PRIMARY OPEN-ANGLE GLAUCOMA IN SUB-SAHARAN AFRICA

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ABSTRACT

Primary open-angle glaucoma (POAG) is a chronic progressive optic neuropathy often associated with increased intraocular pressure resulting in irreversible degeneration of the retinal ganglion cells and their axons, optic disc cupping and characteristic visual field defects. Recently, POAG has become the second major blinding disease worldwide. In most parts of sub-Saharan Africa, it is either the second or the third contributor to blindness. More data needs to be gathered in order to obtain a more complete understanding of its burden, and to allow better public health planning, public education, prevalence assessment and management strategies. The present review gives an overview of available data on prevalence, risk factors and treatment, and highlights the challenges that POAG presents in SSA.

Key words: primary open-angle glaucoma, sub-Saharan Africa

MAGNITUDE OF THE PROBLEM

Primary open-angle glaucoma (POAG) is one of the leading causes of blindness in sub-Saharan African (SSA), where the prevalence of glaucoma blindness ranges between 0.1% and 0.6%.[1-6] Its socio-economic impact on African communities is tremendous, mainly because most affected people remain untreated and go blind at a relatively young age.

Population-based studies conducted outside Africa have repeatedly shown that the prevalence of POAG is greater in individuals who are of African origin than in those of other origins. Only a few epidemiological studies have been carried out on POAG in SSA. Most of these studies are hospital-based and are limited to people who manage to reach the few available hospitals and be examined by the few available ophthalmologists.[7] Community-based studies are difficult to carry out in SSA because they are costly and unlikely to be funded locally. Demographic data are often unreliable, some people being reluctant to provide correct information on questionnaires for various reasons. Moreover, POAG has not received much attention from international funding organizations compared to cataract, trachoma and onchocerciasis.

POAG is the most common form of glaucoma in SSA. It accounts for at least 45% of all forms of glaucoma.[8-12] The other types of glaucoma include primary angle-closure glaucoma, which accounts for 6.6%-15%,[8-11,13] secondary open-angle glaucoma accounting for 17%-37%,[8, 10-12] and secondary closure-glaucoma contributing more or less 2%.[11] Based on available data on POAG in the world's major ethnic groups, its prevalence in Africa has been estimated to be 7%.[14] The few community-based studies ever conducted in SSA have shown a wide variation in its prevalence. In a survey in rural central Tanzania, a prevalence of 3.2% was found.[11] In South Africa, a recent study in an urban black population of the North West Province reported a prevalence of 2.9%.[8] A similar prevalence was reported in the Northern KwaZulu-Natal Province.[10] These figures are two-fold higher than that found in Western Cape.[13] However, the participants in the latter study included not only Blacks, but also people with mixed backgrounds such as a mixture between Blacks and Whites, or with South East Asian descendants, which may explain the low prevalence. The prevalence was 2.7%, 1.02%, 2.1% and 7.7%-8.5% in Nigeria,[15,16] Ivory Coast[17] and Ghana[18] respectively. In general, it appears that stricter diagnostic criteria tend to generate lower prevalences. It is more likely that these rates are lower than the actual figures.[19] Indeed, with the non-availability of advanced techniques for scanning the optic nerve head and the retinal fiber layer (i.e., scanning laser tomography and polarimetry) and computerized visual field assessment (i.e., the Swedish interactive thresholding algorithm) that permit early diagnosis before obvious visual function loss,[20,21] it is likely that a substantial proportion of cases are undiagnosed. On the other hand, another proportion of cases is wrongly diagnosed as having the disease.

Comparison of the prevalence in different regions of SSA should be made with care given the huge ethnic and cultural diversity, which probably expresses underlying

genetic differences that may partly explain the observed differences in epidemiological data.[16,22] In addition, great differences exist in the diagnostic criteria and case selection between studies.

RISK FACTORS

Elevated intraocular pressure (IOP) remains the major risk factor for POAG irrespective of race. A search on PubMed produced only two articles specifically focussing on risk factors for POAG in SSA.[23,24] Both reported the results of hospital-based case-control studies conducted in Kinshasa, Congo and found a strong association between the Mongo ethnic group and POAG. In one of them,[23] a family history of glaucoma, consumption of rice and hyperopia were also significantly associated with POAG. The high proportion of cases with a positive family history is questionable, since this study was hospital-based and therefore subject to various biases, particularly the recall bias for a positive family history in a setting where POAG awareness and knowledge are very poor.[25,26] Though family history plays a key role in the occurrence of POAG, its exact mode of inheritance is yet to be determined. Recently, there has been a growing effort to identify the gene responsible for POAG. In this perspective, two studies have investigated the prevalence and role of myocilin mutations in SSA.[27,28] The results suggested that these mutations do not play a significant role in the pathogenesis of POAG in those populations, which is consistent with the lack of association found between these mutations and the high prevalence of POAG in African American patients.[29]

Studies conducted among Blacks outside Africa have shown either no or only a weak association between refractive status and POAG. Such data remain scarce in SSA where Kaimbo et al.[23] unexpectedly found that hyperopia confers a higher risk of POAG among the Congolese. Community-based surveys are needed to clarify this relationship.

