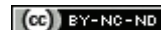


Total Serum Calcium and Ionic Calcium Levels in Birth Asphyxia: A Prospective Study

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ABSTRACT

Introduction: Birth asphyxia is one of the common neonatal problems resulting in significant mortality and morbidity. It is associated with several biochemical abnormalities which may coexist and alter the course of disease process. One of biochemical abnormality is hypocalcaemia and is associated with poor outcome.

Aim: To compare total serum calcium and ionic calcium levels at birth and at 48-hours among asphyxiated and non-asphyxiated neonates.

Materials and Methods: This was a case-control study consisting of 50 term asphyxiated (cases) and 50 term healthy (controls)

neonates admitted under NICU MMIMSR Mullana, Ambala (Haryana) from February 2018 to August 2019. Total serum calcium and ionic calcium levels were estimated and compared at birth and at 48-hours of life among cases and controls.

Results: Total serum calcium and ionic calcium levels at birth were significantly lower in cases (8.04 ± 0.89 mg/dL, 3.62 ± 0.46 mg/dL) as compared to controls (9.32 ± 0.72 mg/dL, 4.79 ± 0.49 mg/dL). Total serum calcium and ionic calcium levels at 48 hours were also significantly lower in cases (9.03 ± 0.84 mg/dL, 4.51 ± 0.41 mg/dL) as compared to controls (9.56 ± 0.49 mg/dL, 4.80 ± 0.69 mg/dL).

Conclusion: Total serum calcium and ionic calcium levels are decreased in birth asphyxia both at birth and at 48-hours.

Keywords: Asphyxiated neonate, Biochemical abnormalities, Calcium supplementation, Hypocalcaemia

INTRODUCTION

Calcium is an important second messenger of body. It acts as co-factor for various enzymatic activities and also plays a significant role in normal muscle function. Hypocalcaemia is known to occur with increased frequency in neonates with birth asphyxia and may trigger seizures or compromise cardiovascular function with deleterious consequences [1]. In serum, calcium occurs in two forms: total serum calcium and ionic calcium. Correlation between ionised and total serum calcium level is poor when serum albumin concentration is low.

Along with prematurity and systemic infections, birth asphyxia is one of three most common causes of neonatal deaths [2]. In India, 2.5 lakh to 3.5 lakh neonates dies every year due to birth asphyxia out of which most of the deaths occur during the first three days of life [3].

Various metabolic derangements have been seen in asphyxiated newborn. Hypoglycaemia, hyperkalemia, hyponatremia, hyperuricaemia, hypocalcaemia, and raised creatinine levels are the biochemical abnormalities associated with poor outcome in birth asphyxia [4]. There is paucity of data on calcium levels in birth asphyxia, so there are no established guidelines for calcium as adjuvant therapy for the same. Hence, the present study aimed to measure both ionised and total serum calcium level in neonates with birth asphyxia and compared with normal healthy neonates.

MATERIALS AND METHODS

A prospective case-control study was conducted in which 50 term asphyxiated (cases) and 50 term healthy (controls) neonates admitted under NICU MMIMSR Mullana, Ambala (Haryana) in the period from February 2018 to August 2019 were recruited. The study was started after taking approval from Ethical Committee of Institute via letter number IEC-1093 and informed consent from one of the parents at admission of mother in obstetric department.

Inclusion criteria: Cases were term neonates, appropriate for gestational age with birth asphyxia as defined by WHO (APGAR score <7 at five minutes of life) [5].

Exclusion criteria: Neonates having gross congenital malformation, neonates of mother having diabetes, chronic renal or hepatic disease were excluded from study.

Basic parameters including gender, mode of delivery, staining of amniotic fluid were compared among cases and controls. Total serum calcium and ionic calcium levels were estimated and compared at birth and at 48-hours of life among them. Calcium supplementation was given to babies with serum calcium level <8 mg/dL or ionic calcium <4 mg/dL.

In both cases and controls, 2 mL of cord blood sample collected at time of birth and 2 mL of venous blood collected at 48-hours was used for assessment of ionised and total serum calcium values at birth and at 48-hours of life by fully automatic biochemical analysers.

