ISSN: 0975-833X

Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 12, Issue, 10, pp.14204-14207, October, 2020

DOI: https://doi.org/10.24941/ijcr.38012.10.2020

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

RESEARCH ARTICLE

CHALLENGES IN CONVENTIONAL MANAGEMENT OF CHRONIC GLAUCOMA: EVIDENCE BASED CALL TO REVISIT ASSUMPTIONS

***Dr. Karan R Gregg Aggarwala and Mark Forman**

Ocular and Metabolism Research Education Consulting Sales Incorporated [OAMRECS], Ph. 212-717-1015

ARTICLE INFO

Article History:

Received 19th July, 2020
Received in revised form
17th August, 2020
Accepted 24th September, 2020
Published online 30th October, 2020

Key Words:

Ocular, ailment, ophthalmoscope, glaucoma, ophthalmology, optometry, pharmacology, surgery, LASER, ablation, blindness, clinical, consumer, ethics, medical, diagnostics, instrument, ophthalmic, innovation, physician

ABSTRACT

Physicians of the years prior to 1952 had significant insight into an ailing client's ocular and bodily pathology by way of personal examination at the other end of an ophthalmoscope and a stethoscope. In the domain of glaucoma diagnostics, optic nerve evaluation came first, and later came the testing of eye pressure at the cornea. The older tests for visual field perimetry, although simple, were reasonably effective, many years prior to computers. The standard of care for Board Certified Ophthalmologists since 1981, has been LASER treatment of the posterior corneal periphery, enlarging "holes" of the trabecular meshwork. Optometrists, however, limit their practice to pharmaceutical agents, applied to the ocular surface. Not to deny the datasets obtained from multi-center, multi-million dollar investigations, much toleration and waiting is required of the client suffering from chronic glaucoma. Ambitions set forth as goals sponsored by the World Health Organization under the leadership of the International Association for the Prevention of Blindness and the World Council of Optometry [collectively termed as the VISION 2020 Initiative] have achieved modestly. Technology as a modality for empowering doctors has great value. The astute consumer of medical consultations, however, must exercise their doubting Thomas. In simplified, but not simplistic terms, the present synthesis is an attempt to bring forth some of the salient features of diagnosing and treating glaucoma that are cause for concern. It is intended by the authors, that any critical remarks presented here, be construed as making good the promise of the Hippocratic Oath, and the tenets of the Declaration of Helsinki.

Citation: ***Dr. Karan R Gregg Aggarwala and Mark Forman.*** **2020.** "Challenges in conventional management of chronic glaucoma: Evidence based call to revisit assumptions.", *International Journal of Current Research*, 12,(10), 14204-14207.

INTRODUCTION

This review paper introduces certain clinical, surgical, and physiological facts concerning the measurement and lowering of intraocular pressure (IOP), a parameter known to influence myopia and glaucoma. Although from years 1990 till 1999 classification of glaucoma emphasized neurodegenerative and inflammatory changes in the retina, soon after, it became a chromosomal entity (1). Despite multiple factors known to influence functional impairment of retinal ganglion cell axons, intraocular pressure (IOP) is regarded clinically as THE primary factor that should be manipulated for managing of glaucoma: primarily by clinical and surgical interventions (2, 3).

Corresponding author:* **Dr. Karan R Gregg Aggarwala,
Ocular and Metabolism Research Education Consulting Sales Incorporated [OAMRECS], Ph. 212-717-1015.

PULSED-AIR EYE PRESSURE

Surface eye drop pharmacological therapy for managing elevation of fluid pressure against the endothelium of the concave back of the cornea is considered "Standard of Care." Today, the best of optometrists tend to champion a medical-metabolic approach whereas the best ophthalmologists might refrain from practicing. Instantaneous pulsed-air eye pressure based on photocell detection of cornea flattening has become commonplace, despite the more sophisticated method of Hans Goldmann. Aside from manometry, any and every clinical method for measuring ocular tonus depends on corneal or sclera elastic resistance. Whereas central corneal thickness is one indicator of elastic resistance, linear correlation can never be assumed. Data suggest that urban samples 18 to 75 years of age, present a wide range (460 microns to 604 microns) in central corneal thickness (4).

