Electroretinography Evaluation in the Göttingen Minipig: Another Animal Model for Ocular Preclinical Safety Assessment

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INTRODUCTION

The minipig eye shares many similarities to the human eye; making them a favorable large animal model choice in ocular toxicology testing. Electroretinography (ERG) is a common end point employed to evaluate retinal toxicity following systemic exposure or ocular administration.

MATERIAL AND METHODS

ERGs were recorded using the EPIC-4000 computerized system with a Ganzfeld dome from LKC Technologies and contact lens electrodes referenced to a sub-palpebral electrode and a ground electrode placed at Cz. The left eyes were dosed by intravitreal injection into the posterior chamber at dose volume of 100 µL using a standard 30G needle attached to a 1-mL syringe. Three different compounds were assessed across three groups of animals; gentamicin (5 mg/eye, 3 eyes), indocyanine green (ICG; 0.25 mg/eye, 4 eyes) and glycine (5 mg/eye, 3 eyes). The right eye served as an untreated control.

The ERG protocol included a scotopic luminance-response curve analysis (-4.09 log cds/m² to 0.90 log cds/m²) with an average of three responses for each light intensity except for oscillatory potentials, where an additional single flash was also used at 0.41 log cds/m². Prior to assessment, the animals were dark adapted for a minimum of 30 minutes. The photopic evaluation included a single flash (averaged response) followed by a flicker response at 30.3 Hz at 0.41 log cds/m². Prior to assessment, the animals were subjected to light adaptation using the Ganzfeld background light, for at least 5 minutes.

RESULTS

When compared to control eyes, there were increases in scotopic a-wave amplitudes in eyes given 5 mg gentamicin (-0.59 to 0.90 log cds/m²) and eyes given 5 mg glycine (0.41 to 0.90 log cds/m²). Scotopic b-wave amplitudes were increased for eyes given 5 mg glycine (-2.09 to 0.90 log cds/m²); whereas decreased amplitudes were observed in eyes given 5 mg gentamicin (-1.59 to 0.90 log cds/m²). Eyes given 0.25 mg ICG were mildly decreased at lower light intensities (2.09 to -0.90 log cds/m²), but at greater light intensities (>0.41 log cds/m²), the amplitudes were generally within the control range. Photopic b-wave amplitudes were decreases in eyes given 5 mg glycine and in eyes given 5 mg gentamicin. There were no treatment-related effects on scotopic or photopic a- or b-wave implicit time and latency. Marked reductions in oscillatory potentials (~4-fold) and flicker response (~3-fold) were noted in eyes given 5 mg glycine and eyes given 5 mg gentamicin. Log K, which is representative of retinal sensitivity, was reduced in the eyes given 5 mg gentamicin, but increased in the eyes given 5 mg glycine when compared with the contralateral untreated control eyes. As previously published, all expected effects were seen following intravitreal glycine or gentamicin administration. The ERG protocol evaluated in minipigs here could be considered in the assessment of retinal toxicity in preclinical toxicology studies.

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