

ROLE OF ALPHA TOCOPHEROL AS AN ADJUVANT THERAPY IN PREGNANCY INDUCED HYPERTENSION

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ABSTRACT

Hypertension is the most common medical problem encountered in pregnancy and remains an important cause of maternal and fetal morbidity and mortality. To conduct a clinical study to evaluate the adjuvant effect of alpha-tocopherol along with routine hypertensive measures in patients with pregnancy induced hypertension. A total of 25 pregnancy induced hypertensive patients with single fetus were prospectively followed up from 24 to 28 weeks of pregnancy till the end of pregnancy. The patients were given capsule alpha-tocopherol 400mg/day as adjuvant therapy. The base line readings and then at 4 weekly intervals of maternal blood pressure and platelets count and evaluated statistically till the end of pregnancy. The mean systolic blood pressure and diastolic blood pressure decreased by 3.5% and 4.36% respectively with significant p value <0.01. The platelet count increased by 5.98% though statistically non significant. Maternal blood pressure decreased and platelet count increased by oral supplementation of alpha tocopherol. Therefore the effect of alpha-tocopherol on these parameters should be considered in future for longer duration and larger scale studies.

Keywords: Pregnancy, hypertension, alpha-tocopherol.

INTRODUCTION

Hypertension is the most common medical problem encountered in pregnancy and still an important cause of maternal and fetal morbidity and mortality. It complicates up to 15% of pregnancies (James and Piercy, 2004). The National High Blood Pressure Education Programme of NHLBI classifies it as Gestational hypertension, Pre-eclampsia and superimposed eclampsia (Hawfield and Freedom 2009) and accounts for approximately a quarter of all antenatal admissions.

Hypertension occurring in the second half of pregnancy in a previously normotensive woman, without proteinuria or other features of pre-eclampsia is termed as gestational

hypertension or pregnancy induced hypertension (James and Piercy, 2004).

Gestational hypertension (PIH) is the hypertension detected for the first time after 20 weeks of gestation in the absence of proteinuria and measured systolic blood pressure greater or equal to 140 mmHg or diastolic blood pressure greater than or equal to 90 mmHg (Hawfield and Freedom 2009).

Pre-eclampsia is associated with several complications and timely management is needed for clinical care of these patients to avert fetal and maternal morbidity and mortality (Duley *et al.*, 2006).

Antihypertensive drugs are used for mild to moderate hypertension during pregnancy to

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prevent or delay progression to pre-eclampsia. Methyldopa is commonly recommended and alternative choice includes Labetolol and calcium channel blockers. Antioxidants primarily vitamin C and E also seem to reduce the risk of pre-eclampsia (Hawfield and Freedom 2009). The reason might be oxidative stress a key factor in the disease process, the over production of reactive oxygen species (ROS) and synthesis of lipid peroxides leads to maternal endothelial cell activation a hallmark of the disease (Chappell *et al.*, 2002). Antioxidants including vitamins C and E and antioxidant cofactors such as selenium, zinc and copper are capable of disposing, scavenging or suppressing the formation of ROS (Mehanty *et al.*, 2006).

Alpha tocopherol (vitamin E) is one of the most important anti oxidant molecule residing mainly at cell membrane and scavenging a wide variety of free radicals (Ruder *et al.*, 2009). Supplemental vitamin E administration in pregnancy appears safe and well tolerated (Shenan *et al.*, 2001).

MATERIALS AND METHODS

This study was conducted in department of Pharmacology and Therapeutics Basic Medical Sciences Institute Jinnah Post-graduate Medical Centre Karachi in collaboration with Department of Gynecology and Obstetrics Unit 2 (ward- 9) JPMC Karachi.

Study was designed to evaluate the adjuvant effect of alpha-tocopherol in pregnancy induced hypertension.

A total of 25 hypertensive pregnant females in second half of pregnancy who were previously normotensive and aged 18 to 40 years were studied till the end of pregnancy.

Written consent was taken from all patients.

