

氪激光联合 Nd : YAG 激光行激光虹膜切除术后一过性眼压升高发病机制

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Study on the pathogenesis of transient intraocular pressure after laser iridectomy with Krypton laser combined with Q -switched Nd : YAG laser

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Abstract

• AIM: To study the pathogenesis of transient intraocular pressure (IOP) after laser iridectomy with Krypton laser combined with Q-switched Nd : YAG laser.

• METHODS: Totally 42 healthy rabbits (84 eyes) provided by the Animal Experimental Center of our hospital were selected, including 18 female rabbits, 24 male rabbits, average weight 2.24 ± 0.31 kg, and they were randomly divided into 6 groups, 7 rats in each group (14 eyes). We observed the change of intraocular pressure after laser iridectomy surgery at 20min, 2, 6, 18, 24h and the nitric oxide (NO), malondialdehyde (MDA), superoxide dismutase (SOD), 6-keto-prostaglandin (6-keto-PGF 1α) and nitric oxide synthase (NOS) content in aqueous.

• RESULTS: There was no significant difference in intraocular pressure, NO, NOS, SOD, MAD and 6-keto-PGF 1α before operation ($P > 0.05$). The intraocular pressure increased after operation, and the difference was statistically significant ($P < 0.05$) at 20min, 2 and 6h after operation, and decreased at 18h after operation, 24h after operation ($P > 0.05$). The levels of NO, NOS and SOD in the aqueous humor of the two groups decreased 20min, 2 and 6h after the operation ($P < 0.05$), while increased after 6h, increased more at 18 and 24h. The difference with control group was no more significant ($P > 0.05$). The levels of MDA and 6-keto-prostaglandin in the aqueous

humor increased after the operation, and the difference was statistically significant at 20min, 2 and 6h after operation ($P < 0.05$), while decreased at 18 and 24h and the difference with control group was not significant ($P > 0.05$).

• CONCLUSION: The increase of transient intraocular pressure after laser iridectomy may relate to the increase of malondialdehyde, 6 - keto - prostaglandin content and the decrease of superoxide dismutase and nitric oxide in the aqueous humor after operation.

• KEYWORDS: Krypton laser; laser iridectomy; intraocular pressure elevation; aqueous

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摘要

目的: 研究氪激光联合 Q-开关 Nd : YAG 激光行激光虹膜切除术后一过性眼压升高的发病机制。

方法: 选取由本院动物实验中心提供的健康家兔 42 只 84 眼, 其中雌兔 18 只, 雄兔 24 只; 平均质量 2.24 ± 0.31 kg; 随机分为 6 组, 每组 7 只 14 眼, 其中 A、B、C、D、E 组分别为激光虹膜切除术后 20min, 2, 6, 18, 24h 组; F 组为正常对照组。观察各组术前及术后眼压和房水内丙二醛 (malondialdehyde, MDA)、一氧化氮 (nitric oxide, NO)、超氧化物歧化酶 (superoxide dismutase, SOD)、6-酮-前列腺素 F $_{1\alpha}$ (6 - 酮 - PGF 1α) 和一氧化氮合酶 (nitric oxide synthase, NOS) 含量的变化。

结果: 手术前各组眼压、房水内 NO、NOS、SOD、MDA、6-酮-PGF 1α 含量对比差异均无统计学意义 ($P > 0.05$)。术后 6h 内眼压升高, A、B、C 组分别与 F 组比较, 差异均有统计学意义 ($P < 0.05$), 术后 6h 以后呈下降趋势, D、E 组分别与 F 组比较, 差异均无统计学意义 ($P > 0.05$)。术后房水内 NO、NOS、SOD 含量呈下降趋势, A、B、C 组分别与 F 组比较, 差异均有统计学意义 ($P < 0.05$), 术后 6h 以后慢慢恢复, D、E 组分别与 F 组比较, 差异均无统计学意义 ($P > 0.05$)。术后房水内 MDA 和 6-酮-PGF 1α 含量呈上升趋势, A、B、C 组分别与 F 组比较, 差异均有统计学意义 ($P < 0.05$), 术后 6h 以后慢慢恢复, D、E 组分别与 F 组比较, 差异均无统计学意义 ($P > 0.05$)。

