EVALUATION OF THE TOXICITY OF INTRAVITREAL CARBOPLATIN INJECTION IN A RABBIT MODEL


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Carboplatin

- **Carboplatin:**
  - belong to the group of platinum based antineoplastic agents
  - chemotherapy drug used in a variety of cancers
  - Carboplatin is a widely used chemotherapy agent in the treatment of retinoblastoma
Retinoblastoma
Retinoblastoma

The leading treatment for retinoblastoma is:

- Intravenous chemotherapy
- Intra-arterial chemotherapy
Retinoblastoma

- **Vitreous seeding** - a limiting factor in the success of globe-preserving therapies

**Melphanan:**

- Toxicity
- Instability
- Cost
Carboplatin

- Carboplatin Delivery methods in retinoblastoma:
  - Intravenous
  - Periocular
  - Intra-arterial

- Intravitreal carboplatin administration toxicity was not examined to date
PURPOSE:
The purpose of this study was to evaluate the toxicity of intravitreal carboplatin injection in a rabbit model.
**Methods:**

- The study included Ten New Zealand albino male rabbits
- Weighing 1.8 to 2.2 kg each
- Handled according to the association for research in vision and ophthalmology (ARVO) Statement for the use of Animals
Methods:

- The rabbits were given a single carboplatin intravitreal injection
- In varied dosage (3-8µg) / 0.1 ml in one eye
- The second eye was used as control
Methods

• **Outcome methods:**
  
  • Anatomical evaluation
  
  • Functional evaluation
  
  • Histopathological evaluation
Methods - clinical evaluation:

- Evaluation of changes in cornea, lens, vitreous, retina, and optic nerve Under Anesthesia

*Baseline day, Weeks 2, 4, 6
Methods - clinical evaluation:

- Intraocular pressure measurement
- Slit lamp examination
- Indirect ophthalmoscopic fundus examination
Methods - toxicity evaluation:

- **Anatomical (in vivo):**
  - Optical Coherence Tomography (OCT)
  - Ultrasound (US) anterior and posterior examinations

*Baseline day, Weeks 2, 4, 6*
Methods - toxicity evaluation:

- **Anatomical (in vivo)**:
- Optical Coherence Tomography (OCT)
Methods - toxicity evaluation:

- **Anatomical (in vivo)**:
  - anterior and posterior Ultrasound (US) examinations
Methods - toxicity evaluation:

- **Functional:**
  - The electroretinogram (ERG) is a diagnostic test that measures the electrical activity generated by the cells in the retina in response to a light stimulus.
  - Repeated electroretinogram (ERG) under photopic and scotopic conditions.

*Baseline day, Weeks 2, 4, 6*
Methods - toxicity evaluation:

- **Histology:**
  - After euthanasia the eyes were fixated and submitted for histopathological evaluation
Results:

- All the eyes (study and control) had Normal:
  - ✔ IOP examination
  - ✔ anterior segment examination
  - ✔ fundus examination
  - ✔ OCT examination
  - ✔ US examination
  - ✔ histopathological evaluation at all the examination points
ERG Results:

Scotopic conditions
ERG Results:
Methods- toxicity evaluation:

- Cell toxicity or cell death
- Retinal cell count:
  - Outer nuclear layer
  - Inner nuclear layer
Methods - toxicity evaluation:

(A) Axial section

(B) Upper & (C) lower Sagittal sections
Methods - toxicity evaluation:

(A) Axial section

(B) Upper & (C) Lower Sagittal sections
Methods - toxicity evaluation:
Retinal cell count results

Average cell count in 3,4,5,6,8 μg carboplatin injections
Conclusions:

- Intravitreal carboplatin injection appears to be safe in the dosage of 3- 4 µg/0.1 ml in a rabbit model.

- Dosage of 5-8 µg/0.1 ml leads to amplitude decline of the ERG reading and decrease in the average retinal cell count but resulted in no anatomical ocular changes.

- Future studies are needed to examine the efficacy of 3- 4 µg/0.1 ml Intravitreal carboplatin injections.
My personal experience with animal studies
“Ethical use in lab’s animal”
Tel-Aviv university
Thank you so very very much.