Meta-Analysis of Carvedilol versus Conventional Treatment in Children with Systemic Ventricle Systolic Dysfunction

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Introduction. Numerous randomized clinical trials in adults with chronic heart failure demonstrated favorable effect of beta-blockers. Treatment in children with systemic ventricle systolic dysfunction includes beta-blockers (carvedilol), although benefit was not recognized sufficiently (mainly due to limited number of pediatric patients).

Methods. We performed meta-analysis, aimed to compare carvedilol and conventional treatment (i.e. digoxin, diuretics, ACE inhibitors) with respect to clinical and echocardiographic outcome in children with chronic heart failure due to impaired systemic ventricle systolic function. We have systematically searched the Medline/PubMed and Cochrane Library for the prospective/observational clinical trials on carvedilol and standard treatment efficacy in pediatric (up to 18 years) heart failure patients. Mean differences for continuous variables, odds ratios for dichotomous outcomes, heterogeneity between studies and publication bias were calculated using Cochrane Review Manager (Rev Man 5.2).

Results. After screening of 391 publications, total of 8 prospective/observational studies (with 516 patients) met established criteria. At the start of studies, there were no differences in the left ventricular end-diastolic diameter (p = 0.17), ejection fraction (p = 0.99) and fractional shortening (p = 0.30) between groups. However, at the end of studies, significantly better ejection fraction (difference 5.2%; 95% CI: 2.4-7.9%; p = 0.0003) and fractional shortening (difference 3.4%; 95% CI: 1.7-5.1%; p <0.0001) was demonstrated in the carvedilol vs. control group. Decrease in the end-diastolic diameter was better during the carvedilol treatment, but without statistical significance. Odds ratio for chronic heart failure related mortality/heart transplantation secondary to carvedilol was 0.52 (95% CI: 0.28-0.97; p = 0.04), with non-significant heterogeneity between studies and no impact of publication bias. Our analysis showed that carvedilol could prevent 1 death/heart transplantation by treating 14 pediatric patients with impaired systemic ventricle systolic function. In addition, odds ratios for clinical improvement and worsened clinical outcome secondary to carvedilol were 1.54 (95% CI: 0.98-2.43; p = 0.06) and 0.60 (95% CI: 0.36-1.00; p = 0.05) respectively.

Conclusions. To the best of our knowledge, our meta-analysis demonstrated, for the first time, clinical outcome and mortality/heart transplantation benefits in carvedilol vs. conventional treatment group of pediatric patients with chronic heart failure.