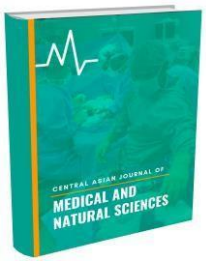

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Article

Study the Levels of Arrestin Beta2 in Patients with Glaucoma in Nassiriya Province, Iraq

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Abstract: Glaucoma, a leading cause of irreversible blindness worldwide, is characterized by visual field anomalies and progressive retinal ganglion cell (RGC) loss. Primary open-angle glaucoma affects over 57.5 million people, with risk factors including age, myopia, hypertension, thin corneal thickness, and family history. This study aimed to evaluate serum arrestin beta2 levels in glaucoma patients and healthy controls. Serum arrestin beta2 was measured in 88 subjects, including 50 glaucoma patients and 38 healthy controls, aged 40-70. Exclusion criteria included retinal diseases, hypertension, and vascular conditions. Results showed a significant decrease in arrestin beta2 levels in glaucoma patients compared to controls ($p < 0.01$), with higher levels observed in older healthy adults (60-70 years). These findings suggest that arrestin beta2 could be a potential biomarker for glaucoma progression, with implications for early detection and targeted treatment.

Keywords: Glaucoma, Ocular neuropathy, Retinal ganglion cells, Primary open-angle glaucoma, Blindness prevention

1. Introduction

"Glaucoma" is a complex collective of ocular neuropathies that are described by anomalies in the visual field and a progressive loss of retinal ganglion cells (RGCs). "Glaucoma" is the most common cause of permanent blindness in the globe (Crabb et al., 2013). "Glaucoma" can be divided into two primary groups.: primary and secondary. Both of these have two major subgroups based on the underlying anatomy and pathophysiology: angle-closure and open-angle.Open-angle and closed-angle glaucoma with no discernible cause can result in primary, or idiopathic, "glaucoma" . On the other hand, increased intraocular pressure is the main factor causing secondary glaucoma, which damages the visual nerve [1]. (POAG) is the most prevalent type of glaucoma; it is thought to be the cause of between 70 and 90 percent of cases [2]. Risk Factors for Glaucoma including: Increased intraocular pressure [3], age, Gender, Genetics and family history, Ethnicity, Smoking and Other health-related issues such as diabetes [4-9], hyper tention [10] and myopia [11].

β-Arrestin2

β-arrestins comprise signal transduction and adaptor proteins, such as arrestins 1, 2, 3, and 4 [12]. which compete with the G protein for the binding of GPCRs, and which were first found to impair G protein-coupled receptor (GPCR)-mediated signaling [13]. Previous

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research has demonstrated the role and mechanism of β-arrestins in the invasion and metastasis of cancer, as well as fibrotic disorders, by serving as multifunctional scaffolds [14,15]. Although β-arrestin2, also referred to as arrestin3, is a crucial member of the arrestin family, its precise function in signal transduction has not been examined.

β-arrestin2 is expressed in the eye in addition to mammalian organs, where it is commonly seen with β-arrestin1. Moreover, β-arrestin2 regulates a number of physiological processes via different receptors, including angiogenesis, autophagy, cell invasion, migration, and an anti-inflammatory action. Frontotemporal degeneration's beginning and progression are associated with these processes [16].

One of the molecular mechanisms linking arrestinBeta2 to glaucoma is its role in modulating the responsiveness of the beta2-adrenergic receptor (β2AR) by receptor phosphorylation and subsequent binding of β-arrestin, which leads to receptor internalization. Arrestin-3 and arrestinBeta2 cooperate to promote β2AR internalization by directly binding to clathrin, an essential protein in coated pits, and facilitating endocytosis. Furthermore, β-arrestins, such as arrestin Beta2, regulate the trafficking of G-protein-coupled receptors like β2AR by acting as adaptors in receptor-mediated endocytosis pathways. These results point to a possible connection between arrestinBeta2 malfunction and diseases such as glaucoma, indicating that the interactions between arrestinBeta2 and β2AR are critical for the internalization and signaling of GPCRs [17].

2. Materials and Methods

Between December 2023 and April 2024 , this investigation was carried out at private laboratories and the Al - Haboubi Teaching Hospital in Nasiriyah . The study included 88 men and women whose ages ranged from 40 to 70 years , as well as 38 control subjects (18 men and 20 women) and 50 patients (32 men and 18 women) . The cases that are not included in this : Retinal obstructive disease , systemic hypertension , cerebral vascular disease , peripheral coronary artery disease , renal failure , and eye infection . Two topic categories were present : There were 38 people in the control group , and they all seemed to be in good general health . The patient group consisted of fifty individuals suffering from glaucoma [18].

