The Effects of Prostaglandin Analogs on Intraocular Pressure in Human Eye for Open Angle Glaucoma

Shabab Akbar, Sapna Ratan Shah

Abstract**:** ***The effects of Prostaglandin Analogs on intraocular pressure and increased aqueous outflow via trabecular meshwork into the schlemm's canal has been studied in this present research paper. Aqueous humor is an outflow, which flows at the back of the iris in the posterior chamber all the way through the pupil aperture, out into the anterior chamber, and drain from the eye via drainage slope. The eye keeps on making aqueous humor in the ciliary body and it passes through the trabecular meshwork into the scheme of the canal, the key drainage from the eye and it finally goes to the "collector channels" and due to the less amount of aqueous humor fluid flow from the drainage angle, the pressure in the eye starts to increase. For this study, the canal of Schlemm is assumed as a permeable channel. And it is connected by trabecular meshwork. The inner layer of the canal's wall has been assumed as permeable. And the aqueous humor drains into the canal through this porous tissue wall. The objective of this paper is to discuss the effect of prostaglandin analogs on intraocular pressure as the Prostaglandin Analogs work by increasing the outflow of aqueous from the eye.***

Keywords**:** ***Collector channel, Open angle Glaucoma, Prostaglandin, Latanoprost, bimatoprost, Latanoprostene.***

I. INTRODUCTION

Glaucoma is an eye disease that describes the process of damaging the optic nerve due to high intraocular pressure (IOP) in the human eye. Normally, three things are happening in the eye. (1) The intraocular pressure in the eye increases. (2) The optic nerve was damaged. (3) The peripheral vision was compromised. Glaucoma can be divide into two types, (a) Open-angle glaucoma (b) Closed-angle glaucoma. Open-angle Glaucoma, the drainage canal, or drainage angel of the eye called the "trabecular meshwork" is not anatomically blocked; it is a kind of clogged drain. The drainage canal becomes clogged or narrow and permits less amount of aqueous humor fluid to leave the human eye. The eye keeps on making aqueous fluid in the ciliary body and hence the pressure in the eye increases. Increased pressure in the eye causes optic nerve damage. In the human eye, vision loss in open angle glaucoma begins with the peripheral vision. A very dangerous thing about open-angle glaucoma is that, it is completely painless and if there is no regular examination of the eye, major damage can occur in the eye without any pain or problem [Avtar and srivastava (2014), [2, 3]].

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Aqueous humor fluid is a very thin, transparent, watery fluid similar to plasma. Aqueous humor fluid is a combination of 99.9% water and the other 0.1% consists of nutrients, vitamins, sugars, and proteins [Fig. (1)]. Aqueous humor fluid sustains the cornea and the lens and gives the eye its regular shape and size. Aqueous humor plays an important role in the health of the human eye. Aqueous humor maintains the health of our eye, as well as lens and cornea by giving nutrition for instance; glucose, nutrients, and amino acids, etc. Aqueous humor maintains the intraocular eye pressure and also it transports the nutrition and vitamin C in the front section to act as an antioxidant agent. It also shows inflation for the development of the cornea and enhances the protection against the wind, dust, poll engrains, and pathogens. Most of the aqueous humor (90%) passes through tissues, which are located in the anterior chamber near the juxtaposition of the iris of the eye between the cornea and sclera. The moving

