ROLE OF 2 GRAM CALCIUM SUPPLEMENTATION IN PREVENTION OF PRE-ECLAMPSIA IN HIGH RISK CASES

Bharti Choudhary (Parihar)¹

HOW TO CITE THIS ARTICLE:

Bharti Choudhary (Parihar). "Role of 2 gram calcium supplementation in prevention of pre-eclampsia in high risk cases". Journal of Evolution of Medical and Dental Sciences 2013; Vol2, Issue 38, September 23; Page: 7205-7210.

ABSTRACT: OBJECTIVE: To select high risk cases which are more prone to develop pre-eclampsia, to study the effect of 2 gram calcium on reduction of pre-eclampsia in high risk patients & to assess the beneficial and adverse effect of calcium on foetal & maternal outcome. **MATERIAL & METHODS:** Two hundred women at high risk of developing pre-eclampsia were randomized to 2 gram of daily calcium & placebo. Subjects & investigators were blinded to treatment allocation. The inclusion criteria were positive roll over test, having at least one high risk factor for pre-eclampsia, between 24 weeks to 32 weeks of pregnancy & blood pressure less than 140/90 mm of Hg. Exclusion criteria were having any chronic condition leading to hypertension. Pre-eclampsia was defined as systolic/diastolic BP over 160/100 mm of Hg plus proteinuria. All subjects were followed up to delivery. **RESULTS:** A statistically significant reduction in the occurrence of pre-eclampsia was seen among the calcium group. 16% cases developed pre-eclampsia out of which 3 were eclampsia, 10% developed uncomplicated gestational hypertension & 74% cases had no hypertension ($p=0.014$). In control group, 54% had no hypertension, 21% had uncomplicated gestational hypertension & 25% had pre-eclampsia out of which 10 patients had eclampsia. Infants born to calcium group on average were 552 gm heavier than Infants born to the control group. ($P<0.05$). **CONCLUSION:** 2 gram calcium supplementation is beneficial for preventing pre-eclampsia in women at high risk for developing pre-eclampsia. No adverse effect in mother or neonate was observed in calcium treated group.

KEY WORDS: Pre-eclampsia, calcium supplementation, high risk pregnancy, roll over test

INTRODUCTION: Pre-eclampsia is a common and serious complication of pregnancy that affects both mother and neonate. It occurs in 7-10% of pregnancies with a case fatality rate of 6-10 %. (1) It relatively more common in developing countries and it probably accounts for more than 40,000 maternal deaths worldwide each year. (2)

Pre-eclampsia is seen more among nulliparous women, with multiple pregnancy, diabetics, women with chronic hypertension, maternal age before 20 or above 35 years, low socioeconomic class, with history of hypertension, with vesicular mole, poly-hydramnios and underlying renal disease. (3)

Several preventive measures have been proposed to decrease morbidity and mortality among pregnant women at high risk of developing pre-eclampsia. The proposed prophylactic measures were antiplatelet therapy (low dose Aspirin), magnesium sulphate and calcium supplementation (4, 5)

Calcium supplementation has been used as a prophylactic measure for pre-eclampsia. Daily supplementation of 2 gram calcium results in overall lowering of blood pressure and overall reduction in the incidence of hypertensive disorder of pregnancy.

With increase in dietary calcium intake and calcium supplementation, there is a fall in parathyroid hormone, vitamin -D, aldosterone and digoxin like substance/other factor. This leads to Na/Ca exchange with Ca/Mg ATPase leading to net efflux of calcium and reduced intracellular calcium. In effect, ionic calcium is transported out of the cell and shifted to the extracellular space. This results in smooth muscle relaxation and lowering of blood pressure and there may be fewer propensities for uterine contractions and onset of preterm labour pains.

On this theoretical ground, it has been suggested through numerous study that 2 gram calcium could be used in the prevention of pre-eclampsia. (6, 7)

MATERIAL & METHODS: The present study was carried out in Department of Obstetrics & Gynaecology, Gandhi Medical College, Sultania Zanana Hospital, Bhopal to evaluate the effect of supplementary calcium on reducing the incidence of pre-eclampsia in women at high risk.

This study was a double blind placebo controlled clinical trial. 200 women at high risk of pre-eclampsia were randomly assigned to 2 gram of calcium supplementation daily and placebo regimen. The preparation of calcium used was calcinol-1000 containing 1 gram of elemental calcium. A high risk woman was defined as having positive roll over test or having at least one risk factor for pre-eclampsia. The inclusion criteria were being high risk for pre-eclampsia, between 24-32 weeks of pregnancy and blood pressure less than 140/90 mm of Hg. Exclusion criteria were negative roll over test and having any chronic condition such as Diabetes, renal disease, cardiovascular disease, chronic hypertension and severe Anaemia. The treatment regimen was a daily intake of 2 gram of elemental calcium as one tablet of 1000 mg taken orally 12 hourly. Each subject underwent a pre-treatment urine and blood biochemistry analysis and she was followed up to delivery. Subjects were instructed to visit the antenatal clinic every fortnight. Blood pressure and proteinuria were evaluated in each visit. Subject's compliance was ascertained by a questionnaire on a weekly basis.

