Dilated Cardiomyopathy in Children: when and how can we use Beta-Blockers

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Dilated cardiomyopathy is characterized by dilatation and impaired contraction of the left ventricle or both ventricles. It may be idiopathic, familial/genetic, viral and/or immune, alcoholic/toxic or associated with recognized cardiovascular disease in which the degree of myocardial dysfunction is not explained by the abnormal loading conditions or the extend of ischemic damage. Histology is nonspecific. Presentation is usually with heart failure, which is often progressive. Arrhythmias, thromboembolism, and sudden death are common and may occur at any stage [1].

The incidence of cardiomyopathy in infants and children is difficult to assess, in part because of the variation in diagnostic criteria in different regions of the world and in part because of the heterogeneous etiologies of the disease [2]. Arola et al reported in Finland the annual incidence of idiopathic dilated cardiomyopathy in children of 0.34 cases per 100.000 of the age-specific population, with 52% occuring in the first year of life [3].

The natural history of dilated cardiomyopathy in children is unclear. A 5-year survival can range from less than 40% to 80%. Undoubtedly this variability is due to the source of patients in individual studies [5-10].

In children, the symptoms of heart failure include tachypnea, tachycardia, poor feeding. The common findings are hepatomegaly, diastolic gallop on physical examination, and cardiac enlargement with or without pulmonary edema on chest radiograph [11]. The class measures developed by the New York Heart association [12] and the Ross scale [13] has been developed to evaluate heart failure in infants, children and adolescents.

Cardiomyopathy investigations should vary with type of heart muscle disease-for example, restrictive, hypertrofic, and dilated. Most new onset heart failure in children is caused by congenital heart disease. Therefore, this should be excluded at the initial assessment. Anomalous left coronary from the pulmonary artery will present with dilated left ventricle and this may cause confusion with dilated cardiomyopathy. Thus, careful general assessment of children with myocardial dysfunction include ECG, echocardiography, investigation of myocarditis, autoimune and mitochondrial diseases [14].

Modern management of heart failure has become more than the normalization of cardiac output and the improvement of symptoms. Neuroendocrine stimulation, myocyte remodeling, cellular energetics and connective tissue/myocyte interations are equally considering when treating children with heart failure [15]. The therapeutic goals include the "normalization" of altered hemodynamics and amelioration of symptoms [16]. To this end inotropes, inodilators, vasodilators and diuretics are the drugs used primarily depending on the clinical features of each patient.

The use of beta-blockers in the treatment of congestive heart failure in adults has been shown to reduce the risk of hospitalization and death in mild-to-moderate heart failure [17,18].

The exact mechanism of action of beta-blocking agents in chronic heart failure is still not entirely clear. The acceptable hypothesis is that the primary mechanism of action of beta-blocking agents in chronic heart failure is to prevent and reverse adrenergically-mediated intrinsic myocardial dysfunction and remodeling [19,20]. First generation beta-blockers (propranolol) are non-selective for beta1 or beta-2 blockade and have no ancillary properties. Second generation beta blockers (e.g. metoprolol, bisoprolol) are selective for beta-1 or beta-2 blockade, but also have no ancillary properties. Third generation beta-blockers (e.g. carvedilol, buncindolol) are either B1 and B2-blockade, however bucindolol has no alfa1-blockade [21]. Carvedilol, a nonselective third-generation beta-blocker, vasodilator secondary to alpha-adrenergic blockade with antioxidant activity and apoptosis inhibition has been demonstrated to favorably affect survival in adult patients with severe chronic heart failure [22].
The experience with beta-blockers in children with congestive heart failure is limited and previous studies were not double-blinded or randomized with placebo controlled group [23-29].

We first reported the results of a prospective, randomized, double-blind, placebo-controlled study of carvedilol experience in children with severe, chronic heart failure, despite the use of conventional therapy [30]. We conducted a study of 22 consecutive children with severe left ventricle dysfunction (left ventricular ejection fraction less than 30%). Patients were randomly assigned to receive either placebo (8 patients) or carvedilol (14 patients) at 0.01 mg/kg/day titrated up to 0.2 mg/kg/day, followed for six months. In patients receiving carvedilol evaluated after six months, a significant increase occurred in left ventricular ejection fraction, from 17.8% (95% confidence interval, 14.1 to 21.4%) to 34.6% (95% CI, 25.2 to 44.0%); p=0.001. New York Heart Association functional class improved in nine patients taken off the transplant waiting list. All nine patients were alive at follow-up. We concluded that carvedilol added to standart therapy may reduce heart failure progression and improve cardiac function, however in our study we recruited only hemodynamic stable patients with severe dilated cardiomyopathy referred for heart transplantation and it must be emphasized that carvedilol therapy was initiated with extreme caution, in small doses and patients were monitored closely to enhance patient safety.

References

Lab. Gador contributed to the Congress