# Comparative Evaluation of Corrected QT and Ionized Calcium in Children

**Zarrin Keihani Douste[1], Mohhamad Taghi Haghi Ashtiani[2], Mamak Shariat[3], and Fatemeh Tehrani[4]**

[1] *Department of Pediatric Neurology, Imam Khomeini Medical Complex, Tehran University of Medical Sciences, Tehran, Iran*

[2] *Department of Pathology, Children Medical Center, Tehran University of Medical Sciences, Tehran, Iran*

[3] *Family Health Institute, Maternal Fetal Neonatal Research Center, Tehran University of Medical Sciences, Tehran, Iran*

[4] *Family Health Institute, School of* Medicine*, Tehran University of Medical Sciences, Tehran, Iran*

***Received: 6 Jan. 2014; Accepted: 23 Dec. 2014***

**Abstract-** Convulsion is one of the most common problems in children and hypocalcemia is one the most frequent etiological items in children's convulsion. Corrected QT (QTc) in EKG is prolonged in hypocalcemia, so it can be a useful tool for evaluation of serum ionized calcium. In three groups (first seizure, multiple seizures, without seizure or control ) every 25 cases, QTc, serum ionized ca, total ca, ABG, and serum albumin level have been checked in the Department of Pediatrics of Imam Khomeini Hospital and outpatient department of Ahari children's medical center in 2008. Prolonged QTc was observed in 72% of convulsive children (36 cases) but only 19% of non-convulsive children (5 cases) showed this pattern. Ionized calcium was significantly higher in non-convulsive than convulsive groups. There was no correlation between prolonged QTc and total serum calcium; however, this correlation with low ionized calcium was significant. QTc is an easy and rapid method for serum ionized calcium evaluation.



*Acta Med Iran* 2015;53(9):579-581.

**Keywords:** QTc; Ionized Calcium; Total serum calcium; Convulsion

## Introduction

Seizure as a common problem in children (nearly 10%) is provoked by somatic disorders originating outside the brain such as high fever, infection, syncope, head trauma, hypoxia, toxins and cardiac arrhythmia. Less than one-third of seizures in children are caused by epilepsy, a condition in which is triggered recurrently from within the brain (1).

Calcium is the fifth most abundant element in the body approximately 99% of the body calcium content in bones, despite the large calcium reserve in the bone cells, extracellular calcium concentration is maintained remarkably constant at approximately 5 meq/lit (10 mg/dl) under normal condition. 40% of extracellular calcium is bound to proteins predominantly albumin, 10% is diffused but combined with cations such as citrate and phosphate and remaining 50% (2.5 meq/lit) is freely diffusible as Ca anion and active form. The freely diffusible fraction is responsible for the physiologic effects of calcium in neuromuscular transmission and as a coupling agent for excitation- transmission in the nervous system and excitation-contraction in the muscles (2,3).

Hypocalcemia can induce convulsion especially in neonates, but convulsion may be the sole clinical abnormality due to hypocalcemia in older children. In hypocalcemia, there is prolong QT interval and corrected QT that QT adjusted to cardiac rate is more sensitive. Using of QTc in ionized calcium evaluation has been reported in some cases series (4). A report showed a case with syncope attack had long QTc (0.48 Sec) and hypocalcemia due to hypoparathyroidism (5). In another study of hypocalcemia, cardiac hypertrophy, autonomic system dysfunction, and long QTc were demonstrated in dialyzed patients (6). In an investigation in pediatric neurologic outpatient of Imam Khomeini Hospital in 497 patients with frequent seizures, 293 had prolonged QTc but lowered total calcium was seen in only 17 patients (7).

Routinely, we evaluate serum calcium level in epileptic children but we need their ionized calcium level, too. As this test is expensive, and a few laboratories in our country analyze this value. It is

**Corresponding Author:** M. Shariat
Family Health Institute, Maternal Fetal Neonatal Research Center, Tehran University of Medical Sciences, Tehran, Iran
Tel: +98 912 3499281, Fax: +98 21 66591315, E-mail address: mshariat@tums.ac.ir

considered that finding alternative methods for checking ionized calcium level could be beneficial.