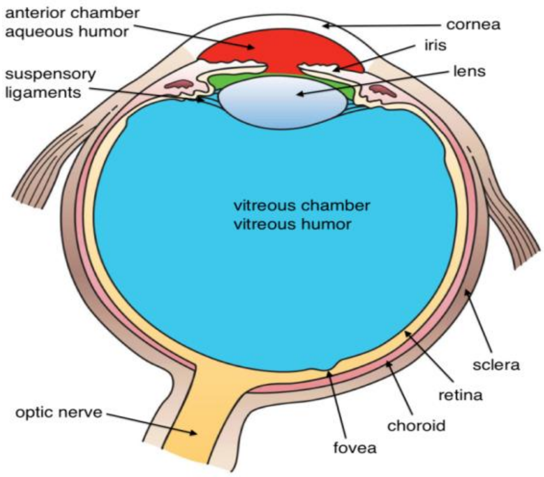

Fig.(1). Flow of Aqueous humor in human eye

exteriorly, and anterior chamber, these special issues are the fibrous connective tissue, trabecular meshwork, Schlemm's canal, collecting duct lined by a collector channel, and endothelium similar to vascular. Aqueous humor going from the anterior chamber drain through the trabecular meshwork into the Schlemm's canal [Canning et al., (2002) [4] and Morris et, al., (2013)[11]]. This fluid flow is responsible for creating a positive intraocular pressure within the eye and has many interesting and important biomechanical consequences and applications. The confrontation in the outflow fluid system of aqueous humor outflow results as the gathering of aqueous humor in the anterior chamber which supervises to increase the amount of fluid and result as an increase in intraocular pressure in the human eye.

The aqueous flow of fluid through the Schlemm's canal plays a major and important responsibility in the regulation and stability of the intraocular pressure, which is necessary to maintain the health and the visual function of the eye. In 2007 Lyubimov et al. [10] have given mathematical modeling of aqueous humor fluid flow and its key consequences of the fluid dynamics where the problem of interaction between the intraocular pressure and the hydrodynamic processes in the eye has described. A lumped parameter model has been taken into account, a wide range of physically permissible mechanisms of the inflow and outflow of intraocular fluid has been investigated. In 2010, Ferreira et al.,[6] and Goel, et al.,[8] have explained the cases of stationary and non-stationary flow regimes, and the consequences of various assumptions have analyzed. The flow in the presence of an external load has been considered. In 2006, Fautsch, et al., [5] and Fitt et, al. [7] have also developed some important aspect of the human eye, where the mechanical properties of the fluid flow, processes have necessary part of numerous aspects of pathology and physiology of the eye. In their research work, they have depicted the particular phenomena of flow in the human eye. They initially focused on glaucoma, and then the condition associated with increased pressure in the eye. The mechanics in "Open-angle Glaucoma" disease is understood. They have presented some mathematical modeling work that gives some partial description of the human eye. And hence they focused on other aspects of fluid dynamics of two focused ocular fluids are Aqueous humor and Vitreous humor. To explain the aqueous humor, they described the problems of proteins, hydration of cornea, transport of heat, and vitreous humor. They have also discussed the prospect of fluid flow, which primarily occurs as a result of jerking or motions of the eyeball. Finally, they described a mathematical model for the degradation of the Bruchs membrane in the retina.

II. FORMULATION OF THE PROBLEM (MODEL DESCRIPTION):

It is considered in the proposed work that the flow is represented by thermal special effects in the front area of the human eye, between the cornea and the iris [Fig. (2)]. It is assumed that the fluid is enclosed by z = 0 and a solid resistant boundary of the cornea (z). And the temperature on the boundary if fixed, it is T_0 and assumed to be very close to the temperature of the body. Here the cornea thickness is constant and it is 0.6mm. The diseased person is taken in an upright position so the gravity acts along the positive x-axis. The continuous production of aqueous humor and outflow phenomena of this transparent fluid in the human eye are essential processes to declare the stability of the intraocular pressure which is very important and essential to maintaining the visual function of the human eye and for the nourishment of vascular tissues of the eye [Avtar, et, al.,(2008) [1]].

