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LETTERS TO THE EDITOR

More on the History of Arrhythmia in Long QT Syndrome

I read with great interest the report by Etheridge et al. (1) entitled "A New Oral Therapy for Long QT Syndrome."

First, I should like to congratulate the investigators for their valuable contribution. They found that in patients with long QT syndrome due to HERG mutations there was an improvement in repolarization in parallel with a normalizing serum potassium level after oral potassium (and spironolactone) administration.

Their final sentence summarizes the present situation as follows: "Further studies are warranted to determine whether they will reduce the incidence of life-threatening events in LQTS patients" (1).

We agree with this statement completely, but I would additionally draw the attention of the authors of the study and the Editorial Comment (2) to the family reported by Gamstorp et al. (3) some 40 years ago. Although the affected members of the family were slightly hypokalemic, the administration of potassium led not only to a diminishment of the electrocardiographic abnormalities but also to cessation of the Adams-Stokes attacks.

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REPLY

We thank Dr. Csanády for his interest in our report (1) and for bringing to our attention the report by Gamstorp et al. (2) of a family whose members presented with syncope associated with hypokalemia. Although hypokalemia is a known trigger for life-threatening arrhythmia in long QT syndrome (LQTS) patients, the consistent finding of hypokalemia in this family suggests a fundamental abnormality of potassium homeostasis. Hypokalemia is a common feature of Andersen-Tawil syndrome, triggering both skeletal muscle paralysis and ventricular arrhythmias. We would like to emphasize that no subject in our study was hypokalemic at baseline, and therefore the therapy did not normalize patients' serum potassium but, rather, increased their serum potassium to the upper limits of normal.

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Impaired Vascular Reactivity in Patients With Erectile Dysfunction

In the January 21, 2004 issue of the *Journal,* Kaiser et al. (1) reported about endothelial function in patients with erectile dysfunction (ED) and no vascular risk factors. They found this group as having significantly less vasodilation to both ischemia (endothelium dependent) and nitroglycerin (endothelium independent) stimuli than normal subjects. These data led the investigators to conclude there was a peripheral vascular defect occurring before the development of overt vascular disease, thus reinforcing the concept of ED as an early marker for systemic vascular disease (1).

We believe that one major point needs clarification. Patients were classified as having ED according to the International Index of Erectile Function (IIEF) (2). This is a 15-item validated self-administered questionnaire that explores five domains of sexual function: erectile function, orgasmic function, sexual desire, intercourse satisfaction, and overall satisfaction. Erectile function is specifically addressed by six questions, 1, 2, 3, 4, 5, and 15, which form the so-called "erectile function domain" of the questionnaire. Each question is scored 0 (or 1) to 5 with a minimum and maximum score of 1 and 30, respectively. Erectile dysfunction is defined as any value <26. Below this cut-off

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point, ED is further defined as mild (22 to 25), mild-to-moderate (17 to 21), moderate (11 to 16), and severe (<10) (3). In the Kaiser et al. (1) study, "normal" subjects had a mean (±SD) score of the IIEF erectile function domain of 21.3 ± 5.3. Assuming a normal distribution, this means that almost 80% of normal subjects were below the cut-off for ED, of whom 40% likely had an IIEF score <20 (mild-to-moderate ED) and 10% <15 (moderate ED). Thus, many "normal" subjects were actually impotent, although to a lesser degree than the true ED group. However, penile color Doppler sonography (the only test that might have further differentiated the two groups) was not performed in normal subjects, and this makes any comment conjectural.

If this observation holds true, differences in the vascular response between groups should be reconsidered. In fact, if the dilation response of "normal" patients with ED is combined with dilation response of the real ED group, one would expect to obtain a higher mean value of percent vascular dilation. For example, percent dilation at 60 s after cuff release was 2.4 ± 0.5 versus 3.7 ± 0.5 in the ED and normal group, respectively. If combined, a mean value of 3% would reasonably become evident. This result, to still be significantly lower, would require normals to show an even higher dilation response, about 4% to 4.5%. This figure seems to be a rather unusual response after wrist occlusion (4).

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REPLY

Dr. Montorsi and colleagues express concerns over the International Index of Erectile Function (IIEF)-15 data presented in our study (1). We inadvertently stated that the data presented were the erectile dysfunction (ED) domain of the IIEF-15, but in fact the data cited in our report were an average of each individual domain of the IIEF-15. In response to their letter to the editor we went back to the raw data and calculated both the ED domain of the IIEF-15 and the IIEF-5 (an abbreviated version of the IIEF-15). These results are presented below.

The IIEF-15 domain consists of six questions (1, 2, 3, 4, 5, and 15) with a maximum score of 30 and a cut-off of <25 for ED (2). The ED group in our study had an IIEF-15 ED domain score of 16.1 versus 26.8 for the normal group ($p = 0.000001$).

The IIEF-5 is a validated brief version of the longer questionnaire (questions 2, 4, 5, 7, and 15 of the IIEF-15) (3,4). These five questions have been found to discriminate most highly between men with and without ED. The maximum score for the IIEF-5 is 25, with a cut-off of <21 for ED. The ED group in our study had an IIEF-5 of 12.9 versus 22.3 for the normal group ($p = 0.000001$).

We appreciate the opportunity to clarify this issue. Based on the results listed above for the ED domain of the IIEF-15 and the IIEF-5, our patients had significant symptoms of ED and our control subjects did not have ED. Therefore, the significance of our original observations is valid, and no further reassessments of the data are warranted.

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