Digitalis Administration: An Underappreciated but Common Cause of Short QT Interval

To the Editor:

I read with interest the recent report by Gaita et al.1 of short-QT syndrome as a familial cause of sudden death. The authors enumerated other factors that shorten QT interval, such as increased heart rate, hyperthermia, hypercalcemia, hyperkalemia, acidosis, and altered autonomic tone.1 I would like to add another important and common, but underappreciated, cause of short QT interval, that is, administration of digitalis preparations.

Because digitalis administration is such a common everyday occurrence in the management of patients with congestive heart failure and in those with atrial fibrillation or paroxysmal atrial tachycardia, its effect on the QT interval should be kept in mind when evaluating ECG changes. Although PR prolongation is a commonly recognized ECG manifestation of digitalis administration, QT shortening is less well known. As a matter of fact, in several case reports in which ECGs were presented,2–5 the short QT interval was not mentioned even though it was present. The property of digitalis preparations to shorten the QT interval is useful clinically in the differential diagnosis of ST-T changes associated with left ventricular hypertrophy, myocardial ischemia, myocardial infarction, or bundle branch block, in all of which the QT-interval is prolonged. The shortened QT interval and the characteristic sagging, “coved,” or “scooped” appearance of the asymmetric and downsloping ST depression, which resembles a reversed check mark, constitute the typical “digitalis effect” on ECG.

The presence of a digitalis effect on ECG does not by itself connote digitalis intoxication. On the other hand, the same mechanism of sudden death in the familial short-QT syndrome as described by Gaita et al.1 could play a role in fatal digitalis poisoning, either iatrogenic or suicidal, besides its association with hyperkalemia in patients with chronic renal insufficiency.

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Response

In the paper recently published in Circulation, we described a new genetic syndrome, in which a short QT interval on ECG was associated with a high incidence of sudden death.1 These subjects also had a high incidence of atrial arrhythmias; at electrophysiological study, effective refractory periods were very short at both the atrial and ventricular level, and ventricular fibrillation was inducible.2 In our families genetic screening has been performed and two different missense mutations have been found, which result in hyperfunction of IKr (human ether-a-go-go gene, HERG).3 The consequence is a heterogeneous abbreviation of action potential duration and refractoriness at both the atrial and the ventricular level. Short and inhomogeneous refractory periods favor reentry and thus arrhythmogenesis.

There are also causes of acquired short QT interval. Some of them are cited in our report, and Dr Cheng is now adding another important one. Digitalis glycosides bind specifically to the Na+/K+–ATPase, decreasing the active transport of sodium. The increase in intracellular sodium causes an augmentation of the exchange of intracellular Na+ for extracellular Ca++. This can cause an increase in K permeability.4 An increased outward current during the plateau is probably the mechanism of the action potential duration and effective refractory period reduction. Digitalis shortens QT interval mainly at high plasma concentrations. Short-QT syndrome has a genetic basis, whereas the short QT of digitalis intoxication is acquired. However, the final mechanism of arrhythmogenesis in some cases of digitalis toxicity could be very similar to that of the genetic short-QT syndrome.

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