The aqueous humor flows in the anterior chamber which is in contact with its posterior surface is warmer than that of in the contact of its anterior surface. The warmer fluid is inclined to rise close to the backside of the chamber into the surrounding cooler fluid and build up a tendency to fall towards the front. The rising warmer fluid is the exchange with surrounding cooler fluid flow. The cooler aqueous humor fluid running into warms up and rises. The result is a thermally compulsive, circulation of aqueous humor in the anterior chamber. This buoyancy- compulsive circulation of aqueous humor in the anterior chamber can be simulated by using the principles of conservation of the mass, momentum, and energy. In most of the aqueous humor, fluid flow that percolates in the Schlemm's canal through the trabecular meshwork must flow fast a little distance along the canal to achieve the collector channel. A canal segment between the two collector channels is known as an elliptical channel. Half of the surface of the elliptical channel is porous in contact with the trabecular meshwork [Gonzalez and Fitt, (2003) [9]]. A mathematical model for the Buoyancy- driven fluid flow of humor arising from the temperature difference between the anterior surface of the Cornia and iris have been described. The model, developed in this research work is based on the Navier-Stokes equation, lubrication theory, and Boussinesq model of fluid density for thermal driven convection flow. In this present model, the heat loss at the corneal surface takes place due to convection as well as due to evaporation and radiation. In the anterior chamber of the human eye, the density varies slightly but the pressure is negligible. The viscosity, density, and expansivity of aqueous humor have similar properties to water and protein. So, there is no inflow through the pupil aperture. The flow is presented by the Navier-Stokes equation.

In the Navier-Stokes equation, the fluid velocity is described as;

$$\hat{q} = u\widehat{e_x} + u\widehat{e_y} + u\widehat{e_z} \tag{1}$$

Where, $\widehat{e_x}$, $\widehat{e_y}$ and $\widehat{e_z}$ are unit vectors in x, y and z detections, in the rectangular co-ordinate system.

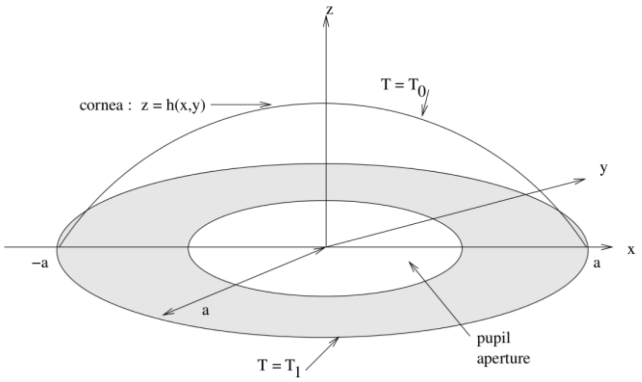

Fig.(2): Schematic diagram of anterior chamber

III. SOLUTION OF THE PROBLEM:

The aqueous humor fluid flow phenomenon had investigated theoretically by [Fautsch, et al., [5] and Fitt et, al. [7] (2006)] where it has described that the limit of Navier-stokes equations, lubrication theory were suitable for the system of equations. Boussinesq approximation equation and the final partial differential equations are as below [Canning, et, al., (2002), [4]]-

$$-\frac{p_x}{\rho_0} + \nu u_{zz} + g\left(1 - \alpha(T - T_0)\right) = 0 \tag{2}$$

$$-\frac{P_y}{\rho_0}+\nu u_{zz}=0 \tag{3}$$

$$u_x+u_y+u_z=0 \tag{4}$$

$$T_{zz}=0 \tag{5}$$

and also the boundary condition are given as follows;

$$u=v=0,\quad w=w_0(x,y),\quad T=T_1 \ on \ \ z=0 \tag{6}$$

$$u=v=w=0,\quad T=T_0 \quad on \ \ z=h(x,y) \tag{7}$$

In the above equation the notations are given as follows; P_x denotes the pressure, T is the temperature, z is the

Table 1: Model Parameters

Control Parameters	Typical physiological value	References No.
Corneal Temperature, T_0 (^oC)	37	[3]
Iris Surface Temperature, T_1 (^oC)	20	[3]
Coefficient of linear thermal expansion, (α)	132	[3]
Gravitational constant, g (ms^{-2})	8.2182	[2]
Height of the Anterior Chamber, (h)	1.2	[2]
Fluid kinematic viscosity, ν (m^2s^{-1})	0.75	[3]
Co-ordinate normal to the iris, (z)	0.79	[3]

co-ordinate normal to the iris and x and y are the co-ordinate in the plane of the iris, q = (u, v, w) is the aqueous velocity, g defines the acceleration because of gravity, α is the coefficient of thermal expansion of aqueous and subscripts denotes differentiation. The cornea's posterior surface has assumed at z = h(x, y) and w = w_0 (x, y).