Exclusion criteria:

Diabetes mellitus, Liver disease, renal disease, Twin pregnancy and patients using aspirin were excluded from the study.

The selected patients were keeping on routine antihypertensive measures along with Vit-E 400mg Capsule Evion (alpha tocopherol) of Merck Marker private Ltd) per day.

The patients were evaluated for blood pressure measured by mercury sphygmomanometer and platelet counts was done at auto analyzer Sysmex K -1000 every fortnightly till the end of pregnancy.

Results were evaluated statistically applying the paired t test.

OBSERVATIONS AND RESULTS

The table-1 and figure 1 show the mean systolic blood pressure of on Day (0) zero was 134 ± 1.00 mmHg and decreased to 125.2 ± 1.43 mm Hg on Day 30 of highly significant p value <0.001 . The mean systolic blood pressure on Day 60 increased to 127.2 ± 1.96 mmHg and on Day of final reading increased to 129.2 ± 2.23 mmHg, both changes statistically non significant. The decrease in systolic blood pressure from Day zero to Day final was statistically significant $p < 0.01$ and percentage decrease was 3.5%.

The mean diastolic blood pressure as shown in Table-1 and Figure 2 on Day zero was 91.6 ± 0.75 mm Hg and decreased to 84.4 ± 1.17 mm Hg on Day 30 with a highly significant $p < 0.001$. It increased to 85 ± 1.41 mm Hg on Day 60 and again increased to 87.6 ± 1.85 mm Hg on Day final with non significant p values. The decrease in mean diastolic blood pressure from Day zero to Day final was statistically significant $p < 0.01$ and the percentage decrease was 4.36%.

The mean platelet count of the patients shown in the table-1 and figure 3 was $236.68 \pm$

Table-1
 Mean Values of Different Variables in Patients on α -tocopherol as an Adjuvant Therapy in Pregnancy Induced Hypertension

Variables	Gestational Age				P Value				% Change
	Day-zero	Day 30	Day 60	Day-Final <or> 36weeks	D-zero - D-30	D-30 - D-60	D-60 - D-Final	D-zero - D-Final	D-zero - D-Final
Systolic BP	134 ±1	125.2 ±1.43	127.2 ±0.96	129.2 ± 2.23	<0.001** *	N.S*	N.S*	<0.01**	3.5% ↓
Diastolic BP	91.6 ± 0.75	84.4 ± 1.17	85 ± 1.41	87.6 ± 1.85	<0.001** *	N.S*	N.S*	<0.0**1	4.36% ↓
Platelet count	236.68 ±11.12	230 ± 12.28	223 ± 12.97	250.84 ± 16.91	N.S*	N.S*	<0.01* *	N.S*	5.98% ↑

*Non significant decrease (P<0.5), **Significant decrease (P<0.01), ***Highly significant decrease (P<0.001)

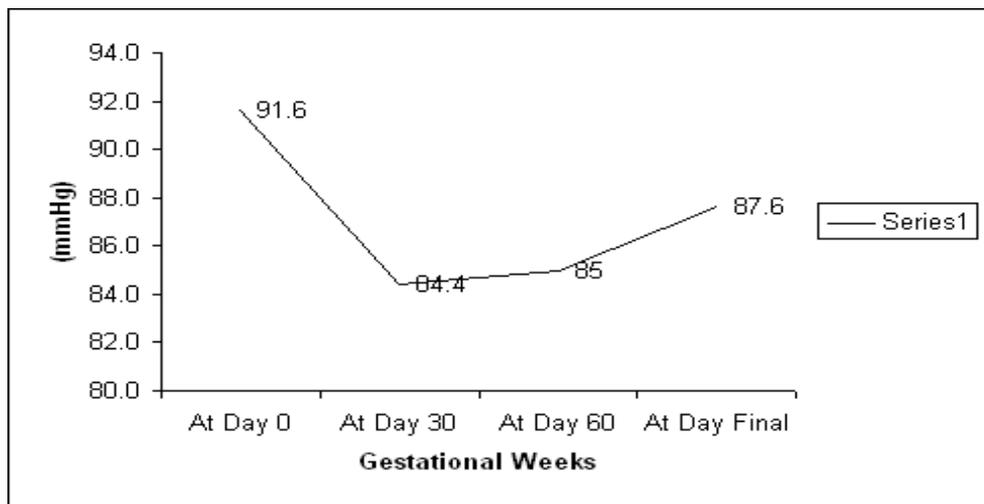


Fig. 1: In Patients with pregnancy induced hypertension changes in means systolic blood pressure (mmHg) at Day 0, Day 30, Day 60 and Day Final.

