THE ESTABLISHMENT OF THE MONKEY MODEL OF ACUTE GLAUCOMA INDUCED BY LASER PHOTOCOAGULATION OF TRABECULAR MESHWORK

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Background: The first article on the laserinduced non-human primate (NHP) high intraocular pressure model was published by Gasterland and Kupfer in 1974. In the past 40 years, this model has gradually matured and has been used in studying the pathogenesis and treatment of glaucoma. An advantage of this model is that the structure anatomy of NHP's optic nerve head is similar to that of humans. This model is also used to study the early damage to the visual system caused by increased intra-ocular pressure.

Purpose: Induce acute ocular hypertension by laser photocoagulation of trabecular meshwork in cynomolgus monkey. Measure the ocular pathophysiological changes caused by ocular hypertension to provide an experimental model for the efficacy of glaucoma and neuroprotective drugs.

Method: A total of 15 cynomolgus monkeys with no abnormal eyes were used in this experiment, including 8 males and 7 females. All animals went through about 3 weeks of behavioral training and intraocular pressure measurement while conscious. The right eye of the animal was photocoagulated with a 532 nm laser via a gonioscope, and the left eye was left untreated as control. In order to reduce inflammation and pain, laser modeling was performed twice, 180 degrees each time and 21 days apart. The last modeling day was set as D1. Before modeling, and on D4, D8, D11, D15, D18, D22, D25 and D29, intra-ocular pressure of both eyes were measured with a pneumatic tonometer while the animals were conscious. Before modeling, and on D8, D15 and D22, slit lamp inspection and OCT (including anterior and posterior segments) and fundus photography were performed. Fundus fluorescein angiography was performed before modeling and on the day of the last inspection (FFA). On D29, all animals were euthanized. Both eyes were taken, retina was separated and plated, and ganglion cells were counted.

Result: The abnormalities observed by the slit lamp after animal modeling include: conjunctival hyperemia, corneal edema, enlarged sputum, slow reflection of the sputum, iris adhesions, anterior chamber cells, and deposits on the surface of the lens. After modeling, the intraocular pressure of the right eye (modeled eye) at each checkpoint was significantly higher than before modeling. There was no statistically significant change in the left eye. Compared with before the operation, the retinal nerve fiber layer (RNFL) on the upper nasal, nasal side, inferior temporal, temporal and optic disc of the modeled eyes increased significantly on D8, and RNFL on the nasal side and optic dis increased significantly on D15 ($P \leq 0.05$), and then gradually recovered. The minimum rim width width (MRW) of the moulding eye decreased after the operation and the differences on D15, D22 and D29 were statistically significant ($p \leq 0.05$). The corneal center thickness (CCT) of the moulding eye increased significantly after the operation. RNFL, MRW and CCT of the areas around the left eye disc did not have statistically significant changes. Compared with the unmoulded left eye, RGC density on the right eye decreased with no statistically significant difference.

Conclusion: Laser photocoagulation of the trabecular meshwork successfully induced an increase in the intraocular pressure in cynomolgus monkeys. 4 weeks after modeling, as the time of increasing intraocular pressure prolonged, minimum rim width decreased and central corneal thickness increased in the modeled eye. RGCs density decreased 4 weeks after modeling. These changes were similar to the manifestations of patients with early clinical glaucoma, suggesting that this model could be used to study the mechanism and effectiveness of the medical treatment of early glaucoma injuries.

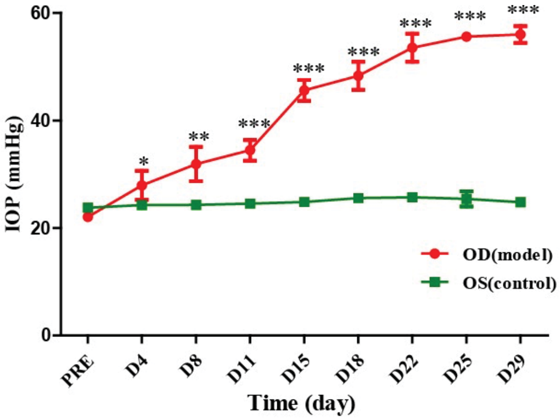


图 1. 激光光凝食蟹猴小梁网后对动物眼内压的影响

Figure 1. The effect of laser photocoagulation on intraocular pressure of cynomolgus monkey trabecular meshwork (modeled right eye compared with control left eye, "*" indicates p≤ 0.05, "**" indicates p≤ 0.01, "***" indicates p≤ 0.001, same as below)