Collection of Blood Sample

Five milliliters of blood were given by venous infusion by both men and women . inserted into a gel tube to draw off the serum . Centrifugation (10 min at 3000 xg) was used to separate the serum after the blood was allowed to clot at room temperature . After that , the serum samples were removed and retained in storage at -20 ° C for later measurements of biochemical parameters , unless they were used immediately .

Statistical Analysis

The data of this study was statistically analysis by using SPSS version 26 , based in using independent sample t test for mean compartment , One way ANOVA for variance analysis , person coefficient for correlation , chi - square for independent , scatter blot for correlation diagram . Statistically significant P-values were defined as $P< 0.001$. The strength at which two variables have a linear link (r=+1) or (r=-1) is measured using the Pearson correlation coefficient (r). Coefficient of correlation between Pearson (r)was employed to investigate any correlations between the various metrics in each patient group.

3. Results and Discussion

Serum Levels of Arrestinbeta2 concentration

The current result was recorded that the levels of arrestin was decreased significantly in patients compared with control group at p. value < 0.01, as in the table (1). Patients with glaucoma exhibit lower expression of arrestinbeta2. This is most likely caused by abnormal GPCR signaling modulation, which has an impact on the internalization and desensitization of beta2-adrenergic receptors. Studies have demonstrated that downregulating the expression of arrestin proteins, including arrestin-2 and arrestin-3, influences the overall regulation of GPCRs in trabecular meshwork (TM) cells by reducing the extent to which agonists promote beta2AR internalization [19].

Furthermore, the pathobiology of glaucoma and ocular hypertension includes the dysregulation of multiple proteins, including vasorin, which is essential for preserving cell viability and preventing TGF-β-induced responses in TM cells, which may aid in the development of glaucoma [20]. Thus, a complex network of molecular pathways underlies the decreased production of arrestinbeta2 in glaucoma patients, and this network is highlighted by the interaction between arrestin proteins and other regulatory factors such as vasorin.

Table 1. Concentration of arrestin in patients and control group

	Patients No. 50	**Control No. 38**	
Arrestin	**Mean ± S. D**		p. value <0.001
	25.6 ± 8.56	49.4 ± 16.3	

Also we found, in control group a significant increase in the third age group than first age group, as the table (2). Elevated β-arrestin-2 levels in elderly control groups could be explained by its vital function in maintaining heart function as we age. Studies reveal that β-arrestin-2 participates in G-protein coupled receptor (GPCR) signaling, a crucial process for preserving cardiac contractility and averting unfavorable alterations in the heart with age [21]. Furthermore, higher levels of β-arrestin have been noted in a number of clinical diseases, including obstructive sleep apnea and heart failure, indicating that its overexpression could represent an adaptive response to aging-related stresses [22,23].

Moreover, it has been demonstrated that β-arrestin-2 modulates inflammatory responses, which may become dysregulated in the elderly, possibly resulting in elevated levels as a defense against inflammation and heart problems [24]. Therefore, the increase in β-arrestin-2 in elderly people could be a result of a defensive adaptation to preserve heart function as well as a reaction to age-related cardiac stress [25].

Table 2. Concentration of arrestin in patients and control group according age.

	Categories	Patients	Control	p. value
	Age groups	Mean ± S. D		
Arrestin	40- 49	23.0 ± 7.67	44.5 ± 12.6[b]	<0.001
	50- 59	23.5 ± 8.42	46.9 ± 18.4[ab]	<0.001
	60- 70	28.8 ± 8.49	60.3 ± 15.8[a]	<0.001
	p. value	0.080	0.041	
	LSD Sig		0.014[1-3]	

4. Conclusion

The study demonstrated a significant reduction in serum arrestin beta2 levels in glaucoma patients compared to healthy controls, with levels notably higher in older adults within the control group. These findings suggest that the dysregulation of arrestin beta2 may play a crucial role in the pathophysiology of glaucoma, potentially linked to abnormal GPCR signaling and impaired receptor internalization. The elevated arrestin beta2 levels in elderly controls may indicate a protective mechanism against age-related cellular stresses, particularly in maintaining cardiac and ocular functions. These results highlight arrestin beta2 as a potential biomarker for glaucoma progression, with implications for early detection and therapeutic intervention. Further research is necessary to explore the precise molecular pathways involved in arrestin beta2 regulation and its broader impact on glaucoma development and progression.

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