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Silent myocardial ischemia in glaucoma and cataract patients

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Abstract ● **Background:** Glaucoma and cataract are multifactorial diseases. They have been described to be associated with cardiovascular risk factors. ● **Methods:** Twenty-four-hour ECG monitoring was done in 22 normal-tension glaucoma patients, 27 open-angle glaucoma patients, 25 cataract patients, and 20 normal controls. The frequency of silent myocardial ischemia (SMI) as well as that of ventricular extrasystoles (VES) was evaluated. ● **Results:** At least one episode of significant asymptomatic ST-T segment depression occurred

in 45% of the normal-tension glaucomas, in 25.9% of open-angle glaucomas, in 12% of cataract patients, and in 5% of normal controls. The frequency of VES was not significantly different among the groups. ● **Conclusions:** Glaucoma, especially normal-tension glaucoma, is significantly associated with the occurrence of episodic asymptomatic myocardial ischemias. Cataract patients, however, had only a slightly, statistically not significantly increased frequency of both SMI and VES compared with normals.

Introduction

The pathogenesis of glaucoma and cataract is not yet fully established and is considered to be multifactorial. The incidence of both eye diseases are statistically somehow associated with systemic diseases. Besides general factors, such as age, race, or gender [24], glaucomatous damage, especially if it develops without increased intraocular pressure, is statistically related to a number of cardiovascular alterations, such as systemic hypotension [8, 11, 32], decreased blood cell velocity in nailfold capillaries [7] and other vessels [22], increased frequency of vasospasm [7], increased diffuse cerebral ischemic changes [30], increased neurosensorial dysacusis [31], increased level of endothelin [12, 20], as well as local constriction and dilatation of conjunctival capillaries [23].

Various risk factors [9, 15, 17] also seem to play a role in the genesis of age-related cataract, such as smoking [3, 13], alcohol consumption [21, 28], systemic hypertension [14, 19, 33], and diabetes mellitus [2].

Furthermore, a decreased life expectancy has been described for both glaucoma [27] and cataract patients [16, 29]. A number of ECG changes, such as rhythm and conduction abnormalities, have been described in glaucoma [25].

In a preliminary study we observed a relatively frequent occurrence of silent myocardial ischemia both in glaucoma and in cataract [10]. The purpose of the present study was to test whether the relative frequency of the occurrence of silent myocardial ischemia is, indeed, larger in this type of patients.

Patients and methods

We examined a total of 94 subjects by means of 24-h ECG: (a) 22 patients with normal-tension glaucoma (NTG), (b) 27 patients with primary open-angle glaucoma (POAG), (c) 25 cataract patients, and (d) 20 normal controls. Their demographic characteristics are listed in Table 1.

NTG was diagnosed when classical glaucomatous damage occurred despite untreated intraocular pressure less than 21 mm Hg

Table 1 Demographic data of control subjects and patients

	Normal-tension glaucoma	Open-angle glaucomas	Cataract patients	Normal controls
Number of patients	22	27	25	20
Sex (female/male)	13/9	17/10	13/12	10/10
Age (years)	64.6 ± 11.6	65.3 ± 9.5	63.4 ± 8.8	61.5 ± 10.4
History of coronary diseases (<i>n</i>)	3	1	4	0
Diabetes mellitus (<i>n</i>)	0	2	2	0
Systemic hypertension (<i>n</i>)	6	1	6	0

in at least two diurnal tension curves. The glaucoma patients were hospitalized for evaluation and treatment of glaucoma; the cataract patients were referred to the hospital for cataract surgery. The control subjects included patients hospitalized for other eye diseases, such as trauma or uveitis, as well as hospital staff members.

No inclusion or exclusion criteria were used. Instead, we included all patients as they entered the hospital, provided they gave their informed consent to take part in the study. One third of the NTG patients and all POAG patients were on local antiglaucomatous drugs (mostly beta-blockers) but none of the normal controls or the cataract patients were taking such drugs.

The ECG was monitored for 24 h using a two-lead ambulatory ECG (Holter system: EPICARDIA/Hellige, Germany). Silent myocardial ischemia (SMI) was defined as positive if at least one episode of ST-T segment depression of 0.1 mV greater during at least 30 s occurred. Ventricular extrasystoles (VES) were defined by the premature occurrence of a QRS complex that was bizarre in shape and had a duration generally greater than 120 ms.

