INTRODUCTION

Chronic open-angle glaucoma, one of the main causes of visual impairment and blindness worldwide, is today considered a form of progressive optic neuropathy often associated with high intraocular pressure (IOP) consequent on anomalous high resistance to drainage of aqueous humour (AH) through the trabecular meshwork (TM) and Schlemm’s channel. Despite in-depth research, the aetiology has not yet been fully clarified, though many authors are favouring more and more the hypothesis of a multifactor pathology, in which an important role is played by both genetic and risk factors.

In the last few years various studies\(^1,2\) have highlighted the fact that in subjects with POAG the alterations of the lipid profile can indirectly favour not only progression of the visual field deficit through systemic arterial alterations, but also directly with alterations of ocular perfusion pressure, both systolic and diastolic.

In a previous paper\(^3\) we showed that type A behaviour can be considered a real risk factor for evolution of visual field impairment. The fact is that subjects with such behaviour present marked nychthemeral oscillation of intraocular pressure values, which facilitates neuronal damage and can thwart the most careful therapy. Such patients are also inclined to alimentary abuses, which, in addition to leading them to be overweight, favour the onset of lipid...
profile disorders.

We considered it useful to examine the serum values of lipids (cholesterol, HDL-cholesterol, LDL-cholesterol and triglycerides) in two groups of patients with POAG, one with characteristics of type A behaviour and one with characteristics of type B behaviour, for the purpose of appraising whether the evolutionary differences in the perimetric damage in the two groups may have a concourse in a possible lipid profile disorder.

**MATERIALS AND METHODS**

The study involved 45 patients, 26 women and 19 men, affected by POAG, without significant differences in disease duration, observed at the Glaucoma outpatient department of the Eye Clinic of the University of Palermo. 25 patients presented characteristics of type A behaviour and 20 characteristics of type B behaviour. The average age of the patients was 64.12 ± 13.5 years without particular differences between the sexes. The patients were submitted to treatment with beta-blockers and/or prostaglandin and/or carbonic anhydrase inhibitors. The study was conducted on the basis of the ethical principles established by the Declaration of Helsinki and informed consent was obtained from all patients. The patients, after determination of type A/B behaviour through a questionnaire in the version modified by the Survey Jenkins Activity, were submitted to the following: (1) Complete bio-microscopic examination; (2) Tonometry and daily tonometric curve; (3) Examination of the visual field through computerized “Octopus 1-2-3” perimeter and evaluation of it through Glaucoma Staging System 2\(^2\). We chose this staging method because it is simple and fast; and (4) Determination of the lipid profile (total cholesterol, HDL Cholesterol; LDL Cholesterol, Triglycerides).

All investigations were repeated after 3 years because it is a time interval that could be considered sufficient for an assessment of the role of the type A behavior and of the lipid profile in the evolution of glaucomatous damage.

**Statistical evaluation**

The data are expressed as average ± SD. Student’s t-test was used to evaluate the significance of the data. Values of \( p \leq 0.05 \) were considered as significant.

**RESULTS**

In patients with type A behaviour, depicted in table 1, the values relating to the single components of the lipid profile both at time 0 and after 3 years proved to be constantly higher.

Table 2 reports the data (average value ± SD) relating to the evaluation of the visual field in the two groups of patients through GSS2 at the time zero and after 3 years.

By using the paired-samples Student t-test in the patients with type A behavior was found a statistically significant difference (\( p = 0.001 \)) at the time zero and after 3 years; no significant difference was found in patients with type B behavior (\( p = 0.18 \)).

**DISCUSSION**

The role of vascular risk factors in glaucoma is still under discussion, though hypothesized as long ago as 1999 by Flammer J et al\(^9\) and highlighted, more recently, by the study by Orzalesi and coll\(^8\), which showed that patients with chronic open-angle glaucoma present a high risk of cardiovascular pathology.

However, there are few studies on the role of atherosclerosis in the genesis and evolution of the glaucomatous process; only a recent study by Agafonova VV et al\(^7\) has highlighted a statistically significant relationship between atherosclerosis and the development of pseudoxfoliation glaucoma. Well consolidated in the literature, by contrast, is the relationship between arterial hypertension and intraocular pressure, along with the fact that the latter presents nychthemeral trend superimposed on that of systemic arterial tension\(^9\).

Alterations of the lipid profile and in particular an increase in total cholesterol and LDL-cholesterol, in addition to being frequent in arterial hypertension, can be associated with atherosclerosis both as a systemic disease of the large vessels and in more specific ocular vascular pathology. As stressed by Martinez and coll\(^10\), in patients with POAG alterations of the ophthalmic artery and the short posterior ciliary arteries detectable in patients with atherosclerosis can in fact determine a diminution of the telediastolic velocity and an increase in vascular resistances to above 0.78 in the ophthalmic artery, involving a risk six times greater of progression of visual field impairment. A statistically significant reduction in flow velocity in the retrobulbar arteries of patients with POAG has been confirmed with Doppler evaluations in other studies\(^11\).