## Materials and Methods

A cross-sectional descriptive, analytical study was carried out in the Department of Pediatric Neurology of Imam Khomeini Hospital and outpatient department of Ahari children's medical center (Tehran-Iran) in 2008. Inclusion criteria were: children with no renal or cardiac abnormalities, no malnutrition, and no antidepressant drug consumption. The target population consisted of 75 children aged 2-10 years divided into three groups; children with a first seizure, frequent seizure and no seizure, each 25 cases. In this study we measured total serum calcium, ionized calcium, ABG, serum albumin as well as QTc (By performing 12 lead EKG and calculating with QTc Bazett Formula) in the case groups (patients with first and frequent seizure) and control group (normal children).

We asked all patients' parents for informed consent. We assured them that all information would remain confidential. Ethics approval for the study was obtained from the institutional review board of Tehran University of medical sciences.

Statistical analysis was performed by SPSS chi-square test and fisher exact test. *P*-value less than <.05 was considered as a significant level.

## Results

In this study, we evaluated total serum calcium, ionized calcium as well as QTc in the patients with a first seizure, frequent seizure, and normal children. Total calcium < 8.6 mg % was seen in 4.6% of control (1 case), 16% of first seizure (4 cases) and 32% of frequent seizures (8 cases).

Total Ca level was higher in control than in case groups (*P*=0.001). The serum ionized calcium in the control group was also more than two other groups, the difference was significant (*P*=0.0001). QTc was normal in 80% of control group, 36% of first seizure and 20% of frequent seizure (below 0.42 Sec), but it was over 0.42 Sec in 19% of control, 64% of first seizure and 80% of frequent seizures. In an analysis by Man-Whitey test these differences were considered significant (*P*=0001) (Table 1).

**Table1. Comparative values in three groups**

| Groups | Control (25) | First seizure (25) | Frequent seizure (25) | *P*-value |
|---|---|---|---|---|
| **Total Ca (mg %)[mean±SD]** | 9.66±0.07 | 8.64±0.19 | 8.16±0.32 | 0.001 |
| **Ionized Ca (meq/L) [mean±SD]** | 3.83±0.08 | 3.26±0.05 | 3.18±0.04 | 0.0001 |
| **Normal QTc [number (%)]** | 21 (80) | 9 (36) | 5 (20) | 0.0001 |
| **Prolong QTc [number (%)]** | 5 (19) | 16 (64) | 20 (80) | |

We observed a significant correlation between QTc and low ionized calcium (r=.93, *P*=0.0001), but we could not find any association between Qtc and total serum calcium.

## Discussion

Seizure is one of the most common problems in pediatric age group; nearly 5% of convulsions in the first year of age is provoked by somatic disorders originating outside the brain.

One of the most common electrolyte abnormalities that induce convulsion is hypocalcemia especially in newborn as well as in cases with frequent seizures due to low appetite, feeding problem, low sun exposure, isolation and mostly due to using frequent antidepressant drugs (1,2).

So serum ionized calcium level is the hallmark of hypocalcemia. But it seems impossible to check in many medical centers in Iran because of its cost. This study is the first investigation in our country for finding a correlation of checking total calcium, ionized calcium, and QTc. QTc is prolonged temporally in hypocalcemia, so it could be used as a method for ionized Ca evaluation

Based on present results total calcium and ionized Ca were higher in the control group than children with a seizure. Current finding was consistent with other studies. Sinert *et al.*, in 2007 stated in their study a significant alteration in serum ionized calcium during certain types of seizures (8). Hypocalcemia is defined as ionized calcium < 1.22 mmol/L may present ranging from myoclonic jerk to seizure, apnea and cardiac arrhythmia (9), Hypocalcemic seizure was seen also in children with rickets and hypomagnesemia that make impairment in Ca absorption (10-12).

We found a significant correlation between seizure and prolonged QTc, that it was compatible with others' study. Sadrnia *et al.,* in 2013 showed long QTc in children with unknown causes of seizure. They pointed to possible link in cardiac and cerebral channelopathy (13). The incidence of prolonged QT in the seizure, syncope and attention deficit hyperactivity disorder has been shown significantly in Jha *et al.,* study in 2010 (14).

