Serum irisin levels in chronic open-angle glaucoma

Abstract

Purpose: To evaluate the levels of irisin in the serum in patients with chronic open-angle glaucoma.

Materials and methods: In this institutional comparative clinical study, the serum irisin levels of age and sex-matched 15 healthy volunteers as controls (Group 1), 15 patients with normal-tension glaucoma (NTG) (Group 2), 15 patients with pseudo-exfoliative glaucoma (PXG) (Group 3) and 15 patients with primary open-angle glaucoma (POAG) (Group 4) were measured with the enzyme-linked immune-sorbent assay (ELISA) method, and were evaluated.

Results: There was no statistically significant difference concerning age and gender among the groups (p>0.05). The mean serum irisin levels in Group 1, Group 2, Group 3 and Group 4 were 24.70±8.53 ng/mL; 15.61±3.56 ng/mL; 17.83±6.06 ng/mL and 16.49±3.39 ng/mL, respectively. Although the mean serum irisin levels in all glaucoma groups seem numerically lower than the control group, there was no statistically significant difference between the serum irisin concentrations of the study groups (p>0.05).

Conclusion: These findings suggest that serum irisin levels are not different among various open-angle glaucoma types. However, theoretically, irisin may contribute to the pathogenesis of glaucoma and may play a neuroprotective hormone in glaucoma. Further studies with large patient population are required for whether irisin plays a role in the pathogenesis of glaucomatous optic neuropathy.

Keywords: open-angle glaucoma, irisin, serum levels

Introduction

Glaucoma is a progressive and neurodegenerative disease characterized by the loss of the axons of retinal ganglion cells (RGCs) at the level of the optic nerve head (ONH) and visual field (VF) loss. Although elevated intraocular pressure (IOP) is considered as most important factor in the pathogenesis of glaucoma, clinical reports demonstrate that treatment strategies on lowering IOP is not alone enough to prevent glaucoma progression in all patients. Thus, neuroprotection may be crucial in the treatment of glaucoma. Neuroprotection is defined as the use of therapeutic agents to prevent, reduce, and even to reverse neuronal cell death because of a neurodegenerative disease or a traumatic or a neurotoxic injury.

Recent studies demonstrated that several neuroprotective treatments have been established in some neurodegenerative diseases of the central nervous system (CNS) disease like Alzheimer’s disease (AD). Irisin is an exercise-induced, 112-amino acid glycosylated protein that is formed by the proteolytic cleavage of fibronectin type III domain-containing protein 5 (FNDC5) in muscle tissue. It has been demonstrated that irisin works in the regulation of glucose homeostasis and the conversion of white adipose tissue to brown. Elevated irisin level increase in energy metabolism, weight loss and improves glucose tolerance causes. Irisin was firstly discovered from mouse skeletal muscle, and it was shown to be present in a variety of a lot of other tissues including rectum, pericardium, intracranial artery, heart, tongue, optic nerve (ON), uvula, brain, ovary, oviduct, pituitary, seminal vesicles, adrenal gland, esophagus, vena cava, kidney, penis, retina, testis, urethra, urinary bladder, spinal cord, liver, small intestine, tonsil, thyroid, and vagina. It has been reported that irisin immunoreactivity is present in the neural retina and muscle fibers in the eye of porcupine. In another study, it has been demonstrated that irisin immunoreactivity was found in all layers of the retina excluding the outer nuclear layer and also in the cornea in hamsters.

Recent reports demonstrated that serum or plasma levels of irisin are decreased in many patients with metabolic syndromes and related diseases. High plasma irisin levels are associated with the stage of diabetic retinopathy (DR). It has been also suggested that irisin might protect against DR with potential anti-IL-17A effects. Additionally, it has been reported that the patients with proliferative DR had decreased serum and vitreous irisin levels compared with the control group and type 2 diabetic patients without DR and that irisin levels were associated with the presence of diabetic nephropathy and DR. However, a specific role for irisin in the CNS has not yet to be identified. Recent studies have suggested that irisin is involved in the process of CNS such as neurogenesis. Additionally, it has been reported that irisin has a beneficial role on brain function by modulating neurotransmitter secretion in the AD. Also, it has been demonstrated that irisin is a neuroprotective peptide in various neurodegenerative diseases. ON is also a part of the CNS and glaucoma is a neurodegenerative disease of the ON in which axonal survival, apoptosis, and neuroprotection are crucial in its pathogenesis and treatment. To the best of our knowledge, there is no previous report in the literature on the blood levels of irisin in patients with glaucoma. In the light of this recent knowledge, we considered that irisin might play a role in the glaucoma pathogenesis and, in this study; we aimed to evaluate the levels of irisin in the serum in patients with open-angle glaucoma.
Materials and methods

Ethics and general information

The study was designed according to the Helsinki Declaration and approved by the institutional ethics committee. Informed consent was obtained from the patients and the volunteers. This pilot work was designed as an institutional controlled study and included age and sex-matched 15 healthy volunteers as controls (Group 1), 15 patients with NTG (Group 2), 15 patients with PXG (Group 3) and 15 patients with POAG (Group 4).

