

Does Anemia Cause QT Prolongation in Patients with Hematologic Disorders?

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To the Editor: Patients with long QT syndrome have an increased risk of torsades de pointes, ventricular fibrillation, and sudden death. It has been reported in recent studies that sickle cell disease, a specific type of anemia, is associated with acquired long QT syndrome (ALQTS), and reduced hemoglobin (Hgb) level is correlated with a longer QT interval in these patients.^[1-3] However, it is unclear whether anemia itself can cause QT prolongation. We hypothesized that QT prolongation should be common in patients with anemia if it can cause ALQTS directly, and aimed to test this hypothesis in patients with anemia caused by conditions other than sickle cell disease.

Upon approval by the Institutional Review Committee of Xinhua Hospital, a retrospective medical record review was conducted in 456 patients initially with Hgb <100 g/L who were admitted to Hematology Department for the treatment of hematologic disorders other than sickle cell disease. Among them, 34% (156/456) had known risk factors for developing ALQTS and, therefore, were eliminated from the study. Fifteen of the excluded patients showed QT prolongation (QTc 464 ± 24 ms) in the presence of one or multiple risk factors of ALQTS such as Hypocalcemia (*n* = 10), hypokalemia (*n* = 5), chronic kidney disease (*n* = 4), left ventricular hypertrophy (*n* = 3), and/or using QT-prolonging drugs (*n* = 5).

The remaining 300 study subjects who met the study inclusion criteria had moderate to severe anemia (Hgb 80 ± 16 g/L, range 19–99 g/L). At the heart rate of 87 ± 17 bpm, their average QTc was normal (414 ± 23 ms). The etiologies leading to anemia are listed in Table 1, and the result of the analysis of variance (ANOVA) revealed no statistical significance between the QTc length between these groups (*F* = 1.280, *P* = 0.247). Twenty-one patients had QTc ≥440 ms, nevertheless 7/21 of them had a wide QRS (>120 ms) including complete left (*n* = 4), right (*n* = 1) bundle branch blocks and right ventricular pacing (*n* = 2), respectively. JT indexes were much less than the cut point of 112 ms^[4] in all subjects showing a wide QRS, indicating their repolarization time was normal. After eliminating those with wide QRS, only 5% (14/300) of anemic patients showed borderline to moderate QT prolongation (461 ± 13 ms, range: 441–479 ms), which is similar to what is seen in the general population. None of them experienced syncope, cardiac arrest, or sudden death. Linear regression analysis revealed no significant correlation between Hgb level and QTc interval (*r* = 0.031, *P* = 0.587). Stepwise

multivariable regression analysis accepted age as the only correlated variable (*r* = 0.262, *P* < 0.01); Hgb (*r* = 0.012, *P* = 0.833), heart rate (*r* = -0.016, *P* = 0.785), serum creatinine (*r* = -0.069, *P* = 0.232), potassium (*r* = -0.076, *P* = 0.190), calcium (*r* = -0.010, *P* = 0.860), sodium (*r* = -0.024, *P* = 0.673), chloride (*r* = -0.025, *P* = 0.668), phosphate (*r* = -0.027, *P* = 0.643), and magnesium (*r* = 0.002, *P* = 0.969) were all excluded from the regression.

To determine whether the severity of anemia affects QTc interval, study subjects were then divided into three groups by Hgb levels. The prevalence of moderate anemia (Hgb 60–90 g/L) was 56%, and severe anemia (Hgb <60 g/L) was 12%. The QTc of each group was calculated, and the result of ANOVA showed no statistical significance between the QTc length in the three groups (*F* = 0.422, *P* = 0.656).

Table 1: Etiologies of anemia in 300 patients

Etiology	Count	Hemoglobin, g/L*	QTc, ms*
NonHodgkin's lymphoma	83	86.3 ± 11.1	416.02 ± 25.51
Acute myelocytic leukemia	58	79.8 ± 14.6	415.05 ± 22.65
Acute lymphocytic leukemia	42	78.9 ± 13.2	408.02 ± 23.95
Myelodysplastic syndrome	26	65.3 ± 16.1	418.62 ± 23.42
Multiple myeloma	23	83.5 ± 12.6	402.57 ± 22.81
Chronic lymphocytic leukemia	16	87.6 ± 9.5	416.56 ± 16.02
Aplastic anemia	12	55.7 ± 20.4	417.92 ± 16.49
Iron-deficiency anemia	9	76.8 ± 16.3	414.44 ± 18.06
Chronic myelocytic leukemia	5	78.6 ± 17.5	410.00 ± 20.17
Others	26	81.2 ± 17.6	417.42 ± 22.10

*Values are mean ± SD. SD: Standard deviation.

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After removing known causes of QT prolongation, we have found that QT intervals are normal in most anemic patients where the anemia is due to hematologic disorders other than sickle cell disease. However, 34% (156/456) of the reviewed anemic patients carried risk factors for ALQTS. It is possible that many of the sickle cell anemia patients in previous studies also carried risk factors of ALQTS. For example, anemia increases heart rate and over time untreated severe anemia could lead to development of tachycardia-cardiomyopathy that could then result in ALQTS based on our unpublished information. In late stages of tachycardia-cardiomyopathy, patients can develop heart failure. Management of heart failure often requires multiple medications that can prolong the QT interval.

In conclusion, based on our study results, anemia itself does not directly cause QT prolongation. However, many anemic patients do carry the risk of developing ALQTS, which is an independent measure of sudden cardiac death.

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Conflicts of interest

There are no conflicts of interest.

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