11.12x 10 / liter on Day zero and decreased to 230 ± 12.28 x 10/ liter on Day 30 and on Day 60 decreased to 223 ± 12.97 x 10/liter. Both changes were statistically non significant. Finally the count increased to 250.84 ± 16.9 x10/liter on Day of final reading i.e. Day final with significant p<0.01. The increase in platelet count of 5.98% from Day zero to Day final was statistically non significant.

DISCUSSION

Early supplementation with antioxidants may be affective in decreasing oxidative stress and improving vascular endothelial function thus preventing and ameliorating the course of pre-eclampsia.

Oxidative stress occurs when the generation of reactive oxygen species (ROS)

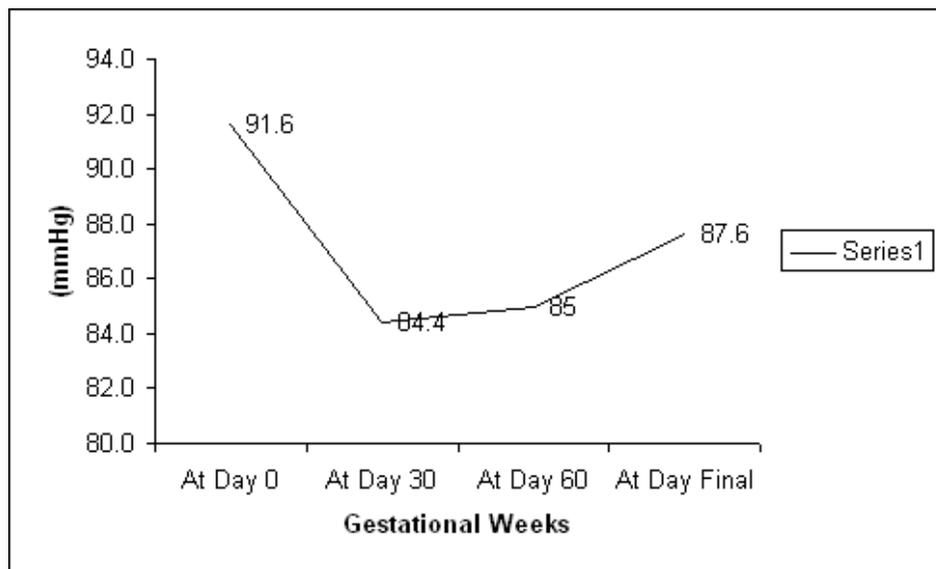


Fig. 2: In patients with pregnancy induced hypertension changes in means diastolic blood pressure (mmHg) at Day 0, Day 30, Day 60 and Day Final.

and other radical species exceeds the scavenging capacity by antioxidants due to excessive production of ROS and/or inadequate intake or increased utilization of antioxidants. Antioxidants (including vitamin C and E) and antioxidant cofactors (selenium, zinc and copper) are capable of disposing and scavenging or suppressing the formation of ROS (Mehanty *et al.*, 2006).

Therefore supplementation throughout the second half of pregnancy with vitamin C and E in pregnant women at high risk for pre-eclampsia had significant beneficial effects on the biochemical markers of the disease and there was a significant reduction in the proportion of women with pre-eclampsia (Utolia *et al.*, 1993).

In our study pregnancy induced hypertensive patients when alpha tocopherol (vitamin E) was administered along with routine antihypertensive measures from 24 to 28 weeks till the end of pregnancy. There was a decrease in systolic and diastolic blood pressure from Day zero to Day final with a significant p value.

