

# Comparison of Erythropoietin, Semaphorins 3A and Pigment Epithelium Derived Factor Levels in Serum and Aqueous Humor of Patients with Neovascular Glaucoma and Cataract

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## ABSTRACT

The aim of this study was to compare the levels of erythropoietin (Epo), semaphorins 3A (Sema 3A) and pigment epithelium derived factors (PEDF) in serum and aqueous humor of those with neovascular glaucoma (NVG) and patients with cataract. It was an experimental study carried out from January 2016 to September 2018. Seventy-three NVG patients were selected as NVG group, and 73 cataract patients were selected as cataract group. The levels of Epo and sema 3A in serum and aqueous humor in NVG group were higher than those in cataract group (both  $p < 0.001$ ), and the level of PEDF in serum and aqueous humor in NVG group were lower than those in cataract group ( $p < 0.001$ ). Compared with cataract patients, NVG patients had higher levels of Epo and sema 3A in serum and aqueous humor and lower levels of PEDF.

**Key Words:** *Neovascular glaucoma, Cataract, Aqueous humor, Erythropoietin, Semaphorins 3A (Sema 3A), Pigment epithelium derived factors (PEDF).*

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Neovascular glaucoma (NVG) is a common secondary glaucoma, caused by neovascularisation on the iris surface and anterior chamber angle, which makes trabecular meshwork and the iris tissue around it adheres to each other and causes intraocular pressure to rise.<sup>1</sup> Although the etiology of iris neovascularisation in NVG is still unclear, most scholars agree with the view of neovascularisation caused by retinal hypoxia.<sup>2</sup> Cataract is the first disease leading to blindness in the world, which is a disorder of lens metabolism caused by high sugar, immunity, abnormal metabolism and so on.<sup>3</sup> The exact pathogenesis of cataract remains unclear.

Erythropoietin (Epo) is the first target recognised by hypoxia inducible factors and is also one of the easiest targets to be activated by hypoxia. Epo can promote angiogenesis. Semaphorins 3A (sema 3A) is a secretory protein with many biological effects. It is involved in the regulation of axonogenesis and angiogenesis of retinal nerve cells during the development of retina. Pigment epithelium derived factors (PEDF) are one of the most important angiogenesis inhibitors, which can inhibit many angiogenesis inducers. At present, there are few reports comparing the levels of erythropoietin, sema 3A and PEDF in serum and aqueous humor of NVG and cataract patients.

The aim of this study was to compare the levels of Epo, sema 3A and PEDF in serum and aqueous humor of patients with NVG and cataract.

This experimental study was carried out at the Department of Ophthalmology, the Affiliated Hospital of Inner Mongolia Medical University, China, from January 2016 to September 2018. This study was approved by the Hospital Ethics Committee. Seventy-three patients (73 eyes) with NVG were collected as NVG group. The inclusion criteria were neovascularisation found on iris surface of patients by slit lamp microscopy and gonioscopy; not responding to conventional antihypertensive medicine; patients had a history of fundus hemorrhage; patients with unsatisfactory medicine control but still had visual acuity; and patients without cataract. Patients with malignant tumors, age-related macular degeneration, vitreous hemorrhage and anterior chamber hemorrhage were excluded.

In addition, 73 patients (73 eyes) with simple cataract treated in the hospital during the same period were selected as cataract group. Cataract group included patients diagnosed as cataract; without other eye diseases or history of eye surgery; with progressive, painlessly reduced vision. Patients with systemic diseases such as diabetes mellitus and hypertension, and those having other ophthalmic diseases or combined with tumors, were excluded.

At admission, fasting elbow venous blood 4mL was taken from both groups in the morning. Before the operation, the patients underwent aqueous humor puncture 1 mm

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**Table I:** Comparison of Epo, sema 3A and PEDF levels in serum and aqueous humor of the two groups.