These alterations in flow involve impairment of perfusion in the head of the optic nerve and have been proposed as a pathogenetic factor for glaucoma\(^11\). In fact the increase in vascular resistances could emphasize the reduction in perfusion during the decrease in arterial tension at night, thus increasing hypoxia, with accelerated apoptosis of the ganglionary cells. A statistically significant reduction in the flow velocity in the retrobulbar arteries of patients with POAG has been confirmed with Doppler evaluations in many studies\(^11\).

Moreover, Rader et al\(^12\) and Kerr et al\(^13\) have been able to show the presence in the retinal peripapillary vessels of patients with systemic arterial hypertension a reduction in flow consequent on an arteriolar spasm probably due to vaso-constrictive hypersensitivity. There would therefore seem to be, both in hypertensive and hypotensive peaks, with a different pathogenetic mechanism, a reduction in retinal perfusion. Further, it is well known that in patients with type A behaviour the particularly marked state of anxiety involves greater oscillation of the arterial pressure values both with repeated diurnal peaks and with greater deflection during the night.

The nychthemeral pressure rhythm is due, as highlighted by Smolensky et coll\(^14\), to various factors like environmental temperature, light, noise and feeding behavioural models, ingestion.

**Table 1** Lipid profile at time 0 and after 3 years.

<table>
<thead>
<tr>
<th>Type</th>
<th>Basal total cholesterol</th>
<th>Total cholesterol after 3 years</th>
<th>Basal HDL-cholesterol</th>
<th>HDL-cholesterol after 3 years</th>
<th>Basal LDL-cholesterol</th>
<th>LDL-cholesterol after 3 years</th>
<th>Triglycerides after 3 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>226 ± 2.14</td>
<td>210 ± 8.25</td>
<td>72 ± 6.57</td>
<td>67 ± 7.88</td>
<td>127 ± 6.98</td>
<td>116 ± 14.54</td>
<td>225 ± 15.62</td>
</tr>
<tr>
<td>B</td>
<td>213 ± 12.6</td>
<td>208 ± 19.34</td>
<td>66 ± 9.29</td>
<td>67 ± 7.88</td>
<td>118 ± 0.98</td>
<td>108 ± 13.07</td>
<td>214 ± 15.02</td>
</tr>
</tbody>
</table>

**Table 2** Variation in the visual field damage in GSS2 in the two groups.

<table>
<thead>
<tr>
<th>Type</th>
<th>GSS2 at time 0</th>
<th>GSS2 after 3 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>2.65 ± 0.83</td>
<td>1.55 ± 0.97</td>
</tr>
<tr>
<td>B</td>
<td>3.09 ± 0.75</td>
<td>1.76 ± 0.84</td>
</tr>
</tbody>
</table>
of liquids and salt and consumption of stimulants. Lastly, a very
important role is played by emotional stress, particularly
accentuated in patients with type A behaviour\(^\text{(19)}\). The fact is that
these patients, according to the classical distinction proposed by
Friedman and Rosenmann, are characterized by marked and diffused
competitiveness, impatience and intolerance towards other people’s
different rhythms and a tendency to want to obtain a limitless number
of things in a limited time period, behaviours that lead to an almost
continual state of anxiety and tension. Moreover, in these people,
reduced physical activity is documentable, with irregular and very
often excessive feeding and the habit of smoking, three conditions
that with disorders of the lipid profile involve faster evolution of
atherosclerotic lesions\(^\text{(17)}\).

In a previous study\(^\text{(15)}\) we highlighted, through the diurnal
tonometric curve, the fact that in patients with type A behaviour there
are more frequent and larger oscillations in intraocular pressure that
repeat in a superimposable way those of the systemic arterial tension.

In our patients with type A behaviour we also noticed impairment
of the lipid profile, with a significant increase above all in the
fractions (total cholesterol and LDL-cholesterol) most involved in
the atherosclerotic process, which remained more or less unchanged
during the whole period of observation.

The more marked perimetric damage in such patients and its more
rapid evolution, with a statistically significant difference compared to
patients with type B behaviour, could therefore perhaps have in
arteriolar alterations, linked to the atherosclerotic process, a concourse
that reduced the effect of the thorough hypotonic therapy to which
these patients were submitted in the three years of observation.

