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RESEARCH ARTICLE

A review of outcomes of laser photocoagulation for Goldberg stage 3 proliferative sickle cell retinopathy

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Abstract

***Topic*:** A review of outcomes of laser photocoagulation for Goldberg stage 3 proliferative sickle cell retinopathy (PSR) in a Eye Foundation Hospital.
***Aims and objectives*:** To report regression of retina neovascularization and visual outcomes after prophylactic scatter retina laser photocoagulation for Goldberg stage 3 PSR in a tertiary private hospital in sub-Saharan Africa.
***Methods*:** A retrospective review of case files of patients who were treated with prophylactic scatter retina laser photocoagulation between January 2017 and June 2022 following a diagnosis of PSR in a Eye Foundation Hospital, Ikeja, Lagos, Nigeria, was done.
***Results*:** A total of 124 eyes of 62 patients with PSR were seen within the period under consideration. A majority of patients (49 (79.0%)) had hemoglobin (Hb) genotype SC, while 13 patients (21%) were Hb genotype SS. At presentation, 29 eyes (23.3%) had Goldberg stage 2 PSR, 55 eyes (44.4%) had Goldberg stage 3 PSR, 27 eyes (21.8%) had stage 4 PSR, while 13 eyes (10.5%) had stage 5 PSR. All 55 eyes (49.2%) with stage 3 PSR were treated with prophylactic retina laser photocoagulation. At the patients' last clinic visit, 34 eyes (61.8%) had the same visual acuity (VA) as at presentation, 11 eyes (20%) had improvements in VA, while 10 eyes (18.2%) had worse VA. Laser treatment success (regression of seafan neovascularization) was seen in 50 eyes (90.9%), while five eyes (8.1%) had unsuccessful laser treatment.
***Conclusion*:** A high percentage (90.9%) of resolution of retina neovascularization secondary to PSR at stage 3 of Goldberg's classification was seen after prophylactic scatter retina laser photocoagulation in our group of evaluated patients. Most patients (81.8%) maintained or had improvements in their visual acuities over the period of follow-up. More clinical research is required to further evaluate outcomes of laser photocoagulation for PSR.

Keywords: *sickle cell retinopathy*; *proliferative sickle cell retinopathy*; *sea fan neovascularization*; *laser photocoagulation*; *regression of sea fans*

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Sickle cell disease consists of a group of inherited hemoglobinopathies affecting multiple organs including the eyes. Ischemia can result from occlusion of vessels by rigid red blood cells with a sickle-shaped appearance [1]. Ocular manifestations of sickle cell disease can occur in both the anterior and posterior segments. Posterior segment manifestations can cause significant visual loss [2]. Goldberg in 1971 had classified retina manifestations of sickle cell into non-proliferative and proliferative types. He further classified proliferative sickle cell retinopathy (PSR) into five stages. Complications of visual loss often occur at stages 4 and 5 from vitreous hemorrhage, retinal detachment, or both. Vitreous hemorrhage is, however, preceded by the formation of abnormal neovascularization called sea fans at Goldberg stage 3. Non-proliferative retina findings include salmon patch hemorrhages, black sunbursts, and atrophic retina holes [3].

Laser photocoagulation is used widely in proliferative retinopathies such as proliferative diabetic retinopathy and has been reported to be effective in PSR also. Some authors, however, still advocate conservative management for PSR rather than prompt laser photocoagulation [4]. It is, therefore, important to evaluate the efficacy and safety of laser photocoagulation treatment for proliferative sickle retinopathy among our cohort of patients.

Eyes presenting at Goldberg stages 2 and 3 are generally believed to be the best stage for prophylactic retina laser photocoagulation [4].

Our study seeks to evaluate regression of sea fan neovascularization (successful retina laser treatment) after prophylactic retina laser photocoagulation for Goldberg stage 3 PSR in our cohort of patients in sub-Saharan Africa.

Aims and objectives

To review regression of retina neovascularization and visual outcome after prophylactic scatter retina laser photocoagulation for Goldberg stage 3 PSR in a tertiary private eye hospital in sub-Saharan Africa.