The debate as to whether diabetes is a risk factor for POAG continues. There is evidence that the large majority of SSA diabetic subjects have no access to treatment, which results in high rates of complications. Whether the incidence of POAG follows the increase in incidence of other diabetes-related complications remains unclear. So far no association has been reported between diabetes and POAG in SSA.[15,23,24]

Numerous studies have investigated the association between systemic hypertension and POAG.[30] To date, there is no agreement as to whether systemic hypertension increases the risk of POAG, although the weight of the evidence suggests the lack of association. The results of the two studies that have evaluated this association in SSA are also conflicting.[15,23] Therefore, there remain some inconsistencies that further studies should attempt to resolve.

The amount of aqueous humour drained to the Schlemn's channel depends on the trabecular meshwork characteristics. Studies have shown both morphological and structural changes mostly consisting of pigments accumulation and reduction of the number of trabecular cells in glaucomatous eyes. Comparison of trabecular meshwork features between Blacks and Whites is important as it may help clarify, for instance, why Blacks present more severe glaucoma. In SSA only one study has provided evidence that Black glaucomatous have much fewer trabecular cells than Whites.[31]

TREATMENT OF POAG

Limiting or slowing the progression of loss of retinal ganglion cells by lowering IOP remains the primary treatment target.[32] There is mounting evidence that the prevalence of POAG and the rate of treatment failure are higher in patients who are of African origin than others.[33,34,35,36] Although medical treatment avoids surgery-related risks, it presents the following problems in SSA:

1. high cost and uncertain availability of drugs and the resulting poor compliance
2. regimens sometimes confusing particularly for less educated people
3. inappropriate drug storage conditions

Consequently, its appropriateness as first line therapy in SSA has been questionned by a number of investigators. Although sound randomized trials are lacking, the situation on the ground indicates that surgery is preferable as the mainstay of treatment.[37,38] Whatever the treatment may be, it should always start by setting a target IOP level and treatment plan on an individual basis, based on factors such as the family history, the current IOP, the extent of visual damage, and the age of the patient. Since there is no unique safe and permanent level of IOP for all POAG patients, the level of IOP that prevents further retinal ganglion loss may be difficult to determine accurately due to the wide diurnal and nocturnal fluctuations of IOP. It is also important that the target pressure is periodically re-evaluated and readjusted over time if necessary, especially if the disease progresses. Based on a considerable amount of new evidence which shows that IOP peak occurs at night in both healthy and glaucomatous individuals rather than during the day (supine IOP greater than sitting IOP around the clock) as initially thought,[39] it is critical that IOP-lowering drugs are effective both during the daytime and at night. At present, only prostaglandins have these features, and they have been shown to be more effective than beta-blockers and carbonic anhydrase inhibitors at any time of the day.

POAG treatment in SSA presents other unresolved issues including poverty, poor understanding of the disease, collapse of health systems, limited number of

ophthalmologists and lack of adequate materials.[37,38,40,41] Most patients cannot afford the cost associated with surgery, lifetime medical treatment and follow-up. Currently, there is roughly only one ophthalmologist for at least one million people.[22,42-44] Most of them reside in cities, aggravating the inaccessibility to eye care in rural areas where most people live. To overcome this problem, the number of ophthalmologists must be increased and the skills of those already available upgraded through surgical training and continuing education. The few existing eye services need to be expanded and reconditioned. Eye care should be made affordable and accessible. Since it seems currently unrealistic to expect support from local governements in most countries, as available funds are used to fight diseases such as malaria, human African trypanosomiasis, AIDS and other deadly diseases, there is a pressing need for support from governmental and non-governmental organizations, universities and individuals from developed countries.

It is unfortunate that trabeculectomy is performed only in major cities and that not all ophthalmologists feel comfortable with the procedure. Studies that have evaluated its effectiveness have found high success and low complication rates.[26,45-51] Long-term follow-up studies after trabeculectomy have shown a decrease in the number of respondents and the success rate over time.[26,47,52,53] The IOP control failure can be ascribed mainly to excessive fibrosis during the healing process. This has led investigators to assess the effectiveness of mitomycin-C (MMC) and 5-fluorouracil (5-FU) in black Africans. Although they significantly reduce the IOP and the risk of surgery failure,[13,54-57] their use is not systematic yet in SSA. All countries should follow the South African policy which recommends trabeculectomy augmented with cytotoxic agents as the first line treatment for POAG.[58] It is, however, important to keep in mind that MMC is more expensive than 5-FU; it must be refrigerated; and has been associated with persistent hypotonia and the eventual maculopathy, the risk of endophthalmitis and early cataract formation or rapid progression of pre-existing lens opacities, and the loss of corneal endothelial cells. The use of post-operative 5-FU has been mostly linked with discomfort related to multiple subconjunctival injections, corneal defects, and subconjunctival leaks.

CONCLUSIONS

Several aspects of POAG in SSA have either never been or have been insufficiently investigated. The diversity of ethnic groups in SSA probably accounts for huge genetic differences, which may partly explain the difference in epidemiological data. Further studies employing more detailed assessment of risk factors are necessary to clarify the possible role of genetic background and certain environmental factors such as food. There is a need to improve POAG diagnosis in the early stages by using very sensitive methods, and to make available affordable therapeutic methods. Because POAG presents a greater public health challenge than other blinding diseases, help is needed urgently to increase the number of glaucoma surgeons. In addition, both local and international health policy makers should work together to find ways to start large-scale screening.

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