24 SECOND VERSUS 24 HOUR IOP

Early biophysics pioneers of the 1950's vouched for the importance of pulsations of IOP, with further developmental research in the late 1980's at John's Hopkins University (5). Changes in eye pressure can occur about once every second from the cardiac ventricular systole, and once every five seconds from thoracic musculature (6). Much has been published and clinically practiced, on diurnal changes in IOP, traditionally with measures at 120 minute time intervals over a 24 hour day-night cyclic period (7-9). From a desire to understand ocular biophysics of glaucoma, the natural question arises: would it be better to monitor IOP dynamically at a frequency ranging from 16 to 60 Hz, for a 24 second duration, than to bother at all about diurnal IOP?

ENERGETIC VASCULAR MUSCLE

Introduction into the eye anterior chamber of nutrient-rich aqueous humor from blood external to the ocular shell, is performed at various sophisticated membranes, most evidence pointing to the Non-Pigment Epithelium, NPE of the anterior assemblage known as the Ciliary Body. Describing the ciliary body as a muscle leaves out its essential vascular property, and perhaps, its description as an energy center: a springy elastic meeting place for the anterior iris and the posterior choroid: embryological related by inversion to the adhering 10-layered cellular synaptic and immensely inter-communicating retinal tapestry. Although the retina does not always remain adhering, its potential for detachment is NOT the subject of this communication.

FLUID PHYSICS HISTORY

The first mathematical modeling of watery fluid is known by the exclamatory remark of "EUREKA," from the annals of the Greek literature describing principles of buoyancy attributed to Archimedes. Many hundreds of years elapsed until the next insightful documentation of water-filled vessels. According to Galileo, the three primary stable legs holding up the tabular science of fluid physics were: Castelli, Magiotti, and Torricelli. Raffaello Magiotti (born 1597) was taught primarily by Benedetto Castelli; their cumulative findings forming the intellectual foundations of the barometer built by Evangelista Torricelli (born 1608), who received instruction from Bonaventura Cavalieri.

COMPRESSION RESISTANCE

Barometric measuring of what we regard as fluid pressure exerted along a radial direction by a cylindrical column of Earth atmosphere has inherent assumptions. Stevin's composition of vector resistance was simplified by Huygens to construct the pendulum based clockwork mechanism for keeping time. The relative compressibility of air in comparison with liquid water is no mystery to the eleven year old boy or girl. There are, however, several unknown ghosts in the machine that alter gross results in response to accumulating rapidly changing atomic, molecular and Brownian orientations and displacements.

PULSATION FLOW

.

With evidence from the relative time constants of iris pupil sphincter dynamics, the authors suggest that the trabecular meshwork drainage process is based on pulsation flow. The bubbles forming at the Inner Wall of Schlemm's Canal, IWSC, are consistent with a dynamic and not passive membrane vacuole formation and dissolution process (10).

DEBRIS AND NUTRIENTS

As the amoeba extends cytoplasm, so cells near the fiber tissue swallow and digest debris and fragments as a way of keeping TM unobstructed. The role of biochemistry of incoming nutrients and their transport into the eye is hardly debated for cellular maintenance and regenerative process. High dosage prescribing of ant-oxidant supplements is not endorsable without concomitant tests for metabolic parameters and biomarkers significant for helping maintain and regenerate vascular, neural, muscle tissue.

BLOOD WATER VOLUME

Just as formation of aqueous humor may be partly by osmotic diffusion biophysical process; so also drainage is posited to be influenced by electrolyte balance and the water volume of blood. This may be one reason for elevation of eye pressure from the water drinking and water loading test known to every eye doctor since the rollout of the Henry Ford tractor.

COLD CRYOGENIC KILLING

Nerve supply of intraocular tissue, not limited to the internal ciliary muscle and external six eye muscles, is generally not described as affecting eye pressure, despite published neurology experiments (11). For the most part, neural mechanisms in the eye and brain have thus far been inaccessible to surgical procedures— aside from age-old cryogenic ciliary body ablative killing by cryogenic applicator. Such tissue freezing device is still in use for seemingly intractable elevation of IOP, above 45 mm Hg 'Pressure" equivalents.

FORMULATING MEDICATION

Eye drops that have been formulated for lowering IOP employ pharmaceutical agents (medically tested and government regulated drugs) that create an effect (12, 13) by at least one of the following general mechanisms of action:

- Reducing production of aqueous humor fluid and electrolytes from the Non-Pigmented Ciliary Epithelium and related cellular assemblies;
- Improving outflow of aqueous humor through the Trabecular Meshwork (TM), also known as Conventional Drainage, or Trabecular Outflow of Aqueous Humor;
- Improving outflow of aqueous fluid through the body of the ciliary muscle, especially through spaces between muscle fiber bundles—termed Uveo-Scleral Aqueous Humor Outflow.