Pre-eclampsia was considered an increase (30 mm of Hg) of systolic BP above 140 mm of Hg and an increase (15 mm of Hg) of diastolic BP above 90 mm of Hg in two measurements at an of 4-6 hours accompanied with proteinuria.

In addition to pre-eclampsia, duration of pregnancy, mode of delivery, maternal and foetal outcome and infant weight at birth were noted for each subject.

RESULTS: Total numbers of cases studied were 200, out of this 100 were in test group and 100 were in the control group. There were no significant difference between the calcium and control groups in terms of important outcome related factors such as baseline calcium intake, age, weeks of gestation, history of Eclampsia or pre-eclampsia, number of pregnancies and BMI index.

In the study group, out of 100 cases, 74% did not developed hypertension, 10% developed uncomplicated gestational hypertension and 16% cases developed complicated pre-eclampsia with proteinuria, retinopathy and eclampsia. In complicated pre-eclampsia group, 75% had proteinuria, 25.5% had eclampsia and 25.5% had hypertensive retinopathy (Table1)

ORIGINAL ARTICLE

	No PIH	Uncomplicated PIH	Complicated PIH				Total
			Proteinuria	Eclampsia	Retinopathy	Total	
No of cases	74	10	10/16	3/16	3/16	16	100
Percentage	74	10	75	25.5	25.5	16	100

Table 1: Follow up of cases in study group

In contrast to study group, in the cases of control group, 54% had no hypertension, 21% developed uncomplicated gestational HT and 25% cases developed complicated pre-eclampsia. In complicated per-eclampsia group, 40% had proteinuria, 40% had eclampsia and 20 % had hypertensive retinopathy. (Table 2)

	No PIH	Uncomplicated PIH	Complicated PIH				Total
			Proteinuria	Eclampsia	Retinopathy	Total	
No of cases	54	21	10/25	10/25	5/25	25	100
Percentage	54	21	40	40	20	25	100

Table 2: Follow up of cases in control group

The calcium group developed hypertension 8 weeks later than control group and the 3 weeks duration was statistically a significant difference ($p < 0.049$). The duration of pregnancy was 2 weeks longer in the calcium group compared to control group and The difference was statistically significant ($p < 0.05$) (table 3)

Variables	Calcium group	Control group
(Mean + SD of mother's age (years))	23.8 ± 4.7	22.5 ± 4.9
Mean + SD of number of pregnancy	1.7 ± 0.1	1.5 ± 0.7
Mean + SD mothers weight (kg) at start of pregnancy	56.2 ± 11.0	55.5 ± 14.9
Mean + SD mothers weight (kg) at start of the study	59.2 ± 10.2	58.3 ± 14.1
Weeks of gestation at the start of the study	25.2 ± 1.2	24.5 ± 1.5
Mean + SD of gestational week for the onset of hypertension	37 ± 2	34.5 ± 1.9
Mean + SD duration of pregnancy in weeks	39.5 ± 0.8	37.5 ± 2.5
Family size	2.5 ± 0.7	2.3 ± 0.6
Family history of hypertension-Number (%)	19 (19%)	34 (34%)
History of PIH in previous pregnancy in multipara-Number (%)	33 (64.86%)	18 (53.34%)
Mean + SD infant birth weight in grams	3316 ± 3.8	2764 ± 761

Table 3: Distribution of pregnancy related, socioeconomic and demographic variables among two group (calcium & control)

- a) No statistically significant difference were seen for these variables between two group
- b) Mean + SD = Mean + standard deviation

ORIGINAL ARTICLE

In the study group, 60% patients delivered vaginally; out of which 3% delivered by forceps application and 37% patients were delivered by caesarean section. In control group, 56% cases delivered vaginally, out of which 4% cases were delivered by forceps application and 40% cases were delivered by caesarean section. (Graph-1)

Graph 1: mode of delivery in calcium & control group

Infants born to the calcium supplemented group had on average 550 grams more weight at birth than infant from the control group (the difference was statistically significant $P < 0.05$) (Graph 2)

Graph 2: distribution of neonates according to birth weight in calcium & control group

DISCUSSION: Despite of the high prevalence of pre-eclampsia in women of child bearing age group, its pathogenesis remains largely unknown. It is known to occur in upto 10% of pregnancy and may cause substantial maternal and foetal mortality and morbidity.

The effect of calcium supplementation on prevention of pre-eclampsia has been a matter of several clinical trials in recent years. The majority of these trials have proven to have favourable effects for calcium supplementation during pregnancy. This study also demonstrated that a daily dose of 2 gram calcium can reduce the occurrence of pre-eclampsia among women at high risk for pre-eclampsia.

There are some trials that failed to demonstrate a beneficial effect of calcium supplementation on occurrence of pre-eclampsia (8,9,10). The discrepancy seen in these trials may be due to low dose of calcium, subject selection or lack of statistical power to detect a favourable effect.

