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A study of Intraocular Pressure trends in Pregnancy and in the third trimester hypertensive patients

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Abstract

Aim and Background: In this present study to investigate that the study of intraocular pressure and certain other visual parameters like visual acuity, corneal edema and fundus examination during normal pregnancy and pregnancy induced hypertension. Intra ocular pressure begins to fall with the progress of pregnancy due to the reduction of the episcleral venous pressure and increased uveoscleral outflow facility. Systolic blood pressure begins to fall during 1st trimester reaches nadir in mid pregnancy and return towards pre gestational levels before term. Diastolic blood pressure decreases more than systolic blood pressure. Reduction in blood pressure is caused by decline in systemic vascular resistance due to vasodilation mediated by gestational hormonal activity, mainly progesterone, estrogen and relaxin. Relaxin relaxes all the ligaments including the corneoscleral ligaments in the presence oestrogen.

Materials and Methods: This is a Comparative study. In this study non-pregnant and pregnant subject in all trimester and pregnancy induced hypertension subjects were selected from the Medical Outpatient Department of Stanley Medical College and Antenatal OP and wards of R.S.R.M. hospital Chennai respectively. They were divided in to five groups of fifty each.

Results: Out of 150 subjects 16 showed corneal edema so it is not significant. But in group III out of 50 subjects 13 showed corneal edema, so it highly significant.

Conclusion: In the Present study we conclude that there is definite tendency for intraocular pressure to drop with the progress of pregnancy, with the least value during the 3rd trimester of pregnancy. So preexisting glaucoma improves during pregnancy.

Keywords: Intraocular pressure in pregnancy, Systolic Blood pressure, Diastolic Blood Pressure, Corneal Edema and hypertension.

1. Introduction

The eye is a peripheral organ of vision. The formation of aqueous humor and maintenance of intraocular pressure are the important aspects of physiology of the eye. Aqueous humor is a clear

fluid, filling the anterior and posterior chamber of the eye. Its refractive index is 1.336 and viscosity 1.025 to 1.040. The osmotic pressure of aqueous humor is slightly higher than plasma. The aqueous humor contains glucose, urea, proteins, inorganic salts, ascorbic acid and some dissolved oxygen.

The walls of the capillaries of the iris, ciliary body, two layers of ciliary epithelium and walls of the retinal capillaries constitute a system of semi permeable membranes, separating blood from aqueous barrier. This barrier is relatively impermeable so that large sized molecules from plasma cannot pass in to the eye. Such a mechanism is necessary for the maintenance of optical transparency of aqueous humor. The circulation of aqueous humor is essential for regulation of the Intraocular pressure as well as for the metabolic activities of the extra ocular structures. Average rate of aqueous humor formation is 2 – 3µl/mt and results from net fluid movement across the epithelial layer of the ciliary process. Fluid transport across the ciliary epithelium occur by three basic mechanisms.
Progesterone increases during pregnancy promotes renal sodium excretion by competitive inhibition of the aldosterone on the renal tubule.

Evertte and Co worker (1978)[1] found that the refractoriness to angiotensin II usually observed during normal pregnancy may be mediated by the action of prostaglandin related substances, that are produced in situ by arteriolar endothelium. Decrease in the rate of prostaglandin synthesis or increase in the rate of prostaglandin catabolism might result in increased vascular responsiveness to angiotensin II, characteristics of the pregnant women who has developed pregnancy induced hypertension.

The same workers in 1978 evaluated the effect of prostaglandin synthase inhibitors on the effective presser dose of angiotensin II, in normal pregnant woman after 28 weeks, they found that indomethacin and aspirin resulted in significant reduction in the amount of infused angiotensin II required to evoke an increase in diastolic blood pressure of 20 mm mercury.

The likelihood of prostaglandin involvement in the regulation of vascular reactivity in pregnant woman was confirmed by Broughton Pipkin and Meirelss (1982)[2] They infused prostaglandin E2 intravenously in to the pregnant women and found that the amount of angiotensin II required to increase diastolic blood pressure by 20 mm of mercury was increased.

Prostaglandins manufactured in the kidney are one possible anti-hypertensive agent. It is thought for example that during pregnancy increased secretion of prostaglandins prevent the rise in blood pressure. If prostaglandin production is impaired then hypertension results, this has been postulated as a mechanism responsible for development of preeclampsia in pregnancy.

