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Steroids versus No Steroids in Nonarteritic Anterior Ischemic Optic Neuropathy

A Randomized Controlled Trial

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Purpose: To examine the role of oral steroid therapy in the treatment of nondiabetic cases of acute nonarteritic anterior ischemic optic neuropathy (NAAION).

Design: Randomized double-blind clinical trial.

Participants: Thirty-eight patients with acute nondiabetic NAAION divided into 2 arms of 19 patients each. One arm constituted the cases and the other constituted the controls.

Methods: Cases received oral steroid therapy and were designated the steroid group, whereas controls received placebo and were designated the nonsteroid group. Best-corrected visual acuity (BCVA), visual evoked response (VER), and OCT were performed at baseline, 1 month, 3 months, and 6 months after recruitment into the trial.

Main Outcome Measures: Best-corrected visual acuity, VER, and retinal nerve fiber layer changes on OCT.

Results: Both groups showed significant improvement in BCVA, VER latency, and resolution of disc edema on OCT parameters over 6 months. Final outcome showed no statistically significant difference with regard to visual acuity, although VER was better in the steroid group ($P = 0.011$). Best-corrected visual acuity, VER amplitude, and VER latency ($P = 0.02$, $P = 0.02$, and $P = 0.04$, respectively) showed a greater percentage improvement in the steroid group, which also saw a faster resolution of disc edema on OCT (1-month follow-up).

Conclusions: Oral steroids in acute NAAION did not improve the visual acuity significantly at 6 months. However, they improved resolution of disc edema significantly and enabled a greater improvement in VER parameters. This subtle benefit of oral steroids in NAAION is clinically unimportant and does not provide support for its use. *Ophthalmology 2018;■:1–5 © 2018 by the American Academy of Ophthalmology*

Nonarteritic anterior ischemic optic neuropathy (NAAION) is an important cause for vision loss in the elderly. It generally manifests with subacute to acute vision loss with disc edema and visual field defects (usually altitudinal). It has limited management options, with control of risk factors—particularly diabetes, hypertension, and hyperlipidemia—being the only universally accepted method. The pathophysiologic factors for optic nerve damage in NAAION indicate a compartment syndrome–like effect caused by disc swelling. It is postulated that reduction of the disc edema through high-dose steroids may reduce this and also may prevent free radical–induced damage. On the basis of anecdotal evidence, steroid therapy has been tried over the past 1 to 2 decades with conflicting results regarding its benefit.[1–6] No prospective, truly randomized controlled study was available for definitive evidence. This study examined the role of oral steroid therapy in NAAION in nondiabetic patients and focused on the structural and functional outcomes and adverse effects of steroid use.

Methods

A prospective, randomized, double-blind placebo clinical trial was conducted at the neuro-ophthalmology services of Dr. Rajendra Prasad Centre for Ophthalmic Sciences (All India Institute of Medical Sciences, New Delhi, India), a tertiary care center, after ethics committee approval and clinical trial registration (www.ctri.nic.in identifier, CTRI/2016/02/006672). All research adhered to the Tenets of the Declaration of Helsinki. The trial started in March 2015 and concluded in August 2016. The primary outcome measure was best-corrected visual acuity (BCVA), and the objective of the trial was to evaluate whether oral steroids improve the visual outcome in acute NAAION. Secondary objectives included evaluating any possible benefit on electrophysiologic or structural parameters and documenting any adverse effects of therapy.

The sampling frame consisted of patients with acute NAAION from 50 to 70 years of age. Patients were diagnosed to have acute NAAION if they (1) demonstrated sudden loss of vision within the preceding month, (2) showed sectoral or diffuse disc edema (hyperemic or pallid), (3) showed field defects corresponding with the disc changes, (4) demonstrated delayed choroidal filling in the

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prelaminar and peripapillary region on fundus fluorescein angiography, and (5) showed no other ocular or systemic conditions explaining the clinical findings. In addition, the presence of a small crowded disc in the fellow eye was documented as a secondary marker to ascertain the diagnosis.[7–11] Patients with symptoms and signs suggestive of an arteritic anterior ischemic optic neuropathy such as scalp tenderness, jaw claudication, temporal headaches, presence of an elevated erythrocyte sedimentation rate, and high C-reactive protein levels were excluded. Diabetic patients, those who previously received steroid or any other treatment for NAAION, and those declining to consent or report for follow-up were excluded from the study.

