

A Comparative Study to Evaluate the Role of Alpha Tocopherol in Pregnancy induced Hypertension

1. Shamama Bashir 2. Sikandar Adil Mughal 3. Khalida Parveen 4. Muhammad Azhar Mughal

1. Asstt. Prof. of Pharmacology & Therapeutics, SMC, DUHS, Karachi 2. Asstt. Prof. of Physiology, PUMHS, Nawabshah 3. Prof. of Anatomy, DMC, DUHS, Karachi 4. Prof. of Pharmacology & Therapeutics, SMC, DUHS, Karachi

ABSTRACT

Objective: To assess the role of alpha tocopherol in Pregnancy Induced Hypertension (PIH) by comparing pregnancy induced hypertensive patients on routine anti-hypertensive measures with pregnancy induced hypertensive patients on alpha tocopherol plus routine antihypertensive measures.

Study Design: Retrospective Randomizing Study.

Place and Duration of Study: This study was conducted at the Department of Pharmacology and Therapeutics, Basic Medical Sciences Institute, Jinnah Postgraduate Medical Centre, Karachi from April 2004 to Sept. 2004.

Materials and Methods: Two groups each comprising of 25 pregnancy induced hypertensive females, age ranging from 18-40 years were studied in this study. Changes in systolic and diastolic blood pressure were assessed from 24-28 weeks of pregnancy and were followed at every 15 days till the time of delivery in Control Group-I (G-I) and Test Group-II (G-II).

Results: On day-0 systolic blood pressure on average showed higher value in G-II compared to G-I. On day 30, 60 and day final, the mean systolic blood pressure showed lower values in G-II although the difference was found statistically insignificant. When diastolic blood pressure studied, it showed on the average same readings for G-I and G-II on day-0. On day 30, day 60 and day final, it also showed statistically insignificant difference between G-I and G-II with higher mean diastolic blood pressure in G-I.

Conclusion Alpha tocopherol exerted better effect on systolic and diastolic blood pressure in test group when compared with control group.

Key Words: Pregnancy Induced Hypertension, Alpha Tocopherol.

INTRODUCTION

Pre-eclampsia (PE) remains to be one of the primary causes of maternal and fetal morbidity and mortality all over the world¹. Pre-eclampsia (PE) and gestational hypertension are the two important conditions mentioned under hypertensive disorders of pregnancy². Gestational hypertension or PIH is the hypertension developing in a female for the first time after 20 weeks of pregnancy³. It is defined as systolic blood pressure greater than or equal to 140 mm Hg or diastolic blood pressure greater than or equal to 90 mm Hg. PE is the gestational hypertension plus proteinuria whereas eclampsia is the occurrence of seizures in the presence of PE⁴. Pathophysiologically PE is characterized by systemic vascular endothelial dysfunction⁵. For the prevention of PIH (gestational hypertension) antioxidants supplementation is helpful. Antioxidants prevent placental peroxide formation and thus endothelial cell damage is prevented⁶. Supplementation of antioxidants in early pregnancy may decrease oxidative stress, improve vascular endothelial function and ameliorate the course of PE⁷. Antioxidants like vitamin C and E seem to reduce the risk of PE⁴.

Therefore, we have designed this study to compare the results of systolic and diastolic blood pressure in Control (G-I) and Test (G-II) groups of pregnancy induced hypertensive patients. Control group was kept on routine antihypertensive measures i.e. lifestyle modifications and antihypertensive drugs as advised by the concerned Obstetrician and Test group was given oral alpha tocopherol in addition to routine antihypertensive measures.

MATERIALS AND METHODS

This study was conducted at the Department of Pharmacology and Therapeutics, Basic Medical Sciences Institute, Jinnah Postgraduate Medical Centre, Karachi in collaboration with Department of Gynecology and Obstetrics Unit II, Ward 9, JPMC Karachi during the year 2004. This comparative study was designed to evaluate the role of alpha tocopherol in pregnancy induced hypertension.

Study groups; Group-I (control group) comprised of 25 pregnancy induced hypertensive females ages ranging from 18 to 40 years. They were enrolled during 24-28 weeks of pregnancy at Day-0. They were kept on routine antihypertensive measures and were

evaluated at every 15 days till the end of pregnancy (day of final reading) for changes in systolic blood pressure and diastolic blood pressure.

Group-2 (Test group) comprised of 25 pregnancy induced hypertensive females age 18 to 40 years. They were enrolled during 24-28 weeks of pregnancy at day-0. They were kept on routine antihypertensive measures plus capsule alpha tocopherol 400 I.U per day and were evaluated at every 15 days till the end of pregnancy (Day of final reading) for changes in systolic blood pressure and diastolic blood pressure.

