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Role of High Dose Calcium in the Prevention of Preeclampsia

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Abstract:

Objectives: *To assess the effect of supplementation of high dose of calcium(2gm) in prevention of preeclampsia.*

Materials & Methods: *A randomized controlled clinical trial on 272 healthy nulliparous woman were randomly allocated into two groups by means of a computer generation randomization list. From 20 weeks of gestation until delivery who received 2gm of oral elemental calcium per day (n=127)were assigned to high dose calcium group or the study group and 145 women were assigned to low dose calcium or control group , receiving 500 mg of calcium per day. Ten women (3.67%) were lost to follow up after randomization (4 in the study group and 6 in the control group) . Thus a total of 123 woman in the study group and 139 in the control group were included in the final analysis. Data was collected by standard questionnaire, clinical examination and investigations and statistical analysis was performed by student's t-test, chi square tests. P<0.05 was statistically significant.*

Results: *Preeclampsia developed in Study Group were 5.7% and Control Group 13.7% and the difference was statistically significant (Chi-squares - 4.65, df =1, p = 0.031). There were 2.43% (3 of 123 women) preterm delivery in the study group and 7.91% (11 of 39 women) in the control group. So, there was a significantly lower risk of preterm delivery in the study group (p = 0.049). Intrauterine growth retardation (IUGR) was found in 3.25% and 9.35% of women in the study and the control groups respectively. The incidence is higher in the control group when compared to the study group (p = 0.045).*

Conclusion: *Calcium intake is beneficial for both pregnant women and her unborn child. Daily supplementation with 2 grams of calcium during pregnancy significantly reduced the risk of preeclampsia, preterm labor and IUGR. So, high dose calcium should be supplemented to all women during pregnancy in developing countries where preeclampsia and preeclampsia related morbidities and mortality are quite high.*

Key Words: *preeclampsia, high dose calcium*

Introduction:

Preeclampsia , as defined by the Working Group of the National High Blood Pressure Education Program, is hypertension (blood pressure > 140/90 mmHg using Korotkoff V sound for diastolic blood pressure) associated with proteinuria (300 mg or more in 24 hour urine)[1]. Preeclampsia community guideline (PRECOG) takes only diastolic blood pressure of e" 90 mmHg to define hypertension[2]. Preeclampsia affects 7% of first pregnancies[3] and responsible for 24% of all maternal deaths in India[4].

The results of several clinical trials and meta-analyses have suggested that calcium supplementation reduces the incidence of preeclampsia[5,6].

Low calcium intake may cause high blood pressure by stimulating either parathyroid hormone or rennin release, thereby increasing intracellular calcium in vascular smooth muscle[7] leading to vasoconstriction. A possible mode of action for calcium supplementation is that it reduces parathyroid release and intracellular calcium and so decreases smooth muscle

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contractility, increases the production of vascular Nitric Oxide (NO)[8] and prostacyclin. Calcium might also have an indirect effect on smooth muscle function by increasing magnesium levels[9].

By reducing uterine smooth muscle contractility it prevents preterm labour[10].

Prevention of Preeclampsia would be a great step forward in prenatal care. One such primary prevention is oral supplementation of high dose calcium(2gm/day) after 20 weeks of pregnancy.

This study was undertaken to evaluate the effect of high dose (2gm) calcium in reducing incidence of preeclampsia in women at high risk of preeclampsia.

Materials and Methods:

A prospective randomized clinical trial on 272 healthy nulliparous women were randomly allocated into two groups by computer generation randomization table. From 20 weeks of gestation until delivery 127 were assigned to high dose calcium group or the study group who received 2 gm of oral elemental calcium (4 tablets of 500 mg each) per day and 145 women were assigned to low dose calcium or control groups , receiving 500 mg of calcium(one active calcium tablet of 500 mg and 3 placebo tablets of the same size, weight, and colours the calcium tablets) per day. Ten women (3.67%) were lost to follow up after randomization (4 in the study group and 6 in the control group. Thus a total of 123 woman in the study group and 139 in the control group were included in the final analysis.

This study was conducted between May 2010 to April 2011, among the pregnant women attending Antenatal Clinic, Department of Obstetrics & Gynecology BURDWAN MEDICAL COLLEGE AND HOSPITAL, BURDWAN, West Bengal, India. This institution serves as a tertiary care hospital catering people of West Bengal and adjoining state like Jharkhand. Nulliparous pregnant mothers (18-30 years) from poor socio- economic status having singleton gestation, Blood pressure (BP) lower than 140/90 mmHg and no proteinuria detectable by a dipstick with first prenatal visit before 20 weeks of gestation were included in the study.

Each subject was informed regarding the details of the study and written consent was obtained from each of them before engaging in the trial. The women were examined every 4 weeks till 28 weeks of gestation then every 2 weeks till 36 weeks and weekly thereafter until delivery.

Initially detailed history regarding personal & family history of hypertension were taken. Height, weight and Blood Pressure of all pregnant mothers were measured.

Apart from routine investigations like estimation of Hb%, Fasting and Post Prandial blood sugar, ABO grouping & Rh typing, VDRL , HIV 1 & 2 testing, Urine for protein, sugar, pus cells, epithelial cells etc. Stool for ova, parasite, cysts etc. anomaly scan at 20wk, the following investigations were done

- Urinary albumin estimation by dipstick method.
- Serum and urinary calcium level.
- Serum urea, creatinine, uric acid estimation
- Liver function test.
- Bleeding time (BT), Clotting time (CT), and platelet count.
- Ophthalmoscopic examination for Retinal changes.

The following parameters were noted in the next all visits –

- BP
- Body weight
- Hb %, BT, CT, platelet count.
- Routine urine examination specially albumin.
- Serum and urinary calcium level.
- USG at 20 weeks, 32 weeks, 36 weeks
- Retinal changes.
- Serum uric acid.
- Liver function test.
- Any medical problems etc.

