INTERNATIONAL JOURNAL OF PHARMACOLOGY AND THERAPEUTICS
ISSN 2249 – 6467

Research Article

Role of Antioxidant Supplementation in preventing Pre-eclampsia

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ABSTRACT

Hypertensive disorders complicating pregnancy are common and WHO estimates the incidence of preeclampsia to be seven times higher in developing countries (2.8% of live births). The prevention of a disease of such a magnitude would have great implications regarding both maternal and perinatal outcome. It has been hypothesized that the pathogenesis of pre-eclampsia is related to an imbalance of increased oxidative stress and lipid peroxidation coupled to a deficiency of antioxidant protection. We conducted a study on 50 antenatal women with roll over test positive, 25 patients formed the study group and 25 patients formed the control group. 22 patients received antioxidant supplentation against 25 patients who did not receive antioxidants. A significant diference was found between cases and control group. Antioxidant supplementation in high risk for pre-eclampsia should be made mandatory.

Keywords: Antioxidants, Pre-eclampsia, Oxidative stress, Lipid peroxidation

INTRODUCTION

Hypertensive disorders complicating pregnancy are common and form one of the deadly triad along with hemorrhage and infection , that results in a large number of maternal deaths.

WHO estimates the incidence of preeclampsia to be seven times higher in developing countries (2.8% of live births) than in developed countries (0.4%). The prevalence of preeclampsia in developing countries ranges from 1.8% to 16.7%. (1)

The prevention of a disease of such a magnitude would have great implications regarding both maternal and perinatal outcome. Prevention of a disease can be achieved only if there is precise knowledge of aetiopathogenesis of the disease. A single pathophysiological mechanism for development of pre-eclampsia has not been identified and multiple pathways may exist which share a common pathway

Role of oxidative stress in the production of pre-eclampsia has been well documented in various studies (2,3, 4). It has been hypothesized that the pathogenesis of pre-eclampsia is related to an imbalance of increased oxidative stress and lipid peroxidation coupled to a deficiency of antioxidant protection.The oxidative stress in the maternal system may be pre-existing(e.g. obesity, diabetes, hyperlipidemia) or may be caused by placental secretion of lipid peroxides. Increased placental secretion of lipid peroxides and/or tumor necrosis factor (TNF-alpha) results in activation of

leucocytes as they circulate through the intervillous space. The activated leucocytes serve as circulating mediators that link the increased oxidative stress of placenta with endothelial dysfunction in the mother (4).

Oxidative stress is kept in check by an increase in maternal antioxidant capacity. Takehara et.al (5) found that the levels of lipoperoxide was 50% lower in placental tissues of 40 weeks gestation than in tissues of 5-11 weeks gestation. Various other studies have also suggested possible increased lipid peroxidation and decreased antioxidant capacity in the third trimester of pregnancy (6).

Decreased levels of antioxidants (alphatocopherol, ascorbate, betacarotene) have been noted in pre-eclampsia (7) . In a systematic review and meta-analysis in 2009 by Gupta S et al. to assess lipid peroxidation and antioxidant status in pre-eclampsia, it was concluded that preeclampsia is associated with increased concentrations of oxidative stress markers including lipid peroxidation products, and a reduction in antioxidant concentrations.(8)

Few studies have been conducted to improve the antioxidant capability of women at risk for pre-eclampsia. This was the rationale for undertaking the present study .

Roll over Test

Roll over test is one of the clinical methods to screen antenatal women at high risk to develop pregnancy induced hypertension. Gant, Chand et al. in 1974 showed that 93% nulliparous ,normotensive young women who developed pregnancy induced hypertension demonstrated an increase in diastolic blood pressure of at least 20 mmHg when turned from lateral recumbent to the supine position between 28-32 weeks of gestation . Over the years many workers have studied roll over test and found varying sensitivity. (9)

OBJECTIVE

To study the role of antioxidant supplementation in pregnant women at high risk for developing pre-eclampsia.

METHODOLOGY

A prospective randomized study was conducted at our instituition for a period of one year from May 2010 to April 2011. Roll over test was done for normotensive antenatal women attending antenatal clinic at 24-28 weeks.With the antenatal women in left lateral position and BP cuff attached to right arm, the blood pressure was recorded. The patient was told to roll over to supine position and blood pressure was recorded immediately and after 5 minutes.A rise of 20 mmHg in diastolic blood pressure was taken as positive. At no time during the test the cuff was removed.

Fifty antenatal women with roll over test positive were recruited. These roll over test positive women were randomly divided into two groups .

a) Study group included 25 primigravidas who received single daily dose of antioxidant supplementation along with iron and calcium tablets till delivery.

b) Control group included 25 primigravidas who did not receive any antioxidant supplementation. Only routine iron and calcium tablets were prescribed.

Written informed consent was taken from antenatal women in both the groups.

Both the groups were followed till delivery for development of pre-eclampsia.