Methods

A retrospective review of case files of patients who were treated with prophylactic scatter laser photocoagulation between January 2017 and June 2022 following a diagnosis of PSR in the Eye Foundation Hospital, Ikeja, Lagos, Nigeria, was done. Only patients who had at least 4 months of follow-up were included in this study. All patients had detailed visual acuity (VA) assessment, and anterior and dilated posterior segment examination. Fundus photographs, Optical Coherence Tomography (OCT), and Fundus Fluorescein Angiography (FFA) were recommended routinely for all patients.

Eyes with cataracts, vitreous hemorrhage, retinal detachment, previous laser photocoagulation, and previous ocular surgery were excluded. Patients with other associated retinopathies like diabetic and hypertensive retinopathy were also excluded.

Visual acuities were classified by World Health Organization (WHO) classification of vision using Snellen's VA charts, and Log MAR notations were used to compare visual outcomes for laser-treated eyes [5]. Demographics were expressed as frequencies and percentages. Statistical analyses were performed using IBM SPSS Statistics Version 22 (IBM Corp., Armonk, NY, USA). Differences in mean were calculated using Student's *t*-test, and *P*-values less than 0.05 were considered to be statistically significant.

The Iridex 532 Argon Laser with slit lamp delivery was used for treatment in all cases. Treatment protocol included extended 1 mm anterior and posterior laser photocoagulation with 1 clock hour on each side of the sea fan neovascularization. Sufficient power to produce mild whitening of the retina was used. The number and extent of burns used depended on the size of the PSR lesion and the surgeons' discretion. Laser photocoagulation was done in sessions depending on surgeons' preference and patients' pain threshold. Successful treatment outcome was defined as clinical regression of neovascularization with no fresh vitreous hemorrhage within 4 months of treatment.

The Goldberg classification of 1971 [3] as represented below was used for classification:

Stage 1: peripheral arterial occlusion and ischemia: It is the earliest abnormality that can be visualized by fundus examination. The occluded arterioles can be seen as dark red lines. They eventually turn into white silver-wire vessels.

Stage 2: peripheral arteriolar-venular anastomoses: Arteriolar-venular anastomoses develop as blood is diverted from blocked arteries to nearby venules.

Stage 3: neovascularization and fibrous proliferation: Neovascularization starts from the arteriolar-venular anastomoses and grows into the ischemic retina. The characteristic fan-shaped appearance due to neovasularization is known as sea fan neovascularization.

Stage 4: vitreous hemorrhage. Peripheral neovascular tufts bleed and cause vitreous hemorrhage.

Stage 5: vitreoretinal traction bands and tractional retinal detachment: Traction on the sea fan and adjacent retina causes traction retinal detachment.

Results

Sixty-two patients were diagnosed with PSR within the period under consideration. Patients ages ranged from 19 to 79 years old with a mean of 40.21 years and a standard deviation of ± 11.11 years; there were 35 (56.4%) males and 27 (43.6%) females. A majority of the patients (49, 79.0%) had HB genotype SC, while the rest of the 13 patients (21%) were HB genotype SS. The mean follow-up period was 3.5 years with a standard deviation of ± 3.4 years. Out of 122 eyes with VA records at presentation, 72 eyes (59.1%) had visual acuities better than 6/18 (mild or no visual impairment), 19 eyes (15.6%) had acuities between <6/18 and 6/60 (moderate visual impairment), and 17 eyes (13.9%) had visual acuities between <6/60 and 3/60 (severe visual impairment), while 14 eyes (11.4%) had VA <3/60 (blindness).

At the patients last clinic visit, 34 eyes (61.8%) had the same VA as at presentation, 11 eyes (20%) had improvements in VA, while 10 eyes (18.2%) had worse VA. A comparison of the mean final LogMAR VA of 0.86 with a standard deviation of ± 1.37 to the mean presenting LogMAR VA of 0.98 with a standard deviation of ± 1.5 in participants who had laser treatment using a paired *t*-test of means showed no significant difference ($P = 0.27$, $t = 1.112$). This result means patients tend to maintain their presenting VA after treatment. At presentation, 29 eyes (23.3%) had Goldberg stage 2 PSR, 55 eyes (44.4%) had Goldberg stage 3 PSR, 27 eyes (21.8%) had stage 4 PSR, while 13 eyes (10.5%) had stage 5 PSR. Prophylactic scatter retina laser photocoagulation was applied to 55 eyes with grade 3 PSR during the period under review.

