Dio...gical heart failure at low serum digoxin concentrations

Digoxin and reduction in mortality in systolic and diastolic heart failure at low serum digoxin concentrations

The DIG trial is the largest trial of digoxin and a very important trial that is not likely to be replicated soon. Therefore, the analyses of Ahmed et al.1 is useful and welcomed. One important conclusion of their study is that 'SCD 0.5–0.9 reduced mortality in a wide spectrum of HF patients and had no interaction with ejection fraction (EF) >45% (P = 0.834).' However, their Figure 4 shows that in patients with EF >45% and SDC 0.5–0.9 ng/dL, the HR (95% CI) for all-cause mortality was not 'significantly' better than placebo. Is this correct? What were the numbers of patients in these subgroups? It would be most helpful if the authors provided Kaplan–Meier curves of mortality and of hospitalization in those with EF >45% and SDC 0.5–0.9 vs. placebo and probably also vs. higher SDC.

Of interest: (i) all-cause mortality in placebo and SDC 0.5–0.9 was similar to our analysis, if one excluded deaths due to 'probable' and 'possible' digoxin toxicity; (ii) it is particularly gratifying that they have dedicated their article to the memories of Thomas W. Smith, M.D. and Richard Gorlin, M.D. as was done in an earlier article.3

References

Dario Giugliano
Division of Metabolic Diseases
Policlinico Seconda Università di Napoli
Piazza L. Miregria
80031 Napoli
Italy
Fax: +39 (0) 81 5665054
E-mail address: dario.giugliano@unina2.it

Katherine Esposito
Division of Metabolic Diseases
Centre of Excellence for Cardiovascular Diseases
University of Naples SUN
Naples
Italy

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Our study also demonstrated that digoxin reduced HF hospitalization regardless of serum digoxin concentrations (SDC). Furthermore, we observed that in patients who achieved low SDC (0.5–0.9 ng/mL), digoxin was associated with reduction in all-cause mortality and all-cause hospitalizations,1 in a subgroup analysis, we found no significant interaction between digoxin and any major patient characteristic, including sex and ejection fraction.

Our subgroup analysis based on low SDC and placebo patients included 4843 patients: 982 patients receiving digoxin who had low SDC and 3861 patients receiving placebo. Of these, 602 (12%) had diastolic HF: 108 patients with low SDC and 494 patients receiving placebo. The magnitude of the absolute and relative reductions in total mortality was comparable between patients with systolic and diastolic HF, and there was no significant heterogeneity in the effect of digoxin between these two groups (adjusted P for interaction 0.834).1

References