Now we can solve the above equation form (1)-(4) easily;

$$T_{zz}=0 \ \rightarrow \ \frac{\partial^2 T}{\partial z^2}=0 \rightarrow \frac{\partial T}{\partial z}=T_c \ \rightarrow T=T_c\, z+T_D \tag{8}$$

$$T=T_0\,, \qquad z=h(x,y) \tag{9}$$

$$T_0=T_c\, h(x,y)+T_D \tag{10}$$

Again applying given boundary condition;

$$T=T_1\,, \quad on \quad z=0 \tag{11}$$

$$T_1=T_c*0+T_D \tag{12}$$

$$T_1=T_D \tag{13}$$

Now the equation (7) takes place;

$$T_0=T_c\, h(x,y)+T_1 \tag{14}$$

$$T_c=\frac{T_0-T_1}{h(x,y)} \tag{15}$$

$$T=\frac{T_0-T_1}{z}\, h+T_1 \tag{16}$$

$$T=T_1+\frac{z}{h(x,y)}\ (T_0-T_1) \tag{17}$$

$$-\frac{P_x}{\rho_0}+\nu u_{zz}+g\big(1-\alpha(T-T_0)\big)=0 \tag{18}$$

$$-\frac{P_y}{\rho_0}+\nu u_{zz}=0 \tag{19}$$

$$-\frac{P_x}{\rho_0}+\nu u_{zz}+g\left(1-\alpha(T_1-T_0)(1-\frac{z}{h})\right)=0 \tag{20}$$

$$u_{zz}=\frac{P_x}{\nu\rho_0}--\frac{g}{\nu}\left(1-\alpha(T_1-T_0)(1-\frac{z}{h})\right) \tag{21}$$

$$u_{zz}=[\frac{P_x}{\nu\rho_0}-\frac{g\alpha}{\nu}(T_1-T_0)-\left(\frac{g\alpha}{\nu}(T_1-T_0)\left(\frac{z}{h}\right)\right) \tag{22}$$

$$u=\frac{\rho_x}{2\nu\rho_0}(z^2-hz)+\frac{g}{\nu}[\frac{hz}{2}-\frac{z^2}{2}+\alpha(T_1-T_0)\left(-\frac{2hz}{3}+\frac{z^2}{2}-\frac{z^3}{6h}\right)] \tag{23}$$

Similarly we also can find that:

$$v=\frac{\rho_y}{2\nu\rho_0}(z^2-hz) \tag{24}$$

$$w=\left[\frac{p_x}{2\nu\rho_0}\left(\frac{hz^2}{2}-\frac{z^3}{3}\right)\right]_x+\left[\frac{p_y}{2\nu\rho_0}\left(\frac{hz^2}{2}-\frac{z^3}{3}\right)\right]_y+\frac{g\rho_0 z^2 h_x}{\nu\rho_0}\left[\frac{1}{4}+\frac{\alpha(T_1-T_0)}{6}\left(\frac{z^2}{4h^2}-1\right)\right]+w_0 \tag{25}$$

IV. RESULTS AND DISCUSSION:

In this present research paper a advance mathematical model for explaining outflow of aqueous flow in meshwork of the eye to give an estimate of effect of velocity profile on flow characteristics of aqueous humor flow and a simple mathematical framework for describing the aqueous outflow through trabecular meshwork have been studied. Computational results for the flow of aqueous humor in anterior chamber of the human eye from proposed work by introducing biological suitable values of the parameters used in this work are listed in the [Table. 1] and has been presented through the graphs in order to illustrate the mechanism of aqueous humor and to investigate the effects of various parameters in human eye. The velocity profile (u), axial distance (z) the linear thermal expansion (α), gravitational constant (g), height of the anterior chamber and (h), fluid kinematic viscosity (ν) especially, thermal parameters, on the aqueous humor flow in human eye have been shown in figure 3, 4, 5 and 6 respectively.

