

CALCIUM SUPPLEMENTATION FOR PRETERM AND LOW BIRTH- WEIGHT NEONATES

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ABSTRACT

Early neonatal hypocalcemia is a common problem in prematurely born infants. To prevent it, therapy with intravenous calcium is often advised. We compared the efficacy and side-effects of intravenous and oral calcium supplementation in preterm and low birth-weight babies. Both the groups were comparable for birth weight, gestational age and cord blood calcium level. Oral calcium administration was as efficacious as intravenous administration in babies of all gestational age groups and birth-weight groups. Side effects associated with therapy were less common and of lesser severity in oral supplementation group. Lower cost and ease of administration were additional benefits.

Keywords: *Early neonatal hypocalcemia, Calcium supplementation.*

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Early neonatal hypocalcemia is a common problem in prematurely born infants. The incidence is reported to be between 26% and 30%(1). This is correlated with delayed surge of parathormone secretion(2) and higher levels of calcitonin(1) in preterm as compared to term neonates. To prevent hypocalcemia in preterm infants, routine supplementation with parenteral calcium is advised. It is, however, also suggested that intravenous calcium supplementation should be reserved for cases with persistent or profound hypocalcemia, tetany and seizure disorders(3). We studied, therefore, the comparative efficacy and adverse effects associated with oral and intravenous calcium supplementation in preterm and low birth-weight babies. If found effective, oral calcium supplementation would be a better choice especially in a developing country.

Material and Methods

We prospectively studied, over a period of two years, 200 preterm or small for gestational age neonates, born in a General Hospital in Bombay. The babies were weighed on a sensitive standard beam scale soon after birth. The gestational age was determined by mother's interview and examination of the neonate using modified Dubowitz examination(4). Three ml of cord blood was obtained in a plain bulb from each of the neonates. The sample was centrifuged, serum separated and then refrigerated till the time of analysis for level of calcium (Ca cord level). One group was given oral calcium supplementation, whereas the other received calcium in a dose of 75 mg of elemental calcium per kg per day in four equally divided doses for 5 days using 10% calcium gluconate solution.

Babies in both the groups received

identical nursing care. Usual care was taken while administering calcium gluconate solution intravenously. The neonates were monitored for signs of hypocalcemia including jitteriness, hypertonicity, hypotonicity, high-pitched cry and convulsions(5). The infants were also watched for problems associated with calcium administration. The side effects were given the following scores: *Mild*: Loose motions, vomiting; *Moderate*: Swelling of surrounding part following intravenous administration, dehydration following diarrhea, vomiting; and *Severe*: Necrotizing enterocolitis, necrosis and/or sloughing of intravenous site, cardiac standstill.

A sample of blood was collected from a peripheral vein on day 5 and serum calcium determined. Estimation of serum total calcium was done using a spectrophotometer 'Spectronic 20' manufactured by Bausch and Lomb using standard procedure(6). Statistical significance was calculated. Statistical analysis was performed using test of significance (standard error of difference between two means and Chi square test).

Results

The two groups were matched for gestational age, birth weight and serum calcium level in cord blood (*Table 7*). The mean (SD) level of serum calcium on day 5 for neonates in the oral group was 9.2 (1.0) mg/dl while that for intravenous group was 9.2 (1.1) mg/dl. To further probe into effectiveness of oral administration of calcium, the babies were divided into different sets depending on their gestational age and birth weight as shown in *Tables II & III*. It was seen that there was no significant difference in the serum calcium levels of babies with gestational age groups of 28-32

TABLE I—*Clinical Characters [Mean (SD)] of Neonates Administered Oral and Intravenous Calcium*

	Oral group	Intravenous group
Birth weight (kg)	1.63 (0.260)	1.58 (0.298)
Gestational age (weeks)	33.9 (2.4)	33.7 (3.2)
Cord calcium level (mg/dl)	7.7 (1.4)	7.9 (1.3)

TABLE II—*Serum Calcium Levels in Relation to Gestational Age*

Gestational age (weeks)	Oral group		Intravenous group	
	No.	Mean (SD) (mg/dl)	No.	Mean (SD) (mg/dl)
28-32	30	9.1 (1.1)	45	9.1 (1.0)
33-37	47	9.2 (1.0)	34	9.4 (1.2)
>37	23	9.4 (0.9)	21	9.3 (0.9)

TABLE III—*Serum Calcium Levels in Relation to Birthweight*

Birth-weight (g)	Oral group		Intravenous group	
	No.	Mean (SD) (mg/dl)	No.	Mean (SD) (mg/dl)
<1000	-	-	2	9.7 (0.3)
1000-1499	13	9.4 (1.1)	35	9.0 (1.0)
>2000	18	9.2 (0.8)	8	9.0 (0.9)

weeks, 33-37 weeks and more than 37 weeks irrespective of whether they were given calcium orally or intravenously. Hence, it can be concluded that calcium given orally or intravenously gives similar serum calcium levels on day 5 in babies of different gestational age groups. As shown in *Table III*, no baby was enrolled in < 1000 g group for oral calcium group and hence this set could not be compared. There was no significant difference in the serum calcium levels in the babies with birth weights 1000-1499 g, 1500-1999 g and more than 2000 g irrespective of route of administration of calcium. A total of 14 babies (7%) developed clinical manifestations of hypocalcemia which was confirmed by serum calcium estimation. The incidence of hypocalcemia in spite of calcium administration was 6% in oral group and 8% in intravenous group. This difference was also not significant statistically.

Ninety eight per cent of neonates in the oral group had no therapy related problems. The corresponding figure for intravenous group was 56% ($p < 0.001$). It was also found that in 21% of babies in intravenous group, the problem tended to be of at least moderate severity. No baby in oral group had moderate or severe complications related to therapy.

Discussion

Low birth weight and prematurity interfere with placental transfer of calcium. After delivery, the neonate has to adapt to sudden withdrawal of calcium supply. This can lead to a decrease in serum calcium levels to about 8.5 mg/dl in term infants and to about 7 mg/dl in preterm infants by 24-48 hours of birth. A preterm baby is in a further disadvantaged state because the ability of her parathyroid gland to respond to hypocalcemic state is limited(2). In

addition, preterm and low-birth weight babies may have high calcitonin levels and organ resistance to the action of parathormone(7,8).

The prospective study enrolled 200 preterm and small for gestational age neonates who were randomly assigned to receive calcium supplementation in a dose of 75 mg of elemental calcium/kg/day either orally or intravenously. It was observed that oral administration of calcium was as efficacious as its intravenous administration in maintaining serum calcium level at all gestational ages. This is in accordance with the observations made by others(9,10). This was also true for babies of birth weights more than 1000 g. Earlier workers(10,11) also found that calcium given orally is as effective as calcium given intravenously in all babies, irrespective of birth-weights. This study also showed that therapy-related problems occurred more frequently with intravenous calcium therapy. The problems were not only less common with oral therapy but were also less severe, when they did occur.

Thus, it can be concluded that administration of calcium orally is as efficacious and much safer than the intravenous administration, in bolus form, in preventing early-onset hypocalcemia in preterm and low birth-weight babies. In addition, there are other advantages like lower cost and simplicity of administration. These are relevant to our country where trained personnel to take care of preterm and small-for-date babies may not always be available.

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