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Pressure responsiveness to angiotensin II and the renin angiotensin aldosterone system is altered remarkably in pregnancy.

Gant and coworkers found that various volume loads including normal saline 100 ml, dextran 500 ml did not alter pressure responsiveness to angiotensin II in normotensive pregnant women despite significant increase in blood volume and decrease in renin plasma level. Therefore the increased refractoriness to angiotensin II characteristic of normal pregnancy is likely to be the consequence of individual vessel refractoriness to angiotensin II. In women destined to develop preeclampsia or a preeclamptic pregnant women the increased sensitivity to angiotension II was the results of alterations in the vessel wall refractoriness rather than the consequence of changes in blood volume or circulating renin angiotensin levels.

2. Materials and methods

In this study non-pregnant and pregnant subject in all trimester and pregnancy induced hypertension subjects were selected from the Medical Outpatient Department of Stanley Medical College and Antenatal OP and wards of R.S.R.M. hospital Chennai respectively. They were divided in to five groups of fifty each. The patients were selected according to the inclusion and exclusion criteria. The inclusion criteria includes Non-pregnant women aged 20 to 30 years with no history of taking contraceptive pills, with no previous history of steroid therapy and asthma, Antenatal women aged 20 to 30 years with no previous history of steroid therapy and asthma and Proven cases of pregnancy induced hypertension aged 20 to 30 years in third trimester of pregnancy and others like Hypertension, Diabetes mellitus, Renal and Cardiovascular diseases was excluded.

Group 0: Control Subjects - Healthy non-pregnant normotensives selected from Medical Outpatient Department of Stanley Medical College Hospital Chennai.

Group I: I trimester normotensive pregnant women selected from inpatient and outpatient departments of RSRM hospital Chennai.

Group II: II trimester normotensive pregnant women selected from inpatient and outpatient departments of RSRM hospital Chennai.

Group III: III trimester normotensive pregnant women selected from inpatient and outpatient departments of RSRM hospital Chennai.

Group IV: Pregnant subjects with pregnancy induced hypertension were selected from Antenatal OP, and Eclampsia wards of RSRM hospital Chennai.

The diagnosis of pregnancy-induced hypertension was mainly based on recording blood pressure, presence of albuminuria & edema. Preeclampsia was defined as a rise in blood pressure after 20 weeks gestation more than 140/90 mm of Hg, on more than 2 occasions, one hour apart in a previously normotensive woman.

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3. Results

The results of our study in the following aspects were analyzed.

1. Intraocular pressure (IOP) in the different trimesters of pregnancy and in PIH(Pregnancy Induced Hypertension)
2. Whether there was any association between intraocular pressure (IOP) and systolic blood pressure (SBP)/ Diastolic Blood Pressure (DBP) in all the groups.
3. Presence of corneal edema in different groups.
4. In cases where corneal was present, the correlation between the intraocular pressure and corneal edema was noted.
5. Visual acuity in all the groups.
6. Fundal changes in all the groups.

On analyzing the IOP in the different groups. It is found that the values though within normal limits, start decreasing from the 1st trimester till the end of the pregnancy. It has reached minimal values towards the end of third trimester (Table 1)

Table.1. Intra ocular Pressure in Group-I, II and III.

Group	**IOP Rt mmHg Mean**	**IOP Lt mmHg Mean**
Group-I	13.80	14.02
Group-II	12.28	12.28
Group-III	11.16	11.04

In group IV the IOP is more than in the groups 1, 2 and 3 subjects but still lower than group 0 values. (Table 2)

Table.2. Introcular Pressure in Different Groups

Group	IOP_{Rt} mmHg mean	IOP_{L+} mmHg Mean
Group 0	19.08	19.44
Group 1	13.80	14.02
Group 2	12.28	12.28
Group 3	11.16	11.04
Group 4	16.90	16.76

On analysis of the results of the effect of blood pressure on IOP, it is found that the association between SBP and DBP independently on IOP is highly significant in group 3 (Table 3).