结论: 激光虹膜切除术后一过性眼压升高与术后房水内 MDA、6-酮-PGF 1α 含量升高和 SOD、NO 降低相关。

关键词: 氪激光; 激光虹膜切除术; 眼压升高; 房水

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0 引言

目前对于预防和治疗因瞳孔阻滞而引发的继发性或原发性青光眼简单且有效的方法为激光虹膜切除术(laser iridotomy, LI)。20世纪60年代已开始应用该手术,伴随着科学水平的发展和医疗技术的进步,该手术已是闭角型青光眼早期治疗的首选^[1-2]。当前我国使用的激光器主要有半导体激光、Nd:YAG激光等,其中Nd:YAG激光使用最多,单独使用它们进行虹膜切除术虽然也能成功,但术中能量使用较大,术后出现并发症的几率较高。近年来根据患者组织致密、基质厚和虹膜色素多等特点,相关专家使用氩激光或者Nd:YAG激光方式实施激光虹膜切除术,优势明显,一次透切成功率较高,术中所需能量低,术后并发症少^[3]。眼压升高是激光虹膜切除术后主要的并发症,虽然持续时间很短,但眼压快速升高会导致视力丧失和视野缺失等并发症。

1 材料和方法

1.1 材料

1.1.1 实验动物和分组 选取由本院动物实验中心提供的健康无眼底和眼前节疾病的家兔42只84眼,其中雌兔18只,雄兔24只,平均体质量 $2.24\pm0.31\text{kg}$ 。随机分为6组,其中A组:7只14眼,激光虹膜切除术后20min组;B组:7只14眼,激光虹膜切除术后2h组;C组:7只14眼,激光虹膜切除术后6h组;D组:7只14眼,激光虹膜切除术后18h组;E组:7只14眼,激光虹膜切除术后24h组;F组:7只14只眼,正常对照组。本研究严格遵守本院实验动物管理条例。

1.1.2 实验试剂和仪器 氧氟沙星眼膏(沈阳兴齐制药公司);Q-开关Nd:YAG激光器(美国Coherent公司);Schiotz眼压计(苏州医疗仪器公司);多波长氩激光仪(美国Coherent公司)。

1.2 方法

1.2.1 激光虹膜切除术 在虹膜切开接触镜下,先选用氪离子激光仪在鼻上方或者颞上方周边虹膜区(2:00或10:00位)进行击射^[4],激光使用黄绿光,激光参数:黄光波长568.2nm,绿光波长520nm;光斑直径200μm,功率300mW,曝光时间0.2s,击射点数30点。使用Q-开关Nd:YAG激光继续击射虹膜直至形成穿孔,直径大于0.3mm,激光参数:波长1064nm,共3个脉冲,能量10nJ。击透依据:可见蘑菇云状色素涌出并可见房水从后房经虹膜击孔涌入前房,前房立即加深或经激光孔见晶状体前囊。

1.2.2 眼压测量 用10g/L地卡因滴眼液点眼3次行表面麻醉,采用双砝码法检测眼压。实验动物取侧卧位,角膜朝上,眼压计垂直置于角膜中央,先用5.5g或7.5g砝码测量眼压,再用10g或15g砝码测量眼压,将5.5g砝码和10g砝码读数对读,或7.5g砝码与15g砝码对读,查眼压校正与眼壁硬度系数表,求得校正的眼压值。

1.2.3 房水检测 各组分别于术前和术后相应时间点测量眼压后取房水0.05mL。采用硝酸镁还原法^[5]检测一氧化氮(nitric oxide, NO)含量。采用分光光度法^[6]检测一氧化氮合酶(nitric oxide synthase, NOS)含量。采用黄嘌呤氧化酶法^[7]检测超氧化物歧化酶(superoxide dismutase,

表1 各组手术前后眼压变化情况 ($\bar{x}\pm s$, mmHg)

组别	眼数	术前	术后
A组	14	21.257 ± 2.067	33.177 ± 4.503
B组	14	21.493 ± 2.166	34.992 ± 7.031
C组	14	20.986 ± 2.148	25.985 ± 4.208
D组	14	21.058 ± 2.593	19.008 ± 3.017
E组	14	20.978 ± 2.561	20.165 ± 3.107
F组	14	21.025 ± 2.014	20.947 ± 2.947

