INTRODUCTION

Glaucoma is a progressive optic neuropathy that leads to irreversible visual impairment if not properly treated ***(Chauhan and Drance, 1992)***. It is the commonest cause of irreversible blindness worldwide ***(Resnikoff et al., 2004)***, and the second leading cause of blindness globally ***(Cook and Foster, 2012)***. Elevated intraocular pressure (IOP) is a major risk factor for the development of glaucoma. It is fundamental and of utmost importance in patients with the suspicion of glaucoma. Diagnosis, prognosis, treatment, and follow-up of glaucoma are still based on IOP. Many scientists believed that its reduction is beneficial in slowing down the glaucomatous changes of the optic nerves and visual field (VF). So the therapeutic strategies designed to reduce the IOP remain the principal method of treatment ***(Leske et al., 2003; Kniestedt et al., 2008; Caprioli and Varma, 2011; Mansouri and Weinreb, 2012)***.

Intraocular pressure in the human eye is regulated by many factors, including the rate of aqueous humor (AH) production, the facility of trabecular outflow, the rate of fluid drainage through the uveoscleral outflow pathway, and the pressure in the episcleral veins ***(Yang et al., 2007)***. It varies throughout the twenty-four hour period due to the changes in these physiologic parameters. In healthy young subjects, there is time variation of IOP with a peak value in most individuals occurring in the late nocturnal / sleep period in either setting or supine body position ***(Liu et al., 2003; Loewen et al., 2010)***.

A significant group of patients still develop glaucomatous progression, despite IOP values considered within normal limits ***(O'Brien et al., 1991)***, because the measurement of IOP taken at a single time point during office hours can render an incomplete picture of IOP due to the diurnal variability of IOP ***(Barkana et al., 2006)***. This IOP fluctuation has been identified as a risk factor for the progression of glaucoma; thus, the IOP profile would be better assessed by a twenty-four hour daily tension curve (DTC) ***(Asrani et al., 2000)***.

Twenty-four hour daily tension curves can estimate IOP peaks and fluctuations to provide the practitioner with more reliable information regarding the short-term IOP profile. However, twenty-four hour IOP monitoring may be unfeasible and time consuming for both patients and physicians; thus, it may be a restricted tool in clinical practice ***(Vasconcelos-Moraes and Susanna, 2008)***.

So the modified diurnal tension curve (mDTC) emerged as an alternative method that involves IOP measurements every 2 or 3 hours during office hours. It is more feasible and may provide better information regarding the IOP profile than single IOP measurements ***(Vasconcelos-Moraes and Susanna, 2008)***.

Intraocular pressure varies in relation to a number of factors, one of them is fluid intake; so another possible way to assess the IOP is the water drinking test (WDT), which was an old fashion test used in the late 1920's to help in the diagnosis of glaucoma ***(Schmidt, 1928; Skuta et al., 2011)***. While we now know that its low sensitivity and specificity make it unhelpful diagnostically ***(Goldberg and Clement, 2010)***. But it may used to evaluate the eye ability to deal with a transient IOP elevation by observing how high the IOP rises and how long it takes to return to baseline ***(De Moraes et al., 2009; Susanna et al., 2006)***.

Like the other widely used stress tests (for example, glucose tolerance test or cardiac stress test), WDT's aim is to stress the trabecular meshwork (TM) by increasing episcleral venous pressure (EVP), secondary to an increase in central and peripheral venous pressure, with resulting transient negative aqueous outflow ***(Diestelhorst and Krieglstein, 1994; Susanna et al., 2006)***. This then would lead to increased IOP as a result of the reduced outflow facility from a decreased pressure gradient across the TM ***(De Moraes et al., 2009)***.

Water drinking test is done by imbibing a volume of water over a short period, with IOP measurements compared before and for some time afterward. It has been either a fixed volume of one liter of water or variable, such as 10 ml/kg body weight in 5 minutes, with no fluid ingestion was allowed 2 hours before the test. This often will lead to increase of IOP after about 30 minutes ***(Goldberg and Clement, 2010; Kerr and Danesh-Meyer, 2010).***

AIM OF THE WORK

To investigate the relation between the intraocular pressure peaks detected during the water drinking test and the modified diurnal tension curve in both normal and glaucomatous eyes.

