



EFFECT OF INTRAVENOUS IMMUNOGLOBULIN IN CHILDREN OF ACUTE MYOCARDITIS IN TERMS OF ECHOCARDIOGRAPHIC FINDINGS

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ABSTRACT

Introduction : Myocarditis is defined as inflammation of heart muscle according to clinical, immunological, and pathological criteria. There have been reports of improved outcomes with the use of IVIG for treatment of myocarditis in paediatric age group. **Aims and Objectives:** The objective of our study was to evaluate the effect of IVIG in children with acute myocarditis in terms of recovery of ventricular function in Echocardiography. **Materials and Methods:** The present study was conducted in the IIMS&R Lucknow. This was an observational study which enrolled children who presented with the fever of acute onset (less than 15 days in duration), and were diagnosed as suspected myocarditis on the basis of clinical features, Troponin I and echocardiography. Children with known cardiac lesions, congenital or acquired, presenting with heart failure were excluded. Their clinical features, cardiac biomarkers and echocardiography findings were compared between Group A, who had received iv immunoglobulin along with standard care and Group B, who had received the standard care alone. Total 90 patients were taken in which 30 patients were in group A and 60 patients were in group B. **Result:** At the time of admission left ventricular ejection fraction <50% was present in 86.6% of Group A and 85 % of Group B patients. At week 1, left ventricular ejection fraction <50% was present in 20% of Group A and 41.6 % of Group B patients. P value was 0.0482 which was significant. Cardiac dilatation (P value= 0.1525), regional wall motion abnormality (P value 0.1905), regional wall hypertrophy (P = 0.3168) between group A and Group B was compared at the time of admission and at week -1, which was found insignificant. At presentation the mean (SD) ejection fraction in group A and group B was 43.6% (11.53) and 44.26 % (5.68), respectively. At week-1, mean (SD) ejection fraction improved from 43.6% (11.53) to 63.6 % (15.25) in group A, and from 44.26% (5.68) to 52.7 % (7.9) in group B. P value in both group at presentation was 0.7161 which was not significant while at week-1 p value was 0.0001 which was statistically significant. (p = 0.0001 between groups A and B). **Conclusion:** The main interest of this study was to know the effect of IvIG in acute myocarditis in terms of improvement in ventricular function based on Echocardiography. All the parameters improved after treatment in both groups. Although, we found only ejection fraction to improve significantly in patients who was given IVIG along with standard care.

KEYWORDS : Acute Myocarditis ,Intravenous Immunoglobulin, Echocardiography.

INTRODUCTION

Myocarditis is an inflammatory disorder of myocardium with necrosis of myocytes and associated inflammatory infiltrate that is categorized into four major types: acute, fulminant, chronic active, and chronic persistent [1]. Myocarditis can manifest a wide spectrum of symptoms, ranging from mild dyspnea or chest pain and sometimes without a specific therapy. It can lead to cardiogenic shock and death [2].

Background

Till now, treatment of myocarditis remains largely supportive. Currently, the standard of care from acute myocarditis remains hemodynamic and cardiovascular support only. Recently many case reports, case control studies and prospective studies including a quasi-randomized trial [3], suggested improved clinical outcomes, if patients with myocarditis with or without encephalitis were administered intravenous immunoglobulin (IVIG) therapy.

There have been reports of improved outcomes with the use of IVIG for treatment of myocarditis in paediatric age group [4]. Similarly, treatment of EV 71 mediated hand foot and mouth disease with IVIG has shown improved outcomes [5]. Our objective was to see the effect of IVIG in terms of echocardiographic findings on the outcomes of children with myocarditis as an adjunct to the symptomatic treatment that is routinely given to these patients.

Aims And Objectives

The objective of our study was to evaluate the effect of IVIG in children with acute myocarditis in terms of recovery of ventricular function in Echocardiography.