注:A组:激光虹膜切除术后20min组;B组:激光虹膜切除术后2h组;C组:激光虹膜切除术后6h组;D组:激光虹膜切除术后18h组;E组:激光虹膜切除术后24h组;F组:正常对照组。

SOD)含量。采用硫代巴比妥酸荧光法^[8]检测丙二醛(malondialdehyde, MDA)含量。采用放射免疫法^[9]检测6-酮-前列腺素F_{1α}(6-酮-PGF1α)含量。

统计学分析: 使用SPSS20.0统计软件进行数据分析,计量资料采用 $\bar{x}\pm s$ 表示,组间两两比较使用独立样本t检验。 $P<0.05$ 表示差异有统计学意义。

2 结果

2.1 手术前后眼压变化情况 术前各组眼压差异无统计学意义($P>0.05$)。术后A、B、C组眼压均升高,分别与F组比较,差异均有统计学意义($t=3.074, 5.190, 4.002, P=0.014, 0.007, 0.031$)。术后D、E组眼压均降低,分别与F组比较,差异均无统计学意义($t=4.177, 6.104, P=0.337, 0.201$),见表1。

2.2 手术前后房水内NO和NOS含量变化情况 术前各组房水中NO和NOS含量差异均无统计学意义($P>0.05$)。术后房水内NO和NOS含量均呈下降趋势,A、B、C组分别与F组比较,差异均有统计学意义(NO: $t=4.184, 3.277, 5.086, P=0.006, 0.004, 0.010$;NOS: $t=4.285, 5.106, 4.772, P=0.026, 0.011, 0.031$);D、E组分别与F组比较,差异均无统计学意义(NO: $t=3.274, 4.001, P=0.206, 0.118$;NOS: $t=5.014, 3.174, P=0.116, 0.253$),见表2。

2.3 手术前后房水内SOD和MDA及6-酮-PGF1α含量变化情况 术前各组房水内SOD、MDA、6-酮-PGF1α含量差异均无统计学意义($P>0.05$)。术后A、B、C组SOD、MDA、6-酮-PGF1α含量分别与F组比较,差异均有统计学意义(SOD: $t=5.985, 3.706, 3.144, P=0.002, 0.007, 0.015$;MDA: $t=5.803, 4.991, 4.074, P=0.041, 0.006, 0.007$;6-酮-PGF1α: $t=4.190, 5.338, 5.072, P=0.001, 0.003, 0.007$)。术后D、E组SOD、MDA、6-酮-PGF1α含量分别与F组比较,差异均无统计学意义(SOD: $t=4.177, 5.003, P=0.219, 0.302$;MDA: $t=3.190, 5.692, P=0.082, 0.395$;6-酮-PGF1α: $t=5.902, 3.186, P=0.104, 0.101$),见表3。

3 讨论

青光眼是由于病理性高眼压致使视网膜的神经纤维遭到损坏,导致患者视力下降的致盲性眼科疾病^[10]。激光虹膜切除术是治疗闭角型青光眼的有效方法,但术后眼压会出现短暂升高,可能会造成视力丧失等后果。术后眼压暂时性升高一般出现在术后6h内,目前其发病机制尚不清楚,有学者认为术后高眼压和术后炎症反应有一定联系^[11-12]。同时也有研究显示,手术后眼压升高和术后房水内的SOD活性降低、6-酮-PGF1α浓度升高有关。本研

表2 手术前后房水内NO和NOS含量变化情况

 $\bar{x} \pm s$

组别	眼数	NO(μmol/L)		NOS(U/L)	
		术前	术后	术前	术后
A组	14	36.89±14.86	20.34±4.97	16.58±3.86	11.96±2.03
B组	14	37.12±16.08	17.06±4.15	16.49±3.77	10.11±2.07
C组	14	36.87±15.34	23.20±5.11	16.89±4.02	11.28±2.48
D组	14	36.99±15.81	38.92±7.08	16.05±3.67	14.18±4.35
E组	14	37.09±16.32	36.27±13.62	16.53±4.10	15.81±3.07
F组	14	37.02±15.08	36.91±18.05	16.82±3.22	16.37±4.05