OVERVIEW OF GLAUCOMA

It is difficult to define glaucoma precisely, as it encompasses a diverse group of disorders. All forms of the disease have in common a potentially progressive and characteristic optic neuropathy which is associated with VF loss as damage progresses, and in which IOP is usually a key modifying factor ***(Kanski and Bowling, 2011).***

Epidemiology of Glaucoma:

Globally, there are an estimated 60 million people with glaucomatous optic neuropathy and an estimated 8.4 million people who are blind as the result of glaucoma. These numbers are set to increase to 80 million and 11.2 million by 2020. Glaucoma is the second leading cause of blindness globally ***(Cook and Foster, 2012).***

It affects up to 2 % of those over the age of 40 years globally, and up to 10 % over the age of 80; 50 % may be undiagnosed. In European or African ethnic origin, primary open angle glaucoma (POAG) is the most common form. On a worldwide basis, primary angle-closure glaucoma (PACG) constitutes up to half of cases, with particularly high prevalence of far Eastern descent ***(Kanski and Bowling, 2011).***

World health organazation estimated the global population of people with high IOP (>21 mm Hg) at 104.5

million. The incidence (newly identified cases) of POAG was estimated at 2.4 million people per year ***(Skuta[A] et al., 2011).***

Epidemiology In Egypt:

The earliest population-based survey for the patterns of visual acuity and blindness in Egypt was done between 1965 and 1968 in which the prevalence of glaucoma was 2% in urban population and 9% in the rural one ***(Said et al., 1971).***

Eldaly et al, in 2013 presented information regarding blindness and visual impairment among 988 eyes of 494 Egyptian glaucoma patients attending the Cairo University Hospital's General Ophthalmology Clinics. Prevalence of glaucoma in their study was 8.1% among hospital ophthalmology outpatient clinics. Up to date, these are the only available figures describing prevalence of glaucoma in the Egyptian population ***(Eldaly et al., 2014).***

Classification of Glaucoma:

There are many separate anatomic, gonioscopic, biochemical, molecular, and genetic views of the classification of the glaucomas, among others, each with its own merit. Traditionally, glaucoma has been classified on anatomical basis into open angle (of anterior chamber), closed angle and developmental glaucoma (Table 1) and as primary (when no anatomically identifiable underlying cause of the events that led to outflow obstruction and IOP elevation can be found) or secondary (when an abnormality is identified and a putative role in the pathogenesis can be ascribed to this abnormality). Further subdivisions separated the open-angle glaucomas (OAG) into pretrabecular forms, usually due to membranous overgrowth; trabecular forms, where the site of AH outflow obstruction resides in the TM; and post-trabecular forms, due to obstruction in Schlemm's canal or, more usually, elevated EVP. Angle-closure mechanisms consisted of anterior conditions, usually resulting from contraction of pretrabecular membranes and peripheral anterior synechiae, and posterior conditions that "push" the iris forward to close the angle, either with or without pupillary block. Differentiation of OAG from closed-angle glaucoma is essential from a therapeutic standpoint to identify the cause of the pressure elevation and can lead the clinician to the appropriate method of controlling the pressure. The concept of primary and secondary glaucomas is also useful, but it reflects our lack of understanding of the pathophysiologic mechanisms underlying the glaucomatous process ***(Skuta[A] et al., 2011; Morrison and Pollack, 2003).***

Table (1): Anatomic classification of glaucoma ***(Morrison and Pollack, 2003)***

Open - angle glaucomas
Pretrabecular
Trabecular
Post-trabecular
Closed-angle glaucomas
Pupillary block
Nonpupillary block
Developmental glaucomas

Another classification (Table 2) depending on the etiology of the disease and based on the underlying ocular or systemic disorder is becoming increasingly useful, this approach allows more effective treatment of the abnormal IOP because the underlying condition itself can be addressed to augment standard antiglaucoma therapy. In addition, identifying the basic cause allows the clinician to recognize conditions that can eventually develop into glaucoma, before producing ocular pathology. This provides the opportunity to apply specific therapy to prevent the patient from developing glaucoma at all. An additional advantage is that this classification can include forms of glaucoma that can be less pressure dependent, such as normal-tension glaucoma, and improve our ability to treat and protect the optic nerve itself ***(Morrison and Pollack, 2003).***