If the patients had to have surgery, the test was done at least 2 days after the operation. Before starting the examination, resting 12-lead electrocardiography was performed. In no case did this show any alterations of ST-T segments or abnormal rhythms.

During the 24-h monitoring the patients could move around normally. However, they had to perform at least one forced physical activity, such as walking up and down stairs, for several minutes. Smoking was prohibited for the total 24-h period.

Results

The four groups were comparable with regard to age (Table 1). However, a history of systemic diseases was clearly more frequent in the cataract and glaucoma groups (Table 1) than in the normal controls.

Ten (45.5%) of the 22 NTG patients, seven (25.9%) of the 27 POAG patients, three (12%) of the 25 cataract patients, and one (5%) of the 20 normal controls had significant SMI. The relative frequency is depicted in Fig. 1. The difference between NTG and normal controls was statistically significant ($P=0.003$; chi-square) the difference between NTG and POAG, however, was not significant ($P=0.15$). If the glaucoma patients were pooled ($n=49$), 34.7% had myocardial ischemia. This was again statistically significantly different from normal controls ($P=0.01$). The relative frequency of SMI in the glaucoma group was not influenced by the patients' histories. If the four patients with a history of coronary heart diseases were excluded from the analysis, the relative frequency remained 35.6%. If the two diabetic pa-

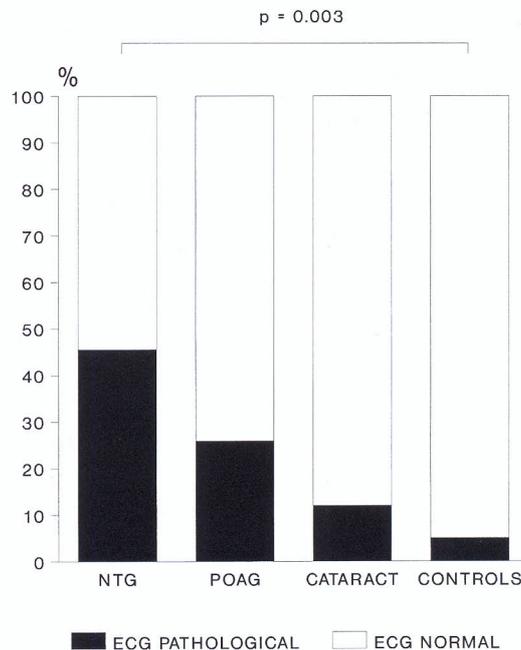


Fig. 1 Relative frequency of silent myocardial ischemia in the four groups (NTG normal-tension glaucoma, POAG primary open-angle glaucoma)

tients were excluded, the relative frequency was 34.0%. When the seven patients with systemic hypertension were excluded, the relative frequency was 33.3%. When all patients with a history of any type of systemic diseases were excluded, the relative frequency was 35.1%. Patients included in this remaining group were without systemic medication.

Seventy-five percent of all observed silent ischemic episodes occurred while the patient was sitting at ease or during sleep. Only 25% of the episodes occurred during physical exertion. Most of the patients who experienced myocardial ischemia had two episodes during 24 h, although the frequency varied between one and three. The frequency of VES was the same in NTG and POAG patients and in normal controls (Fig. 2). In the group of cataract patients, however, two patients had very frequent VES, though the difference did not attain statistical significance.

