· Original article ·

Acute reversible lens opacity affects retinal HRA + OCT imaging in mice

Cai-Rui Li[1,2], *Shu-Guang Sun*[1], *Ireni Ali Rahman*[2,3], *Chooi May Lai*[2,3]

[1]Department of Ophthalmology, the Hospital of Dali University, Dali 671000, Yunnan Province, China
[2]Lions Eye Institute, Molecular Ophthalmology Department, Nedlands, Australia
[3]Centre for Ophthalmology and Visual Science, University of Western Australia, Nedlands, Australia
Correspondence to: Cai-Rui Li. Department of Opthalmology, the Hospital of Dali University, Dali 671000, Yunnan Province, China. lcrbrett@ hotmail. com
Received:2009-11-17 Accepted:2009-12-28

Abstract

• AIM: To assess the affect of ketamine and xylazine (ketamine/xylazine) to the transient lens opacity in mice.
• METHODS: Kimba mice (n = 10) and wild-type mice (wt, n = 8) were sedated with intraperitoneal injection of ketamine (60mg/kg for mice) and xylazine (10mg/kg) at 4, 8, 12 and 16 weeks old respectively. Pupils were dilated with tropicamide 25g/L alone to allow imaging lens status and retina using Spectralis HRA + OCT.
• RESULTS: All Kimba mice and wt presented extreme proptosis, suppression of the eye-blink reflex, corneal surface drying and lens opacities which occurred as early as 21 ± 6 minutes after giving anesthesia and the lens opacities lasted up to 150 ± 24 minutes.
• CONCLUSION: Ketamine/xylazine can cause transient lens opacity that may be related with the drugs' side-effect.
• KEYWORDS: ketamine; xylazine; proptosis; lens opacity; mouse
DOI:10. 3969/j. issn. 1672-5123. 2010. 01. 007

Li CR, Sun SG, Rahman IA, Lai CM. Acute reversible lens opacity affects retinal HRA + OCT imaging in mice. *Int J Ophthalmol (Guoji Yanke Zazhi)* 2010;10(1):21-22

INTRODUCTION

Spectralis HRA + OCT offers a combination of OCT imaging with fluorescein angiography (FA). The system can track ocular movement and image the mice retina longitudinally with high accuracy. Combined administration of ketamine and xylazine is used increasingly for safe, effective anesthesia of small laboratory animals. We reported that mice injected with ketamine and xylazine at doses recommended for effective anesthesia[1] developed transient lens opacities that interfere with the retinal imaging using HRA + OCT.

MATERIALS AND METHODS

Materials Kimba mice(n = 10) and wild type mice(wt, n = 8) in the study were divided into 4 groups (4, 8, 12 and 16 weeks old group). All the mice were housed in cages at a constant temperature of 22℃, with a 12∶12h light/dark cycle, and food and water were available. All animal procedures were performed in accordance with the ARVO statement for the use of animals in ophthalmic and vision research and with approval from the animal ethics committee at the University of Western Australia, Australia.

Methods Mice were anesthetised with ketamine (60mg/kg intraperitoneal, Morris Plains, NJ) and xylazine (10mg/kg intraperitoneal, Leverkusen, Germany) 0. 1mL. Kimba mice (n = 10) and wt (n = 8) were examined at 4, 8, 12 and 16 weeks postnatal respectively. Following pupil dilation (25g/L tropicamide, Alcon, Fort Worth, TX), the retinal image and lens status were examined using Spectralis HRA + OCT (Heidelberg, Germany) at equally spaced angular orientations (30°) and both eyes were examined.

RESULTS

All Kimba mice and wt presented extreme proptosis, suppression of the eye-blink reflex, corneal surface drying and lens opacities which occurred as early as 21 ± 6 minutes after giving anesthesia. Total cataract formed in 30 ± 7 minutes (Figure 1) and the lens opacities lasted up to 150 ± 24 minutes since the mice waked up from anesthesia.

The FA image became vague and OCT scan could not be completed because of lens opacity (Figure 2). The retina can not be imaged any more when total cataract is formed.

DISCUSSION

Mice are important model organisms in many fields of science. Spectralis HRA + OCT is a novel method of retinal imaging. When we used HRA + OCT to analyze the retinal vascular and retinal thickness change in Kimba and wt mice, all the mice presented proptosis and lens opacities after intraperitoneal ketamine/xylazine anesthesia. Lens opacities occurred as early as 21 ± 6 minutes after the beginning of anesthesia and total cataract formed in 30 ± 7 minutes and the retina can not be imaged any more by HRA + OCT. The lens opacities lasted up to more than 150 ± 24 minutes since the mice waked up from anesthesia. Mice given the same drug doses were similarly affected. We think that the lens opacity is induced by the ketamine and xylazine side-effect. It was reported that ketamine can cause reversible changes in the rat brain and 40mg/kg may result in fluid-filled cavities appearing inside cells. The cavities disappeared after several days[2]. In a study of 9 daily ketamine users, biopsies revealed epithelial denudation and inflammation with a mild eosinophilic infiltrate[3].