Table (2): Clinical (etiologic) classification of glaucoma ***(Morrison and Pollack, 2003)***

Glaucoma condition	Open-Angle	Angle-Closure with pupillary block	Angle-Closure without pupilary block
Primary open- angle glaucoma	X		
Primary angle-closure glucomas			
With papillary block		X	
Without papillary block			X
Childhood glaucomas	X	X	X
Glaucomas associated with ocular and systemic disorders (secondary glaucomas)			
Steroid-induced glaucoma	X		
Pigmentary glaucaoma	X		
Pseudoexfoliation glaucoma	X		
Neovasuclar glaucoma	X		X
Iridocomeal endothelial syndromes	X		X
Elevated eopiscleral venous pressure	X	X	X
Glaucoma from ocular trauma and hemorrhage	X	X	X
Lens-induced glaucoma	X	X	X
Glaucoma from ocular inflammation	X	X	X
Glaucoma from disorders of the retina, choroid, and vitrous	X	X	X
Glaucoma following anterior segment surgery	X	X	X
Glaucoma from intraocular tumors	X	X	X
Systemic diseases	X	X	X

Primary Open Angle Glaucoma:

Primary open-angle glaucoma also referred to as chronic simple glaucoma, is a generally bilateral disease of the adult onset characterized by an IOP > 21 mmHg at some stage, glaucomatous optic nerve damage, an open anterior chamber angle, characteristic VF loss as damage progresses, absence of signs of secondary glaucoma or a non-glaucomatous cause for optic neuropathy ***(Kanski and Bowling, 2011).***

Primary open-angle glaucoma accounts for the majority of patients in the OAG category, and this group includes normal-tension glaucoma. The initiating event, or underlying etiology, may reside in the TM, increasing aqueous outflow resistance and increasing IOP. It could also be a genetic predisposition for structural alterations in the optic nerve head that affect the support or nutrition of the optic nerve axons ***(Morrison and Pollack, 2003).***

Diagnosis:

Glaucoma is diagnosed by the assessment of a combination of findings, including IOP levels, optic disc appearance, and VF loss ***(Skuta[C] et al., 2011).***

In addition to the progress brought on in the last years by automated VF testing, there are three outstanding features that have proven to be a significant step forward in the early diagnosis of glaucoma. These features are: improvements in detecting the actual changes in the optic disc related to glaucoma; the detection of changes in the nerve fiber layer which point to the diagnosis of glaucoma before the onset of VF loss; a better understanding of the relationship between IOP and glaucoma and the risk factors that predispose to the actual development of glaucoma ***(Boyd and Luntz, 2002).***

Intraocular pressure is one of the strongest risk factors for glaucoma progression. At high enough levels, IOP can be causative. Variability in diurnal IOP and large IOP differences between fellow eyes were found to be more common in patients with POAG (36%) than in normal subjects (6%). The diurnal IOP range and the IOP range over multiple days were found to be significant risk factors for progression, even after adjusting for age, race, and VF damage. In the analysis of the Early Manifest Glaucoma Trial with a median follow-up of 8 years the results confirmed the earlier findings that elevated IOP is a strong factor for glaucoma progression, with a hazard ratio increasing by 11% for every 1mmHg of higher IOP. ***(Wilensky, et al., 1993; Asrani et al., 2000; Kass et al., 2002; Bengtsson et al., 2007).***

The optic nerve head appearance is a significant risk factor and diagnostic sign as its alteration basically defines glaucoma in most patients ***(Epstein et al., 1989; Schulzer et al., 1991).***

Optical coherence tomography allows precise cross-sectional imaging of the eye and enables noncontact and non-invasive imaging of the RNF layer and optic nerve head ***(Schuman and Williams, 2002).***