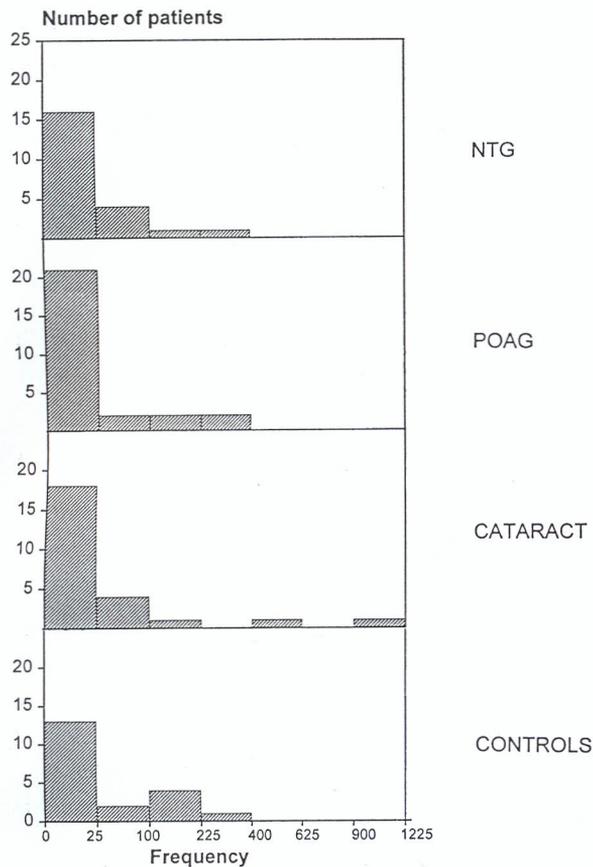


Fig. 2 Frequency distribution of ventricular extrasystoles in the four groups

Discussion

In the present study we searched for episodes of SMI and for VES with the help of 24-h ECG monitoring in glaucoma and cataract patients and in normal controls. All subjects entering this study had normal 12-lead ECGs. The results confirm the findings of a previous pilot study [10] that the frequency of SMI is increased significantly in patients with NTG and, to a lesser extent, in patients with POAG. In cataract patients, however, the frequency was only slightly, statistically not significantly, greater than in normal controls.

The ischemic episodes occurred mainly when patients were sitting at ease or during sleep. This indicates that the major cause might not be arteriosclerotic changes of the coronary arteries but rather functional vascular dysregulation [4, 18]. This is in agreement with the currently prevailing concept of vascular involvement in the pathogenesis of glaucoma [5]. Although the level of intraocular pressure is positively correlated to the level of the blood pressure [32], the vascular risk factors for glaucomatous damage are not so much arteriosclerosis [26] or hypertension [32] as functional vascular dysregulation and systemic hypotension [6].

The observed high prevalence of SMI, especially in NTG, without increase in VES [1] supports the hypothesis that vascular dysregulation might be one of several risk factors for the development of glaucomatous damage.

Cataract, however, seems to be more related to arteriosclerosis and its risk factors. The chance of finding ischemias in cataract patients may, therefore, be greater if ECG is done during exercise. This, however, remains to be proved. The slight increase in the frequency of VES in the cataract patients also points towards arteriosclerosis.

References

- Bethge KP (1982) *Langzeit-Elektrokardiographie bei Gesunden und bei Patienten mit koronarer Herzkrankung*. Springer, Berlin Heidelberg New York
- Chen TT, Hockwin O, Dobbs R (1988) Cataract and health status: a case-control study. *Ophthalmic Res* 20: 1-9
- Christen WG, Manson JE, Seddon JM (1992) A prospective study of cigarette smoking and risk of cataract in men. *JAMA* 268: 989-993
- Coffman JO, Cohen RA (1981) Vasospasm ubiquitous? *N Engl J Med* 304: 780-782
- Flammer J (1995) The role of ocular circulation in the pathogenesis of glaucomatous damage. In: Krieglstein GK (ed) *Glaucoma update V*. Kaden, Heidelberg, pp 81-86
- Flammer J (1996) To what extent are vascular factors involved in the pathogenesis of glaucoma? In: Kaiser HJ, Flammer J, Hendrickson P (eds) *Ocular blood-flow*. Karger, Basel, pp 12-39
- Gasser P, Flammer J (1991) Blood-cell velocity in the nailfold capillaries of patients with normal-tension or high-tension glaucoma and of healthy controls. *Am J Ophthalmol* 111: 585-588
- Graham SL, Drance SM, Wijsman K, Douglas GR, Mikelberg S (1995) Ambulatory blood-pressure monitoring in glaucoma. *Ophthalmology* 102: 61-69
- Italian-American Cataract Study Group (1994) Incidence and progression of cortical, nuclear, and posterior subcapsular cataracts. *Am J Ophthalmol* 118: 623-631
- Kaiser HJ, Flammer J, Burckhardt D (1993) Silent myocardial ischemia in glaucoma patients. *Ophthalmology* 207: 6-8