Parameter	NVG group (n=73)	Cataract group (n=73)	p-value
Serum Epo (U/L)	25.85 ±1.26	23.14 ±1.55	<0.001
Aqueous humor Epo (U/L)	168.42 ±14.93	27.03 ±3.08	<0.001
Serum Sema3A (ng/mL)	0.96 ±0.29	0.25 ±0.07	<0.001
Aqueous humor Sema3A (ng/mL)	2.21 ±0.75	0.74 ±0.33	<0.001
Serum PEDF (pg/mL)	12.15±1.86	13.47 ±2.02	<0.001
Aqueous humor PEDF (pg/mL)	216.98 ±28.59	238.61 ±31.16	<0.001

of corneal limbus with a syringe with sterile No. 25 needle under the slit lamp. The 0.15 to 0.2 mL aqueous humor was taken. The levels of Epo, sema 3A and PEDF in serum and aqueous humor were measured by ELISA, and the differences between the two groups were compared. Collected data were analysed using independent sample t-test for quantitative variables and chi-square test for qualitative variables by SPSS version 25. The value of  $p < 0.05$  was considered significant difference.

Among the 73 patients in NVG group, 43 (58.90%) were males and 30 (41.10%) were females, the age ranged from 50 to 72 ( $64.75 \pm 2.81$ ) years. In the cataract group, there were 44 males (60.27%) and 29 females (39.73%), the age was from 51 to 73 ( $65.54 \pm 3.23$ ) years. There was no significant difference in gender and age between the two groups ( $p=0.866, 0.117$ ). Epo and sema 3A levels in serum and aqueous humor of NVG group were higher than those of cataract group (both  $p < 0.001$ ), and PEDF levels in serum and aqueous humor of NVG group were lower than those of cataract group ( $p < 0.001$ , Table I).

Studies have shown that Epo concentration in aqueous humor of neovascular glaucoma patients combined with cataract is higher than that of patients with primary open angle glaucoma (POAG) and pseudoexfoliation glaucoma (PXFg).<sup>4</sup> The results showed that Epo levels in serum and aqueous humor of NVG group were higher than those of cataract group, which illustrated that comparing with cataract patients, Epo levels in serum and aqueous humor of NVG patients expressed highly.

A study has shown that upregulation of sema 3A expression can promote retinal vascular occlusion and inhibit vascular regeneration.<sup>5</sup> The author found that comparing with cataract patients, sema 3A levels in serum and aqueous humor were significantly higher in NVG patients. It is speculated that sema 3A can inhibit vascular remodelling, aggravate ischemia and hypoxia, promote apoptosis of retinal ganglion cells, and aggravate NVG formation and ocular damage.

PEDF belongs to the serine protease inhibitor gene family, and it is regarded as one of the most effective angiogenesis inhibitors because of its physiological role of protecting the retina and controlling the growth of blood vessels in the eye. Low levels of PEDF can weaken the inhibition of neovascularisation. A study found that PEDF might be expressed by the iris tissue in

patients with NVG associated with proliferative diabetic retinopathy.<sup>6</sup> The results of this study showed that comparing with cataract patients, PEDF levels in serum and aqueous humor were lower in NVG patients.

In conclusion, comparing with cataract patients, NVG patients have higher levels of Epo and sema 3A in serum and aqueous humor, and lower levels of PEDF. The results of this study are helpful regarding the basic etiological study of NVG and cataract, as well as to the clinical diagnosis of these two diseases.

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#### ETHICAL APPROVAL:

This study was approved by the Hospital Ethics Committee.

#### CONFLICT OF INTEREST:

Authors declared no conflict of interest.

#### AUTHORS' CONTRIBUTION:

YS: Contributed to the conception/design of the work, analysed and interpreted data for the work, drafted the work; and finally approved the version to be published.

HZ: Drafted the work; analysed and interpreted data for the work.

YS: Drafted the work, and revised it critically for important intellectual content.

WG: Contributed to the conception/design of the work, and drafted the work.

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