

CORRESPONDENCE

Letters to the Editor

Carvedilol for Anthracycline Cardiomyopathy Prevention

Kalay et al. (1), in a population of apparently unselected patients receiving their first 6 cycles of anthracyclines, found in their control group a high incidence of functional cardiomyopathy: 24% of their patients had at the final examination an ejection fraction of 50% or less. This incidence of cardiac dysfunction is higher than the expected one for patients beginning their exposure to anthracyclines (2); this must be clearly explained, because it is the base of the suggested treatment effect: only one patient of the carvedilol group developed functional cardiomyopathy. The only risk factor for cardiomyopathy development that is apparently present in this relatively young population is a high accumulated dose, with a mean of 513.6 mg/m² for adriamycin users and of 770.4 mg/m² for epirubicin users, in the control group. The carvedilol-treated group received about the same mean doses.

Unfortunately, the investigators do not report the standard deviation of the total doses administered. If there is a large dispersion of data, the “nonsignificant” Student *t* test reported for the comparison of total doses between groups loses confidence. Large dispersion of data in this regard may imply different distribution of total doses, with consequent different risks to both groups, independently of the influence of treatment on cardiac prognosis. When one is trying to reach conclusions with a small set of data, meticulous presentation of both data and appropriate statistics is mandatory.

Also, the total dose of adriamycin and epirubicin appears unusually high in a population naïve to previous anthracycline exposure: we calculate cycles of about 87 mg/m² for adriamycin users and about 130 mg/m² for epirubicin users, which are not the usual doses for breast cancer or lymphoma treatment. This also requires clarification.

***Fernando Florenzano, MD**
Pamela Salman, MD

*Department of Medicine
University of Chile
Av Salvador 486
Santiago
Region Metropolitana
Chile
E-mail: fflorenz@med.uchile.cl

doi:10.1016/j.jacc.2007.03.016

REFERENCES

1. Kalay N, Basar E, Ozdogru I, et al. Protective effects of carvedilol against anthracycline-induced cardiomyopathy. *J Am Coll Cardiol* 2006;48:2258–62.
2. Swain MS, Whaley FS, Ewer MS. Congestive heart failure in patients treated with doxorubicin. *Cancer* 2003;97:2869–79.

Reply

We thank Drs. Florenzano and Salman for their valuable comments regarding our study (1). Four types of anthracycline cardiotoxicity are described: acute, subacute, chronic, and late onset. Acute complications can be seen in 0.4% to 41% of patients (2). We performed echocardiography after chemotherapy and evaluated both acute and subacute cardiotoxicity. Dilated cardiomyopathy is the most important complication of chemotherapy. It is associated with certain risk factors: dose, administration rate, gender, age, underlying heart diseases, hypertension, irradiation, and the human epidermal growth factor receptor-2.

Mean decrease in left ventricular ejection fraction (LVEF) in our control group was 16.6%. It was demonstrated that gradual decrease in LVEF was 1.9% with every 50-mg anthracycline dose. Decrease in LVEF in our study was concordant with this information. However, both LVEF and cardiomyopathy incidence may change with risk factors. The incidence of subclinical cardiomyopathy is not exactly known. It has been demonstrated that doxorubicin-induced subclinical cardiomyopathy can be 27.6% (3), and the troponin I increase can be 33% of patients after chemotherapy, and this increase is associated with decreased LVEF (4). In another study (5), patients who had received chemotherapy were randomized either to receive or not to receive an angiotensin-converting enzyme inhibitor, and the primary end point was >10% decrease in LVEF. The primary end point was 0% in the treatment group and 43% in control subjects. These results suggest that systolic dysfunction may occur in many patients. Decompensated heart failure was shown in one patient in our groups, but subclinical cardiomyopathy was demonstrated in additional patients.

The main result of our study showed that carvedilol may prevent anthracycline-induced cardiomyopathy. Our study is a preliminary one in this issue. We enrolled cancer patients, so patients with different types of disease at different stages were included in the trial. Although we had a small number of patients, the distribution of disease types and the anthracycline dose used in the patient group were well balanced between the groups. The dose of anthracycline changes with the treatment scheme. Moreover, the number of standard cycles is 6; in some cases additional cycles may be used depending on the scheme employed and the oncologist's preference. Most of our patients received adriamycin, and the regular dose was 65 to 75 mg/m², but higher doses were used in some patients. Furthermore, it is known that the cardiotoxicity incidence increases with increased doses of adriamycin and epirubicin above 550 and 900 mg/m², respectively (6).

***Nihat Kalay, MD**
Ibrahim Ozdogru, MD
Ozlem Er, MD
Emrullah Basar, MD