Table.3. Association between intraocular pressure and Systolic blood Pressure/Diastolic pressure in all the groups

Group	IOP vs SBP	IOP Vs DBP
Group 0	0.24	0.23
Group 1	0.01	0.36
Group 2	0.08	0.34

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Group 3	0.34	0.53
Group 4	0.14	0.17

The blood pressure in group 0,1,2,3 both SBP and DBP have almost similar values except in group 0, were the values are higher than in the other 3 groups. There is no significant difference between 0,1,2 and 3 groups. However in group 4 subjects the mean values of systolic and diastolic blood pressure is much higher compared to the other groups (0,1,2,&3) (Table 4)

Table.4. Blood Pressure in different groups

Group	SBP mmHg Mean	DBP mmHg Mean
Group 0	114.0	74.1
Group 1	109.1	72.2
Group 2	111.2	70.6
Group 3	107.2	69.8
Group 4	145.6	96.24

As all our subjects from group 3 and 4 (PIH) belong to the 3rd trimester of pregnancy it would be worthwhile comparing the effects of intra ocular pressure, blood pressure both systolic and diastolic between the group 3 and 4 subjects. Blood pressure has an influence on the intra ocular pressure (table 5).

Table.5. Comparison between blood pressure and intra ocular pressure

Group	SBP mmHg Mean	DBP mmHg Mean	IOP mmHg Mean
Group 0	114.04	74.12	19.08
Group 3	107.20	69.80	11.16
Group 4	145.56	96.24	16.90

Correlation of intraocular pressure between group 3 & 4 are highly significant (Table 6)

Table.6. Correlation of Intraocular Pressure between Group 3 and Group 4

Group	**Number**	**Mean**	**SD**	**t Value**	**P value**
Group 3	50	11.16	1.13	98.01	.001 Significant
Group 4	50	16.90	1.09		

In all 250 subjects slit lamp examination was done detect corneal edema out of which 16 subjects showed mild corneal edema and stromal opacities (table 7)

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Table.7. Corneal edema in all groups

Groups	Corneal edema		
	Both Eyes	Right Eye	Left Eye
Group	0	0	0
Group 1	0	0	0
Group 2	0	2	1
Group 3	6	4	3
Group 4	0	0	0

Out of the 50 subjects in group 2 only 3 subjects had corneal edema. Its significance is low (table 8).

Table.8. Correlation between intraocular pressure and corneal edema (CE) group2

Group 2	**Number**	**Mean IOP**	**SD**	**t Value**	**P value**
CE(Ab)	47	12.40	1.01	5.68	.01 Significant
CE (P)	3	10.33	.58		

However out of the 50 subjects in group 3, 13 subjects showed corneal edema. This is highly significant (table 9).

Table.9. Correlation between intraocular pressure and corneal edema (CE) group3

Group 2	**Number**	**Mean IOP**	**SD**	**t Value**	**P value**
CE(Ab)	37	11.49	1.04	5.56	.001 Significant
CE (P)	13	9.77	.93		

Therefore in pregnancy, out of 150 subjects 16 showed corneal edema so it is not significant. But in group III out of 50 subjects 13 showed corneal edema, so it highly significant.

4. Discussion

This study reports that with advancing pregnancy, intraocular pressure decreases. These results are consistent with many other studies. The physiological mechanisms responsible for the decrease of intraocular pressure (IOP) during pregnancy are not clearly known. A number of possible mechanisms can be postulated. It is well documented that levels of progesterone, estrogen, relaxin and prostaglandin are increased during pregnancy and continues to be high throughout the pregnancy. Therefore it can be speculated that decreased IOP in pregnant women might be due to hormonal changes of pregnancy.

Increased concentrations of estrogen were thought to be associated with glaucoma. Some investigators reasoned that if estrogen is the cause of increased IOP, the use of its antagonist progesterone might lower it. To test this hypothesis Posthumus injected progesterone intraperitoneally and noted a reduction in intraocular pressure in glaucoma patients. Progesterone pharmacological properties might be steroid related, with steroid blockade as a possible explanation. Paterson and Miller found that during pregnancy the out flow facility rose steeply for about twenty weeks. It then underwent a sudden reduction following by a slow recovery with another sharp decrease at term. Since progesterone levels gradually rise through out, they believed that the fall in IOP was not attributable to progesterone alone. The same investigator administered relaxin 20 mg intra muscularly to a small group of glaucoma patients. Both male and female patients responded with decreased intraocular pressure and increased out flow facility.

According to Philips and Gore[3] physiological softening of ligaments in late pregnancy might extend to that of the corneoscleral envelope to produce reduced corneoscleral rigidity and therefore cause fall in IOP. Improved corneoscleral out flow, which result from the hormonal changes of late pregnancy, is a more likely explanation for the decrease of intraocular pressure.