11. Kaiser HJ, Flammer J, Graf T, Stümpfig D (1993) Systemic blood pressure in glaucoma patients. *Graefe's Arch Clin Exp Ophthalmol* 231: 677-680
12. Kaiser HJ, Flammer J, Wenk M, Lüscher T (1995) Endothelin-1 plasma levels in normal-tension glaucoma: abnormal response to postural changes. *Graefe's Arch Clin Exp Ophthalmol* 233: 484-488
13. Klein BE, Klein R, Linton KLP, Franke T (1993) Cigarette smoking and lens opacities: the Beaver Dam Eye Study. *Am J Prev Med* 9: 27-30
14. Klein BE, Klein R, Jensen S, Linton KL (1994) Hypertension and lens opacities from the Beavers Dam Eye Study. *Am J Ophthalmol* 119: 640-646
15. Klein R, Klein BE, Jensen SC, Moss SE, Cruickshanks KJ (1994) The relation of socioeconomic factors to age-related cataract, maculopathy, and impaired vision. *Ophthalmology* 101: 1969-1979
16. Klein R, Klein BE, Moss SE (1995) Age-disease and survival. The Beaver Dam Study. *Arch Ophthalmol* 113: 333-339
17. Lesiewska-Junk H (1994) Senile and presenile cataract. *Acta Ophthalmol* 72: 602-605
18. Miller D, Waters DD, Warnica W, Szlachet J, Kreeft J, Thérout P (1982) Is variant angina the coronary manifestation of a generalized vasospastic disorder? *N Engl J Med* 304: 763-766
19. Mohan M, Sperduto RD, Angra SK (1989) India-US case-control study of age-related cataracts. *Arch Ophthalmol* 107: 670-676
20. Moriya S, Sugiyama T, Shimizu K, Hamada J, Tokuoka S, Azuma I (1992) Low-tension glaucoma and endothelium (ET-1). *Folia Ophthalmol Jpn* 43: 554-559
21. Munoz B, Tajchman U, Bochow T, West S (1993) Alcohol use and risk of posterior subcapsular opacities. *Arch Ophthalmol* 111: 110-112
22. Nasemann JE (1992) Die Fluoreszenz-Perfusions-Szintigraphie - eine neue Methode zur Quantifizierung okulärer Durchblutungsstörungen. *Habilitationsschrift, University of Munich*
23. Orgül S, Flammer J (1995) Perilimbal aneurysms of conjunctival vessels in glaucoma patients. *Ger J Ophthalmol* 4: 94-96
24. Orgül S, Flammer J, Gasser P (1995) Female preponderance in normal-tension glaucoma. *Ann Ophthalmol* 27: 355-359
25. Peräsalo R, Peräsalo J, Raitta C (1992) Electrocardiographic changes in institutionalized geriatric glaucoma patients. *Graefe's Arch Clin Exp Ophthalmol* 230: 213-217
26. Pillunat LE, Stodtmeister R (1988) Inzidenz des Niederdruckglaukoms bei hämodynamisch relevanter Karotisstenose. *Spektrum Augenheilkd* 2: 24-27
27. Ringvold A, Blika S, Guldahl J, Brevik T, Hesstvedt P, Hoff K (1991) The middle-Norway eye-screening study. *Acta Ophthalmol* 69: 273-280
28. Ritter LL, Klein BEK, Klein R, Mares-Perlman JA (1993) Alcohol use and lens opacities in the Beaver Dam Eye Study. *Arch Ophthalmol* 111: 113-117
29. Street DA, Javitt JC (1992) National five-year mortality after in-patient cataract extraction. *Am J Ophthalmol* 113: 263-268
30. Stroman GA, Steward WC, Golnik KC, Curé JK, Olinger RE (1995) Magnetic resonance imaging in patients with low-tension glaucoma. *Arch Ophthalmol* 113: 168-172
31. Susanna R, Basseto KL (1992) Hemorrhage of the optic disc and neurosensory dysfunction. *J Glaucoma* 1: 248-253
32. Tielsch JM, Katz J, Sommer A, Quigley HA, Javitt JC (1995) Hypertension, perfusion pressure, and primary open-angle glaucoma. *Arch Ophthalmol* 113: 216-221
33. Unakar NJ, Johnson M (1994) Lenticular alterations in hypertensive rats. *Exp Eye Res* 59: 645-652
34. West SK, Valmadrid CT (1995) Epidemiology of risk factors for age-related cataract. *Surv Ophthalmol* 39: 323-334