AQUEOUS HUMOR DYNAMICS AND FORMATION

The parameters of AH dynamics include the rate of AH production, the facility of trabecular outflow, the rate of fluid drainage through the uveoscleral outflow pathway and the pressure in the episcleral veins (Fig. 1) ***(Yang et al., 2007).***

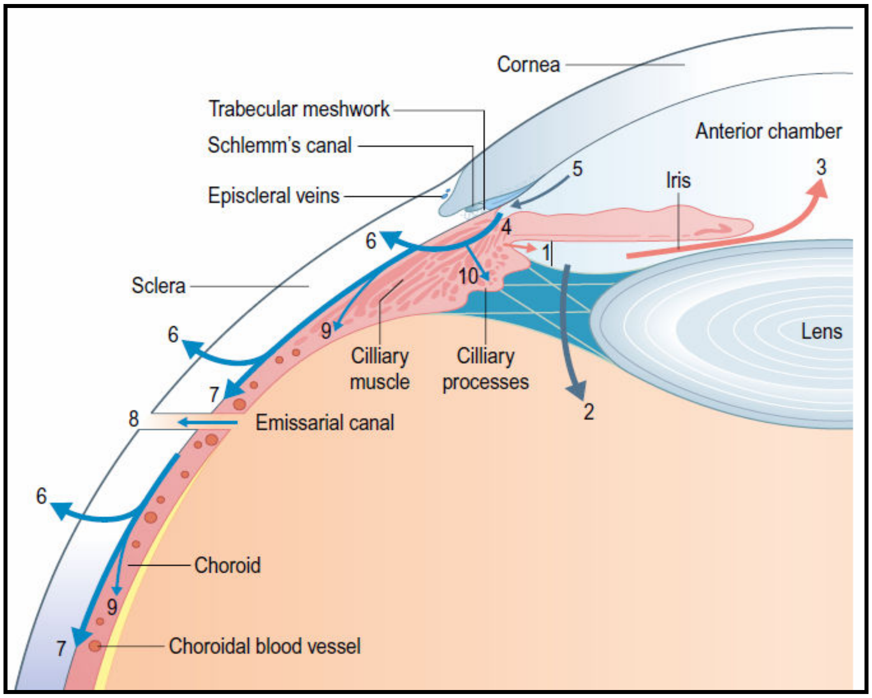

Figure (1): Aqueous humor dynamics. Aqueous humor that is secreted into the posterior chamber (1) flows across the vitreous cavity (2) or through the pupil into the anterior chamber (3). Fluid circulates around the anterior chamber and eventually drains into the anterior chamber angle (4). Aqueous humor drains from the anterior chamber angle via two routes, the trabecular meshwork, Schlemm's canal, and episcleral veins (5), or the uveoscleral outflow route. The latter route starts with the ciliary muscle. From there, fluid may flow in many directions, including: across the sclera (6), within the supraciliary and suprachoroidal spaces (7), through emissarial canals (8), into uveal vessels (9) and vortex veins (not drawn), and possibly into ciliary processes (10) where it could be secreted again ***(Toris, 2009)***.

When one or more of these parameters is altered and the balance between inflow and outflow is disturbed, various pathological conditions affecting IOP can result. Understanding the complex mechanisms that regulate AH circulation is essential for better management of glaucoma ***(Yang et al., 2007).***

Anatomical Consideration:

- ### Anatomy Of The Ciliary Body:

The ciliary body, along with the iris, forms the anterior uvea. The ciliary muscle, which forms the outer portion of the ciliary body, is a triangular tissue consisting of three groups of muscle fibers, with its apex pointing posteriorly, ending at the ora serrata. Outermost, longitudinal fibers insert as tendinous bands into the scleral spur, with some extending in front of the spur, into the TM. The middle radial and inner circular fibers form the base of this triangle and can be seen gonioscopically as the ciliary body band ***(Morrison et al., 2003).***

Internal to the ciliary muscle, approximately 70 radial ciliary processes and intervening minor processes extend into the posterior chamber (PC), forming the pars plicata (Fig. 2) ***(Morrison et al., 2003).***

