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Reversibilities of Visual Fields and Optic Nerve Cupping in Ocular Hypertensive and Glaucoma Patients Treated With Topical Anti-Glaucoma Medications.

By

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Advisor: Nada J. Lingel, O.D.
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A literature review to investigate the reversibilities of visual field defects and optic nerve cupping in glaucoma, glaucoma suspects and ocular hypertensive patients with current topical glaucoma therapy regimens.
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INTRODUCTION

Glaucoma is a multifaceted disease with limited information on its natural course. There are many different management regimens for glaucoma.\textsuperscript{1,2} No matter what type of treatment modality is used, present glaucoma management is directed at the reduction of IOP,\textsuperscript{2} and cannot be considered successful unless functional vision loss can be controlled, or possibly reversed. Can a reversal of clinical findings be achieved? A current article review suggests that reversals of optic disk cupping and visual field loss are possible in a large enough percentage of patients to warrant consideration. The unpredictable progression of the disease, combined with the variability of patient response to treatment, poses a difficult management task for the clinician, but one with the possibility of a successful outcome.

As with other diseases, glaucoma presents and follows a working model which shows progression with specific signs and symptoms. The classic glaucoma model begins with an initial increase in IOP, development of abnormalities of the optic disc and, finally, the appearance of visual field defects. It should be understood that this model is correct for the majority of cases, but not all cases present themselves in this specified way. For example, IOP elevation is not necessarily the first indication of glaucoma and significant visual field loss can occur in patients whose IOP's are not elevated; as found with low tension glaucoma. This suggests that more than one mechanism may contribute to the visual field losses associated with glaucoma.

The glaucomas show a great patient variability regarding progression of the disease. Other variabilities include patient reactions to treatment, and variability of the IOP needed to prevent further functional vision loss. Goldman described a pressure level below which the optic nerve can function for an extended period of time without damage as the critical intraocular pressure. The
critical IOP differs for each patient, but is the point at which functional vision has the greatest opportunity for stability or even reversal. At present, there is no known way to accurately predict what level, if any, of IOP will be associated with the stabilization of the disease and thus stabilization of visual field loss.

The most popular method of treatment is one of trial and error. The intraocular pressure is lowered to a predetermined "normal" amount while visual fields are monitored. If vision loss still progresses, a more aggressive approach is initiated to further reduce the IOP. This management approach combined with the precaution against overtreatment due to side effects, tends to allow progression of the disease in many cases. This universal modality of treatment does not take into consideration the individual patient's critical IOP. Further study must be made to identify individual factors concerning glaucoma treatment.

The current care of patients with chronic glaucoma is based on a conceptual framework in which it is assumed: one, that untreated chronic glaucoma is an inexorably progressive disease and two, that the deterioration can in some cases be halted by lowering IOP. Other studies, discussed later in the paper, have documented that decreases in IOP, achieved by different agents, may have very different consequences with respect to preservation of the visual fields. Findings of this type indicate that researchers and clinicians must consider multiple modes of glaucoma in designing screening and treatment programs for the disease.

IOP

Although IOP control is how we attempt to manage glaucoma, it may not be the factor that best determines successful outcome. At present, the efficacy of
antiglaucoma therapy is usually judged on the basis of its intraocular pressure reducing effect. Our literature review stresses the possibility that lowering IOP to each individuals' critical pressure can result in improvement of the visual field in a large percentage of patients. Clinical experience along with the work of other authors, suggests that this is not always the case.

Rolando and co-workers evaluated the effect of IOP drop and visual field changes in the short term. The results showed a visual field deterioration in 60% of the eyes, visual field improvement in 30% and no change in the final 10% of cases. To add to these percentages is a study by Zeimer, concerning the diurnal variation among patients. Approximately 30% of patients with glaucomatous visual field loss first present with a "normal" IOP. Patients may have an undetected diurnal curve that spikes above the "normal borderline" of 21 mmHg. Only 40% of POAG patients have their spike between 8:30AM and 5:00PM, therefore, a patient may be erroneously diagnosed as having a "normal" IOP. Thus, one-third of glaucoma suspects may go undetected until physically visible changes occur in the optic nerve or repeatable visual field defects are noted. If these percentages resemble the general population, then the percentage of visual field improvements, as found by Rolando, could possibly be higher with early diagnosis and treatment.

In another study by Pecori-Giraldi, 55 eyes with pressures of greater than 24mm were studied. Hypotonia was induced with glycerol, and IOP was remeasured. Visual fields were retested when IOP had fallen by 6 to 10 mm Hg and maintained with medical therapy for at least 5 months. A significant increase in the total sensitivity of the visual field occurred when IOP was decreased an average of 8 mm. No significant differences were apparent on visual field examinations prior to hypotonization, confirming the latter visual field changes were due to IOP reduction and not to chance. As one may expect, the
greater the IOP reduction, the greater the visual field improvement as demonstrated in Shin's study where 13 patients were monitored. 

