Commentary

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Although nonarteritic anterior ischemic optic neuropathy (NA-AION) is a common disease, its pathogenesis, clinical features and management have been subjects of much controversy and confusion. This is primarily due to lack of in-depth knowledge of the various aspects of the disease.

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Most importantly, the understanding and management of the disease is a 3-step procedure.

- A good knowledge of the basic scientific facts of the disease is the foundation. Unfortunately, the primary cause of controversy is poor understanding of this in NA-AION
- That basic scientific knowledge leads to a logical understanding of the pathogenesis of the disease
- That, then, finally results in its rational management

I have discussed these three issues about NA-AION briefly, previously, and, in 2011 in detail in my book entitled "Ischemic Optic Neuropathies."[1,2] Most recently, with more information available, I updated the information on the subject in my keynote lecture at the German Ophthalmology Society Congress and German Neuro-ophthalmology Society meeting in Berlin in September 2012.[3]

Al Zubidi and colleagues provide a brief overview of the current controversy on the role of corticosteroid therapy in NA-AION. This controversy is based fundamentally on the following three misconceptions about NA-AION, which arise from lack of thorough knowledge of the subject.

I. That its pathogenesis is not known

I have discussed this subject at length previously, in the light of currently available scientific information.[1,2] Based on those findings, I have concluded that "*the pathogenesis of NA-AION is known, though it is highly complex"*

II. That NA-AION and ischemic cerebral stroke are similar in nature, pathogenetically and in management

Ischemic cerebral stroke is usually a thromboembolic disorder and occasionally hypotensive. In sharp contrast, NA-AION is a hypotensive disorder in the majority of cases, and only rarely a thromboembolic disorder. I have discussed this subject at length elsewhere.[4] This is very well demonstrated by the fact that aspirin helps thromboembolic disorders, whereas, two large studies[5,6] have shown that aspirin has no benefit of reducing the risk of NA-AION. This is because aspirin has no effect on blood pressure. Biousse[7] while discussing corticosteroid therapy in NA-AION, made the following dogmatic statement: "Oral corticosteroids in the setting of acute cerebral stroke are contraindicated," which is based on this basic misconception. I have discussed in detail [2,8] the invalidity of various objections by Biousse[7] to my study[8] on the role of corticosteroid therapy in NA-AION.[2,9]

III. That corticosteroids have no rationale in NA-AION

This has been a common objection by neuro-ophthalmologists to the use of corticosteroids in NA-AION. I have discussed this subject at length previously.[1-3] Following is the rationale:

- It is well-known that corticosteroids reduce capillary permeability, and that reduces fluid leakage and edema. A comparison of the time it took for resolution of optic disc edema in NA-AION patients treated with corticosteroid therapy versus untreated patients showed a faster resolution of optic disc edema in the treated group ($P = 0.0006$).[10] In view of all these facts, the scientific rationale for visual improvement with corticosteroid therapy in NA-AION is this: The faster resolution of optic disc edema with corticosteroid therapy[10] → progressive decrease of compression of the capillaries in the optic nerve head → restoration of better blood flow in the capillaries → improved circulation in the optic nerve head → improved function of the surviving but not functioning hypoxic axons → improved visual outcome
- Bernstein *et al*. showed in experimental NA-AION that "cellular inflammation plays a major early role following white-matter (optic nerve) infarct,"[11] and that "inflammation is a prominent early histological feature."[12] Based on their studies, they concluded "selective inflammatory modulation also may be relevant in the NAION of human NAION."[12] Corticosteroid therapy is the treatment of choice in inflammatory disorders.

Therefore, the faster resolution of optic disc edema and presence of an inflammatory reaction in NA-AION constitute a rationale for the beneficial effect of corticosteroid therapy in NA-AION.[10-12]

Most neuro-ophthalmologists have been unwilling to accept the findings of my study,[8] because, they have argued (apart from the belief that corticosteroid therapy has no rationale in NA-AION) that my study[8] had no "conventional randomization." This naturally raises the question about critical criteria of "conventional randomization;" these are that *treated and untreated groups at baseline must be comparable in demographic and clinical characteristics*. My "patient choice randomization"as discussed by Al Zubidi *et al*., and discussed by me,[1-3,8,9] does meet that crucial criterion. Unfortunately, there is a tremendous amount of unnecessary genuflexion to "conventional randomization" or "class I studies."

