

## Glaucoma Chronic Angle-Open, Endocrinopathy and Obstructive Sleep Apnea Syndrome: Fortuitous Association or Interaction?

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### ABSTRACT

On the basis of the literature data the relationships between chronic open-angle glaucoma, endocrinopathies and nocturnal apnoea syndrome are re-examined. It is assumed that the onset of glaucoma in different endocrinopathies has an only pathogenetic mechanism: OSAS.

**Key words:** Open-angle glaucoma; Acromegaly; Hypothyroidism; Cushing syndrome; Diabetes mellitus type 2; Obstructive sleep apnea syndrome

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### REVIEW

Chronic open-angle glaucoma, the main cause of irreversible blindness, is a neurodegenerative illness characterized by

irremediable loss of the ganglionic cells of the retina. From numerous studies aiming at pathogenetic identification of the mechanism it emerges that it is sometimes associated with other pathologies and in particular with endocrine ones. Besides, the eye in its components presents various receptors for different hormones (Table 1) that account for its involvement in many endocrinopathies.

Particularly numerous are studies aiming to underline a correlation between thyroid pathology, particularly hypothyroidism and glaucoma. Girkin *et al*<sup>[1]</sup> observed that subjects with hypothyroidism present a greater risk of developing glaucoma. Cross too<sup>[2]</sup>, in a study on 12,376 patients, noticed that glaucoma affected 6.5% of subjects with thyroid pathology. By contrast, Ozturk<sup>[3]</sup> believes that the higher frequency of glaucoma in hypothyroid subjects is not due to the hormonal deficit but to the age of these subjects, over fifty, the age of highest frequency of the glaucoma.

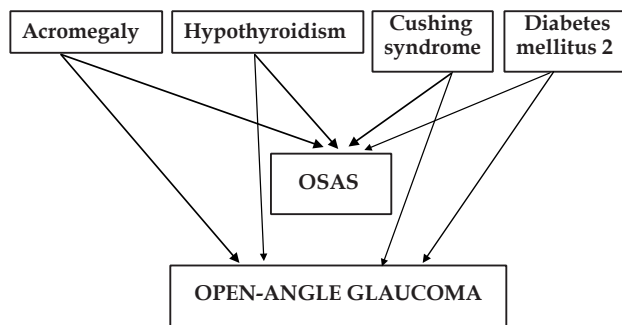
No less numerous are studies carried out in subjects with type 2 diabetes mellitus, which highlight the high frequency (4.5%) of primary open-angle glaucoma (POAG) among these patients<sup>[4,5]</sup>. This increased prevalence may nevertheless only be apparent in that, as maintained by some authors, it is due to overestimation on account of the more frequent ophthalmological examinations to which diabetic patients are submitted. Other studies, however, have suggested that this type of bias cannot entirely explain the positive association between diabetes and the risk of glaucoma<sup>[6,7]</sup>.

The effect of corticosteroid hormones on intraocular pressure (IOP) is an incontrovertible datum. The fact is that use of these, through either a general or an ocular pathway, especially for a period of some length, can involve an increase in IOP, above all through alterations to Schlemm's trabecular network where receptors for these hormones have been highlighted. In the literature, recently, cases of glaucoma onset have also been reported in patients with Cushing's syndrome<sup>[8]</sup>.

Although the eye participates in hypophyseal pathology, especially in cases of increased secretion of GH<sup>[9,10,11]</sup>, a glaucomatous pathology in subjects with acromegaly is exceptional. The hypothesis that GH could favour the onset of POAG, formulated by Greco and coll<sup>[12]</sup>, has not found confirmation, and the finding of increased values of IOP in subjects with acromegaly, reported in the past few decades, is probably to be connected to variations in the thickness of the cornea

**Table 1** Distribution of the hormonal receptors in the structures of the eye.

	GH	Thyroxine	Glucocorticoids	ER-alfa	ER-beta	Progesterone	Androgenic steroids
Meibomio gl.				+	+	+	
Lacrimal gl		+		+	+	+	+
Conjunctiva				+	+	+	+
Cornea	+			+	+	+	+
Irides-cliairy corp	+		+	+	+	+	+
Crystalline lens			+	+	+		+
Retina	+			+	+	+	+
Optic nerve	+						
Schlemm's trabecular meshwork	+		+				



**Figure 1** Pathogenetic hypothesis of the POAG during endocrinopathies.

induced by the GH, which were not taken into account.