MEDICAL EMERGENCY

Although needles are rarely employed in the management of chronic glaucoma, and generally, topically administered eye drops are standard of care—ophthalmologists, emergency room doctors, and veterinarians (14, 15) do employ intravenous hyper-osmotic agents (mannitol) to rapidly

reduce IOP and have done so for over the past one hundred years. Tragically, such practice can cause sudden bleeding into intraocular spaces (16) damaging renal tissue (17) as well. When a hyper-osmotic agent such as mannitol is used for highly elevated IOP, occlusion etiology for rise in pressure is not addressed, such as inflammation or ischemia. Apposition of the colored iris tissue against the anterior lens OR against the posterior corneal periphery disables painfully: known either as Acute Pupillary Block Glaucoma OR Acute Angle Closure Glaucoma, ACG (18). Other various classes are intermittent and chronic without symptom angle closure, and the related Plateau Iris phenomenon.

MANAGING OCCLUSION RISK

Competent physician assisted clinical examination of the anterior segment of the eye, especially after age 35, can test for tendency for pupil or angle occlusion before morbidity takes place. Risk for ACG can be evaluated by ophthalmologists (traditional "eye doctors"), as well as by a trained optometrists— varied by geography and personal proclivity and clinical practice model. Anterior chamber (A/C) angle of Grade II can be easily detected ***even without*** a physician administered slit-lamp bio-microscope exam. To find risk for ACG, simply point a penlight from the left or right side of the lateral corner (canthus): an Iris Shadow forms nasally. The need for lower cost and portable LASER IRIDOTOMY surgical instrumentation is quite apparent to serve less fortunate communities.

REFLECTIONS ON LATANOPROST

Changes in mode of action of dominant prescribed topical eye-drops transitioned from beta blockers to prostaglandin analogs: from the late 1990s. To fulfill a market need by yet another version of the same drug is NOT truly creative innovation (19). To understand human physiology and factors that promote disease is necessary to innovate based on unmet need. The original research for developing prostaglandin analogs is attributed mainly to Lazlo Bito, but noted physiologist on the blood-brain interfaces, Hugh Davson (20) played equal part (See 1976 article in Journal of Physiology and his physiology textbook). For the years 1976 till 2001, Bito (21) documented reflections and suggested appropriate criteria for developing new drugs to control elevation of IOP. Despite many honorable efforts in collaborative drug development by accomplished Principal Investigator scientists and clinicians at Medical and Pharmaceutical Companies, a recent meta-analysis published in year 2019 reveals (22) that the most efficacious currently employed drug of the prostaglandin variety is the one with the least ocular surface tolerability. This surprising result directs us, as responsible physicians and scientists, to recognize some of the palpable challenges for clinical management of glaucoma.

DYNAMIC OCULAR TONOMETRY

Known and speculated physiological mechanisms linking accommodation biomechanics to onset and progression of myopia and glaucoma point to the necessary development of a recording tonometry system. A synthesis published on biophysical, ergonomic, and metabolic factors that alter eye pressure (23) suggests that pulsations of IOP (ocular pulse) could be an indicator of impending pathology, with both ocular and systemic components. Subarachnoid pressure on the optic nerve (24) may lead to advancing neurodegenerative changes in glaucoma, and a good means for evaluation is needed. Measures of corneal indentation pulse at the Institute of Physics (Wroclaw, Poland) indicate early changes in blood flow dynamics within the eye, are associated (in part) with advancing age.

INSIGHTFUL ENGINEERING

Although busy inventors and writers can express their competences unheeded, busy clinical and surgical professionals can be stymied. Application of critical thinking, more efficient experimental design, and training across disciplines is sorely needed. Strategic planners may often have to work alone buried among journals that present authenticated wisdom, cutting through convention and habitual rote process. Insight must be gleaned from clinical as well as scientific sources for genuine innovation.

INDUSTRY AND ACADEMIA

Today, there appears to be not even one ocular tonometry (eye tonus measuring) system that adequately controls for biomechanical tension properties of the tested region. This tragic paucity of insightful engineering has major public health and economic consequences. It may not speak poorly of faculty researchers but it certainly deprecates University programs for Technology Transfer and collaborations with industry. If a University demands ANY more than seven (7) percent (%) of revenues from commercial development by a Professor or PhD Student, that would grossly violate very fundamental principles of established business practice for commissions designated as royalty payback. Reducing University Institutional demands will break at least one delusion (25) that every Dean and Chancellor suffers as badly as any Corporate Executive.