In this study, authors also observed that children with low ionized calcium had prolonged QTc. QTc is affected by different factors such as hypocalcemia and hypomagnesemia (15). Kumar *et al.*, in 2000 reported prolonged QTc and hypocalcemia in patients with cerebral malaria convulsion (4). Hypocalcemia, cardiac hypertrophy, and autonomic nervous system dysfunction have been reported in a study from Japan (5). In our previous study, among 497 cases of frequent seizure, we found prolonged QTc (> 0.42 Sec) in 40.84% patients, which after 3 days intravenous calcium administration, QTc was below 0.4 sec, total calcium was between 9-11 mg% but only 17% (34 cases ) had hypocalcemia (total calcium level below 8mg%). Unfortunately, we could not check ionized Ca in that study. This study may improve our previous knowledge for finding a correlation of checking total calcium, ionized calcium and QTc. Checking QTc in suspicious hypocalcemia could be a rapid and easy method for its documentation in seizure cases. This research could be continued in several centers for better evaluation and giving more information.

## Acknowledgment

This study was conducted in Department of Pediatric Neurology of Imam Khomeini Hospital and outpatient clinic of Children Medical Center of Tehran University of Medical Sciences.

This work was supported by a grant from Tehran University of Medical Sciences.

## References

1. Johnston M. Seizures in childhood. In: Kliegman RM, Berhman RE, Jenson HB, et al, editors. Nelson' textbook of pediatrics. 18th edition. Philadelphia: Saunders Elsevier Can 2007; p. 2457
2. Frank Y. Ashwa S. Neurologic disorders associated with the gastrointestinal disease. Nutritional deficiencies and fluid electrolyte disorders. In: Swainnan KF, Ashwal S, Ferroiero MD, editors. Pediatric Neurology Principles and Practice. 4th ed. Philadelphia; Mosby Elsevier Co; 2006; p.2327-8.
3. Rasmussen H. The calcium messenger system. N Engl J Med 1986;314(17):1904-101.
4. Soniel Kumar MR, Gupta BK. Prognostic implication of hypocalcemia and QTc interval in malaria. Indian J Malariol 2000;37(3-4):61-7.
5. Huang TC, Cechin FC, Mahoney P, et al. Corrected QT interval prolongation and syncope associated with pseudo hypoparathyroidism and hypocalcemia. J Pediatr 2000;136(3);404-7.
6. Kurosu M, Ando Y, Akimoto T, et al. Factors related to the QT prolongation in chronic renal failure. Nihon Jinzo Gakkai Shi 1999;41(2):70-6.
7. Azarfar A. Comparative evaluation between total calcium serum and prolonged corrected QT interval.
8. Sinert R, Zehtabchi S, Desai S, et al. Serum ionized magnesium and calcium levels in adult patients with seizures. Scand J Clin Lab Invest 2007;67(3):317-26.
9. Thomas TC, Smith JM, White PC, et al. Transient Neonatal Hypocalcemia: Presentation and Outcomes. Pediatrics 2012;129(6):e1461-7.
10. Visudhiphan P, Visudtibhan A, Chiemchanya S, et al. Neonatal seizures and familial hypomagnesemia with secondary hypocalcemia. Pediatr Neurol 2005;33(3):202-5.
11. Lynch BJ, Rust RS. Natural history and outcome of neonatal hypocalcemic and hypomagnesemic seiures. Pediatr Neurol 1994;11(1)23-7.
12. Bellazzini MA, Howes DS. Pediatric hypocalcemic seiures: A case of Rickets. J Emerg Med 2005;28(2):161-4.
13. Sadrnia S, Yousefi P, Jalali L. Correlation between seizure in children and prolonged QT interval. ARYA Atheroscler 2013;9(1):7-10.
14. Jha OP, Khurana DS, Carvalho KS, et al. Assessment of the QT interval in the electroencephalography (EEG) of children with syncope, epilepsy, and attention-deficit hyperactivity disorder (ADHD). J Child Neurol 2010;25(3):284-6.
15. Bednar M, Harrigan EP, Anziano R, et al. The QT Interval. Prog Cardiovasc Dis 2001;43(5 Suppl 1):1-45.
16. Moseley B, Bateman L, Millichap J, et al. Autonomic epileptic seizures, autonomic effects of seizures, and SUDEP. Epilepsy Behav 2013;26(3):375-85.