CLINICAL STUDY

Intraocular pressure and gonioscopic findings in rural communities mesoendemic and nonendemic for onchoceriasis, Kaduna State, Nigeria

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Abstract

Purpose **To report on glaucoma-related ocular parameters, namely intraocular pressure and peripheral anterior synechiae, in the presence of onchocercal infection.**

Methods **Two computer-generated random samples of individuals were drawn from communities mesoendemic and nonendemic for onchocerciasis respectively. Applanation tonometry and gonioscopy were carried out on these individuals.**

Results **Four hundred and thirty-six and 319 individuals from the mesoendemic and nonendemic communities were examined respectively. The mean intraocular pressure was 1.58 mmHg lower in the individuals from the mesoendemic communities compared with those from the nonendemic communities ($p < 0.001$) despite the prevalence of peripheral anterior synechiae being higher in the mesoendemic communities. In these communities, there was strong evidence that the prevalence of peripheral anterior synechiae increased with increasing microfilarial load.**

Conclusions **Onchocercal infection produces a low-grade inflammatory process, which may result in a lowering of intraocular pressure despite the formation of peripheral anterior synechiae. Glaucomatous optic nerve damage may therefore not be the primary cause of visual loss in ocular onchocerciasis as this occurs late and is probably preceded by other blinding onchocercal pathology.**

Key words Glaucoma, Gonioscopy, Intraocular pressure, Nigeria, Onchocerciasis, Peripheral anterior synechiae

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The World Health Organization (WHO) has estimated that 17.7 million people are infected with *Onchocerca volvulus*, of whom 270 000 are blind and a further 500 000 severely visually disabled. Over 99% of infected individuals live in the tropical belt of Africa.[1] Several population-based studies in Africa have confirmed onchocerciasis as one of the major causes of blindness (12.5–73.1%) in endemic areas.[2–6] Ocular onchocerciasis is known to cause blindness by a variety of mechanisms: sclerosing keratitis, chronic anterior uveitis, chorioretinal atrophy, chorioretinitis, optic neuritis and optic atrophy.

Glaucoma has also been implicated as another blinding lesion caused by the infection. Since Hissette first noted that 'if the ciliary body is much affected, hypertonia is produced, often causing atrophy of the eyeball',[7] a number of other publications have appeared to corroborate this finding.[8–12] The literature to date suggests that two forms of glaucoma may be associated with onchocercal infection. The first is early-onset glaucoma in the absence of other ocular signs of inflammation or onchocercal infection, and the second an end-stage, post-inflammatory glaucoma. The aetiology of this first form of glaucoma has been attributed to both increased aqueous production as a result of ciliary body irritation by microfilariae, and diminished aqueous outflow from peripheral anterior synechiae.[13] However, low intraocular pressures (IOPs) have also been reported in individuals with onchocerciasis.[14–16]

A large WHO placebo-controlled trial of ivermectin for onchocerciasis in Kaduna State, Northern Nigeria afforded the opportunity for a population-based investigation of ocular parameters in the presence of onchocercal infection. This paper presents the findings with respect to IOP and gonioscopic findings in populations mesoendemic and nonendemic for onchocerciasis.

Table 1. *Demographic and ocular characteristics of the individuals examined*

	Mesoendemic communities (n = 436)	Nonendemic communities (n = 319)
No. (%) of males	200 (46%)	163 (51%)
Age (years)		
Mean (SD)	30.3 (17.1)	29.7 (18.1)
Median (range)	27 (5–81)	28 (5–85)
No. skin-snip positive (%)	270 (62%)	0
No. of successful right IOP measurements	382 (88%)	262 (82%)
No. of successful left IOP measurements	381 (87%)	262 (82%)
Right IOP mmHg		
Mean (SD)	13.5 (4.6)	15.1 (4.7)
Median (range)	13 (4–42)	14 (6–40)
Left IOP mmHg		
Mean (SD)	13.4 (4.2)	14.8 (4.0)
Median (range)	13 (2–42)	14 (6–28)
No. (%) of individuals with PAS in right eye	51 (14.1%)	23 (9.3%)
No. (%) of individuals with PAS in left eye	46 (13.1%)	23 (9.9%)

IOP, intraocular pressure; PAS, peripheral anterior synechiae.