Our study matches with the study of Chappell *et al* (1999) who administered Vitamin C 1000 mg/day and vitamin-E 400 IU/day or placebo at 16 to 22 weeks of gestation in patients who were identified as being increased risk of pre-eclampsia by abnormal uterine artery Doppler analysis. The study revealed the number of women who developed pre-eclampsia was significantly lower in vitamin group than in placebo group. This shows the antioxidant effect of both vitamins against the reactive oxygen species.

Our study also matches with the study of Tackacs *et al* (2003) who studied the role of vitamin E in inhibiting the production of interleukin-6. They demonstrated significantly high systolic and diastolic blood pressure in pre-eclamptic patients than in normal pregnant females and also demonstrated that vitamin-E significantly reduced the production of interleukin-6 by endothelial cells that were cultured with pre-eclamptic plasma and observed no effect on interleukin-6 production by endothelial cells that were cultured with normal plasma. They used 50 micro grams/liter vitamin-E which is comparable to

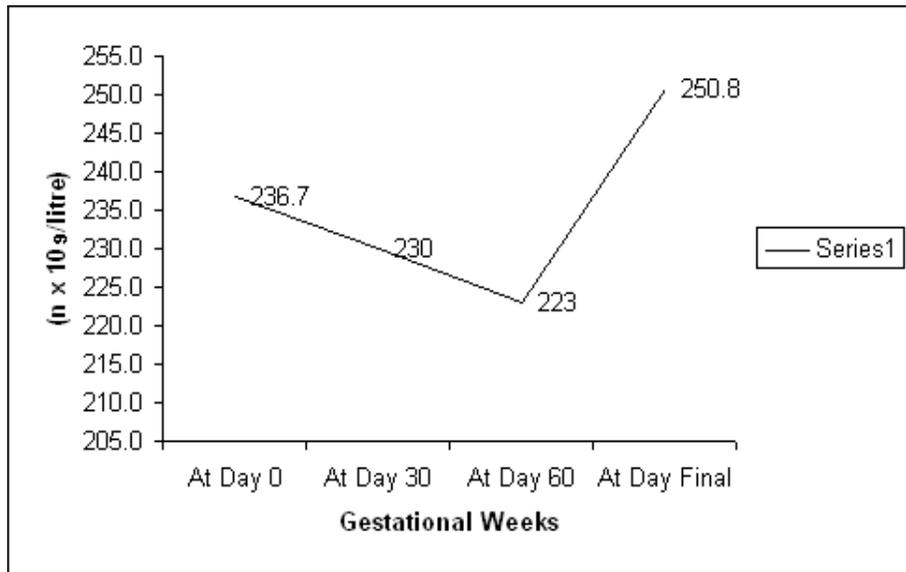


Fig. 3: In patients with pregnancy induced hypertension changes in means platelet count (n x 10⁹/litre) at Day 0, Day 30, Day 60 and Day Final

serum levels from taking 400IU/day vitamin-E orally the dose that was used in our study. They showed beneficial effect of antioxidant therapy in prevention of pre-eclampsia.

Our study does not match with the study of Oken *et al* (2007) who did not observe a lower risk of gestational hypertension or pre-eclampsia with a greater intake of vitamin C, D or E, the difference might be due to the fact that they have examined association of first trimester intake of vitamin C, D and E with pre-eclampsia and gestational hypertension. Whereas we have studied the adjuvant role of vitamin E with antihypertensive measures in pregnancy induced hypertensive patients.

In our study there was an inverse relationship of platelet count with systolic blood pressure at the end of gestation and this observation accords with the statement of Bolo *et al* (2002) who stated that there was an inverse correlation between platelet count and systolic blood pressure suggesting that in severe pre-eclampsia thrombocytopenia is likely.

CONCLUSION

In our study maternal blood pressure decreased and platelet count increased by oral supplementation of oral alpha tocopherol with routine anti hypertensive measures thus the effect of oral alpha tocopherol on these parameters should be considered in design of future studies.

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