When reducing the IOP in glaucoma patients, there are two important questions. One, how low do I set my goal for IOP reduction?; and two, what means of treatment do I select for this IOP reduction? In the previously mentioned study by Pecori-Giraldi, it was reported that in the 55 eyes studied, IOP reduction with timolol resulted in visual fields that either remained stable or improved over a three year follow-up time. In contrast, patients treated with pilocarpine to an equivalent decrease in IOP showed progressive visual field loss. 

In conclusion the effect of medical therapy in glaucoma can be evaluated in the short term with IOP measurements. Careful visual field examination can indicate the efficacy of antiglaucoma therapy which is not always related to IOP values. Visual field improvements in glaucoma seem to be a rather frequent event, and often are the only indicator of efficacy of therapy.

OPTIC CUP

Optic nerve evaluation is an essential part of the optometric examination and unlike other tests, it is a subjective measurement made by the practitioner. The majority of early glaucoma changes occur in the optic disc. Such changes include increased cup/disc ratio with thinning of the neural rim, vertical elongation of the cup, bearing of circumlinear vessels, striated lamina, and bayonetting. It has been shown in studies that cup changes may precede changes in pallor due to the loss of nerve tissue. Other studies have shown that loss of optic nerve fibers occurs before glaucomatous field loss appears. Stereo photographs and computerized image analysis provide objective
quantification of the contour of the optic nerve head and should be used in the future evaluation of the optic cup.

The question as to what occurs first in the glaucomatous eye is a topic for further study. The reversal of rim tissue thinning is a question of greater relevance when considering the return of functional vision. It seems consistent that if there is an improvement in the rim tissue, then a visual field reversal should also occur. This was noted by Shin and co-workers who reported that a direct correlation existed between the amount of IOP reduction, amount of decrease in cup/disc ratio, increase in neuroretinal rim area, and the decrease in cup volume. The visual field response may not correspond directly to the cup/disc ratio changes due to variability of IOP reduction. In a study by Katz, 75 eyes were studied over a 10 year period and cup/disc ratio improvement was noted in nearly one third of the glaucomatous eyes that had at least a 30% decrease of IOP. Of those with less than a 20% decrease in IOP, a 0% improvement was noted. Shin's study also suggested a 50% decrease in IOP was needed to cause a decrease in the cup/disc ratio. This data reinforces the importance of adjusting treatment for each individual patient. It is not just a matter of decreasing the IOP, but rather decreasing IOP a critical amount for each patient. Perhaps a critical IOP reduction must be attained before a clinically noticeable change in the optic disk can occur. One fact does seem consistent; the greater the magnitude of IOP reduction, the greater the reversal effect. Those with a low percentage of IOP reduction tend to show no reversal and may even show progression. These studies have shown that lowering intraocular pressure can reverse disc cupping.

It appears that the optic disc cup reversal is complete during the first 2 weeks of IOP reduction, with little more occurring beyond that time. A decrease in cup volume, an increase in neural rim area, and a decrease in the cup to disc
ratio occurred within two weeks in 62% of the eyes with POAG after the IOP had been reduced by 50% or more. Again a critical IOP reduction had to be achieved for visible results. Even though most cup/disc ratio reversals occur in the first two weeks of IOP reduction, cup/disc changes have been shown to occur later on in the treatment of some patients. The reversal of the backward bowing of the lamina cribrosa may bring about a mechanical relief of stretching, compression, and strangulation on axons and capillaries. It appears that in patients with long standing increased IOP's, there may be a reversal of the cup/disc ratio but not an improvement in visual field with a decrease in the IOP. Visual field improvement occurs more often in cases where cupping of the optic disc does not extend to the edge of the disc. Visual field improvement occurs less in cases involving total loss of neuroretinal rim tissue, as seen in long standing IOP elevation. Even so, improvement in the appearance of the optic disc has been shown to accompany improvement in the visual field of many glaucoma patients. Though the data is grim, chronically elevated IOP should not be ignored. Rehabilitation of some of the compromised, but not atrophied, optic nerve fibers may occur with treatment.

Reversibility of glaucomatous disc changes has been an accepted phenomenon in infantile and juvenile glaucomas. Adult reversibility has been noted in recent literature on a less frequent basis. There are at least two possible explanations for this difference. One, the immature eye may be more plastic than the older eye. Two, reversible cupping in older eyes may be more subtle and hence often missed. Perhaps the reversal in older patients is often unnoticed because observers do not expect change and therefore fail to look for it.