Methods

Thirty-six communities in two areas of Kaduna State, Northern Nigeria, expected on entomological grounds to be mesoendemic for onchocerciasis were censused in 1988. Ethics approval and informed consent were obtained. Individuals aged 5 years and over were photographed, registered and skin-snipped. A brief history, including previous diethyl carbamazine (DEC) intake, was obtained from the patient. The 34 communities with the highest skin-snip positivity were selected for inclusion in the ivermectin trial. In 1990, two further communities in a non-onchocercal area of Kaduna State were censused as a control group. These individuals were similarly registered and skin-snipped. Findings of the ivermectin trial have been published.[3,17,18]

A random sample of registered individuals from each of these populations was generated by computer. In the mesoendemic communities, 6% of the population was included in the random sample and in the nonendemic communities, 21% of the population was included. The random samples were weighted with respect to age to give an increased representation of those aged 20 years and over in each community. An extensive ophthalmic examination was performed on all individuals in the random samples prior to any treatment with ivermectin.[3,17,18] The ocular examination used a slit-lamp biomicroscope and included applanation tonometry using a Haag Streit tonometer and gonioscopy using a Goldmann two-mirror gonioscope. A variety of gonioscopic features were documented including the estimated total number of degrees of angle closed or affected by peripheral anterior synechiae (PAS). Gonioscopy was initially performed in 40 eyes by two ophthalmologists in order to ensure that readings obtained by each observer were comparable. There was a mean difference of 12° between the number of degrees of PAS recorded by each ophthalmologist for the same eyes. The difference between the two observations was not significant (p = 0.11). The ophthalmologists were unaware of the individuals' skin-snip status at the time of the examination.

Statistical analyses were performed using the Generalized Estimating Equations approach (GEE) to account for correlation between each individual's two eyes.

Results

Between-community comparison

There were 436 individuals in the random sample drawn from the communities mesoendemic for onchocerciasis and 319 individuals in the random sample drawn from the communities nonendemic for onchocerciasis. Just under two-thirds (62%) of those in communities mesoendemic for onchocerciasis had positive skin-snips whilst none had positive skin-snips in the nonendemic random sample. Of a total of 1510 eyes, 1299 (86%) had successful applanation and 1194 (79%) had successful gonioscopy. Failure of tonometry and gonioscopy was strongly age-related, with most failures occurring in children aged less than 10 years. Table 1 shows demographic and ocular characteristics of the study sample. Fig. 1 shows the distribution of IOPs within each community. Using data from both eyes and controlling age and sex, the mean IOP was 1.58 mmHg lower in the mesoendemic communities compared with the nonendemic communities (95% CI 0.94–2.21; $p < 0.001$). The prevalence of PAS was higher in the mesoendemic communities than in nonendemic communities (odds ratios controlling age and sex = 1.92, 95% CI 1.18–3.15; p = 0.009). Taking only those eyes with PAS, the mean angle of PAS was 31° greater in mesoendemic communities (95% CI 0–62; p = 0.05).

Within-community comparison

Within the mesoendemic communities the mean right IOP was 13.1 (SD 4.5, median 12, range 4–42) mmHg in those with positive skin-snips compared with 13.9 (SD 4.3, median 13, range 6–37) mmHg in those with negative

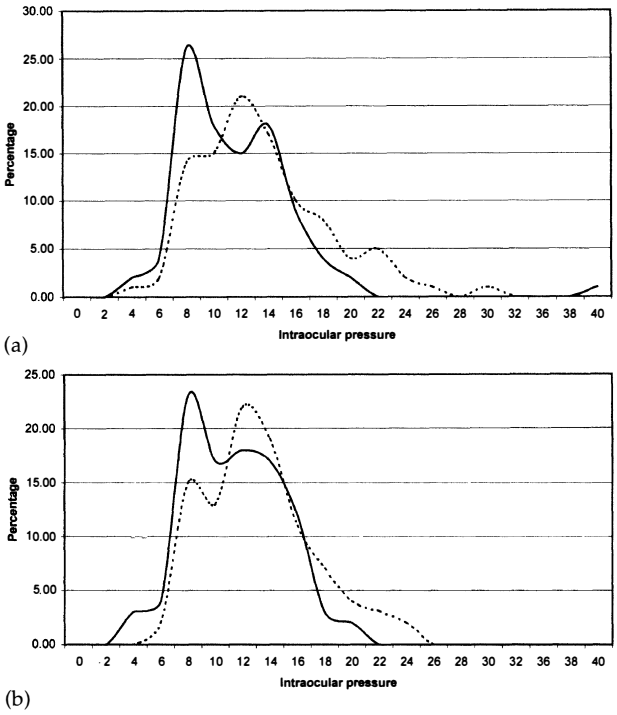

Fig. 1. *Distribution of (a) right eye and (b) left eye intraocular pressures in the mesoendemic (continuous line) and nonendemic (broken line) random samples.*