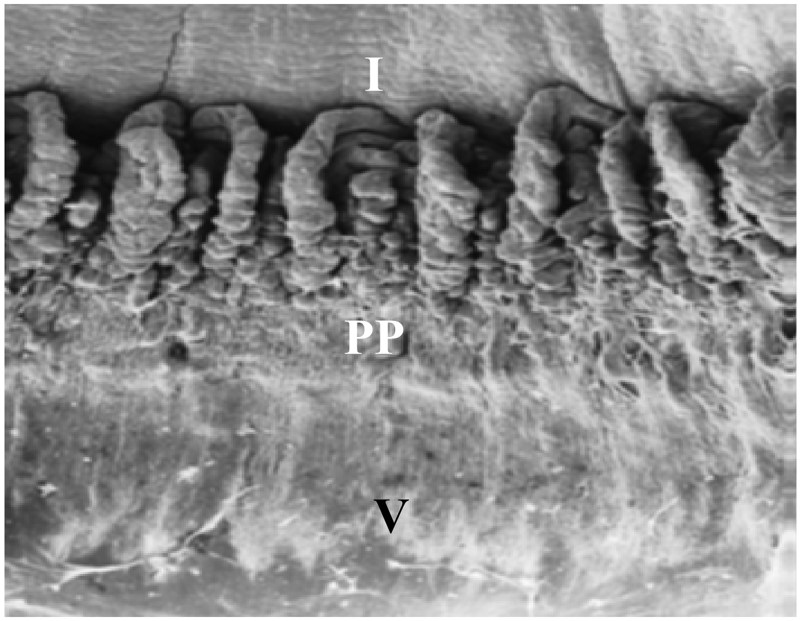

Figure (2): Scanning electron micrograph of the posterior chamber with lens and zonules removed demonstrates posterior surface of the iris (I), major and minor ciliary processes (pars phiata), and pars plana (PP). Ora serrata and vitreous base (V) are located at the bottom of photo-graph (X42) ***(Morrison et al., 2003).***

These processes arise just posterior to the iris root, forming the ciliary sulcus. Major processes are approximately 2 mm long and 1 mm high and have irregular, convoluted surfaces. The more posterior pars plana, which only overlies the ciliary muscle, extends from the ciliary processes to the ora serrata. Lens zonules arise from between the nonpigmented epithelial cells and are channeled in between the ciliary processes to insert into the anterior and posterior lens capsule ***(Morrison et al., 2003).***

- ## Ultrastructure of The Ciliary Process Microvasculature:

Capillaries of the ciliary muscle have a continuous endothelial lining that is impermeable to injected tracer substances. In contrast, the capillaries of the ciliary processes have fenestrations, consisting of circular "pores" where the cell membranes are fused ***(Holmber, 1959).*** These fenestrations, which line the entire circumference of these capillaries, allow for the passage of macromolecules, including tracer substances, into the ciliary process stroma (Fig. 3). This forms the ultrastructural basis for ultrafiltration ***(Smith and Rudt, 1973).***

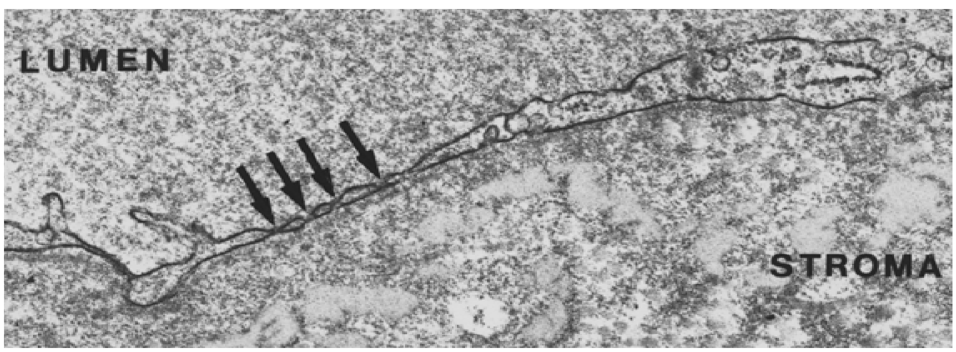

Figure (3): Ciliary process capillary wall. Arrows indicate endothelial fenestrations X26,000 ***(Morrison, et al. 2003).***