Development of an Intracameral Administration and Ocular examination for Beagle Dogs

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Rationale:

A rapid expansion of new technologies in ocular drug delivery and new drug candidates to treat challenging ocular diseases have recently emerged. These approaches are necessary as the eye has many unique barriers to drug delivery. Intracameral administration is a technique that involves injecting a drug directly into the anterior chamber of the eye. Intracameral administration has the advantage of rapidly achieving high intraocular concentrations of drug directly at the target tissue; however, sudden increase in drug concentration may cause toxicity to the cornea, development of cataract and inflammation[1].

Different assessments and capabilities in nonclinical ocular evaluation are in high demand and this poster reports a few of the evaluations available in laboratory Beagle dogs.

The objective of the study was to assess an intracameral administration method along with ocular examination procedures that will be used for upcoming nonclinical toxicology ocular studies.

Experimental Procedures:

- Povidone and saline solution flushes were performed prior to the injection. Medetomidine and isoflurane were used for the anesthesia prior to and/or during the procedure as needed and Atipamezole was used as a reversal agent.
- Two Beagle dogs were administered a single bilateral intracameral administration of 20 µL saline or had a needle inserted through the cornea at approximately 1 mm from the limbus and parallel to the iris.
- Aqueous humor samples were collected 3 days after the injection from the left eye of 2 dogs.
- Ocular examinations were performed 3 to 15 days after the injection.

Ocular parameters monitored during the study:

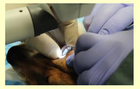
-Ocular evaluation was performed using a hand held slit lamp biomicroscope and indirect ophthalmoscope.

Pupillometry (Pupil diameter)

Tonometry (Intraocular pressure)

Pachymetry (Corneal thickness)

Gonioscopy (Iridocorneal angle)



Specular Microscopy (Corneal endothelium)

RESULTS

Ocular clinical signs: mild redness, eye discharge and pupil dilation were seen a few days after the injection.

Biomicroscopy (slit lamp) and Indirect Ophthalmoscopy Observation:
Minor changes related to the injection and aqueous humor collection procedure were observed, including corneal opacity and vascularization (superotemporal aspect of cornea at the injection site), and were not considered adverse. The pupil light response was normal for all dogs.

OCULAR PARAMETERS (RIGHT EYE)

PUPIL DIAMETER (mm)							INTRAOCULAR PRESSURE (mmHg)									CORNEAL THICKNESS (µm)						
	PRE-INJECTION			POST -INJECTION				PRE-INJECTION				POST -INJECTION					PRE-INJECTION			POST -INJECTION		
ANIMALS	#1	#2	MEAN	#1	#2	MEAN	ANIMALS	#1	#2	#3	MEAN	#1	#2	#3	MEAN	ANIMALS	#1	#2	MEAN	#1	#2	MEAN
#1	9.1	9.3	9.2	8.9	8.9	8.9	#1	21	20	19	20	25	25	23	24	#1	663	655	659	658	650	654
#2	9.5	10.0	9.8	9.7	10.0	9.9	#2	26	23	25	25	22	22	19	21	#2	578	580	579	581	582	582
MEAN	9.3	9.7	9.5	9.3	9.5	9.4	MEAN	24	22	22	23	24	24	21	23	MEAN	621	618	619	620	616	618
SD	0.28	0.49	0.42	0.57	0.78	0.71	SD	3.5	2.1	4.2	3.5	2.1	2.1	2.8	2.1	SD	60.1	53.0	56.6	54.4	48.1	51

CORNEAL ENDOTHELIAL CELL LAYER (RIGHT EYE)

PRE-INJECTION												POST-INJECTION											
CENTRAL CORNEA						CENTRAL INFERIOR CORNEA						CENTRAL CORNEA						CENTRAL INFERIOR CORNEA					
ANIMAL	No. of Cells	Cell Density (cell/mm²)	Hexagonal Cells (%)	CV	SD	ANIMAL	No. of Cells	Cell Density (cell/mm²)	Hexagonal Cells (%)	CV	SD	ANIMAL	No. of Cells	Cell Density (cell/mm²)	Hexagonal Cells (%)	CV	SD	ANIMAL	No. of Cells	Cell Density (cell/mm²)	Hexagonal Cells (%)	CV	SD
#1	197	2764	70	22	75	#1	131	2677	66	25	90	#1	198	2623	72	20	74	#1	145	2721	66	25	88
#2	188	2386	66	22	87	#2	123	2497	72	19	72	#2	222	2524	73	18	68	#2	145	2490	71	22	83
MEAN	193	2575	68	22	81	MEAN	127	2587	69	22	81	MEAN	210	2574	73	19	71	MEAN	145	2606	69	24	86
SD	6.4	267.3	2.8	0.0	8.5	SD	5.7	127.3	4.2	4.2	12.7	SD	17.0	70.0	0.7	1.4	4.2	SD	0.0	163.3	3.5	2.1	3.5

Aqueous humor collection:
One sample of 0.1 mL was successfully collected 3 days after the injection.

Gonioscopy:
Iridocorneal angle size of 3 and 4 was measured in each eye according to the Shaffer scoring scale[2].

Discussion:

A single bilateral intracameral administration of saline or an insertion of a needle (sham dosing) as well as different ocular parameters were easily performed in laboratory Beagle dogs with no significant changes.

A volume of 0.1 mL of aqueous humor fluid was collected from the left eye without important ocular side effects.

A single bilateral administration of saline or needle insertion in the anterior chamber eye caused only minor ocular changes such as corneal opacity and vascularization and were considered procedure-related.

The pupil diameter, intraocular pressure and corneal thickness had similar values before and 3 to 15 days after the saline administration or needle insertion.

The corneal endothelium in the central and inferior aspect of the cornea were easily evaluated in these dogs. The dosing procedure and sampling collection of the aqueous humor did not affect the endothelial cell layer.

Reference:

1-Bartlett J. and A.P. Cullen. (1989) Clinical Ocular Pharmacology, (2nd edition, Butterworth-Heinemann, pp. 55). Elsevier, Stoneham.

2-Shaffer, R.N. (1960). Primary glaucomas. Gonioscopy, ophthalmoscopy and perimetry. *Trans Am Acad Ophthalmol Otolaryngol,* Vol 64, (Mar-Apr 1960) pp.112-127.