skin-snips. A similar pattern was observed in left eyes. Considering both right and left eyes and controlling for age and sex, the IOP was 0.66 mmHg lower on average in eyes of skin-snip-positive individuals (95% CI 1.56 lower to 0.24 higher) but this difference was not statistically significant ($p = 0.15$). Controlling for age and sex, the prevalence of PAS was higher in eyes of those with positive skin-snips (18.9% vs 8.4%) but again this difference was not statistically significant (OR = 1.30; 95% CI 0.63–2.67; $p = 0.5$).

Among those with positive skin-snips there was no evidence of an association between microfilarial load and IOP after controlling age and sex ($p = 0.54$). In the same group, however, there was strong evidence that the prevalence of PAS increased with increasing microfilarial load ($p < 0.001$). In those eyes with PAS, there was no evidence of correlation between microfilarial load and number of degrees of PAS ($p = 0.96$). Amongst the individuals with no PAS within the mesoendemic communities, there was some evidence that those with positive skin-snips had lower IOPs that those with a negative skin-snip (12.7 mmHg, $n = 173$ vs 13.5 mmHg $n = 99$; $p = 0.06$).

A total of 40 individuals had unequivocal glaucoma. Thirty-seven were from the mesoendemic communities. Unequivocal glaucoma was diagnosed if a typical optic disc appearance was seen in one or both eyes, or if there was an equivocal glaucomatous disc appearance with a raised IOP over 21 mmHg on phasing. If the optic disc was not visible, a raised IOP in excess of 30 mmHg or previous glaucoma surgery was required for diagnosis.

The history obtained from the patient regarding past history of DEC consumption was found to be of dubious validity and was excluded from analysis.

Discussion

This finding of a lower mean IOP in the mesoendemic communities compared with nonendemic communities is consistent with those of Anderson[14] and Thylefors *et al.*[15,16] Within the mesoendemic communities, IOPs were slightly lower in the eyes of the individuals who were skin-snip-positive for onchocerciasis, but the difference was not statistically significant. Nor was there any evidence of a correlation among the skin-snip-positive individuals between microfilarial load and IOP. There are (at least) three possible explanations for our findings. One possibility is that onchocercal infection does lead to a decrease in IOP, but that our sample of individuals within the mesoendemic communities was too small to demonstrate this effect within these communities. Alternatively, onchocercal infection may have no impact on IOP and the difference that we observed at the community level is due to some difference between the mesoendemic and nonendemic communities other than onchocercal infection. Thirdly, it may be that the spread of microfilarial load was too small to show such an effect in our population.

To our knowledge this is the first study including systematic gonioscopy to determine the association of PAS with onchocercal infection. Observations in 22 individuals who had gonioscopy in the study by Thylefors *et al.*[16] suggested that PAS may be associated with onchocerciasis and the possibility was also mentioned by Buck.[19] Other authors have attributed open angle glaucoma to onchocercal infection but have not reported gonioscopic findings.[11,12] We found that the prevalence of PAS was higher in mesoendemic than nonendemic communities, higher in infected individuals within endemic communities (though not achieving statistical significance) and increased with increasing microfilarial load.

An end-stage post-inflammatory glaucoma has been widely reported in ocular onchocerciasis.[7–13,15,16,19] In our population the few eyes that were blind with a high IOP also had other severe onchocercal pathology, suggesting that the high pressure in itself was probably not the primary cause of visual loss but rather a late secondary phenomenon as first suggested by Thylefors *et al.*[16]

Putting these findings together we hypothesise that current onchocercal infection produces a low-grade inflammatory process in the eye which results in a lowering of the IOP due to inflammation in the ciliary body and also results in the formation of PAS. The possibility that low-grade inflammation is produced even prior to PAS formation is suggested by the finding that amongst those with no PAS in the mesoendemic community, those with a positive skin-snip had a lower IOP than those with a negative skin-snip. Overall sufficient functional trabecular meshwork is maintained for the lower IOP to be the main outcome until the very late stages of ocular disease, at which time PAS may completely occlude the angle resulting in a rise in IOP.

By this stage, however, the eye is often already blind from other pathological sequelae of onchocercal eye disease.

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