According to Camras CB in 1987[4] topical prostaglandin are very effective at reducing intra ocular pressure in a variety of animals and in humans, with relatively few side effects. PGF2 increase aqueous outflow facility (uveoscleral) accounting for most of the intraocular pressure reduction.

Prostaglandins are synthesized by human trabecular endothelial cells in culture and therefore could conceivably play a role in the normal physiological regulation of aqueous humor outflow. However the marked intraocular pressure lowering effects of exogenously administered PGF2 in monkeys is not the result of altered trabecular outflow facility (which changes only slightly) but rather of increased uveoscleral drainage. The latter apparently results from widening and dissolution of collagen types I and III within the connective tissue filled spaces between the longitudinally oriented bundles of the ciliary muscle.

Given extra ordinarily small topical of PGF2 required to produce this effect (less than 1 microgram) it seems possible that PG produced by the trabecular endothelium could be carried with the aqueous humor through the uveoscleral routs, where it exerts its action. Thus the meshwork itself might regulate uveoscleral outflow with PG acting as the regulatory autocoid.

According to D. Paterson and J.H miller[5] described as the 3rd ovarian hormone relaxin and was discovered by Hisaw (1926). It is a polypeptide of low molecular weight and is present in blood serum as conjugates which vary with species. (eg) Human relaxin softens the symphysis pubis of the guinea pig, but not that of the mouse. It has an action on connective tissue which is

presumably effective throughout the body including the eye. Using sponge biopsy technique dilatation of the blood vessels in the connective tissue followed by edema and splitting of the collagen fibers. Relaxin exerts its action only in the presence of estrogen and thus subjects have to be estrogen primed before the administration of relaxin. It is to be noted that, in pregnancy relaxin is already primed by estrogen. A more likely state of affair would seem to be that a balance is maintained by the three hormones working together estrogen and progesterone providing a background against which relaxin can take effect.

Results indicate that relaxin may increase the facility of outflow in the presence of estrogen.

According to Horven and Halvard Gjennaess[6] in the controls the IOP averaged 14.0 mm Hg, by both Schiotz and applanation tonometry was performed in only 20 of the 27 control patients. In pregnancy and during the 1st two months after delivery a statistically significant decrease in the IOP was found with both methods.

Wilke[7] noted lower episcleral venous pressure in pregnant women. It has been reported that the reduction of episcleral venous pressure was consistent with the generalized reduction of peripheral vascular resistance during. All these data support the concept that increased outflow facility and reduced episcleral venous pressure are in large part responsible for the ocular hypotensive effect of pregnancy.

The most impressive results disclosed in the study is significantly higher mean intraocular pressure in third trimester hypertensive pregnant women (16.90 mmHg). The difference between them is found to be 5.74 mmHg. The physiological basis for the IOP relationship may be an increased production of aqueous humor induced by increased Blood Pressure.

According to C.J.Bulpitt Charles hodes and M.G.Everitt B.J Opthal (1975)[8]. An increase systemic pressure will however increase the amount of aqueous fluid filtered through the ciliary body although probably affecting the amount produced by filtration and not active secretion (Macri 1967).

Most reports are in agreement with the present study that the IOP decrease in pregnancy. The reduction in IOP could be explained by a reduction of the episcleral venous pressure and increased outflow facility.

It has been reported that systemic blood pressure is positively related to intraocular pressure. Thus chronic simple glaucoma patients and ocular hypertensive subjects have relatively high blood pressure as compared with normal subjects. Decreased intra ocular pressure has been reported during pregnancy especially during third trimester and after delivery. The clinical

impression has been recorded that relatively few cases of glaucoma occur and that preexisting glaucoma improves during pregnancy.

Cornea is devoid of blood vessels. It gets its nutrition and oxygen from the aqueous humor and atmosphere. Aqueous humor is reduced during pregnancy due to increased outflow. So the intraocular pressure is reduced. Due to reduction of aqueous humor the oxygen supply to the cornea is reduced. Therefore the cornea is subjected to hypoxia.

The earliest anatomic consequence of hypoxia is edema characterized by increased corneal thickening. About 2% thickening can be recognized by pachometry, around 4 to 6 % by appearance of posterior striae and 8 to 10 % by routine biomicroscopy. Vertical striae develop after 3 to 4 hours after reduced oxygenation and may be seen by slit lamp near the posterior third of the stroma.