If the relationship is undisputed between endocrinopathy and glaucoma, extremely controversial is the pathogenetic mechanism, although the presence of hormonal receptors in Schlemm’s trabecular network could explain the increase in IOP at least in some endocrinopathies.

In the case of diabetes mellitus, moreover, the metabolic disorder could act with a complex mechanism, at the basis of which there are probably anomalies of the small vessels, with consequent damage to the optic nerve and the nervous fibres as well as to the retinal ganglionic cells, with acceleration of their apoptosis. Confirming this hypothesis, some studies<sup>[4]</sup> stress the importance of the duration of diabetes, which significantly proves to be associated with an increase in the prevalence of glaucoma.

In the last years of the past century stress was laid on the importance of pressure disorders in subjects with Obstructive Sleep Apnoea Syndrome (OSAS)<sup>[13]</sup>, for which, as is well known, endocrine pathology is one of the predisposing conditions. The fact is that the functional alterations of almost all the endocrine glands (pituitary, thyroid, adrenal capsules, ovary, pancreas) involve an increase in bodily weight with accumulation of fat, above all in the organs that favour frequent episodes of collapse of the upper airways during sleep.

In acromegaly there is an elevated prevalence of sleep apnoea, as underlined by Hernandez-Gordilo *et al*<sup>[14]</sup>, and equally high values (80%) are reported by Tsoi UA *et al*<sup>[15]</sup>.

The association between hypothyroidism and OSAS is confirmed by various studies and particularly by Ozcan KM *et al*<sup>[16]</sup>, who in a group of 203 patients with OSAS noticed the presence of clinical or subclinical hypothyroidism in 12. 77% of patients.

There are more and more numerous studies that stress that between OSAS and type 2 diabetes mellitus there is a two-way relationship with additive or synergic effects. In a recent review of the literature, Greco and Spallone<sup>[17]</sup> noticed that OSAS involves the appearance of insulin resistance that precedes both reduced tolerance to carbohydrates and diabetes proper and that the severity of the latter is related to the severity of the OSAS.

The role of OSAS among the risk factors of open-angle glaucoma<sup>[18]</sup> is now consolidated in the literature and a study by Lin CC *et al*<sup>[19]</sup> highlighted the fact that the risk of a subsequent diagnosis of glaucoma during a 5-year follow-up clearly increased in comparison to a population of comparable age and ethnic characteristics. The potential association between OSAS and glaucoma may depend on repeated nocturnal episodes of transitory hypoxemia with increased vascular resistance and consequent impairment of perfusion of the head of the optic nerve and its oxygenation, above in glaucoma with normal or low IOP. The fact is that in this form, even more than in the form associated with high IOP, reduction in arterial tension involves reduction in perfusion, favouring the onset of apoptosis of the ganglionic cells.

In glaucoma associated with an increase in IOP, OSAS may act, instead, by further increasing IOP through an increase in sympathetic tone and an alteration of the architecture of sleep<sup>[13,20]</sup>.

Hence the increased frequency of glaucoma during endocrinopathies would not be an accidental coincidence, but, on the contrary, a component of the endocrinopathy, which would play its role both directly and, above all, by triggering the onset of OSAS.

Hence chronic open-angle glaucoma is confirmed not to be a single illness but a heterogeneous group of optic neuropathies all characterized by progressive degeneration of the optic nerve with irreversible loss of sight.

## CONFLICT OF INTERESTS

There are no conflicts of interest with regard to the present study.

