏(典必舒,爱尔康公司,比利时)涂眼,包扎术眼。

1.3.3 术后处理 氯替泼诺混悬滴眼液、普南扑灵滴眼液用 4 周,第 1 周 1 日 4 次,第 2 周 1 日 3 次,第 3 周 1 日 1 次,第 4 周 1 日 1 次;左氧氟沙星滴眼液用 1 周,一日 2 次;人工泪液用 4 周,一日 4 次。

1.4 随访

患者需在术后 1 周、术后 1 个月、3 个月、6 个月和 1 年进行复查随访,所行眼科检查同术前 1 天,所有基线和术后评估由同一名医生完成,这名医生对患者是否有糖尿病并不知情。

1.5 数据分析

统计学分析:采用 SPSS 19.0 软件分析,采用重复测量方差分析。以 $P < 0.05$ 为差异有统计学意义

2 结果

2.1 人口统计学和术中数据

所有在 12 个月内能够完成随访的患者纳入此研究分析,人口统计情况和临床特征见表 1。糖尿病组患者的平均糖尿病病史为 4.4 年,且不患有严重的糖尿病并发症,如糖尿病肾病,糖尿病视网膜病变,糖尿病神经病变,下肢血管病变,心血管疾病或糖尿病足。这些患者依据中国 2 型糖尿病指南(2013 年编,表 2)^[1],通过健康饮食、规律锻炼、口服降糖药或胰岛素治疗,其糖尿病均控制良好。糖尿病组与对照组在年龄、性别、白内障超声乳化时间、眼压、核分级和冲洗液使用量上无明显差异($P > 0.05$,表 1)。所有患者在手术期间无特殊事件发生,且无糖尿病患者发展为增生性糖尿病视网膜病变。

表 1 人口统计学和术中数据

Table 1 Demographic and intraoperative data of patients with cataract

Parameter	Nondiabetic	Diabetic
Age(y)	62.8± 2.2	61.1± 2.1
Gender, n(%)		
Male	48(48)	46(46)
Female	52(52)	54(54)
Duration of diabetes(y)	-	4.4 ± 1.5
Intraocular pressure(mmHg)	16.5 ± 2.1	17.2 ± 2.0
Cataract nuclears opalescence, n:		
1	18	15
2	34	33
3	40	46
4	8	6

Note: Data are presented as mean± SD or percentage.

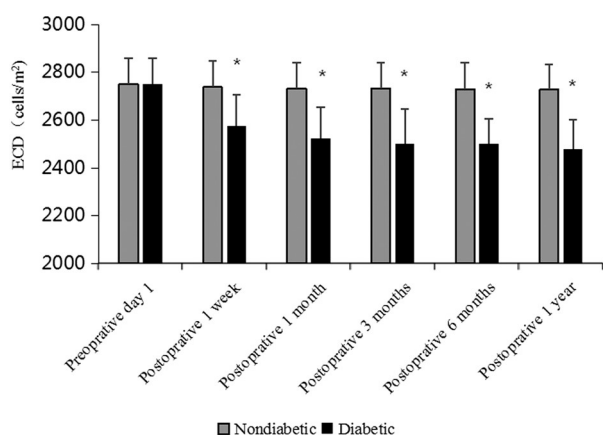


图1 糖尿病组和非糖尿病组患者术前1天、术后1周、术后1个月、术后3个月、术后6个月和术后1年的ECD相互联系和变化
注:* 糖尿病组合非糖尿病组术后各时间点有差异($P_{\text{组间}} < 0.05$)。
Fig.1 Comparisons of endothelial cell density between the diabetic and nondiabetic groups at preoperative day 1 and postoperative 1 week, 1 month, 3 months, 6 months and 1 year.

Note: Data are shown as mean $\pm$ standard error(SE).

*Diabetic group differed from nondiabetic group postoperatively at the time point ($P_{\text{group}} < 0.05$).