A favourable effect of calcium intake on PIH was first reported in 1960 by Hamilton when he reported a lower rate of PIH among Ethiopians who have a diet rich in calcium (11)

Several mechanism have been postulated for the effect of calcium on blood pressure, a low calcium intake increases blood pressure through stimulating rennin release, which in turn causes vasoconstriction, another possible mechanism is through lowering parathyroid release and intracellular calcium resulting in smooth muscle contractility.

An interesting finding in the present study was that Muslims comprises 45% and Hindus 55%. Among Hindus, Sindhi community formed a single large community which appeared to be susceptible to develop PIH. Among Hindus, 55.3% were Sindhis. Similarly in control group, out of total 60% cases, there were 33.1% were Sindhis. No present study has categorized the high risk cases according to community

In our study we measured duration of pregnancy (in terms of gestational age) and infants birth weight among two group of study and control group. A favourable effect both on infant's birth weight and duration of pregnancy were seen in our study confirming other studies. (12, 13)

The mode of delivery in the study and control group was also compared. Walterberg & colleagues reported an increase in total number of LSCS for PIH and eclampsia in the control group. These results were comparable to our study also (14).

All the above studies though relatively small in number in terms of patient's number, demonstrate a consistent beneficial aspect of calcium in high risk pregnancies particularly in reducing the incidence and severity of pre-eclampsia and in addition enhancing foetal growth and gestational age.

CONCLUSION: In conclusion, it could be stated that the high risk patients could be screened for pre-eclampsia by simple methods and put on 2 gram of daily calcium supplementation. In the light of our observation and other studies, calcium supplementation is beneficial for both mother and neonate. This preventive measure is easy to administer and cost effective. It is very effective in reducing risk of pre-eclampsia among high risk pregnant women. More studies are needed to address the optimal dosage of calcium.

REFERENCES:

1. WHO, Technical Report Series No. 758: The Hypertensive disorders of pregnancy. Geneva: 198-193
2. Duley L: Which anticonvulsant for women with Eclampsia. Evidence from the collaborative Eclampsia Trial. Lancet 1599;345:1455-1463
3. Cude –Agudelo A, Beliz'an JM. Risk factors for pre-eclampsia in a large cohort of Latin American and Caribbean women. Br J Obstet Gynaecol 2000;107(1):75-83
4. Lippert TH, Muke AO. Is prevention of pre-eclampsia with low dose aspirin possible. Critical assessment of available studies. Geburtshilfe Frauenheilkd 1996;56(2):88-92
5. Chien PF, Khan KS, Arnott N. Magnesium sulphate in the treatment of Eclampsia and pre-eclampsia; an overview of the evidence from randomized trials. Br J Obstet Gynaecol 2006; 103 (8898);619-629
6. Lopez – Jaramillo P, Narvaez M, Weigel RM. Calcium supplementation reduces the risk of PIH in an Andes population. Br J Obstet Gynaecol 1989;96:648-655
7. Sanchez-Ramos L, Briones DK, Kaunitz AM, Delvalle GO, Gaudier FL, Walker KD. Prevention of PIH by calcium supplementation in angiotensin II-sensitive patients. Obstet Gynaecol 1994;84;349-353
8. Marya RK, Rathee S, Manrow M, Effect of calcium and vitamin D supplementation on toxemia of pregnancy. Gynaecol Obstet Invest 1987;24;38-42
9. Villar J, Say L, Shennan A, Lindheimerzn, Duley L, Conde-Augdo A- Methodological and technical issues related to the diagnosis, screening, prevention and treatment of pre-eclampsia and eclampsia. Int J Gynaecol Obstet 2004 s28-s41
10. Repke J, Villar J. Pregnancy induced Hypertension and low birth weight: the role of calcium. Am J Clin Nutr 1991;54.237s-241s
11. Atallah AN, Hofmeyr GJ , Duley L. Calcium supplementation during pregnancy for preventing PIH .The Cochrane review Library, Issue 3, Oxford; Update Software, 2000.
12. Hamlin RHJ. Prevention of pre-eclampsia. Lancet 2002;1;864-865
13. Niromanest S, Lagaii S, Mosavi- Jarrahi A. Supplementary calcium in prevention of pre-eclampsia. Int. J Gynaecol Obstet 2001 July 74 (1):17-21
14. GJ Hofmeyr, L Duley, A Atallah. Dietary calcium supplementation for prevention of pre-eclampsia and related problems – a systematic review and commentary: BJOG 2007; 114:933-943.

AUTHORS:

1. Bharti Choudhary (Parihar)

PARTICULARS OF CONTRIBUTORS:

1. Assistant Professor, Department of Obstetrics & Gynaecology, Gandhi Medical College, Sultania Zanana Hospital, Bhopal, M.P.

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Bharti Choudhary (Parihar),
115/5, OPD Block,
Sultaniya Lady Hospital Campus,
Bhopal, M.P. – 4962001.
Email- drbhartiparihar@gmail.com

Date of Submission: 12/09/2013.
Date of Peer Review: 13/09/2013.
Date of Acceptance: 16/09/2013.
Date of Publishing: 18/09/2013