REFERENCES

1. Ritch R (2003) Narrative on 5 questions, July.
2. Liebmann JM (2000) Glaucoma diagnosis and management. Ophthalmology Clinics of North America, 13(3).
3. Shields MB (2006) Shields' Textbook of Glaucoma, Fifth Edition.
4. Aggarwala KRG (2020) Personal Communication with Rashmi Gora Mahajan, Candidate for PhD (Unpublished Data).
5. Aggarwala KR (1992) ARVO Conference presentation by David Silver, PhD.
6. Aggarwala KRG (2020) Communications with Professor Krishnananda Nayak of Manipal University of Health Sciences (Cardiology).
7. Kniestedt C, Punjabi O, Lin S, Stamper RL (2008) Tonometry through the ages. Survey of Ophthalmol. Nov-Dec; 53(6): 568 to 591.
8. Ericson LA (1958). Twenty-four hourly variations of the aqueous flow. Examination with peri-limbal suction cup. Acta Ophthalmol; 50:1-95.
9. Phelps CD, Woodson RF, Kolker AE (1974). Diurnal variation in intraocular pressure. Am J Ophthalmol, 77:367-77.
10. Ujiie K and Bill A (1984) The drainage routes for aqueous humor in monkeys as revealed by scanning

electron microscopy of corrosion casts. Scan Electron Microsc (Pt 2): 849-5.
11. 11.McDougal, David H and Gamlin, Paul D (2015) Autonomic control of the eye. Compr Physiol. January; 5(1): 439–473.
12. Kanner E and Tsai JC (2006) Glaucoma medications: Use and Safety in the Elderly Population. Drugs Aging. 23(4): 321-32.
13. Costagliola C, del'Omo R, Romano MR et al (2009) Pharmacotherapy of intraocular pressure: Part I. Parasympathetic, Sympathomimetic and Sympatholytics. Expert Opin Pharmacother Nov 10 (16), 2663-77.
14. Mandell DC (2000) Ophthalmic Emergencies. Clin Tech Small Anim Pract. May: 15(2): 94-100.
15. Mauger TF Nye CN, Boyle KA (2000) Intraocular pressure, anterior chamber depth and axial length following intravenous mannitol.J Ocul Pharmacol Ther. Dec 16(6): 591-94.
16. Saluja K, Naik M, Vemparala R et al. (2017) Idiopathic Bilateral Suprachoroidal Haemorrhage: A Rare Case Presentation. Case Rep Ophthalmol Med.
17. Shi J, Qian J Li H et al (2018) Renal tubular epithelial cells injury induced by mannitol and its potential mechanism. Ren Fail November, 40 (1): 85-91.
18. Yanoff, Myron (1998) Ophthalmic Diagnosis and Treatment. Glaucoma Chapter: pages 100-129 (Elliot B. Werner, MD) Butterworth-Heinemann Handbook, Current Medicine, Inc., Philadephia.
19. Csikszentmihalyi, Mihaly (1996) Creativity: Flow and the Psychology of Discovery and Invention. New York: Harper Perennial.
20. Maurice DM (1996) In Memoriam: Hugh Davson, 1909-1996. Experimental Eye Research. December; 63(6): 611-12.
21. Bito LZ (2002) Prostaglandin postscript: a personal reflection. Surv Ophthalmol. August 47. Suppl. 1: S231.
22. Tang W, Zhang F, Liu K et al (2019) Efficacy and safety of prostaglandin analogues in primary open-angle glaucoma or ocular hypertension patients: A meta-analysis. Medicine (Baltimore); July, 98:(30).
23. Aggarwala KRG (2020) Ocular accommodation, IOP, development of myopia and glaucoma. Med Hypothesis Discov Innov Ophthalmol 9 (1) pp5.
24. Sigal IA, Roberts MD, Albert DM (2011) Biomechanical Changes of the Optic Disc. In: Ocular Disease: Mechanisms and Management, Edited by Levin LA and Albert DM. Elsevier, Saunders.
25. Rosenzweig, P (2007) The Halo Effect: and Eight other Business Delusions that Deceive Managers. Free Press: Simon & Schuster; New York.

****