Could the QTc prolongation seen in diabetic ketoacidosis be due to more than just a raised anion gap?

To the Editor:

Perez et al[1] demonstrated that nearly one-third of patients presenting with diabetic ketoacidosis (DKA) had QTc prolongation. The authors demonstrated a significant correlation between the QTc and anion gap and, therefore, hypothesized that the QTc prolongation seen was secondary to an elevated anion gap and metabolic acidosis.

The authors evaluated whether the change in QTc was related to electrolyte abnormalities, but they did not assess other features of the clinical presentation that may have caused the QTc prolongation observed.

The patients' temperatures are not documented in the study. As cold sepsis could be a precipitant for ketosis, the associated hypothermia should, therefore, be considered as a cause for QTc prolongation.[2]

Hypothyroidism is another autoimmune endocrine condition that is closely associated with type 1 diabetes mellitus and often related to poorer diabetic control.[3] Raised thyroid-stimulating hormone levels is a well-established cause of QTc prolongation,[4] however, thyroid function was not assessed in the acute setting or during follow-up of the Perez et al study.[1]

Lastly, a well-established complication of DKA treatment in the pediatric population is cerebral edema.[5] Raised intracranial pressures are another cause of QTc prolongation, but the authors have not assessed whether this may have occurred during their study.

Although we acknowledge that there is a strong correlation between QTc prolongation and anion gap in patients with DKA, the above confounding factors that could also cause QTc prolongation should be assessed.

Rebecca Clarke, MBBS, BSc
Pediatric Emergency Medicine
North Middlesex Hospital
London, United Kingdom

Adam Ioannou, MBBS, BSc, MRCP
Department of Cardiology
Hammersmith Hospital
London, United Kingdom

https://doi.org/10.1016/j.jpeds.2020.12.027

The authors declare no conflicts of interest.

References

1. Perez MM, Medar S, Quigley L, Clark BC. QTc Prolongation in pediatric patients with diabetic ketoacidosis. J Pediatr 2021;228:235-9.e2.
2. Aslam AF, Aslam AK, Vasavada BC, Khan IA. Hypothermia: evaluation, electrocardiographic manifestations, and management. Am J Med 2006;119:297-301.
3. Fatourechi A, Ardakani HM, Sayarifard F, Sheikh M. Hypothyroidism among pediatric patients with type 1 diabetes mellitus, from patients' characteristics to disease severity. Clin Pediatr Endocrinol 2017;26:73-80.
4. Akın A, Unal E, Yıldırım R, Ture M, Balık H, Haspolat YK. Evaluation of QT dispersion and Tp-e interval in children with subclinical hypothyroidism. Pacing Clin Electrophysiol 2018;41:372-5.
5. Jayashree M, Williams V, Iyer R. Fluid therapy for pediatric patients with diabetic ketoacidosis: current perspectives. Diabetes Metab Syndr Obes 2019;12:2355-61.

Reply

To the Editor:

We read with interest the letter from Clarke and Ioannou regarding our study. Although we acknowledge the risk of confounding, given the retrospective nature of our manuscript, we feel it is highly unlikely that these factors had an impact on our results.

Although hypothermia has been associated with QTc prolongation,[1] infection is a rare cause of diabetic ketoacidosis (DKA) in developed countries and accounts for only 15% of cases of DKA.[2] Hypothermia could not be attributed as a cause of QTc prolongation in our cohort, as none of the 96 patients had a temperature <35°C during their course of illness on further review of the data.

The authors acknowledge the association between type 1 diabetes mellitus and thyroid disorders; however, DKA has been shown to be associated with sick euthyroid syndrome and a normal thyroid-stimulating hormone.[3] It is difficult to imagine a consistent relationship between DKA severity and thyroid-stimulating hormone elevation that could drive the association with QTc prolongation.

Cerebral edema occurs in <1% of cases of DKA,[4] so this rare potential confounder was not specifically assessed. Our data (Table I) did demonstrate a statistically significant heart rate elevation by severity of DKA, which would challenge the assertion that increased intracranial pressure had a clinical impact, especially in the severe DKA group. Furthermore, the association between elevated intracranial pressure and QTc prolongation has mostly been observed in cases of subarachnoid hemorrhage.[5]

We would again like to thank our colleagues for their interest in our article.

Michelle M. Perez, MD
Bradley C. Clark, MD
Children's Hospital at Montefiore, Bronx
New York

https://doi.org/10.1016/j.jpeds.2020.12.028