In our study incidence of the intraocular pressure is least in group 3 that is third trimester of pregnancy. Corneal edema in group 3 is high when compare to group 1 & 2. There is a good correlation between intraocular pressure and corneal edema.

Visual acuity don by Snellens chart does not show any variation during pregnancy whether in normal or in pregnancy induced hypertension. However there seems to be a change in the distance of comfortable reading before and 2 weeks after delivery in some of the cases through to a very small extent.

Corneal edema with a normal lens and retina should affect the visual acuity. In our study edema has been very minimal and that is why there is no effect on visual acuity. One of our eclamptic patient showed fundus changes in whom the visual acuity was not done.

5. Conclusion

Certain visual parameters like intraocular pressure, corneal edema, visual acuity and fundus examination was done from first to third trimester of pregnancy and in pregnancy induced hypertension subjects, belonging to 3rd trimester of pregnancy. Our results showed that there is definite tendency for intraocular pressure to drop with the progress of pregnancy, with the least value during the 3rd trimester of pregnancy.

Even though there is a slight increase intraocular pressure in pregnancy induced hypertension cases the value was found to be within normal limits. Minimal corneal edema was found to be in 16 out of 250 subjects. But these 16 subjects are from group 2 & 3 i.e. in 100m subjects (16%). There was no change in visual acuity and the fundus of the eye was also normal except in one case of eclampsia.

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References

1. Evertt. R.B. Worley RJ Macdonald PC, Gant NF. Modification of vascular responsiveness to angiotensin II in pregnant women by Intravenously infused 5αdihydropregesterone. Am. J. Obst and Gynaecol, 1978; 131:352.
2. Broughton pipken F Meirells R.S. Prostaglandin E2 attenuates the pressor response to angiotension II in pregnanat subjects, but in non pregnant subjects. Am. J. Obst and Gynaecol. 1982;142:168
3. Philips C1 Gore SM ocular hypotensive effect of late pregnancy with and without high blood pressure. Br.J. Ophthalmol 1985; 525-60.
4. Camras CB . Multiple dosing of prostaglandin F2 α or epinephrine on cynomolgus monkey eyes. Aqueous humor dynamics. Invest ophthalmal Vis Sci. 1987:28;463.
5. Paterson G. Miller SJH hormonal influence in simple glaucoma. A preliminary report. Br.J. ophthalmol . 1963:47;129-37.
6. Horven I gzonnaess H Kreeze A blood circulation changes in the eye and limits with relation to pregnancy and female sex hormones. Acta Opthalmol. 1976: 54:503-7
7. Wilke K episcleral venous pressure and Pregnancy Acta Ophthalmal. 1975:125; 40-5
8. Bulpitt C J Hoder C Everitt MG. Intraocular pressure and systolic blood pressure SBP in the elderly. Br. J ophtholmol. 1975:59;717-20
9. Differential expression of Helios, Neuropilin-1 and FoxP3 in head and neck squamous cell carcinoma (HNSCC) patients A.A.Mohamed Adil, Anil Kumar Bommanabonia, Anandraj Vaithy, Sateesh Kumar 3biotech 9 (178)
10. Protagonist of Immuno-Profiling, Immuno-Scoring, and Immunotherapy Towards Colitis-Associated Cancer: Systematic Review, Mohamed Adil a.a, AK Pandurangan, M Waseem, N Ahmed Diagnostic and Treatment Methods for Ulcerative Colitis and Colitis 2020
11. Emerging Role of Mitophagy in Inflammatory Diseases: Cellular and Molecular Episodes, Mohamed Adil AA, S Ameenudeen, A Kumar, S Hemalatha, N Ahmed, N Ali 2020 Curr Pharm Des. 2020;26(4):485-491. doi: 10.2174/1381612826666200107144810
12. Increased Expression of TGF-β and IFN-γ in Peripheral Blood Mononuclear Cells (PBMCs) Cultured in Conditioned Medium (CM) of K562 Cell Culture AAM Adil, L Vallinayagam, K Chitra, S Jamal, AK Pandurangan, N Ahmed Journal of Environmental Pathology, Toxicology and Oncology 38 (2)
13. Cancer immunotherapy: Targeting immunosuppressive tumor microenvironment NA A.A Mohamed Adil Oncobiology and Targets 2014