On the other hand, it is also well known that LDL-cholesterol stimulates
local production of endothelin-1 with strong vaso-
constrictive action on the ciliary arteries, with a further unbalancing
of the relationship with nitric oxide, with vaso-dilating action\(^\text{(18)}\), and
deregulation of aqueous outflow through the trabecular meshwork
(TM). This hypothesis also seems to be confirmed by other studies
emphasizing that the reduction in cholesterol, though at levels initially
within the norm, involves a reduction in the risk of developing
POAG and a slowing of the evolution of the campimetrical damage
in affected people\(^\text{(19)}\). The role of the impairment of the lipid profile
is also underlined by the observation that therapy with statins\(^\text{(20,21)}\), which markedly influence the reduction in LDL-cholesterol levels, is
what ensures the best protection against glaucomatous damage. Some
studies, also on particularly vast population samples, have shown that
this favourable result might also be due to a direct protective
action on the ganglionary cells, which would be added to the action
consequent on the reduction in the lipid component of plasma.

From our study, the limitation of which is the low number of
samples, it emerges that the more rapid progression of visual field
impairment in patients with type A behaviour, could be the resultant
of a double pathogenetic process: mechanical and metabolic.

The greater instability of the IOP characteristic of such patients
would seem to be responsible for the mechanical damage on the head
of the optic nerve while the impairment of perfusion, consequent
on the atherosclerotic alterations with accentuated reduction in
perfusion, especially at night, could favour the process of apoptosis
of the ganglionary cells.

It follows that if on one side this hypothesis confirms the
multifactor pathogenesis of POAG, on the other it also imposes the
need not only to check the IOP, but also to undertake dietary and
therapeutic treatment of the possible alteration of the lipid profile,
above all with statins, to slow the impairment of the visual field,
which remains the fundamental objective of glaucoma therapy.

REFERENCES

1. Modrezewska M, Grzesiak W, Zaborski D, Modrezewska
   A. The role of lipid dysregulation and vascular risk factors

2. Marcus MW, Miskens RP, Ramdas WD, Wolfs RC, De Jong
   PT, Vingerling JR, Hofman A, Stricker BH, Janssouin NM. Cholesterol-lowering
   drugs and incident open-angle glaucoma: A population-based cohort study.
   *PloS One* 2012; **7**(1): e29724. [PMID: 22236844]

3. Moreale-Bubella R, Moreale Bubella D, Cillino S. Type A
   behaviour pattern: it is a risk factor for open-angle chronic
   [DOI: 10.1097/IJO.0b013e31827095b5]

   2) for classifying functional damage in glaucoma. *J Glaucoma.
   2006; 15*: 40-46. [PMID: 16378017]

5. Flammer J, Haefliger IO, Orgül S, Resink T. Vascular
dysregulation: A principal risk factor for glaucomatous damage? *J

6. Orzalesi N, Rossetti L, Omboni S; OPTIME Study Group
   (Osservatorio sulla Patologia glaucomatosa, Indagine Medico
   Epidemiologica); CONPROSO (Collegio Nazionale dei Professori
   Ordinari di Scienze Oftalmologiche). Vascular risk factors in
   glaucoma: the results of a national survey. *Graefes Arch Clin Exp
   [DOI: 10.1007/00147-006-0457-5]

7. Agafonova VV, Frankovska-Gerlak MZ, Sokolovskaia TV,
   Brizhak PE, Bessarabov AN. Occurrence and characteristics of cardiovascular
   2013 Nov-Dec; 129**(6)**: 34-7 [PMID: 24624800]

8. Jürgens C, Grossmann R, Tost FH. Relationship of systemic
   blood pressure with ocular perfusion pressure and intraocular
   pressure of glaucoma patients in telemedical home monitoring.

   The role of systemic blood pressure in glaucoma progression. *Rom J

10. Martínez A, Sanchez M. Predictive value of colour Doppler
    imaging in a prospective study of visual field progression in
    **83**(6): 716-22. [PMID: 16396650]

    hemodynamics and glaucoma prognosis: A color Doppler imaging
    archophthalmol.121.12.1711. [PMID: 14662590]

12. Marjanović I, Martinez A, Marjanović M, Kontić D, Hentova-
    Senčanić P, Marković V, Bozić M. Changes in the retrobulbar
    circulation of 24-hour blood pressure regulation and patterning.
    24502088]

    in the glaucomas and the anterior ischemic optic neuropathies. *Am J

    untreated primary open-angle glaucoma and ocular hypertension.

15. Smolensky MH, Hermida RC, Portaluppi F. Circadian
    mechanisms of 24-hour blood pressure regulation and patterning.
    *Sleep Med Rev.* 2016 Mar; **2**: S1078-0792(16)00019-8. [PMID:
    27076261]; [DOI: 10.1016/j.smrv.2016.02.003]

16. Özşelit ME, Özşelit E Doğan NB, Pekel N, Ozyurtlu F, Yılmaz A,
    Saygi S, Tengiz I, Ercan E. Impact of anxiety level on circadian


**Peer Reviewer:** Ronald Frenkel