Written consent was taken from all the participants before they were enrolled in study. Exclusion criteria

for both groups were diabetes mellitus, any evidence of liver disease, renal disease or twin pregnancy and patients who were using aspirin therapy.

Blood pressure was measured by standard mercury sphygmomanometer. The results were evaluated by paired *t* test, student *t* test and percentage.

OBSERVATIONS AND RESULTS

The observations of both groups-I and II were evaluated on day 0 i.e. at 24-28 weeks of gestation, day 30 i.e. 28-32 weeks, day 60 i.e. 32-36 weeks and at day of final reading (DF) which was ≥ 36 weeks of gestation.

Table No.1: Comparison of mean Systolic Blood Pressure (mmHg) in patients with Pregnancy Induced Hypertension (PIH) (group-I) with Pregnancy Induced Hypertension (PIH) taking Alpha Tocopherol Group-II of different gestational age ranges from 24-36 weeks, recorded from day- 0 to day-final.

Mean Systolic Blood Pressure (mmHg) in different Gestational age ranges from 24-36 weeks					P Value				% age Change
Groups	At Day-0 24-28 Week	At Day-30 28-32 Weeks	At Day-60 32-36 Weeks	At D. F ≥ 36 Weeks	D0-D30	D30-D60	D60-DF	D0-DF	D0-DF
G -I (n=25)	132.4 \pm 1.05	127.6 \pm 1.76	127.6 \pm 2.26	130.8 \pm 2.51	<0.001	N.S	N.S	N.S	↓ 1.20%
G - 2 (n=25)	134 \pm 1	125.2 \pm 1.43	127.2 \pm 1.98	129.2 \pm 2.23	<0.001	N.S	N.S	<0.01	↓ 3.50%

Key: G-I = Control Group DF = Day of final reading N.S = Non Significant
G-2 = Test Group Figures in Parentheses indicate number of patients

Table No.2: Comparison of Mean Diastolic Blood Pressure (mmHg) in Patients with Pregnancy Induced Hypertension (PIH) (Group-I) with Pregnancy Induced Hypertension (PIH) taking Alpha Tocopherol (Group-II) of different Gestational age ranges from 24-36 weeks, recorded from day 0 To day final.

Mean Diastolic Blood Pressure (mmHg) in different gestational age ranges from 24-36 weeks					P Value				%age Change
Groups	At Day-0 24-28 Weeks	At Day-30 28-32 Weeks	At Day-60 32-36 Weeks	At D.F. ≥ 36 Weeks	D0-D30	D30-D60	D60-DF	D0-DF	D0-DF
G -I (n=25)	91.6 \pm 0.75	86.4 \pm 1.28	87.6 \pm 1.85	88 \pm 1.63	<0.001	N.S	N.S	<0.01	↓ 3.9%
G -2 (n=25)	91.6 \pm 0.75	84.4 \pm 1.17	85 \pm 1.41	87.6 \pm 1.85	<0.001	N.S	N.S	<0.01	↓ 4.3%

Key: G-I = Control Group D.F = Day of final reading N.S=Non Significant
G-II = Test Group Figures in parentheses indicate number of patients

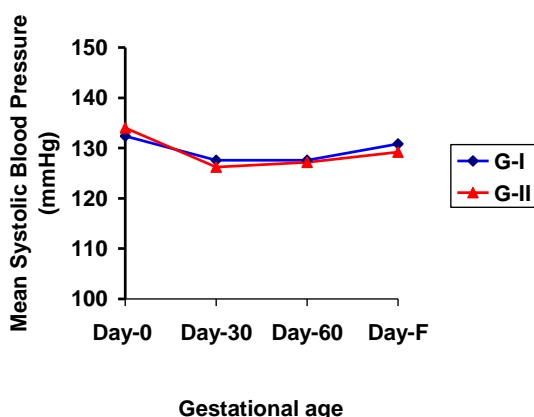
Systolic Blood Pressure

Control group-I: All the 25 enrolled pregnancy induced hypertensive patients were studied till the day of final reading. Mean systolic blood pressure as shown in **Table-1** and **Figure-1** was decreased from 132.4 \pm 1.05 mm Hg on day-0 to 127.6 \pm 1.76 mm Hg on day-30, the decrease was found statistically highly significant, it remained same on day-60 and increased to 130.8 \pm 2.51 mm Hg on the day of final reading. The reduction in systolic blood pressure was statistically highly significant from day 0 to day 30. Whereas,

insignificant results were obtained when this reduction was compared from day 30-60 and rise in systolic B.P compared from day 60 to day of final reading. The decrease in systolic blood pressure from Day-0 to Day of final reading was statistically insignificant. The change in systolic blood pressure was found to be 1.2% reduction from day-0 to day of final reading.

