Evaluation of prolonged action growth factors neuroprotective effects in the experimental optic nerve damage model

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Glaucoma is the leading cause of the inevitable blindness in the world. Glaucoma causes damage of retinal ganglion cells (RGC), which take visual information from the photoreceptors and send it to the brain through axons. Therefore RGC death induces optic nerve degeneration and defects in visual field. Modern glaucoma medicinal and surgical treatment is concentrated to the reduction of the main risk factor - intraocular pressure. Unfortunately, adequate intraocular pressure control does not always guarantee the stability of visual functions and glaucomatous alterations proceed to progress even under normal intraocular pressure conditions. This is why we need innovative treatment methods, directed to the main damage target RGC, that could ensure direct neuroprotection. According to the recent researches, one of the causes of RGC death is the deficiency of neurotrophic factors. This is the reason why more attention is centered to the scientific researches trying to prove neurotrophic factors' neuroprotective effect towards RGC. In the first part of this project we will be introduced to the experimental preclinical optic nerve damage model. In the second part of the project we will seek to evaluate prolonged growth factors neuroprotective effect in the experimental optic nerve damage model. At this point of our research there is not enough data considering the exact mode of action and direct neuroprotective effect on the RGC. This is why preclinical research is so important for pharmacokinetics, pharmacodinamics and toxicity evaluation.

Purpose

Introduce experimental optic nerve damage model and evaluate prolonged growth factors effect on RGC apoptosis.

Objections

- To cause RGC death in the experimental nerve damage model.
- To evaluate factors, that could effect RGC death in the experimental nerve damage model.

- To evaluate prolonged growth factors‘ effect on RGC proliferation apllying the experimentaloptic nerve damage model.
- To evaluate prolonged growth factors‘ effect on RGC apoptosis apllying the experimentaloptic nerve damage model.;
- To compare RGC proliferation between two experimental animal groups, one of which had the prolonged growth factors treatment applied and the placeb group.
- To evaluate the adverse effects of prolonged growth factors.

Materials and methods

We will have the total count of 156 BALBc male mice. We will apply intraperitoneal anesthesia with medetomidine hydrochloride and ketamine. We will apply optic nerve damage model – mechanical crush – for 3 s on all experimental eyes.

Experimental groups:

Group I – experimental animal (BALBc mice, 39 units) group, which had the experimental optic nerve crush applied.

Group II – experimental animal (BALBc mice, 39 units) group, which had the experimental optic nerve crush and intravitreal saline injection applied.

Group III – experimental animal (BALBc mice, 39 units) group, which had the intravitreal injecton of prolonged growth factors in the undamaged eye.

Group IV – experimental animal (BALBc mice, 39 units) group, which had the experimental optic nerve crush and the intravitreal injecton of prolonged growth factors applied.

Experimental animal groups will be examined in 3 stages. We will euthanise the experimental animals with cervical dislocation after these stages. After we extract the eyeball, we will separate the retina and the optic nerve away from other tissues. The optic nerve and the randomly chosen retinal parts will be analyzed imunohistochemically, concentrating on RGC count. Furthermore, we will analyze optic nerves using electronic microscopy.

Expected results

1) Introduced preclinical optic nerve damage model.

2) Evaluation of the effectiveness of prolonged growth factors treatment and comparison to the placebo group.

3) Evaluation of the adverse effects of prolonged growth factors treatment.