

Myocardial Dysfunction Due to Hypocalcemia

MUNESH TOMAR, SITARAMAN RADHAKRISHNAN AND SAVITRI SHRIVASTAVA

From the Department of Pediatrics and Congenital Heart Surgery, Escorts Heart Institute and Research Centre, Okhla Road, New Delhi, India.

Correspondence to :

Munesh Tomar, Department of Pediatrics and Congenital Heart Surgery, Escorts Heart Institute and Research Centre, Okhla Road, New Delhi 110 025, India.

muneshthomar@yahoo.co.in

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Hypocalcemia is a curable cause of myocardial dysfunction and clinical congestive cardiac failure, with only stray reports available in literature. We describe 15 infants presenting with severe left ventricular dysfunction, who were found to have hypocalcemia with or without hypomagnesemia. Vitamin D deficiency was identified as the main cause of hypocalcemia. These children improved on supplementation of vitamin D and calcium.

Key words: *Child, Congestive cardiac failure, Myocardial dysfunction, Hypocalcemia, Vitamin D deficiency.*

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Calcium has a central role in myocardial contraction coupling, and hypocalcemia reduces myocardial function. Congestive cardiac failure (CCF) due to hypocalcemia is also reported, though rare. There are scattered reports of hypocalcemia related myocardial dysfunction that improved after treatment with therapeutic dose of vitamin D and calcium. We herein report our experience with 15 infants who were referred to us with a diagnosis of dilated cardiomyopathy.

METHODS

Medical records of 94 children admitted with a diagnosis of left ventricular dysfunction without any structural heart defect over 7 years (June 2001-October 2008), were retrospectively analyzed. Sixteen percent ($n=15$, 12 males) had hypocalcemia as the main cause of ventricular dysfunction and included in this retrospective analysis.

RESULTS

The age of 15 infants ranged from 45 days to 5 months (median 2 mo). Their weight at the time of

presentation was within normal limit (50th to 78th percentile). The clinical presentation was congestive heart failure in 12 cases and congestive heart failure with shock in 3. Seven children also had convulsions at presentation. The duration of illness was 4-6 weeks. Babies were on combination of breastfeed and formula feed, none was on cow's milk. Anterior fontanel was widely open in all; no other sign of rickets was found. There was history of undiagnosed sudden death in siblings in two families, who had died at a similar age.

Chest radiograph revealed cardiomegaly in all cases. Twelve lead ECG showed sinus tachycardia, normal frontal QRS axis for age and prolonged corrected QT interval. Serum calcium was low while alkaline phosphatase was high in all infants. Serum parathyroid hormone level (Chemiluminescent Immunoassay) was elevated (secondary hyperparathyroidism) in all cases except in one case, who was found to be hypoparathyroid. Serum vitamin D (25 hydroxy) assayed in 12 cases (Chromatography Radioreceptor H3 assay), was low in 6 cases and near normal in 4. Maternal serum calcium, alkaline phosphatase and serum phosphorus were within

normal limit in all cases. Maternal serum vitamin D level was found to be low in one case. Hemoglobin ranged between 8 and 10 g/dL. Screening for inborn errors of metabolism, including carnitine level, was done in 4 infants and was normal. Myocardial biopsy was not done in any of the patient. Echocardiography revealed dilated left ventricle (Z score +3-4), severely decreased left ventricle ejection fraction (LVEF), fractional shortening (FS), normal coronaries and no structural heart defect in all cases. All cases received decongestive therapy (digoxin, frusemide and ACE inhibitor). Calcium was started as continuous intravenous infusion (dose 100-200 mg/kg/day) till serum calcium normalized, after which we switched to oral calcium in the same dose. Injection vitamin D (cholecalciferol) was given intramuscularly (600 000 IU) followed by oral maintenance dose of 400 unit/d for 6 months. Injection magnesium sulfate (50%) (0.1 mL/kg) was given intramuscularly to all infants on day 1 and day 2 of the treatment. Serum calcium levels normalized in 2-4 days in all, except in one infant who had hypoparathyroidism. In this baby, resistant hypocalcemia was treated with oral 1,25-dihydroxycholecalciferol, which led to normalization of serum calcium level. One infant had recurrent hypocalcemia along with tonic spasm leading to aspiration and death, after initial normalization of calcium level. Ten children received packed cell transfusion (15mL/kg) for low hemoglobin level (8-8.9 g/dL).

Fourteen infants were discharged after normalization of their calcium levels and QTc interval. There was a definite improvement in their LVEF and it normalized over 8-12 weeks.

DISCUSSION

Fifteen out of 94 (16%) babies with severe left ventricular dysfunction had severe hypocalcemia. Primary cause of hypocalcemia in our series was found to be vitamin D deficiency. Vitamin D levels were at lower limit of normal, but they were definitely low for that degree of hypocalcemia(14). All infants except one responded dramatically to therapeutic doses of vitamin D and calcium. Clinical findings, investigations, and response to treatment with vitamin D and calcium strongly support

hypocalcemia as a cause for myocardial dysfunction. However, contribution of coexistent hypomagnesemia for left ventricular dysfunction can not be ruled out.

Available literature has only case reports of hypocalcemia as the cause of cardiomyopathy in pediatric age group in available literature. Vitamin D deficiency, vitamin D dependent resistant rickets, or idiopathic factors have been implicated for hypocalcemia(1-3). Maiya, *et al.*(9) reported 16 cases of cardiomyopathy in children associated with vitamin D deficiency leading to hypocalcemia over a period of 6 years. In adults with ventricular dysfunction, hypoparathyroidism was found to be the main reason for hypocalcemia(4-8). Hypomagnesaemia was not mentioned as an association in these reports. There is one prospective study investigating cardiac function in patients with rickets(10). All patients were asymptomatic though echocardiographic abnormalities were noted.

Possible explanations of myocardial dysfunction in patients with hypocalcemia are well described in the literature(1-10). The reason for vitamin D

TABLE I INVESTIGATIONS AT ADMISSION IN THE STUDY CHILDREN (N=13)*

Investigations	Lab findings Median (range)	Normal value
Calcium		
Total (mg/dL)	5.4 (5-8.6)	8.8-10.8
Ionized (mmol/L)	0.5 (0.3-0.7)	1.12-1.23
Magnesium (mg/dL)	1.8(1.3-2.1)	1.6-2.6
Phosphorus (mmol/L)	1.4 (1.1-7)	1.1-2.1
Alkaline phosphatase (U/L)	2400 (1200-3240)	145-420
Vitamin D level (pg/mL)*	12 (5-25)	24-45
Parathyroid hormone (pg/mL)	404 (9-809)	7-53
Chest X-ray (CT ratio %)	65 (60-78)	<55
ECG: QTc (s)	0.52 (0.51-0.58)	<0.45
LVEF (%)	20 (15-30)	>55%

* Two infants referred after getting treatment outside are not shown, both had normal serum calcium, vitamin D and parathyroid levels; *Done in 10 children each; ECG-electrocardiogram, QTc-corrected QT interval, CXR-chest roentgenogram CT ratio-cardiothoracic ratio, LVEF-left ventricular ejection fraction.

WHAT THIS STUDY ADDS?

- Indian children with low serum calcium as the sole reason for left ventricular dysfunction are described.

deficiency(9) in developing countries is possibly nutritional. In addition, deficiency may occur in dark skinned infants or in breast fed infants of mothers unexposed to sunlight. This problem may thus be more dispersed in this part of the world or a particular ethnic group in more developed countries. We conclude that serum calcium and magnesium levels must be estimated in all children presenting with cardiomyopathy.

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