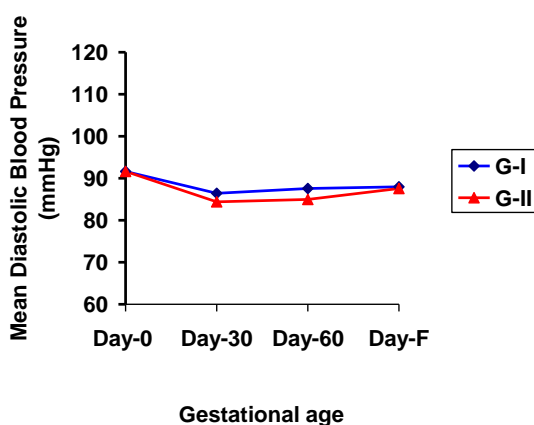
Test group -II: In this group 25 enrolled pregnancy induced hypertensive patients were studied from day-0 to day of final reading. The mean systolic blood pressure as shown in **Table-I** and **Figure-I** was

decreased from 134 ± 1.0 mm Hg to 125.2 ± 1.43 mm Hg from day 0 to day-30 that showed highly significant decrease ($p < 0.001$). Then systolic blood pressure was increased to 127.2 ± 1.98 mm Hg on day-60 and again it increased to 129.2 ± 2.23 mm Hg on day final, both of these changes were found statistically insignificant. Whereas, the decrease in blood pressure from day-0 to day final reading was statistically significant ($p < 0.01$) and it was reduced by 3.5 %.



Key: G-I=Control Group, G-II=Test Group
Day-F=Day-Final reading

Figure No.1: Changes in Mean Systolic Blood Pressure(mmHg) in different gestational age ranges from 24-36 weeks recorded from Day-0 to Day Final of patients Group-I (G-I) & Group-II(G-II)



Key: G-I=Control Group, G-II=Test Group
Day-F=Day-Final reading

Figure No.2: Changes in Mean Diastolic Blood Pressure(mmHg) in different gestational age ranges from 24-36 weeks recorded from Day-0 to Day final of patients Group-I (G-I) & Group-II (G-II)

Diastolic Blood Pressure

Control group-I: The mean diastolic blood pressure as shown in **Table-2** and **Figure-II** was decreased from 91.6 ± 0.75 mm Hg on day-0 to 86.4 ± 1.28 mm Hg on day-30 with highly significant reduction ($p < 0.001$).

Whereas, an increase was observed 87.6 ± 1.85 mm Hg on day-60 which was further increased to 88 ± 1.63 mmHg on day of final reading but both results were found to be statistically non-significant. The decrease in diastolic blood pressure from day-0 to day of final reading was found statistically significant (3.9%).

Test group-II: The mean diastolic blood pressure as shown in **Table-2** and **Figure-II** on day-0 was 91.6 ± 0.75 mm Hg and it significantly decreased to 84.4 ± 1.17 mm Hg on day-30 ($p < 0.001$). It was also increased to 85 ± 1.41 mm Hg on day-60 and it again increased to 87.6 ± 1.85 mm Hg on day of final reading; however, both changes were found statistically non-significant. The decrease in mean diastolic blood pressure from day-0 to day of final reading was noted statistically significant ($p < 0.01$) with a decrease of 4.3%.

Comparison of Change in Blood Pressure Systolic Blood Pressure

G-I vs. G-II: On day-0, the difference in systolic blood pressure on the average showed slightly higher value in G-II, however, when tested statistically the difference was found non-significant between G-I and G-II. On day-30, 60 and day final the mean systolic blood pressure on the average showed lower values in G-II, and the difference was found insignificant statistically. The change in mean systolic blood pressure from day-0 to day final in G-I was found less decreasing i.e. (-1.2%) as compared to G-II (-3.5%).

Diastolic blood pressure

G-I vs. G-II: On day-0, diastolic blood pressure on the average has shown same readings for G-I and G-II. On day-30, day-60 and day final the results showed statistically non-significant differences between G-I and G-II with higher mean diastolic blood pressure in G-I. The change in mean diastolic blood pressure from day-0 to day final reading in G-I was less decreasing (-3.9%) as compared to G-II (4.3%).