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Among the 55 eyes treated with prophylactic scatter retina laser photocoagulation, treatment success (regression of sea fan neovascularisation) was achieved in 50 eyes (90.9%). On multivariate analysis Hb genotype, sex of patients, age, number of laser sessions, presence of rubeosis, and associated systemic conditions had no significant relationship with laser treatment success or failure.

Discussion

The ideal treatment for PSR remains a subject of debate among retina specialists. Previous randomized controlled trials showed significant regression of neovascularization and prevention of vitreous hemorrhage among treated eyes [4]. However, because of the small number of participants in those trials, the high rate of spontaneous regression, and the fact that regression was seen mostly in individuals younger than 25 years, a lot of controversy persist. Some specialists presently prefer observation until vitreous hemorrhage becomes eminent, while others treat earlier [6, 7].

Due to the few facilities for laser photocoagulation in sub-Saharan Africa and a high likelihood that patients are lost to follow-up [8–10], more specialists in our region prefer to treat PSR with laser photocoagulation rather than observe. Patients who present to the retina specialist might not be able to comply with strict observation protocols. Despite above reasoning, it is still important to evaluate the outcomes of treated patients to ensure they are acceptable and within international standards. Our study evaluates treatment outcomes for Goldberg stage 3 PSR among our cohort of patients in sub-Saharan Africa. Treatment success was defined as clinical regression of neovascularization with no fresh vitreous hemorrhage within 4 months of treatment was seen in 90.9% of eyes in our study. This result is better than initial reports of 81.2 and 85.7% regression of neovascularization in previous studies [7, 11]. It should also be noted that despite regression of sea fan neovascularization, recurrences could still occur in up to 34% [7] of cases; hence, continuous monitoring is important for eventual successful outcomes. Retina specialists within our group practice consider Goldberg stage 3 PSR as an idea stage to treat as controversy remains among proponents of prophylactic laser photocoagulation for PSR if patients at Goldberg stage 2 should be treated or not, especially as a high rate of spontaneous resolution or auto infarction is reported [4].

To reflect the variable differences in eyes presenting at stage 3, further classification has been proposed as follows: grade A: flat sea fan with leakage < 1 disc area; grade B: elevated sea fan with hemorrhage; grade C: elevated sea fan with partial fibrosis; grade D: complete sea fan fibrosis without well demarcated vessels; grade E: complete sea fan fibrosis with well demarcated vessels [12, 13]. Traditionally, flat sea fans (grade A) are reported to have good responses to laser photocoagulation, while elevated ones, especially the large ones, respond less favorably. Regression of sea fans did not differ between treated and untreated eyes when flat sea fan was less than 1 disc area [11].

Scatter laser photocoagulation was done for all our patients, and no feeder vessel technique of photocoagulation was done for any patient. Treatment protocol included extended 1 mm anterior and posterior laser photocoagulation with 1 clock hour each side of the sea fan neovascularization and sufficient power to produce mild whitening of the retina. The number and extent of burns used depended on the size of the PSR lesion. Laser photocoagulation was done in sessions depending on surgeons' preference and patients' pain threshold.

Scatter laser photocoagulation is reported to have an indirect effect. Ischemic retina produces vascular endothelial growth factor (VEGF), which promotes neovascularization. Scatter laser coagulation destroys this ischemic retina converting a hypoxic retina to an anoxic retina, thus preventing vitreous hemorrhage, retinal detachment, and vision loss [1]. Like other regions of the world, it is important that attention be drawn to visual complications of sickle cell retinopathy in sub-Saharan Africa, well designed protocols need to be developed, and a better understanding of factors associated with regression of neovascularization is much needed. Well-designed screening protocols are also required as well as better training for care givers [14–16].

Our study shows a benefit of laser photocoagulation for the treatment of PSR at stage 3 of Goldberg's classification. Figure 1 shows Fundus photographs and FFA of a patient with stage 3 PSR, showing vitreoretinal traction bands and epiretinal membranes, sea fan neovascularization, and fluorescein dye leakage from sea fans. In view of the small number of eyes evaluated and the paucity of data for outcomes in sub-Saharan Africa, it is important to have further research into this topic particularly a randomized clinical trial [1].