Clinical examinations

All participants underwent a complete ophthalmologic examination including best-corrected visual acuity, slit-lamp biomicroscopy, intraocular pressure (IOP) measurement using Goldmann applanation tonometry, gonioscopy, dilated fundoscopy using a 90-diopter lens, and VF examination with full-threshold strategy, by a Humphrey VF analyzer.

Diagnostic criteria

Group 1 (Control group) included the healthy subjects with no history of ocular disease (except refractive error) and had a normal eye examination including normal IOP (<22 mmHg), an open-angle, normal appearance of the optic disks and retinal nerve fiber layer (RNFL), and normal VFs. Group 2 (NTG group) included the patients having glaucomatous cupping, RNFL, and VF defect in at least one eye in two consecutive visits and an IOP lower than 22 mmHg. Group 3 (PXG group) included the patients having typical pseudoexfoliative material on the anterior lens capsule, an open-angle, IOP higher than 22 mmHg, typical glaucomatous cupping, RNFL and VF defects in at least one eye in two consecutive visits. Group 4 (POAG group) included the patients having an open-angle, IOP higher than 22 mmHg, typical glaucomatous cupping, RNFL and VF defects in at least one eye in two consecutive visits.

Exclusion criteria

The systemic examination was performed and a detailed medical story was obtained to identify the patients with risk factors for vascular disease such as hypertension, diabetes mellitus, morbid obesity, hyperlipidemia, cardiovascular, and cerebrovascular diseases. The patients with any cardiac disease such as cardiomyopathy or prior myocardial infarction, renal insufficiency, diabetes mellitus, systemic hypertension, peripheral or coronary artery disease, cerebrovascular disease, ocular inflammation, retinal occlusive disease, vasculitis, renal or hepatic dysfunction, morbid obesity, pregnancy, psychiatric illness, and/or chronic alcohol abuse were excluded from the study.

The measurement of serum irisin levels

Blood samples were taken from patients and healthy controls to measure irisin levels at 08.00 hours after overnight fasting in all subjects. All participants were rested for 15 minutes before blood-collection process. Samples were delivered to the laboratory within 20 min, centrifuged (2000g for 10 min at 4°C) and the sera aliquot is stored at −80°C until assayed. Commercial kit (Sunredbio, Baoshan, Shanghai) was used in salusin- beta measurements and samples were assayed by enzyme-linked immunosorbent test (ELISA) according to the manufacturer’s instructions. The minimum detectable level (sensitivity) was less than 0.157ng/mL and the assay range was 0.2-60 ng/mL. Intra- and interassay CVs were less than 10% and 12%, respectively. All samples were measured spectrophotometrically via ELx800TM Absorbance Microplate Reader (BioTek Instruments, Inc., Winooski, VT, USA) at 450 nm. The biochemist was blind to the identity of samples during processing. The results are presented as ng/mL.

Statistical analysis

Results are given as means±SD. The Statistical Package for Social Sciences, version 11.0 (SPSS Inc., Chicago, IL) was used for statistical analysis. Individual group parameters were assessed with the one-sample Kolmogorov–Smirnov Z test and were found to be abnormally distributed (p<0.05). Hence, statistical comparisons between groups were performed by the non-parametric Kruskal–Wallis and the Mann–Whitney U test. Spearman’s Rank order correlation coefficients were used to assess significant associations between irisin levels and demographic findings. For all comparisons, statistical significance was defined by p<0.05.

Results

There was no statistically significant difference concerning age and gender among the groups (p>0.05). The mean serum irisin levels in Group 1, Group 2, Group 3 and Group 4 were 24.70±8.53 ng/mL; 15.61±3.56 ng/mL; 17.83±6.06 ng/mL and 16.49±3.39 ng/mL, respectively. Although the mean irisin levels in all glaucoma groups seem numerically lower than the control group, there was no statistically significant difference between the serum irisin concentrations of the study groups (p>0.05) (Controls vs NTG, PXG and POAG: p=0.922; p=0.775 and p=0.905, respectively; NTG vs PXG: p=0.914; NTG vs POAG: p=1 and POAG vs PXG: p=0.726) (Table1).