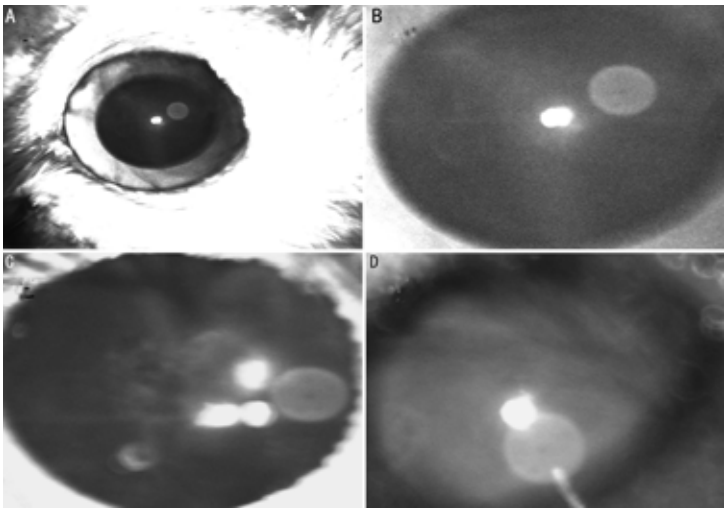

Figure 1　Lens opacity after anesthesia in mice　A: The eye with contact lens; B: Clear lens 5 minutes after anesthesia; C: Partial lens opacity formed 21 ± 6 minutes after anesthesia; D: Total cataract formed 30 ± 7 minutes after anesthesia.

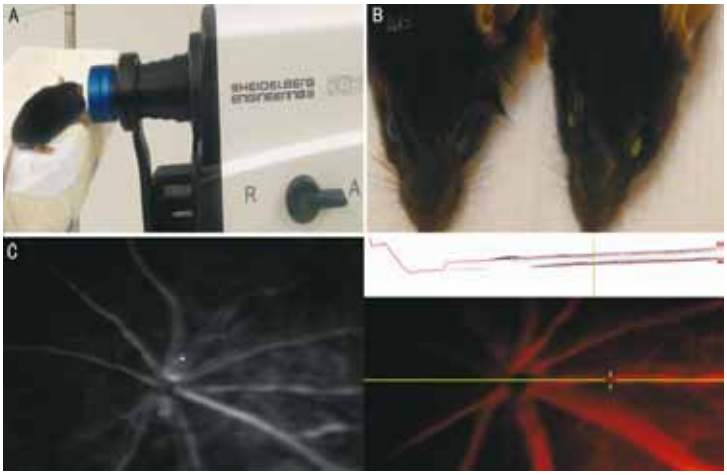

Figure 2　HRA + OCT examination　A: Testing; B: Cataract and proptosis in two mice; C: Vague FA and OCT because of lens opacity.

Some reports found that expression of TNF-alpha and VEGF increased in the aqueous humor of the patients undergoing ketamine anesthesia[4]. Others thought the appearance of lens opacities were associated to varying degree with proptosis, suppression of the blink reflex and corneal surface drying[5]. Ketamine/xylazine anesthesia can facilitate the development of UVR-induced cataract in the rats[5]. A plausible explanation of ketamine/xylazine-induced transient lens opacification is that ketamine/xylazine can cause extreme proptosis and corneal surface drying, alter the aqueous cytokines and cause reversible protein change in the lens. Therefore, the side-effect of ketamine/xylazine combination should be considered as the main cause of transient lens opacity in mice.

REFERENCES

1 Calderone L, Grimes P, Shalev M. Acute reversible cataract induced by xylazine and by ketamine-xylazine anaesthesia in rats and mice. *Exp Eye Res* 1986;42:331-337

2 Olney JW, Labruyere J, Price MT. Pathological changes induced in cerebrocortical neurons by phencyclidine and related drugs. *Science* 1989;244(4910):1360-1362

3 Shahani R, Streutker C, Dickson B, Stewart RJ. Ketamine-associated ulcerative cystitis: a new clinical entity. *Urology* 2007;69(5):810-812

4 Tu KL, Kaye SB, Sidaras G, Taylor W, Shenkin A. Effect of intraocular surgery and ketamine on aqueous and serum cytokines. *Mol Vis* 2007;12(13):1130-1137

5 Zhang F, Löfgren S, Söderberg PG. Interaction of anaesthetic drugs and UV-B irradiation in the anterior segment of the rat eye. *Acta Ophthalmol Scand* 2007;85(7):745-752

影响小鼠视网膜检查的突发性可逆性晶状体混浊

李才锐[1,2], 孙曙光[1], Ireni Ali Rahman[2,3], Chooi May Lai[2,3]
(作者单位:[1] 671000 中国云南省大理市,云南大理学院附属医院眼科;[2] 澳大利亚狮子眼科研究所分子眼科中心;[3] 西澳大学眼科和视光学中心)
作者简介:李才锐,博士,副教授,副院长,研究方向:玻璃体视网膜病变。
通讯作者:李才锐. lcrbrett@ hotmail. com

摘要

目的:评价氯胺酮/甲苯噻嗪麻醉对小鼠晶状体的影响。

方法:用氯胺酮(60mg/kg)/甲苯噻嗪(10mg/kg)腹腔注射,分别麻醉 4,8,12 和 16wk 的 Kimba 小鼠(n = 10)和野鼠(n = 8)。托吡卡胺眼液(25g/L)扩大瞳孔后用 HRA + OCT 检查晶状体状态和视网膜病变。

结果:所有的 Kimba 小鼠和野鼠都出现严重的眼球突出,眨眼反射消失,角膜干燥和晶状体混浊。最早的晶状体混浊发生在麻醉后的 21 ± 6min,晶状体混浊可持续 150 ± 24min。

结论:氯胺酮/甲苯噻嗪麻醉可导致暂时性晶状体混浊,晶状体混浊与氯胺酮/甲苯噻嗪的副作用有关。

关键词:氯胺酮;甲苯噻嗪;眼球突出;晶状体混浊;小鼠