注:A组:激光虹膜切除术后20min组;B组:激光虹膜切除术后2h组;C组:激光虹膜切除术后6h组;D组:激光虹膜切除术后18h组;E组:激光虹膜切除术后24h组;F组:正常对照组。

表3 手术前后房水内SOD和MDA及6-酮-PGF1α含量变化情况

 $\bar{x} \pm s$

组别	眼数	MDA(nmol/mL)		SOD(U/mL)		6-酮-PGF1α(pg/mL)	
		术前	术后	术前	术后	术前	术后
A组	14	3.026±1.453	5.995±2.031	113.52±25.74	44.91±16.08	144.65±50.21	3027.31±864.20
B组	14	3.159±1.529	8.264±1.605	112.66±26.81	54.38±23.04	146.02±48.73	1521.50±506.80
C组	14	2.997±1.608	8.816±1.442	114.02±25.39	66.31±25.09	145.66±51.29	953.90±264.20
D组	14	3.216±1.735	4.367±1.208	114.97±27.30	82.55±29.10	145.87±50.21	322.50±83.40
E组	14	2.985±1.408	2.556±0.448	113.64±26.85	100.33±41.72	144.09±49.65	185.10±67.20
F组	14	3.055±1.641	2.957±1.384	112.95±25.37	112.85±31.92	145.36±50.16	145.20±57.80

注:A组:激光虹膜切除术后20min组;B组:激光虹膜切除术后2h组;C组:激光虹膜切除术后6h组;D组:激光虹膜切除术后18h组;E组:激光虹膜切除术后24h组;F组:正常对照组。

究表明,术后20min、2、6h组眼压和房水内NO、NOS、SOD、MDA、6-酮-PGF1α含量和正常对照组比较,差异均有统计学意义($P<0.05$),而术后18、24h组和正常对照组比较,差异均无统计学意义($P>0.05$)。

氪激光产生的热效应与Nd:YAG激光产生的机械效应对虹膜组织细胞膜上磷脂酶有激活作用,使细胞膜磷脂裂解成花生四烯酸,在环氧化酶的作用下合成前列腺素G₂(prostaglandin G₂,PGG₂),再经一系列的氧化反应生成PGE2,从而增加眼部的炎症反应使眼压升高。Gabelt等^[13]采用放射性碘为示踪剂,用放射自显影法间接证明前列腺素(prostaglandin,PG)通过增加巩膜葡萄膜外流量发挥降压作用。氪激光虹膜切除术时,氪激光对虹膜组织产生光化学反应、压强效应与热效应,使房水和虹膜组织内氧自由基生成增加,SOD大量损耗,当氧自由基增多超过SOD等酶系清除能力时,过多的氧自由基可沉积在小梁网上,导致小梁内皮细胞的膜脂质和膜蛋白受损。同时氧自由基还可损伤小梁内皮的ATP泵,使小梁内皮细胞的水代谢发生障碍,致使内皮细胞水肿,小梁间隙变窄。此外,氧自由基可阻止酸性磷酸酶对酸性粘多糖的解聚作用,使小梁基质增多,小梁网增粗,小梁间隙变窄,房水流阻力增加,房水排出量减少,导致眼压升高^[14]。近年来一些血管内源性调节因子对小梁网运动的调节失衡越来越引起关注,特别是NO。NO是一种重要的信号分子,其可通过激活腺苷酸环化酶,提高环磷酸腺苷水平而发挥生物学效应,参与各种病理生理过程。Nathanson等^[15]研究发现正常人的睫状肌特别是从巩膜突伸向小梁网的纵行肌纤维和房水流通道中富含还原型辅酶染色阳性的物质即NOS;利用三种类型合成酶的抗体进行的免疫组化实验结果表明这些区域有大量的内皮结构类型的NOS表达,为NO维持正常眼压及其参与青光眼的发病过程提供了解剖学依据,同时发现在慢性开角型青光眼中此部位的

NOS明显降低。

综上所述,激光虹膜切除术后一过性眼压升高与术后房水内MDA、6-酮-PGF1α含量上升和SOD、NO含量降低相关。

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