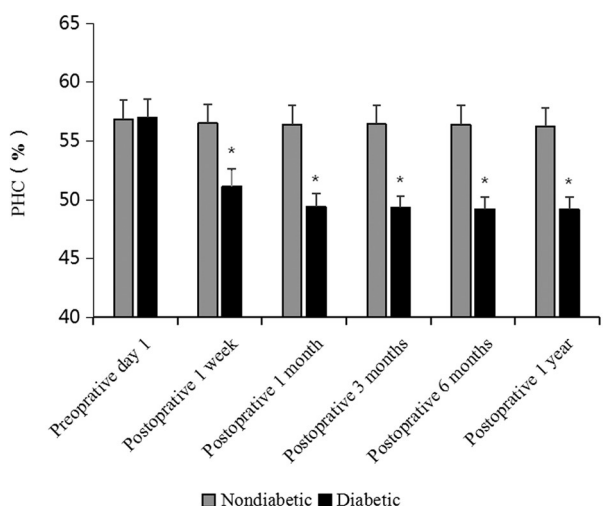


图2 糖尿病组和非糖尿病组患者术前1天、术后1周、术后1个月、术后3个月、术后6个月和术后1年的PHC的相互联系和变化
注:* 糖尿病组合非糖尿病组术后各时间点有差异($P_{\text{组间}} < 0.05$)。
Fig.2 Comparisons of percentage of hexagonal cells between the diabetic and nondiabetic groups at preoperative day 1 and postoperative 1 week, 1 month, 3 months, 6 months and 1 year. Data are shown as mean $\pm$ standard error(SE). *Diabetic group differed from nondiabetic group postoperatively at the time point($P_{\text{group}} < 0.05$).

2.2 ECD, PHC, CV 和 CCT 各项指标结果

所有指标在糖尿病组和非糖尿病组患者行白内障超声乳化手术前无明显差异($P > 0.05$)。在术后12个月的随访中,两组的ECD和PHC下降(图1和图2, $P_{\text{时间}} < 0.05$), CV升高(图3, $P_{\text{时间}} < 0.05$)。并且,糖尿病组在术后各时间点的ECD, CV, PHC值改变比非糖尿病组更为显著($P_{\text{时间}} < 0.05$)。

两组的CCT值在不同时间点会产生波动且有各自的峰值(图3, $P_{\text{时间}} < 0.05$)。糖尿病组在术后12个月的随访中,中央角膜厚度较厚。并且,三项指标的组内和组间差异都有统计学意义($P_{\text{组间,时间}} < 0.05$)。

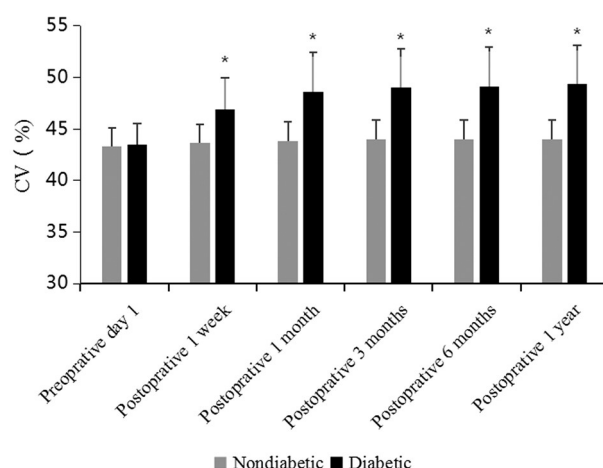


图3 糖尿病组和非糖尿病组患者术前1天、术后1周、术后1个月、术后3个月、术后6个月和术后1年的CV的相互联系和变化
注:* 糖尿病组合非糖尿病组术后各时间点有差异($P_{\text{组间}} < 0.05$)。
Fig.3 Comparisons of CV between the diabetic and nondiabetic groups at each time of preoperative day 1 and postoperative 1 week, 1 month, 3 months, 6 months and 1 year. Data are shown as mean $\pm$ standard error (SE). * Diabetic group differed from nondiabetic group postoperatively at the time point($P_{\text{group}} < 0.05$).

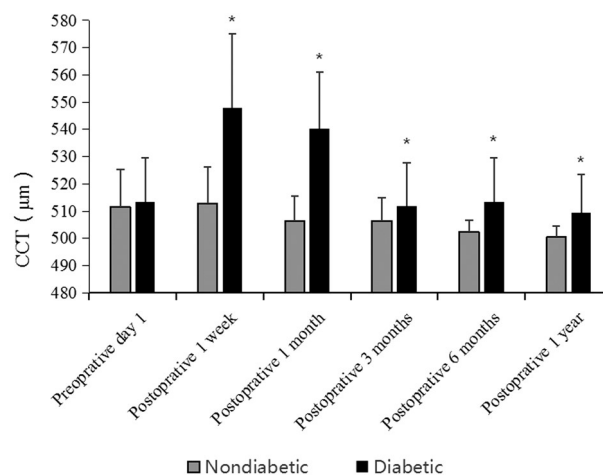


图4 糖尿病组和非糖尿病组患者术前1天、术后1周、术后1个月、术后3个月、术后6个月和术后1年CCT比较。用平均值 $\pm$ 标准误差表示
注:* 糖尿病组和非糖尿病组术后各时间点有差异($P_{\text{组间}} < 0.05$)。
Fig.4 Comparison of central corneal thickness(A) between the diabetic and nondiabetic groups at preoperative day 1 and postoperative 1 week, 1 month, 3 months, 6 months and 1 year. Data are shown as mean $\pm$ standard error(SE). *Diabetic group differed from nondiabetic group postoperatively at the time point($P_{\text{group}} < 0.05$)