STATISTICAL ANALYSIS

Statistical analysis was done by statistical SPSS[®] 25.0 and chi-square and t-test was applied to data. The significance level for p-value was taken as $p < 0.05$.

RESULTS

In the present study, APGAR score at 5 minutes was significantly less in cases as compared to controls ($p < 0.001$) [Table/Fig-1].

Total serum calcium and ionic calcium levels at birth and at 48-hours after birth were also significantly lower in cases as compared to controls [Table/Fig-2].

DISCUSSION

The present study was conducted to check levels of total serum calcium and ionic calcium in birth asphyxia in which no statistically significant difference was found based on gender, birth weight and mode of delivery among asphyxiated and non-asphyxiated neonates.

In the present study, both total serum calcium and ionic calcium levels were estimated at birth and 48-hours of post-natal life in cases and controls. Jajoo D et al., studied total serum calcium at birth, 6-hours and 24-hours of life and, then at the 5th day of life in asphyxiated neonates as cases and healthy neonates as controls and was observed that asphyxiated infants had significantly lower serum calcium levels than control infants during each of the time period studied [4]. A study

Characteristics		Cases (50) N (%)	Controls (50) N (%)	p-value
Gender	Male	29 (58%)	31 (62%)	0.838
	Female	21 (42%)	19 (38%)	
Birth weight	Mean±SD (grams)	2720±440 gm	2800±400 gm	0.341
Period of gestation	Mean±SD (weeks)	37.98±1.15	38.10±3.49	0.582
APGAR at 5 minutes	Mean±SD (minutes)	5.60	9.18	<0.001
Amniotic fluid	Clear	45 (90%)	41 (82%)	0.388
	Stained	5 (10%)	9 (18%)	
Parity	Primigravida	26 (52%)	28 (56 %)	0.688
	Multigravida	24 (48%)	22 (44%)	
Mode of delivery	Vaginal delivery	27 (54%)	27 (54%)	1
	Caesarean	23 (46%)	23 (46%)	
Booking status	Booked	32 (64%)	35 (70%)	0.523
	Unbooked	18 (36%)	15 (30%)	

[Table/Fig-1]: Base line parameters of both cases and controls.

		Cases (50) Mean±SD	Controls (50) Mean±SD	p-value
At birth (mg/dL)	Total serum calcium	8.04±0.89	9.32±0.72	<0.001
	Ionic calcium	3.62±0.46	4.79±0.49	<0.001
At 48-hours of birth (mg/dL)	Total serum calcium	9.03±0.84	9.56±0.49	<0.001
	Ionic calcium	4.51±0.41	4.80±0.69	0.014

[Table/Fig-2]: Comparison of cases and controls based on mean total serum calcium levels and mean ionic calcium levels at birth and 48-hours of life.

was conducted by Alphonsus NO, in which {among asphyxiated compared to non-asphyxiated neonates ($p < 0.001$)} mean total serum calcium at the ages of 12, 24 and 48-hours were significantly lower [6]. Jayaprakash K and Murali B, studied serum calcium levels among asphyxiated and non-asphyxiated neonates and found lower total serum calcium levels among asphyxiated neonates [7]. The results of all these studies are similar to the results of the present study. However, the study conducted by Jain BK et al., (p -value 0.3) had found no statistically significant difference between asphyxiated and non-asphyxiated neonates based on mean total serum calcium levels [8], and this is contradictory to the present study.

Study conducted by Basu P et al., compared total serum calcium levels at birth among asphyxiated and non-asphyxiated neonates and found the level of total serum calcium to be statistically significantly lower among asphyxiated neonates (p -value <0.01) [9]. Another study conducted by Rai S et al., (p -value <0.05) also reported similar results to the present study [10]. In this study at birth and 48-hours of life, ionic calcium levels were statistically lower among cases than controls, and this difference was statistically significant (p -value <0.5).

Results similar to the present study have been reported in various earlier conducted studies by Yoneda S et al., (p -value <0.001) and Lila A et al., (p -value <0.001) [11,12].