Pre-eclampsia was defined as hypertension with blood pressure >= 140/90mmHg with proteinuria > 300mg / 24 hour, dipstick >=1+ ; and /or high BP in presence of severe features / end organ damage.

Blood pressure was measured from right brachial artery. Systolic blood pressure corresponded to Krotkoff 's Phase I and diastolic to Phase IV of auscultatory method.

Composition of antioxidant preparation was- Vitamin A 2500 IU, Vitamin E 10 IU, Vitamin C 50mg, Beta Carotene as 20% suspension 50 mg, Zinc sulfate 27.45 mg, monohydrate selenium dioxide 70 mcg.

Inclusion Criteria
Normotensive primigravidas with singleton pregnancy.

Exclusion Criteria
Multigravida, Antenatal women with chronic hypertension, twin pregnancy, Diabetes mellitus, hypothyroidism, renal disease .

RESULTS

Out of a total of 50 roll over test positive patients, 25 patients formed the study group and the other half i.e. 25 patients formed the control group. 3 patients were lost to follow up from the study group. Hence, 22 patients received antioxidant supplentation against 25 patients who did not receive antioxidants.There was no statistically significant difference in age among both the groups. Majority of patients belong to 20-25 years of age in study and control group.(Table 1)

There was a significant diference in the preventive effect of antioxidant supplementation in patients at high risk for developing pre-eclampsia. Only 36.4% of patients in the supplemented group developed pre-eclampsia whereas 80% of non-supplemented women developed pre-eclampsia .(Table 2)

Chi square test was applied to compare the disease outcome in supplemented group and non-supplemented group. The proportion of disease development in non-supplemented group (control group) compared to supplemented group (study group) was found to be significant with p value 0.002.

Table 1: Age distribution among study and control group

Age Group(years)	Study Group(n=22)	Control Group(n=25)
20-25	14	13
26-30	7	12
31-35	1	0

Table 2: Effect of anti oxidant supplementation in roll over test positive patients

Roll over test positive patients		
	Study Group(n=22)	Control Group(n=25)
Normotensive	14 (63.6%)	5 (20%)
Preeclampsia	8 (36.4%)	20 (80%)

DISCUSSION

Pressman et al. in a randomized double blind study , supplemented Vitamin E daily to 20 pregnant women and measured amniotic fluid Vitamin C levels. He demonstrated increase in the maternal plasma vitamin E levels in the supplemented women but not in the control subjects. No Changes in vitamin C levels in maternal plasma as well as in amniotic fluid was noted. Also maternal vitamin E levels correlated with chorioamnion concentration of vitamin E at the time of delivery.(10) This study clearly demonstrated that there is transfer of antioxidants from maternal plasma to feto-placental unit. Hence, fall in antioxidant concentrations can be corrected by supplementation to prevent the occurrence of disease.

Chappell et al. conducted a blind, randomized placebo controlled trial of antioxidant vitamins to prevent pre-eclampsia. He found a 60% reduction in the occurrence of pre-eclampsia(OR 0.39, 95% CI 0.17-0.90) from 17% in those who received antioxidants to 8% in women who received placebo. Even the patients who received Vitamin C and E demonstrated a reduction in measures of oxidative stress.(11,12)

Similar result was seen in our study as it was found that 63.6% of patients who received antioxidants remained normotensive throughout pregnancy compared to only 20% patients who did not receive antioxidants.

However, Beazley et al. in a blind placebo controlled study of 109 patients noted no difference between treatment and control groups in the rate of pre-eclampsia or for the total antioxidant status. These results are contradictory to the resultin the present study.(13)

Similar results were noted by Sharma et al. , in a prospective clinical trial which randomized 251 primigravida women to receive oral lycopene (2mg twice daily beginning at 16-20 weeks) or matched

placebo. Women randomized to lycopene were less likely to develop preeclampsia (8.6% vs 17.7%, P<0.05) than those who received placebo.(14)

A study in Beijing(15) randomized 52 women at high risk for developing preeclampsia to receive 1000mcgm per day of liquid selenium or placebo for 6-8 weeks during late gestation . There was a decreased incidence of pregnancy induced hypertension from 22.7% to 7.7% in the treatment group.

CONCLUSION

There is increasing evidence that oxidative stress is an important contributory factor to the pathogenesis of preeclampsia. So trial of antioxidant therapy to prevent the development of preeclampsia in high risk patients is warranted. Few studies have noted success in this regard. The beneficial effect of supplementing antioxidants in the present study though in small number of cases is a premature document on the role of antioxidant therapy in high risk cases for developing pregnancy induced hypertension. Larger multicentric randomized controlled trials are required to prove the preventive role of antioxidants before implementing use of these supplements as part of public health policy .

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Paper cited as :

Himsweta Srivastava , Richa Sharma .Role of Antioxidant Supplementation in preventing Pre-eclampsia .International Journal of Pharmacology and Therapeutics. Volume 2 Issue 2 2012 ,pp 33-38.