Table 1 Mean irisin levels and comparisons in study groups

<table>
<thead>
<tr>
<th>Group</th>
<th>Number</th>
<th>Mean irisin levels±SD (ng/mL)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>15</td>
<td>24.70±8.53</td>
<td></td>
</tr>
<tr>
<td>NTG</td>
<td>15</td>
<td>15.61±3.56</td>
<td>Controls vs. NTG: p=0.922</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Controls vs. PXG: p=0.775</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Controls vs. POAG: p=0.905</td>
</tr>
<tr>
<td>PXG</td>
<td>15</td>
<td>17.83±6.06</td>
<td>NTG vs.PXG: p=0.914</td>
</tr>
<tr>
<td>POAG</td>
<td>15</td>
<td>16.49±3.39</td>
<td>POAG vs. PXG: p=0.726</td>
</tr>
</tbody>
</table>

Abbreviations: NTG, normal tension glaucoma; PXG, pseudoexfoliative glaucoma; POAG, primary open-angle glaucoma; SD, standard deviation

Discussion

Neuroprotection is crucial in the treatment of glaucoma and other neurodegenerative or apoptosis-associated diseases. Recent studies have shown the beneficial role of irisin on AD, neurodegenerative disease and that irisin enhances brain function by modulating neurotransmitter secretion, and that irisin plays crucial roles in the processings such as neurogenesis in the CNS. Previous studies have reported that irisin is observed in the cerebrospinal fluid.
Serum irisin levels in chronic open-angle glaucoma

and hypothalamus, and irisin is known to be highly expressed in astrocytes and microglia and neurons in various brain regions. It has been demonstrated that irisin is synthesized in the muscle tissue and is present in cerebellar Purkinje cells and intercellular nerve endings. Zhang et al. reported that injection of irisin into ventricular sytem in the brain increases in the locomotor activity. Brailoiu et al. suggested that irisin promotes neuronal depolarization of cardiac projecting neuron nucleus. Another study showed that irisin contributes to neural differentiation by modulating metabolic responses in the CNS. Irisin is found in several brain regions, such as the midbrain and the hippocampus in rodents. It has been reported that the skeletal muscle-derived irisin is linked to reward-related processes and motivation. Additionally, it has been demonstrated that irisin has antidepressant-like effects via modulation of energy metabolism in the prefrontal cortex. Some studies have emphasized that irisin secreted following exercise has a beneficial role in brain function in neurodegenerative diseases such as AD.

Irisin is a peptide that secreted by muscle and regulates energy metabolism. However, it has been suggested that it mediates muscle-adipose-bone-neuron connectivity. It has been well-known that brain-derived neurotrophic factor (BDNF), the widely existed neurotrophin in the brain has a critical role in synaptic functions and neuronal survival. Exercise-induced irisin stimulates the expression and activation of BDNF in the hippocampus, and improves learning and memory function. In the other hand, it has been reported that irisin can prevent the ischemia-induced neuronal injury due to oxidative stress via attenuation of the secretion of a pro-inflammatory cytokine such as tumor necrosis factor (TNF)-α through activation of Akt/ERK1/2. Additionally, a recent study suggested that irisin has neuroprotective effect via the suppression ROS-NLRP3 inflammatory signaling, expression of interleukin (IL)-1β, and the activation of caspase 1 signaling as apoptosis signaling in ischemic conditions. In another report, it has been also showed that significantly elevated reactive oxygen species and malondialdehyde levels in cerebral ischemia were reduced by irisin treatment in peri-infarct brain tissues. Some studies have been demonstrated that high dose irisin administration has provided the regulation in mitochondrial metabolism in the prefrontal cortex.

Author Contributions

The authors declare that there is no conflict of interest regarding the publication of this paper.

References

Serum irisin levels in chronic open-angle glaucoma.


46. Li DJ, Li YH, Yuan HB, et al. Mitochondrial-derived hormone irisin protects against neuronal injury via activation of the Akt and ERK1/2 signaling pathways and contributes to the neuroprotection of physical exercise in cerebral ischemia. Metabolism. 2017;68:31–42.

Serum irisin levels in chronic open-angle glaucoma