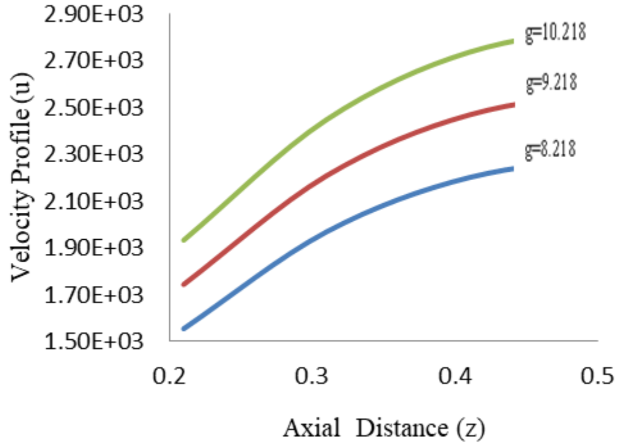

Fig.(4). Velocity profile (u) with axial distance (z) for different Gravitational constant (g) and Iris surface temperature (T_1), Corneal temperature (T_0)

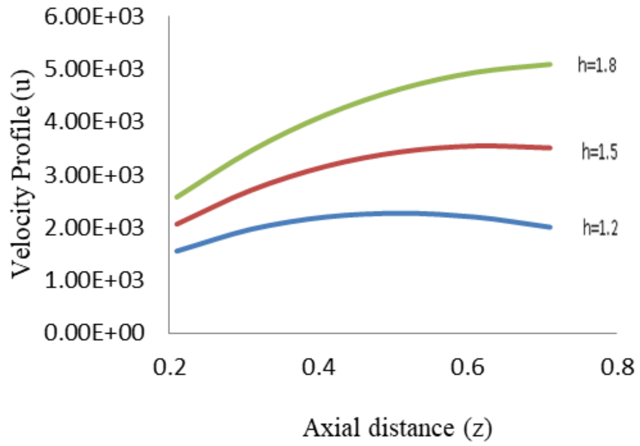

Fig.(5). Velocity profile (u) with Height of the anterior chamber (h) and Iris surface temperature (T_1), Corneal temperature (T_0)

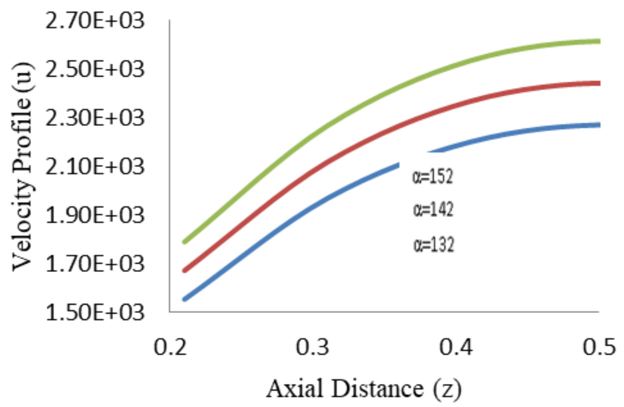

Fig.(3). Velocity profile (u) with axial distance (z) for different linear thermal expansion (α) and Iris surface temperature (T_1), Corneal temperature (T_0)