Thirty-eight patients were randomized into 2 study groups of 19 each using a computer-generated random number table after each patient provided written informed consent. The sample size was calculated based on the initial findings of a pilot study carried out at the center on 20 patients in 2 groups. The assumed effect size was 30%; other assumptions were confidence level of 95% (α error of 5%), study power of 80%, and a dropout rate of 10%. The standard deviation of the outcome in the population was 0.3. The intervention and treatment were provided by an ophthalmologist (treating clinician, unmasked investigator) in the neuro-ophthalmology clinic. The patients were followed up by a different ophthalmologist (D.S.) (observing clinician, masked investigator) during the course of the study. The observing clinician (masked investigator), ophthalmic technician, and patient were blinded to the therapy being received by each arm. One of the study groups (steroid group) received oral steroids (Tab. prednisolone 80 mg for 2 weeks, and then tapered to 70 mg for 5 days, 60 mg for 5 days, and then decreasing by 5 mg every 5 days until stopping), whereas the other (nonsteroid) group was given a placebo. Oral methylcobalamin was given to both groups. Patients also underwent a general physical examination, a Mantoux test, and chest radiography to rule out tuberculosis before starting therapy. All patients were treated by a physician to control any systemic risk factors and adverse effects of medications. Ophthalmic evaluation included recording BCVA in logarithm of the minimum angle of resolution (logMAR) units, Goldmann kinetic perimetry (where possible), visual evoked response (VER), and OCT (retinal nerve fiber layer [RNFL] thickness, disc area, and central macular thickness). The tests were carried out at presentation (baseline). Best-corrected visual acuity, VER, and OCT were repeated in all patients at 1, 3, and 6 months of follow-up, whereas Goldmann kinetic perimetry was performed whenever possible. Additionally, a general physical examination and blood glucose testing (fasting and postprandial) were carried out at each follow-up examination to look for any adverse effects of steroids. Statistical analysis was carried out using SPSS software version 14.0 (SPSS, Inc., Chicago, IL). Quantitative data were expressed as mean ± standard deviation or median and range, as appropriate. Appropriate parametric and nonparametric tests, including the Mann–Whitney U test and chi-square test, were applied. A P value less than 0.05 was taken as statistically significant.

Results

A total of 59 patients with NAAION of less than 1 month's duration visited the center during the period of recruitment for the study. Of these, 15 patients were excluded because of diabetes, 2 were excluded because of possible arteritic anterior ischemic optic neuropathy, 2 already were using steroids, and 2 declined to consent to the study. All 38 patients with acute NAAION recruited to the study completed the follow-up. Age was similar in both groups, with an overall mean ± standard deviation of 56.8±6.1 years ($P = 0.30$, Mann–Whitney U test). The median duration between onset of symptoms and presentation was 12 days (range, 1–30 days), with a median of 14 days and 10 days for the nonsteroid and steroid groups, respectively. There was a male preponderance in both groups, and both groups were statistically similar with regard to all baseline demographic and clinical parameters (Tables 1 and 2). The systemic risk profile of both groups was alike. Fourteen patients in both the groups showed associated systemic risk factors, including hypertension (5 patients in the nonsteroid group vs. 7 patients in the steroid group), hyperlipidemia (4 patients in the nonsteroid group vs. 5 patients in the steroid group), hypertension with hyperlipidemia (3 patients in the nonsteroid group vs. 1 patient in the steroid group), obstructive sleep apnea (2 patients in the nonsteroid group vs. 1 patient in the steroid group), and no systemic risk factors (5 patients in each group). Visual field defects included an inferior altitudinal or inferonasal defect (25 patients), a superior altitudinal defect (7 patients), and generalized field depression (6 patients).

The nonsteroid group showed a median baseline BCVA of 0.8 logMAR (range, 0–2.7 logMAR), whereas the steroid group showed a median baseline BCVA of 1 logMAR (range, 0.5–3 logMAR; $P = 0.16$). The final median BCVAs of the nonsteroid group and steroid group were 0.6 logMAR (range, 0–2.7 logMAR) and 0.5 logMAR (range, 0.2–1.8 logMAR), respectively ($P = 0.78$). Both groups showed a statistically significant improvement in BCVA from baseline during a 6-month follow-up ($P = 0.01$ and $P = 0.003$ for the nonsteroid and steroid groups, respectively); however, the steroid group showed a greater change in vision compared with the nonsteroid group (Tables 1 and 2; Fig 1).

Baseline OCT showed increased thickness and edema in the superior or inferior RNFL, or both, in most patients which improved and revealed RNFL thinning at the final follow-up visit. Significant RNFL thinning was noted in all quadrants over the course of the follow-up (barring the temporal quadrant in the nonsteroid group). There was no difference between the RNFL parameters in the 2 groups either at baseline or the final follow-up visit. However, the superior and inferior RNFL showed a greater reduction of edema at the 1-month follow-up visit ($P = 0.028$ and $P = 0.031$, respectively) compared with the placebo group. There was a higher change in the superior and inferior quadrants ($P = 0.03$ and $P = 0.03$, respectively) at the first-month follow-up visit in the steroid group compared with the nonsteroid group. However, the change in the nasal and temporal quadrants was similar in both groups. The percentage change in RNFL in both groups was statistically similar (Table 2).

Median VER amplitude at baseline in the nonsteroid and steroid groups were 5 μv (range, 2–10 μv) and 5 μv (range, 3–10 μv), respectively ($P = 0.90$), which showed an insignificant change to 5 μv (range, 2–10 μv) and 6 μv (range, 3–10 μv), respectively. However, the percentage change was more in the steroid group compared with the nonsteroid group ($P = 0.02$). Median VER latency at baseline in the nonsteroid and steroid groups was 131 ms (range, 99–154 ms) and 137 ms (range, 87–158 ms), respectively ($P = 0.46$), which showed an insignificant change to 128 ms (range, 99–144 ms) in the nonsteroid group ($P = 0.16$) and a statistically significant change in the steroid group to 128 ms (range, 120–140 ms; $P = 0.03$). Although the percentage change was more in the steroid group compared with the nonsteroid group ($P = 0.04$), the final VER latency in both groups was comparable ($P = 0.48$; Tables 1 and 2).

Follow-up results of the intergroup analysis (steroid vs. nonsteroid groups) are presented in Table 2. Additionally, both groups showed a similar speed of recovery of optic disc edema and BCVA. No serious adverse effects of steroid therapy were noted in this study. The adverse effects in both groups included gastrointestinal symptoms, including nausea and dyspepsia