3 讨论

本研究评估了糖尿病和非糖尿病患者在行白内障超声乳化吸出联合人工晶体植入手术后角膜内皮和中央角膜厚度的演变过程。在术后1年的观察期内,糖尿病和非糖尿病患者的ECD、PHC、CV和CCT都发生了显著变化。

角膜内皮细胞位于角膜最内层,为单层扁平六角形细胞,通过其屏障和泵功能对维持角膜脱水状态、厚度和透明度有重要作用^[4,5]。角膜内皮细胞在胚胎学上由神经嵴细胞发育而来^[6],可以分泌粘多糖基质胶原纤维维持其脱水状态。因此,有限的角膜内皮细胞对于角膜上皮细胞的正常转运功能有关键作用^[7,8]。

角膜内皮细胞在创伤和病理状态下会受损,如内眼手术和Fuchs 角膜内皮营养不良等,而内皮细胞的增殖能力有限不能再生^[9],角膜内皮细胞通过周边细胞的移行和扩展,可以起到代偿作用^[10],当损伤超过代偿范围,便可导致角膜不可逆的水肿和混浊,从而引起视力下降。角膜内皮细胞的丢失受多种因素影响,如手术史、白内障核硬度、角膜切口类型、年龄和术前视力等^[11]。所以 ECD 常为内眼手术常规检测指标,尤其在白内障、青光眼的术前和术后。

近期研究证实,一些因素如白内障术后、角膜移植术后等可以引起角膜内皮细胞损伤^[12]。在发病机制的探索中,有研究证实眼内微环境的改变可能导致角膜内皮细胞的丢失,并伴随白介素、单核细胞趋化蛋白和干扰素等因子^[13-15]。糖尿病可以增加内皮素的分泌,使眼部动脉收缩频率加快,血液循环受阻,导致无法正常供给角膜内皮细胞所需要的营养,角膜内皮细胞的结构发生改变^[16]。糖尿病患者角膜内皮细胞密度(mean cell density, ECD)、六角形细胞百分比(percentage of hexagonal cells, PHC)较正常人偏低^[17]。

本研究发现糖尿病组比非糖尿病组的 ECD 和 PHC 术后发生明显变化,提示内皮细胞减少, CV 值升高,提示发生了移行和扩展,它们的重新分布受糖尿病的影响。

通过对糖尿病患者和非糖尿病患者术后 1 年内 CCT 的观察证明,糖尿病患者的角膜内皮细胞功能较差,并在术后远期内恢复能力较差。角膜依靠内皮细胞的 Na^+/K^+ ATP 酶的泵作用维持基质中水和离子的平衡,使角膜处于脱水状态而保持透明。 Na^+/K^+ ATP 酶失活,使泵功能减弱,是导致糖尿病患者角膜水肿的重要机制^[18,19]。Herse 发现 69%-76%的糖尿病动物模型的内皮细胞 Na^+/K^+ ATP 酶活性减低^[20],导致角膜增厚,角膜增厚不是由于基质成分的增加,而是水的渗透增加。并且,角膜水肿已被证实与许多特殊因子相关,Tsaousis 等发现,除 2 型糖尿病外,超声能量是引起角膜水肿的决定性因素,尽管超声能力消失后不影响临床转归^[21]。糖尿病患者的基底膜和内皮细胞可能会由于自身结构的改变导致形态学改变,因此,糖尿病患者承受眼部手术创伤的能力较差^[2]并有研究发现糖尿病患者病程越长,血糖控制越不理想,其角膜厚度会显著增加^[22]。

本研究仍有许多局限性,如 HbA1c 和平均血糖值没有被纳入,尽管所有患者的血糖控制情况良好。术前和术后血糖的变化水平也没有进行检测,更多研究需要进行来观察血糖变化是否为影响术后的一个因素。在此情况下,本研究证明了糖尿病患者比非糖尿病患者行白内障超声乳化吸出联合人工晶体植入术后角膜内皮的形态和中央角膜厚度在术后远期内变化更明显。因此,在进行白内障超声乳化手术时,应该注意防止声波震动、高温和物理创伤的直接作用。

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