Paradigm shift in chronic glaucoma

Syed S. Hasnain M.D.

History.

After the invention of ophthalmoscope in 1851 by Helmholtz, ophthalmologists were able to see the optic discs of simple glaucoma subjects, which were described as ***cupped*** by Heinrich Muller, an ophthalmic pathologist in 1856. The phenomenon of cupping occurring in glaucomatous disc was endorsed by prominent ophthalmologists like Von Graefe. It was believed that the high intraocular pressure was causing the cupping or excavation of the optic disc. Interestingly there was one dissenter, in 1864 Dr. Dixon, who disagreed that cupping of the disc was caused by high intraocular pressure (IOP). He argued that if the mechanical force of high IOP is strong enough to cause excavation of the disc then the same force should also displace the lens and iris forward as well. But his opinion was turned down by another prominent ophthalmologist Sir William Bowman, who was in favor of cupping. Since then the term cupping has become synonymous with chronic glaucoma. No questions were raised about the validity of the term ***cupping*** but instead it was given further credence 100 years later in 1960's by introducing another term known as cup-to-disc ratio.

I believe the term cupping was mistakenly given 150 years ago which has misled us about glaucoma pathogenesis. In this article, I have presented my arguments against **cupping** and in favor of **sinking,** but my colleagues are the judge**.**

You may like to read my article "**Optic disc may be sinking in chronic glaucoma**" which had explained in more details on my website hasnaineye.com why I got involved in this research and how I reached at the above conclusion.

Points against the cupping of the optic disc

- Physiological cup of an optic disc is a superficial depression in the center of an otherwise flat optic disc which is produced by the atrophy of the Bergmeister's papilla in fetal life. Histology of the normal optic disc identifies this cup as a central connective tissue meniscus. It is difficult to believe that the physiological cup made of fibrous tissue would enlarge in response to high IOP and then reverse in size when the IOP is lowered. If the cup is being affected by raised IOP then the mechanical force of high IOP should have deepened rather than concentrically enlarged the cup. If the high IOP is concentrically enlarging instead of deepening the cup then it may be defying the laws of physics.

- If there is a true concentric enlargement of the physiological cup then it would imply that the subjects born with small cups such as 0.2 cup/disc ratio would take longer time to become 100 % cupped or totally blind, whereas the subjects born with large cups like 0.8 cup/disc ratio would become totally blind sooner since they are already 80 % cupped to start with. But this is not the case.

- If cupping is produced due to high IOP then why is it not occurring in acute glaucoma where the IOP goes very high whereas the cupping is occurring in normal tension glaucoma (NTG) in which the IOP is within normal range?

- True concentric enlargement of the physiological cup cannot selectively destroy the arcuate fibers as it should be involving the entire 360 degrees of axons in the optic disc and not only the arcuate.

- Axons for the central vision are located in the central part of the disc and also superficial (closer to the vitreous). If the cupping were occurring then the central axons should have been destroyed first but instead the peripheral axons because of their deeper location are being destroyed first in glaucoma.

- Ophthalmic literature and textbooks describe the phenomenon of reversal of cupping when the IOP is lowered. This may be a fallacy. The cases described are usually those in which the IOP has been suddenly and drastically lowered by glaucoma surgery. Due to too much lowering of the IOP there is rebound hyperemia or papilledema of the optic disc resulting in reduction in the size of cups. If there is a true reversal of cupping then we should have also witnessed the reversal of lost vision and of visual fields and also regaining of the lost axons but this is not occurring.

- If the original cup was enlarging concentrically then the central blood vessels should have remained centrally and not have displaced nasally.

Points in favor of sinking of the optic disc.

- Sinking of the optic disc may explain the excavation of the optic disc since the axons are being severed and depleted unlike flat disc atrophy in which the axons are being atrophied and not severed. Arcuate shaped defects in the retina due to total disappearance of the arcuate axons as seen on red-free ophthalmoscopy can only be explained if the axons are being axotomized, not atrophied in glaucoma. Above arcuate or wedge shaped defects are not present in non-glaucomatous optic atrophy in which the atrophy, not severing of the axons is occurring. End –stage glaucomatous disc is an empty crater due to axotomy of all the axons.
  Axotomy of the axons is the characteristic feature of glaucoma

- Sinking of the disc may explain as to why glaucoma cannot be halted despite maximally lowering of IOP. Once the disc starts sinking the cascade of loosening and sinking of the disc will ensue until all the axons are axotomized

- Sinking of the optic disc may explain loss of peripheral field first since the peripheral axons because of their deeper and closer to the scleral edge location will be axotomized first and the central axons at the end.

- Sinking of the optic disc may explain the manifestation of single or double arcuate field defects in the earlier stages of glaucoma.

- Sinking of the optic disc may explain the nasal shifting of the blood vessels due to loss of anchorage created by the severance of the temporal fibers more so than the nasal fibers due to usually temporally tilted optic disc.

- Sinking may explain the occurrence of splinter hemorrhage which may due to severing of the smaller blood vessels, a fate similar to that of axons.

- Sinking may explain progressive thinning of RNF layer as revealed by OCT due to continuous severing and depletion of the axons.

- Sinking of the disc may explain the thinning of the ganglion cell complex of the macular area in early stages of glaucoma because the macular fibers are also being axotomized along with the arcuate fibers.

- Sinking of the optic disc may explain sloping and kinking of the blood vessels at the entire disc margin occurring prior to any change in the contour of the physiological cup.

- Sinking of the optic disc may explain higher incidence of chronic glaucoma in myopia due to inherent thinning and weakness of the border tissue making the 'O' ring seal weaker thus myopic discs more prone to sinking.

In summary, the morphology and the histology of the glaucomatous discs support the phenomenon of the sinking disc. Border tissue of Elschnig, not lamina cribrosa may be the primary site of injury. The axons are being ***severed, not atrophied*** in chronic glaucoma. I believe the terms cupping and cup-to-disc ratio have made the glaucoma diagnosis very complicated. With the concept of cup-to-disc ratio the subjects born with large cups but with normal IOP and normal visual fields may be treated as normal-tension glaucoma whereas those born with small cups but high IOP may be ignored treatment as ocular hypertension.

Ironically, no where else in medicine the same phenomenon or parameters are being used to describe both healthy and the diseased state of an organ as the term cupping is being used to describe both the physiological and pathological cupping. No wonder there is great inter-clinician variance in glaucoma diagnosis despite the OCT and other high technological procedures. If we see a new patient with large cups with normal visual fields, then how can we know if these large cups are physiological or glaucomatous if the previous photographs are not available?

The sinking optic disc will be a paradigm shift to the cupping theory. Cupping of the optic disc implies that the problem starts from the center of the disc end extends towards the peripheral part or in other words the central axons (for central vision) should be destroyed first and the peripheral axons (for the peripheral vision) at the end, but this is not occurring in glaucoma. Sinking of the disc will imply that the deeper peripheral axons will be destroyed first and the superficial central axons at the end and this is exactly what is revealed by visual field examination in glaucoma.

All I ask my colleagues is to view the glaucomatous discs as **sinking** rather than **cupping** (gestalt switch), and then they for themselves can decide if the disc is cupping or sinking in glaucoma.

At the end I would like to mention a quote from Thomas Kuhn, a great philosopher of science, "***Almost every significant breakthrough in the field of scientific endeavor is first a break with tradition, with old ways of thinking, with old paradigms"***

Syed S. Hasnain M.D.
Porterville, California

For comments or feedback email at: hasnain40@sbcglobal.net

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