Intravenous Immunoglobulin in Children with Acute Myocarditis and/or Early Dilated Cardiomyopathy

We retrospectively studied medical records of all children with acute myocarditis and/or early DCM admitted to the Pediatric Critical Care Unit of our hospital between January 2010 and December 2012 were reviewed. 28 patients were included in the study, of which 12 were treated with IVIG (1 g/kg per day) for two days. The patients who received IVIG therapy had a higher left ventricular ejection fraction and a reduced left ventricular end diastolic diameter six months after treatment, as compared to children who had not received IVIG (*P*<0.001 and *P*=0.002, respectively).

Keywords: *Cardiomyopathy*, *Management*, *Myocarditis, Outcome, Steroid.*

Acute myocarditis is defined as inflammation of the myocardium, leading to the sudden onset of heart failure, arrhythmia, fulminant hemodynamic collapse and sudden mortality [1]. They may lead to dilated cardiomyopathy (DCM) and cardiac dysfunction, with serious and lethal consequences. This retrospective study was performed to evaluate the effect of intravenous immunoglobulin (IVIG) on the cardiac function and cardiac rhythm of children with acute myocarditis and/or early DCM.

This was a retrospective analysis of case records of children who presented with acute myocarditis and/or early DCM and admitted in pediatric critical care unit of our tertiary hospital between January 2010 and December 2012. Inclusion criteria were children (age <12 y), acute onset (duration <3 months) congestive heart failure and impaired left ventricular function (On echocardiography, either a left ventricular ejection fraction (LVEF) ≤0.45, left-ventricular end-diastolic volume (LVEDD) of >2 SD above the norm, or a shortening fraction (SF) >2 SD below the mean) following a recent viral illness. Patients with structural heart disease, Kawasaki disease and other specific causes of acute cardiomyopathy were excluded. The study was approved by the Ethics committee of the hospital. Data were collected through patient chart review. Searches were screened and data extracted independently by two reviewers. Quality was assessed by two reviewers using the Jadad scale.

The patients were divided into IVIG therapy and non- IVIG therapy (control) groups. Data analysis of laboratory tests including blood levels of myocardial enzymes, troponin, and C reactive protein; other investigations including electrocardiography, chest *X*-ray and echocardiography were performed prior to and following treatment. Gender, age, cardiac function classification, parameters of echocardiography, blood test data and incidence of complications were compared between the two groups. Echocardiography data was analyzed for by standard methodology. Left ventricular ejection fraction (LVEF), diameter of the left atrium (LA), left ventricular end diastolic diameter (LVEDD), left ventricular systolic diameter (LVSD), diameter of the right atrium (RA) and diameter of the right ventricle (RV) were analyzed. The recovery of left ventricular function was assessed in hospital and post-treatment at 3 and 6 months. IVIG was administered at a dose of 1 gm/kg per day for two days. Other conventional therapies were administered as required in both groups. The primary outcome was survival. Secondary outcomes measures were improve-ment in LVEF and LVEDD on echocardiography; and incidence of fatal cardiac arrythmias. All statistical analyses were performed with the Statistical Package for Social Sciences version 16.0 (SPSS Inc., Chicago, IL, USA).

A total of 35 children were initially eligible for the study; however, 7 were excluded due to insufficient clinical data/non comparable factors. Twenty-eight children were ultimately included. Of these, 12 patients, (7 males) had received treatment with IVIG (1gm/kg per

TABLE I CARDIAC PARAMETERS IN THE TWO GROUPS

Variable measures	*IVIG group (n=12)*	*Control group (n=16)*
LVEF baseline (%)	35.3 (12.2)	33.5 (8.6)
3 mo post-treatment*	50.8 (12.2)	38.6 (14.4)
6 mo post-treatment*	62.2 (10.2)	43.3 (10.4)
LVEDD baseline (mm)#	47.4 (12.4)	50.6 (10.4)
3 mo post-treatment*	42.2 (5.8)	49.6 (10.3)
6 mo post-treatment*	40.6 (4.8)	46.8 (6.2)
VT/VF recovered*	2/3	1/3
AV block recovered*	4/5	1/3
Deaths	2	7

**P<0.01; #P<0.05, VT: Ventricular tachycardia, VF: Ventricular fibrillation; AV: Atrioventricular.*

day) for two days, while the remaining 16 patients (9 males) had not received IVIG therapy. At baseline, children of the two groups did not differ significantly with regard to the echocardiographic data of left ventricular function *i.e.* LVEF and LVEDD. At both three months and six months post-treatment, the mean LVEF and LVDD in the IVIG group was significantly better than control group (P=0.003). The LVEF of both groups had improved significantly at 6 months; however, children treated with IVIG had a significantly higher LVEF than those without IVIG. The episodes of ventricular tachycardia/fibrillation and atrioventricular block were reduced significantly in the IVIG group. There were two mortalities in the IVIG therapy group and seven in the non IVIG therapy group (P=0.032).

Previous studies have indicated the therapeutic effects of the high dose IVIG in acute myocarditis. [2-7]. High dose IVIG is commonly used at dosage of 1gm/kg/day for 2 days [5,8]. However, evidence from Cochrane collaboration review of 2010, based on one trial did not support the use of IVIG for the management of adults with presumed viral myocarditis, and observed that there are no randomized pediatric trials [8]. A randomized controlled trial (RCT) suggested that IVIG did not augment the improvement in LVEF for 62 patients with recent onset dilated cardiomyopathy [9]. We observed that IVIG therapy improved the outcome in such patients. The retrospective nature of the study, no comparison of baseline clinical data of patients, and non-availability of reasons for starting IVIG were the shortcoming of this study.

In conclusion, this study suggests that IVIG for the treatment of acute myocarditis and/or early dilated cardiomyopathy is associated with improved recovery of left ventricular function and a reduction in the episodes of fulminant arrhythmias.

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