Cause of decreased calcium levels in birth asphyxia is not completely understood, possible explanations could be that hypoxic-ischaemic injury can cause reperfusion injury which can cause either necrosis or apoptosis and rapid influx of calcium into cells leading to cell death. Widespread calcium influx into cells of multiple damaged organs in asphyxiated newborns may lead to lower serum calcium levels. Decrease of calcium levels in hypoxic-ischaemic encephalopathy has also been postulated due to excretion of calcium in urine caused by hypoxic ischaemic reperfusion injury [13]. Jajoo D et al., had stated the cause of lower calcium level in birth asphyxia as impaired function of parathyroid gland due to hypoxia [4]. Other cause of hypocalcaemia may be due to late initiation of feeds, amplified production of calcitonin, increased endogenous phosphate load due to breakdown of tissues, metabolic acidosis, and renal failure [14].

Limitation(s)

Small sample size due to limited study period.

CONCLUSION(S)

Birth asphyxia leads to decrease in both total serum calcium and ionic calcium levels both at birth and at 48-hours of life. Although these findings are promising but further extensive studies are needed with a large sample size as there are no standard guidelines to use calcium as adjuvant treatment in asphyxiated newborns as they are at higher risk of hypocalcaemia and more prone to complications associated with it.

REFERENCES

- Gupta BD, Sharma P, Bagla J, Parakh M, Soni JP. Renal failure in asphyxiated neonates. *Indian Pediatr.* 2005;42(9):928-34.
- Liu L, Johnson HL, Cousens S, Perin J, Scott S, Lawn JE, et al. Child Health Epidemiology Reference Group of WHO and UNICEF Global, regional, and national causes of child mortality: An updated systematic analysis for 2010 with time trends since 2000. *Lancet.* 2012;379(9832):2151-61.
- Network N. National Neonatal-Perinatal Database (Report 2002-2003). In: National Neonatology Forum NNPD Network, New Delhi, India. 2005.
- Jajoo D, Kumar A, Shankar R, Bhargava V. Effect of birth asphyxia on serum calcium levels in neonates. *Indian J Pediatr.* 1995;62(4):455-59.
- Chacham S, Pasi R. Hypoxic-Ischemic Encephalopathy and Intracranial Hemorrhage. In: IAP Textbook of Pediatrics. 7th ed. Pp. 80-88.
- Alphonsus NO. Prevalence of neonatal hypocalcaemia among full-term infants with severe birth asphyxia. *Pac J Med Sci.* 2011;8(1):04-12.
- Jayaprakash K, Murali B. Study of electrolyte status, glucose and uric acid levels in perinatal asphyxia. *J Evol Med Dent Sci.* 2014;3(18):4786-90.
- Jain BK, Singh D, Singh H, Narang APS, Sobti PC, Gupta A. Serum ionised calcium in birth asphyxia. *Indian J Clin Bio Chem.* 2000;15(1):36-39.
- Basu P, Sabyasachi S, Das H, Choudhuri N. Electrolyte status in birth asphyxia. *Indian J Pediatr.* 2010;77(3):259-62.
- Rai S, Bhatiyani KK, Kaur S. Effect of birth asphyxia on serum calcium and glucose level: a prospective study. *Int J Sci Study.* 2015;3(7):03-06.
- Yoneda S, Ibara S, Kobayashi K, Kato E, Maruyama Y, Maruyama H, et al. Low adjusted serum ionised calcium concentration shortly after birth predicts poor outcome in neonatal hypoxic-ischaemic encephalopathy. *J Obstet Gynaecol Res.* 2005;31(1):57-64.
- Lila A, Abdrabuo IA, Elsayed AH, Alkhesen GA, Ibrahim MA. Ionised serum calcium and serum total magnesium, predicts outcome in neonatal hypoxic-ischaemic encephalopathy. *Nat Sci.* 2015;13(3):127-31.
- Allen KA, Brandon DH. Hypoxic ischaemic encephalopathy: Pathophysiology and experimental treatments. *Newborn Infant Nurs Rev* 2011;11(3):125-33.
- Salle BL, Delvin E, Glorieux F, David L. Human neonatal hypocalcaemia. *Biol Neonate.* 1990;58 Suppl 1:22-31.

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