PDo05-12
Anaesthesia during corneal transplantation in children
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Background: Corneal transplantation (= keratoplasty) is the only therapy of choice for most causes of corneal blindness and is a procedure consisting of full-thickness replacement of the corneal. During surgery, reduced intraocular pressure is necessary and expulsive bleeding to be avoided.

Aim: We present anaesthesiological experience in paediatric keratoplasty.

Methods: This retrospective study includes 17 children (mean age 9.8 ± 4.9 years, min 1.5 years, max 15.8 years) having had keratoplasty from 2008 to 2015 at the Saarland University Medical Centre in Homburg, Germany. All patients received intravenous fentanyl, propofol, and atracurium (0.5 mg·kg⁻¹·“body weight”⁻¹) before endotracheal intubation. Anaesthesia was maintained with desflurane (MAC 0.5) and remifentanil (0.25 μg·kg⁻¹·“min”⁻¹). All children received acetazolamide (1 mg·kg⁻¹·“body weight”), mannitol 10% (1 g·kg⁻¹·“body weight”), and the upper part of the body was elevated by 30°. Before surgical opening of the eye, intravenous atracurium (0.1 mg·kg⁻¹·“bodyweight”⁻¹) was administrated if the train-of-four was not elevated by 30°. Intraocular pressure was monitored by surgeons using subjective grades of vis a tergo (grade 0–4).

Results: Two patients had vis a tergo grade 1. Thirteen cases had vis a tergo grade 2, and two cases had an iris prolapse beyond the level of corneal incision (vis a tergo grade 3). Expulsive haemorrhage was not observed in this survey. In all patients, corneal transplantation was successful.

Conclusion: Measures to reduce intraocular pressure and full relaxation should be used to ensure successful keratoplasty in children.

Keywords: ocular pressure, ophthalmology, paediatric, surgery, keratoplasty

PDo06-01
Efficacy of novel small molecule-based NLRP3 inhibitors in retinal pigment epithelial cells
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Purpose: Activation of the NLRP3 inflammasome has been reported in the retinal pigment epithelium (RPE) of patients with atrophic age-related macular degeneration (AMD) and has been suggested to contribute to disease pathogenesis. Recently developed small molecule-based specific NLRP3 inhibitors may provide a novel therapeutic strategy for atrophic AMD. We tested these NLRP3 inhibitors for their efficacy in human RPE cells, using different in vitro models of oxidative and photooxidative damage-induced inflammasome activation.

Methods: Human primary RPE cells (Lonza, Cologne, Germany) and ARPE-19 cells primed with IL-1α were subjected to either lysosomal membrane permeabilisation (LMP) by Leu-Leu-OMe, oxidative damage induced by hydrogen peroxide (H₂O₂), or lipofuscin-mediated phototoxic digestion induced by incubation with 4-hydroxynonenal (HNE)-modified photoreceptor outer segments and subsequent blue light irradiation. Inflammasome activation was assessed by measuring release of IL-1β, IL-18, and lactate dehydrogenase (LDH). For NLRP3 inhibitor treatment, cells were incubated with IFM-632 (IFM Therapeutics, Bonn, Germany) or MCC950 (Merck, Darmstadt, Germany). Caspase-1 inhibitor Z-YVAD-FMK served as control.

Results: Induction of LMP, oxidative damage, and photooxidative damage each resulted in pronounced inflammasome activation in primed RPE cells with release of IL-1β and IL-18 as well as pyroptotic LDH release. NLRP3 inhibitors IFM-632 and MCC950 suppressed inflammasome activation in all three models with reduction of IL-1β, IL-18, and LDH release. E.g., oxidative stress by incubation with 5 mM H₂O₂ resulted in 27.9% pyroptosis which was reduced by co-incubation with 0.01 μM IFM-632, 0.01 μM MCC950, and 20 μM caspase-1 inhibitor Z-YVAD-FMK to 9.6% (p < 0.001), 20.6% (p = 0.001), and 9.7% (p < 0.001), respectively. In all models, IFM-632 exhibited a stronger effect compared to MCC950 at equimolar concentration.

Conclusion: Novel small molecule-based NLRP3 inhibitors are effective in human RPE cells and thus represent promising drugs for the evaluation of inflammasome inhibition as a new therapeutic strategy in atrophic AMD.

PDo06-02
Topological distribution and potential role of beta-synuclein in the aging RPE in vitro
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Background: Next to age-related changes of refracting optic media and neuroretina, age-related alterations occur also within the retinal pigment epithelium (RPE). These conditions include increasing oxidative stress, accumulation of lipofuscin and protein degradation. In previous studies, an age-related increase of the protein beta-synuclein (SNCA) in parts of the visual system including neuroretina has been shown. SNCA may function as an antagonist of neurotoxic alpha-synuclein (SNCA) and may reduce pro-apoptotic p53-activity and inflammation. The underlying mechanisms of SNCA within the RPE are not sufficiently known. The aim of this study is a morphological characterization of the aging RPE and the possible role of SNCA within the RPE in vitro.

Methods: Paraffin-embedded eyes of the marmoset monkey Callithrix jacchus of different ages were studied regarding morphological and histological characteristics under consideration of macula and periphery. Furthermore, the intracellular occurrence and expression pattern of SNCA and SNCA was examined in paraffin-embedded eyes of C. jacchus, ARPE-19 cells and primary porcine RPE (ppRPE) cells in vitro. To analyze the functions of SNCA including cell viability; apoptosis and the p53-MDM2 signaling cascades. ARPE-19 cells and ppRPE cells were incubated with different SNCA concentrations and viability, apoptosis and protein and gene expression (e.g., p53, MDM2) were analyzed.

Results: Histological results indicate age-related morphological changes with varieties especially in the cell shape and characteristics of intracellular pigmentation of the aging RPE. Distinct alterations have been found in the macula in contrast to peripheral regions. While an exposition of ARPE-19 and ppRPE cells with different concentrations of SNCA did not influence the viability of the cells, a decrease in apoptosis was shown. The expression of SNCA was influenced by the presence of SNCA. Analysis of the p53-MDM2 pathway revealed an activation.

Conclusion: The present work shows, that the aged RPE shows morphological changes with distinct differences between the macular and peripheral localizations. Next to alterations of the SNCA expression between macular and periphery, an influence of SNCA on essential cellular functions suggests, that SNCA is relevant in age-related processes in the RPE. However, further studies are mandatory to characterize the role SNCA within the aging RPE.

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