Plan for Analysis of Data :

Data were analyzed with SPSS 9 statistical software. Results were presented as mean ± SD, comparison between the groups were analyzed by unpaired student's t test. The Chi-square analysis was done where appropriate and $P<0.05$ was considered as statistically significant

Results:

Table I showed 5.7% and 13.7% cases of preeclampsia developed in the study group and the control group respectively. This difference was statistically significant (Chi-squares - 4.65, df =1, p = 0.031).

Table II have shown a higher percentage of eclampsia in the control group (36.84%) than the study group(28.57%).

Table III depicts maternal and neonatal outcome in both the study and the control groups. There was a significantly lower risk of preterm delivery in the study group (2.43%) in comparison to control group (7.91%) .

From Table 4 we have found that Mean Systolic Blood pressure (SBP, mmHg) in study group was 130.03 ± 10.68 and in control group was 132.15 ± 14.5 (p < 0.0001). Diastolic Blood Pressure (DBP, mmHg) in study and control group were 81.44 ± 8.65 and 83.94 ± 12.54 respectively (p = 0.0009).

Table-I

Number of Preeclampsia detected in Study (n=123) and Control (n=139) Group

	Preeclampsia	Normal Pregnancy	Total	Percentage (%)	p Value
Study Group	7	116	123	5.7	0.031[a]
Control Group	19	120	139	13.7	
Total	26	236	262	9.9	

[a] significant value.

Table-II

Eclampsia detected among Pre eclamptic mothers both in study and Control Group

	Study Groupn=7	Control Groupn=19
Eclampsia	2 (28.57%)	7 (36.84%)

Table-III

Maternal and Neonatal outcome both in Study and Control Group.

Variable	Study Group (n=123)	Control Group (n=139)	p value
Preeclampsia	7 (5.7%)	19 (13.7%)	0.03[a]
Preterm delivery	3 (2.43%)	11 (7.91%)	0.04[a]
Gestational age at delivery(week)	38.02 ± 1.25	38.08 ± 1.26	0.0042[a]
Birth weight(gm)	2900 ± 313.48	2775 ± 277.69	0.038[a]
IUGR	4 (3.25%)	13(9.35%)	0.045[a]
Stillbirth	3 (2.43%)	7 (5.03%)	0.27

Values are given as mean±SD or number (percentage).
[a]significant value.

Table -IV

Comparison of changes in blood pressure (BP) both in Study and Control Group

Variable	Study group(n=123)	Control group(n=139)	p value
Systolic BP, mmHg	130.03 ± 10.68	132.15 ± 14.55	< 0.0001[b]
Diastolic BP, mmHg	81.44 ± 8.65	83.94 ± 12.54	0.0009[b]

Values are given as mean±SD (range).
[b]significant value.

Discussion:

The randomized control trial shows that supplementation of 2 gm calcium per day decreases the incidence of hypertensive disorders in pregnancy

Kumar A. et al.[11] reported that the overall incidence of preeclampsia was 7.8% (41 of 524 women) and the incidence was 4.0% in the calcium group and 12.0% in the placebo group (OR, 0.31; 95% CI, 0.15-0.63). A 66.7% reduction in preeclampsia was observed in the calcium group.

The above report corroborated with our study (Chi-squares - 4.65, df =1, p = 0.031 ,Table 1)and there was 58.39% reduction of preeclampsia in the present study which nearly corresponds to the study by *Kumar A. et al.*

Kumar A. et al.[11] also reported that none of the women in either group (calcium and placebo group) developed eclampsia, but our study does not correlate well with their study because eclampsia detected in control and study group were 36.84% and 28.57% respectively (Table2)

In the present study, it was noted that 2.43% preterm delivery was in study group and 7.91% in control group (p = 0.04) and there is 69.27% reduction of preterm delivery (table-3) which is more significant than other study[11].

The mean birth weight was significantly greater in the study group (2900 ± 313.48) than control group (2775 ± 277.69) (p = 0.038). The incidence of IUGR was more higher in control group when compared to study group (9.35% and 3.25% respectively) (p = 0.045). Stillbirths were also reduced in study group (2.43%) than control group (5.03%) (p = 0.27)

Herrera JA et al.[12] reported that mean birth weight was significantly greater in the calcium group (2979 ± 448 g) than placebo group (2705 ± 433g), and the difference was statistically significant, p < 0.01.

According to *Niromanesh S et al*[13] the infants born in the calcium supplemented group had on an average of 500 g or more weight at birth than infant from the placebo group (infant birth weight for calcium group was 3316 ± 308g and Placebo group was 2764 ± 761 g, the difference was statistically significant < 0.05).

So, our study also corroborated to the above two studies. The mean birth weight was significantly greater in the study group (2900 ± 313.48 g) when compared to control group (2775 ± 277.69 g), and p = 0.038.

Herrera JA et al [12] reported that mean maternal diastolic blood pressure at delivery was significantly higher in the placebo group (p =0.005).

We found that Diastolic Blood Pressure (DBP, mmHg) in study and control group were 81.44 ± 8.65 and 83.94 ± 12.54 respectively (p = 0.0009) and both were almost similar.

So calcium supplementation in high dosage is very popular for reduction of incidence of preeclampsia and chances of renal stone formation is less as the duration of supplementation is short.

Conclusion:

In the light of our observation, calcium intake is beneficial for both pregnant women and their unborn child. Daily supplementation with 2 grams of calcium during pregnancy significantly reduced the risk of preeclampsia, preterm labor and IUGR. So, high dose calcium should be supplemented to all women during pregnancy in developing countries where preeclampsia and preeclampsia related morbidities and mortality are quite high.

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