The other objection raised has been that my study was not masked and therefore must have biased data collection and analysis. In my paper, I clearly discussed what steps were taken to mask data collection and analysis.[8] I responded to this objection by pointing out that the visual acuity outcome in my untreated group was exactly the same as in the untreated group in the "conventional randomized" Ischemic Optic Neuropathy Decompression Trial,[13] that is, 41% versus 43%; that proves that there was no bias in my data collection.[9]

I have pointed out that claims of beneficial effects of intravitreal steroid injection are flawed; indeed, it can be harmful.[14]

In conclusion, in spite of my meeting all the objections several times over, some neuro-ophthalmologists are unwilling to believe that corticosteroid therapy has any beneficial effect in NA-AION.[1-3,8] However, scientific knowledge is constantly evolving; as our knowledge advances, our concept of disease and its management must change too. Therefore, one has to evaluate findings in the light of current knowledge and scientific evidence, rather than outmoded conventional thinking. Over my 58 years of research, based on my findings, I have often challenged dogmas and conventional wisdom. Whenever conventional wisdom is challenged, even if new scientific information shows that it is no longer valid, the initial reaction is usually skepticism or even ridicule. I have faced that problem many times during my research over the years; fortunately, the findings of my studies have stood the test of time. Eventually, new knowledge becomes part of accepted practice.

References

1. Hayreh SS. Ischemic optic neuropathy. Prog Retin Eye Res 2009;28:34-62.
2. Hayreh SS. Ischemic Optic Neuropathies. Heidelberg: Springer-Verlag; 2011. p. 265-415.
3. Hayreh SS. Ischemic optic neuropathies-Where are we now? Graefes Arch Clin Exp Ophthalmol 2013;251:1873-84.
4. Hayreh SS. Non-arteritic anterior ischemic optic neuropathy versus cerebral ischemic stroke. Graefes Arch Clin Exp Ophthalmol 2012;250:1255-60.
5. Beck RW, Hayreh SS, Podhajsky PA, Tan ES, Moke PS. Aspirin therapy in nonarteritic anterior ischemic optic neuropathy. Am J Ophthalmol 1997;123:212-7.
6. Newman NJ, Scherer R, Langenberg P, Kelman S, Feldon S, Kaufman D, *et al.* The fellow eye in NAION: Report from the ischemic optic neuropathy decompression trial follow-up study. Am J Ophthalmol 2002;134:317-28.
7. Lee AG, Biousse V. Should steroids be offered to patients with nonarteritic anterior ischemic optic neuropathy? J Neuroophthalmol 2010;30:193-8.
8. Hayreh SS, Zimmerman MB. Non-arteritic anterior ischemic optic neuropathy: Role of systemic corticosteroid therapy. Graefes Arch Clin Exp Ophthalmol 2008;246:1029-46.
9. Hayreh SS. Role of steroid therapy in nonarteritic anterior ischemic optic neuropathy. J Neuroophthalmol 2010;30:388-9.
10. Hayreh SS, Zimmerman MB. Optic disc edema in non-arteritic anterior ischemic optic neuropathy. Graefes Arch Clin Exp Ophthalmol 2007;245:1107-21.
11. Salgado C, Vilson F, Miller NR, Bernstein SL. Cellular inflammation

in nonarteritic anterior ischemic optic neuropathy and its primate model. Arch Ophthalmol 2011;129:1583-91.

12. Bernstein SL, Johnson MA, Miller NR. Nonarteritic anterior ischemic optic neuropathy (NAION) and its experimental models. Prog Retin Eye Res 2011;30:167-87.
13. Ischemic Optic Neuropathy Decompression Trial Research Group. Optic nerve decompression surgery for nonarteritic anterior ischemic optic neuropathy (NAION) is not effective and may be harmful. JAMA 1995;273:625-32.
14. Hayreh SS. Intravitreal triamcinolone for nonarteritic anterior ischemic optic neuropathy. J Neuroophthalmol 2008;28:77-8.

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