## REFERENCES

- Gukin CA, McGwin G Jr, McNeal SF, Lee PP, Owsley C. Hypothyroidism and the development of open angle glaucoma in aq male population. *Ophthalmology* 2004; **111**: 1649-52
- Cross JM, Gukin CA, Owsley C, McGwin G Jr- The association between thyroid problems and glaucoma. *Br J Ophthalmol* 2008. **92**: 1503-5
- Ozturk BT, Ksarimoglu H, Dabas O, Pekei H, Gonen MS. Ocular changes in primary hypothyroidism. *BMC Res Notes* 2009; **29**: 286-294
- Zhao D, Cho J, Kim MH, Friedman D, Guallar E. Diabetes, glucose metabolism, and glaucoma: the 2005-2008 National Health and Nutrition Examination Survey. *PLoS One*. 2014 Nov 13; **9(11)**: 1255-1258
- Zhao D, Cho J, Kim MH, Friedman DS, Guallar E. Diabetes, fasting glucose, and the risk of glaucoma: a meta-analysis. *Ophthalmology*. 2015 Jan; **122(1)**: 72-8
- Mitchell P, Smith W, Chey T, Healey PR Open-angle glaucoma and diabetes: the Blue Mountains eye study, Australia. *Ophthalmology*. 1997; **104**: 712-718.
- Pasquale LR, Kang JH, Manson JE, Willett WC, Rosner BA, et al. Prospective Study of Type 2 Diabetes Mellitus and Risk of

- Primary Open-Angle Glaucoma in Women. *Ophthalmology* 2006; **113**: 1081-108
- 8 Virevialle C, Brasnu E, Fior R, Baudouin C. Open-angle glaucoma secondary to Cushing syndrome related to an adrenal adenoma: case report. *J Fr Ophthalmol.* 2014 Dec; **37(10)**
  - 9 Ciresi A, Amato MC, Morreale D, Lodato G, Galluzzo A, Giordano C. Cornea in acromegalic patients as possible target of growth hormone action. *J Endocrinol Invest.* 2011; **34**: 30-5
  - 10 Ciresi A, Amato AM, Morreale Bubella R, Cillino S, Giordano C. Cornea in children with growth hormone deficiency: the effect of GH treatment. *Growth Hormone & IGF Research* 2014; **24**: 150-4
  - 11 Morreale Bubella R. L'occhio nella patologia endocrina. 1a Edizione. *Italia. Ed. Danaus* 2014: 131-142
  - 12 Greco AV, Ricci B, Altomonte L, Rebuzzi AG, Manna R, Ghirlanda G. Gh secretion in open-angle glaucoma. *Ophthalmologica* 1979; **179**: 168-72.
  - 13 Shi Y, Liu P, Guan J, Lu Y, Su K. Association between glaucoma and obstructive sleep apnea syndrome: a meta-analysis and systematic review. *PLoS One.* 2015 Feb 23; **10(2)**: 9
  - 14 Hernández-Gordillo D, Ortega-Gómez Mdel R, Galicia-Polo L, Castorena-Maldonado A, Vergara-López A, Guillén-González MÁ, Torre-Bouscoulet L. Sleep apnea in patients with acromegaly. Frequency, characterization and positive pressure titration. *Open Respir Med J.* 2012; **6**: 28-33
  - 15 Tsoi UA, Sviryaev IuV, Korostovtseva LS, Semenov AP, Vaulina DA, Nepran VI, Kravchenko SO, Konradi AO, Grineva EN. Clinical features of obstructive sleep apnea syndrome in patients with acromegaly. *Ter Arkh.* 2015; **87(4)**: 47-52.
  - 16 Ozcan KM, Selcuk A, Ozcan I, Ozdas T, Ozdogan F, Acar M, Dere H. Incidence of hypothyroidism and its correlation with polysomnography findings in obstructive sleep apnea. *Eur Arch Otorhinolaryngol.* 2014 Nov; **271(11)**: 2937-41
  - 17 Greco C, Spallone V. Obstructive Sleep Apnoea Syndrome and Diabetes. Fortuitous Association or Interaction? *Curr Diabetes Rev.* 2015; **12(2)**: 129-55.
  - 18 Bendel RE, Kaplan J, Heckman M, Fredrickson PA, Lin SC. Prevalence of glaucoma in patients with obstructive sleep apnoea—a cross-sectional case-series. *Eye (Lond)* 2008; **22**: 1105-1109.
  - 19 Lin CC, Hu CC, Ho JD, Chiu HW, Lin HC. Obstructive sleep apnea and increased risk of glaucoma: a population-based matched-cohort study. *Ophthalmology.* 2013 Aug; **120(8)**: 1559-64
  - 20 Faridi O, Park SC, Liebmann JM, Ritch R. Glaucoma and obstructive sleep apnoea syndrome. *Clin Experiment Ophthalmol.* 2012 May-Jun; **40(4)**: 408-19

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