In figure 3, the variation of velocity profile (u) with z for the different values of coefficient of linear thermal expansion (α) have been shown. Figure depicts that the velocity profile increases as the axial distance (z) increases. It is also seen in the figure that the velocity profile (u) increases as coefficient of linear thermal expansion increases (α ie. 132, 142 and 152). Figure. 4, shows the variation of velocity profile (u) with axial distance (z) for the different values of gravitational constant (g). It is shown in the figure that u, increases as the axial distance (z) increases. It is also shown in the figure that the velocity profile increases as the value of gravitational constant (g) increases. Velocity is depends on the axial distance in the trabecular meshwork. Aqueous humor flows behind the iris in the posterior chamber throughout the pupil aperture, out into anterior chamber to drainage canal of the eye called trabecular meshwork. In open eye glaucoma there is a clogged drain and as the axial distance increases the velocity increases that describe the increased high pressure in eye. Prostaglandin analogs gives the immediate rise in out In figure 5, the variation of velocity profile (u) with axial distance for different value of height of anterior chamber (h) have been shown. It is shown in the figure that velocity profile (u) increases as the axial distance (z) increases. It can also be seen in the figure that the velocity profile increases as the value of height of anterior chamber (h) increases [2].

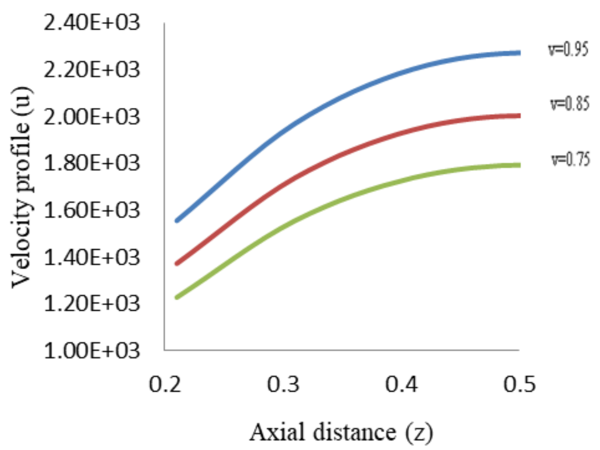

Fig.(6). Velocity profile (u) for fluid kinematic viscosity (v) and Iris surface temperature (T_1), Corneal temperature (T_0)

Figure 6, shows the variation in velocity profile (u) with axial distance (z) for different values of fluid kinematic viscosity (v). The figure also reveals that the velocity profile (u) increases as the axial distance (z) increases. It can also be seen from the figure that the velocity profile increases as the value of fluid kinematic viscocity (v) increases for the values of 0.75, 0.85 and 0.95 [Fautsch, et al., (2006), [5]]. Aqueous humor is an out flow, which flows behind the iris in the posterior chamber through the pupil aperture, out into the anterior chamber and drain from the eye via the drainage angle and maintain the intraocular pressure (IOP). The eye keep on making the aqueous humor in the ciliary body and it passes through a biological filter trabecular meshwork into the schelmm's, of canal. The intraocular pressure in the human eye increases if the drainage route is blocked or narrow. So to decrease the intraocular pressure, the Prostaglandin analogs helps to better drain of aqueous humor fluid flow and to increase fluid flow from the eye to the "collector channnels [Lyubimov et, al., (2007)].

V. CONCLUSION

This study can help us to gain some significant and important insights concerning the identifications of the factors which may involve in build up some medical problems in the eye and enrich our present realising of the role of buoyancy-driven flow of aqueous humor in the development of some ocular diseases. Also, the study may alleviate the design of some therapeutic methods to neutralize adverse contribution of the convection to the growth of some pathological states in the eye. The significance of this paper is to find out the effects of Prostaglandin analogs on aqueous fluid outflow and to decrease the intraocular pressure (IOP) in the human eye. Prostaglandin analogs is a combination of latanoprost, bimatoprost, travoprost, tafluprost and latanoprostene bunod and they work by increasing the Aqueous humor outflow of fluid from the drainage angle through trabecular meshwork to the canal of schlemm's to lower down the intraocular pressure.

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