The idea of reversing damage to the optic nerve opens new doors for treatment of glaucoma, but the prevalence and clinical significance has not
been established. More studies are needed to determine what percentage of reduction in IOP might be necessary to see cup/disc ratio reversibility and which patients are likely to demonstrate such reversibility.

**VISUAL FIELDS**

In general, an association between high IOP and the development of glaucomatous visual field loss is well accepted. However, recent studies have shown that such a correlation is not clear and direct. Until recently the possibility of reversibility of visual field loss was not considered. Now several studies have reported a visual field improvement with significant decrease in IOP.\(^2,10,11\) The single point that appears to separate one study from another is the amount of IOP decrease needed to obtain a visual field reversal. All studies agree that a large reduction, in the range of 30-40\% is necessary for visual field improvement. Thus, not unexpectedly, patients with POAG should show more improvement in perimetry results than those with low tension glaucoma.

More studies are needed to explore the idea of visual field reversal with IOP reduction. For any treatment regimen to be considered a success, it must endure in the long term. In a study by Spaeth, of the 19\% of patients presenting with visual field improvement none showed a deterioration during the time of the study.\(^3\) This was also evident in the study by Pectori-Giraldi previously mentioned in which stabilization and in some cases improvement of all 55 eyes was seen over the 3 years of the study.\(^6\) The endurance of treatment is yet another crucial area for further investigation.

In a study by Tsai, the global indices were correlated to one another to rule out patient unreliability and familiarity with the perimeter as the cause of improved visual field. No correlation was found between an increase in visual
field and patient familiarity. The learning effect was minimal. Furthermore, it should be emphasized that the statistically significant improvement of visual field global indices was demonstrable mainly in patients with higher initial IOP level and larger magnitude of IOP reduction, rather than in all patients that showed optic disc cupping reversal after IOP reduction.¹¹

When treating glaucoma, controversies exist as to what stage of glaucoma is most successful in bringing about reversibilities in visual fields and optic nerve cupping. The most common and accepted theory, however, seems to point to early stages of glaucoma as having a higher prognosis for vision function improvement.⁴,⁷,¹³ Eyes with greater damage may require greater pressure reduction than healthier eyes for a disc and visual field improvement to become manifest. This is in agreement with the concept that visual field improvement is less likely to occur in patients with severe advanced cupping versus those with moderately damaged optic nerves. In addition, eyes with more severe cupping are more sensitive to elevated IOP.¹³ Demonstrable visual field changes have been noted with early to moderate glaucoma patients and not with the advanced glaucoma patient.⁷,¹¹

The lack of a consistent association between disc and visual field changes over time may be explained at least partially by the current limitations of perimetry and optic disc analysis. With the better quantification and increased sensitivity that will become possible with more sophisticated technology, such as computerized imaging, a greater correlation of visual field and optic disc changes may be detectable. The validity and consequence of timely treatment may need further study as technology increases to help obtain a true correlation.
CONCLUSION

Perhaps in the future we might find cause to change our therapeutic goals in an attempt to achieve reversal of optic nerve cupping and visual field loss. However, at present, our goal as clinicians should be to keep IOP's low enough to prevent progressive damage to the disc and progressive field loss. Estimates show a 30-40% decrease or more as being most beneficial. Furthermore, the development of sensitive and reproducible methods for measuring visual fields, such as automated perimetry, and optic discs such as photogrammetry and computerized image analysis, may show that reversibility of field and disc changes occurs more often than has previously been appreciated. These are the avenues that will lead to better management of glaucoma patients due to dependable feedback mechanisms. IOP reduction seems to vary from one individual to another, and from one study to another. In our opinion this is not a question of each study's validity, but rather of the importance of "individual" glaucoma management.

Another problem with glaucoma evaluation and management is the lack of a clear definition concerning the progression of the disease. There is no unanimous opinion on what constitutes the first signs of glaucomatous damage and when a glaucoma suspect become an established glaucoma patient. As revealed in this literature review, early to moderate glaucoma management holds the highest prognosis for visual function improvement.7,11 Further study is needed to address the relationship of optic cup reversal and visual field reversal with IOP decrease. The ideal definition of glaucoma control is a lowering of ocular pressure associated with an improvement in the disc and visual field.12 The ideas of reversals in optic disk cupping and visual fields are exciting and encouraging. Too many variables still exist to determine exact
standards for therapy and management to obtain these reversals. It is important that clinicians begin to look for these reversible signs in their glaucoma patients. Soon, because of technological advances, glaucoma management will have a protocol that can be followed and lead to the desired reversibilities in most or all patients.


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