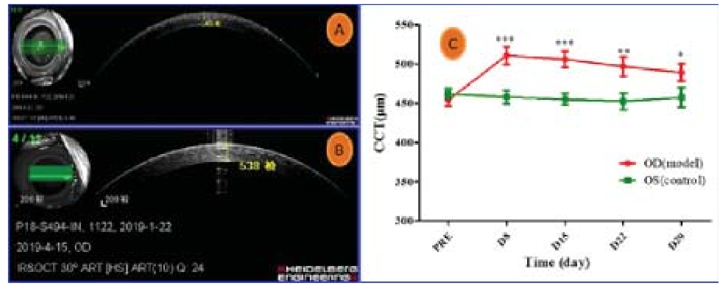


Figure 4. Changes of corneal thickness in the center of the eyes after laser photocoagulation of cynomolgus trabecular meshwork

(A Measurements of corneal thickness in the center of the modeled eye; B Corneal thickness increased 2 weeks-D15 after laser photocoagulation; C Graph of changes in corneal thickness.)

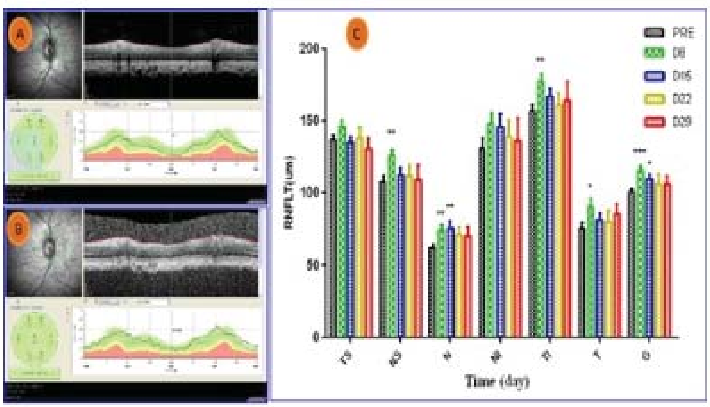


Figure 2. The effect of laser photocoagulation of cynomolgus monkey trabecular meshwork on the thickness of the retinal nerve fiber layer around the optic nerve head of the animal model

(A Illustration of the thickess of RNFL around the modeled eye disc before laser photocoagulation; B RNFL thickness increased after 1 week-D8 of laser photocoagulation; C Histogram of changes in RNFL thickness around the optic nerve head.)

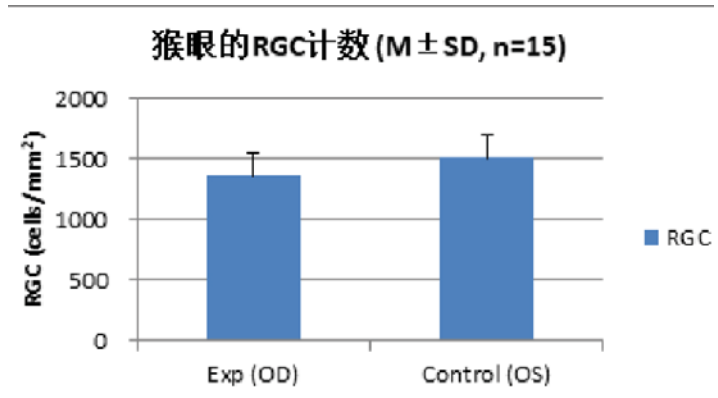
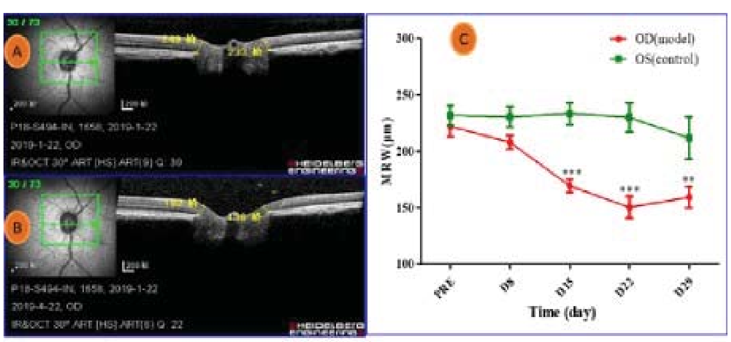


Figure 5. Counting results of retinal ganglion cells (RGCs) in the eyes of animals after laser photocoagulation of cynomolgus trabecular meshwork



小 目 小 的变化
(A 激光光凝前，造模眼最小盘沿宽度测量图例；B 激光光凝后 4 周 -D29，造模眼最小盘沿宽度减小；C 双眼最小盘沿宽度 。

Figure 3. Changes in MRW of both eyes after laser photocoagulation of cynomolgus monkey trabecular meshwork

(A Illustration of MRW measurement before laser photocoagulation; B MRW decreased 4 weeks-D29 after laser photocoagulation; C Graph of changes in MRW.)