DISCUSSION

A large number of studies have shown that gestational hypertension or pregnancy induced hypertension (PIH) and pre-eclampsia can result in substantial infant and maternal mortality worldwide. Regarding PE, vascular endothelial damage is the basic pathophysiological mechanism. Free radical mediated lipid peroxidation may be involved in this endothelial damage⁸. Free radicals i.e., Reactive Oxygen Species (ROS) may produce a state of oxidative stress. Oxidative stress develops when reactive oxygen species level exceeds the scavenger capacity by antioxidants. Anti-oxidants like vitamin E and C can disperse, remove or decrease the formation of (ROS)⁹.

In view of the importance of PIH and PE that can lead to eclampsia in developing countries like

Pakistan. we have conducted a comparative study to evaluate the role of alpha tocopherol in pregnancy induced hypertension. In our study Group-2 patients were compared with Group-1 patients for changes in systolic and diastolic blood pressure. The fall in systolic and diastolic blood pressure in our study at the end of pregnancy i.e. on the day of final reading was more in G-II as compared to G-I but the difference was found statistically insignificant.

The study of Shennan *et al*¹⁰ and Chappell *et al*⁷ targeted preeclampsia by keeping their patients on the prophylactic treatment, they had supplemented with vitamin C 1000 mg and vitamin E 400 I.U in women who were at higher risk of PE from second trimester of pregnancy. They have evaluated that there was at least 50% reduction in the development of PE by this supplementation. Their findings are in correlation with the results of our study in which we have also found comparatively better effects in treated group.

According to study results of Duley *et al* 1996, the risk of preeclampsia can be reduced by using antioxidant therapy. Whereas, the study of Chappel *et al* in 1999 has compared early supplementation of vitamins E and vitamin C with placebo in women with increased risk of PE from 16-22 weeks of pregnancy and continued throughout pregnancy, his results match with our results, there was a significant reduction in systolic or diastolic blood pressure in the proportion of women with PE who had received vitamin therapy.

CONCLUSION

The results of this study show that a better control on systolic and diastolic blood pressure in pregnancy induced hypertensive patients that was observed when alpha tocopherol was administered orally along with anti-hypertensive measures. Future studies need to be carried out on various parameters and on larger scale to confirm the role of alpha tocopherol as antioxidant in controlling pregnancy induced hypertension and pre-eclampsia.

REFERENCES

- 1) Perez-Cuevas R, Fraser W, Reyes H, Reinharz D, Daftari A, Heinz CS, Roberts JM. Critical pathways for the management of preeclampsia and severe preeclampsia in institutionalised health care settings. BMC Pregnancy and Childbirth 2003;3: 61-65
- 2) Oken E, Ning Y, Rifas-Shiman SL, Rich-Edwards JW, Olsen SF, Gillman MW. Diet during pregnancy and risk of pre-eclampsia or gestational hypertension. Ann Epidemiol 2007;17(9): 663-668.
- 3) James PR, Nelson-Piercy C. Management of hypertension before, during, and after pregnancy. Heart 2004; 90: 1499-1504.
- 4) Duley L, Meher S, Abalos E. Management of pre-eclampsia. BMJ 2006; 332: 463-468.
- 5) Mutter WP, Karumanchi SA. Molecular mechanisms of preeclampsia. Microvasc Res 2008; 75(1): 1-8.
- 6) Bhosale L, Padia D, Malhotra H, Thakkar D, Palep HS, Algotar KM. Capsule "SUJAT" for comprehensive antenatal care and prevention of pregnancy induced hypertension. Online Original Research Article. http://bhj.org/journal/2000_4201_jan00/original_136.htm
- 7) Chappell LC, Seed PT, Briley AL, Kelly FJ, Lee R, Hunt BJ, et al. Effect of antioxidants on the occurrence of pre-eclampsia in women at increased risk: a randomized trial. Lancet 1999; 354: 810-816.
- 8) Mikhail MS, Anyaegbunam A, Garfinkel D, Palan PR, Basu J, Romney SL. Preeclampsia and antioxidant nutrients: Decreased plasma levels of reduced ascorbic acid, α -tocopherol, and beta-carotene in women with preeclampsia. Am J Obstet Gynecol 1994; 171: 150-157.
- 9) Ruder EH, Hartman TJ, Goldman MB. Impact of oxidative stress on female fertility. Curr Opin Obstet Gynecol 2009; 21(3): 219-222.
- 10) Shennan AH, Chappell L. Pre-eclampsia. Contemp Clin Gynecol & Obstet 2001; 1(4): 353-364

Address for Corresponding Author:

Dr. Shamama Bashir,

Assistant Professor,
Department of Pharmacology & Therapeutics,
Sindh Medical College,
Dow University of Health Sciences, Karachi.
E-mail: dr.shamama@hotmail.com