In conclusion, a high percentage (90.9%) of resolution of retina neovascularization secondary to PSR at stage 3 of Goldberg's classification was seen after prophylactic scatter retina laser photocoagulation in our group of evaluated patients. Most patients (81.8%) maintained or had improvements in their visual acuities over the period of follow-up. More clinical research is required to further evaluate outcomes of laser photocoagulation for PSR.

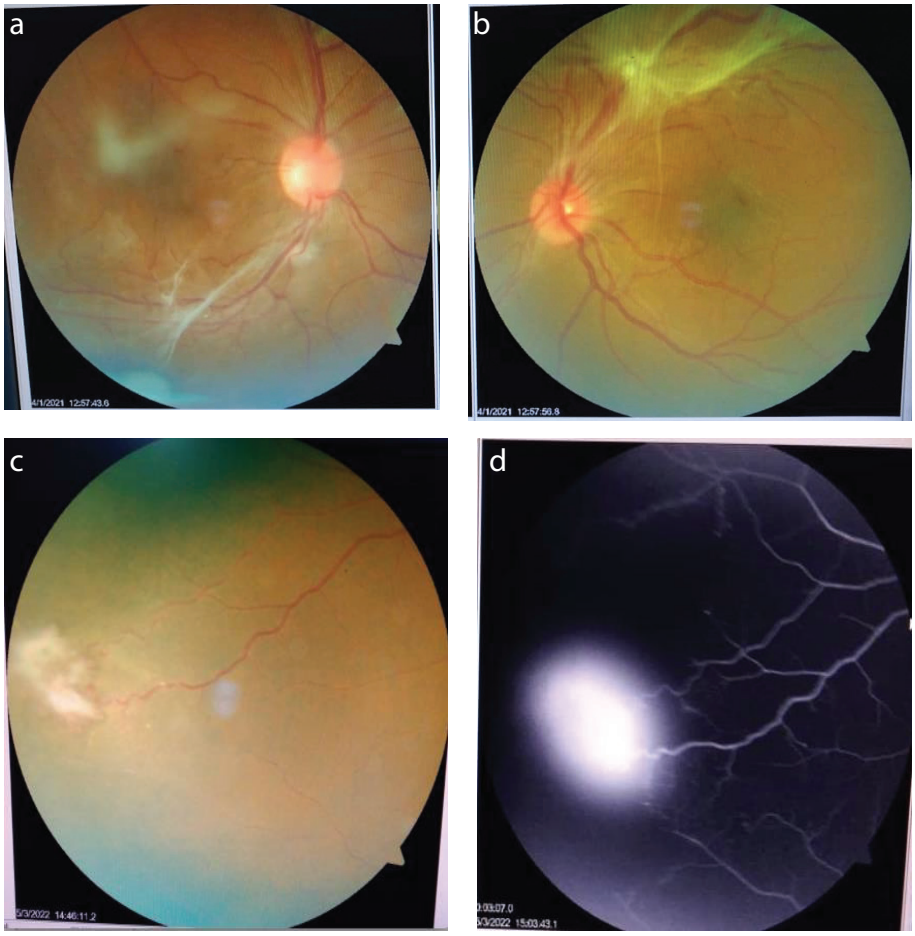

Fig. 1. (a) Fundus photograph of the posterior pole of the right eye of a patient with stage 3 proliferative sickle cell retinopathy , showing vitreoretinal traction bands and epiretinal membranes. (b) Fundus photograph of the posterior pole of the left eye of a patient with stage 3 proliferative sickle cell retinopathy , showing vitreoretinal traction bands and epiretinal membranes. (c) Fundus photograph of the inferotemporal periphery of the right eye of a patient with stage 3 proliferative sickle cell retinopathy, showing seafan neovascularization with fibrosis. (d) Fundus Flourescein Angiography picture of the right eye of a patient with stage 3 proliferative sickle cell retinopathy, showing hyperflorescence from seafan dye leakage.

Conflict of interest and funding

The authors report no conflict of interest. Funding for this study was provided by authors only.

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