MATERIAL AND METHODS

The present study was conducted in the Department of Pediatrics IIMS&R Lucknow. This was an observational study which enrolled children who presented with the fever of acute onset (less than 15 days in duration), and were diagnosed as suspected myocarditis on the basis of clinical features, Troponin I and echocardiography [6].

Study Type

An observational study was planned to evaluate the efficacy of IVIG as an adjunct therapy in children with acute myocarditis in terms of recovery of ventricular function in Echocardiography.

Study Design

A cross-sectional study was planned to evaluate the study.

Study Population

Case material for this study was the patients admitted to Department of Pediatrics, Integral Institute of Medical Science & Research, Lucknow, as a case of acute myocarditis.

Sample Size

A sample of 90 patients were calculated at 95% confidence interval and 10% absolute precision assuming 30% prevalence of myocarditis from previous study data and 10% dropouts.

Inclusion Criteria

- Recent history of viral prodrome in children aged 1- 15 year, with fever of less than 2 weeks duration
- Development of acute and severe heart failure following this illness – Difficulty in breathing, edema, hepatomegaly, tachycardia, gallop rhythm, muffled heart sound.
- Myocardial dysfunction characterized by raised Troponin- I level(>0.05IU/dl) and/or acute myocarditis according to echocardiography–

Exclusion Criteria

- Pre-existing cardiac illness (congenital or acquired).
- Condition known to be associated with acute congestive heart failure other than viral illness.

Group-a

Patients from 1-15 years groups fulfilling clinical diagnostic criteria of acute/ fulminant myocarditis who had received the drug A (i.e. iv immunoglobulin) along with standard care.

Group-b

Patients from 1-15 years groups fulfilling clinical diagnostic criteria for acute myocarditis who had received the standard care alone.

Standard care included decongestive therapy in the form of oxygen, angiotensin converting enzyme inhibitor, loop diuretics and fluid restriction for myocarditis.

Data collection and work-up of study children

In the PICU details of the patient were recorded in a structured proforma by the principal investigator on a daily basis in the form of history, clinical examination, routine investigation, chest X ray, ECG and echocardiography.

Statistical analysis

Data was collected and analyzed using SPSS version 16. Fisher's exact test (used where expected frequency was less than 5), was used for categorical variables and Student's T- test was used for continuous variables depending on whether they are normally distributed or not. P value of less than 0.05 was considered significant.

Sample Collection

Cases with suspected myocarditis were studied for their clinical features, recovery patterns and other biochemical and imaging parameters.

- 1) **Blood investigation-** CBC, random blood sugar, general blood picture, renal function test (serum urea, serum creatinine), liver function test (SGPT, SGOT), and ABG was done by standard methodology.
- 2) **Chest x-ray** (cardiomegaly, pulmonary congestion)
- 3) **ECG** (for myocarditis)
- 4) **2D echo**
- 5) **CPK-MB** and/or **Trop-I** enzyme marker.

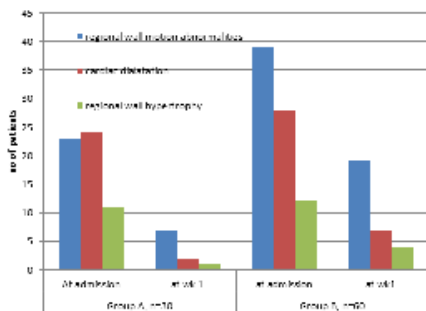
Observation

We have observed the effect of IV immunoglobulin given in Group-A as compare to Group-B as an adjunct therapy in children with acute myocarditis in terms of echocardiographic findings.

Table-1: Echocardiography Finding

Parameter	Group A (N=30)		Group B (N=60)		P value
	At admission (%)	At week 1 (%)	At admission (%)	At week 1 (%)	
Regional wall motion abnormalities	23(76.6)	7(23.3)	39(65)	19(31.6)	0.1905
Cardiac dilatation	24(80)	2(6.6)	28(46.6)	7(11.6)	0.1525
Regional wall hypertrophy	11(36.6)	1(3.3)	12(20)	4(6.6)	0.3168

Echocardiography finding



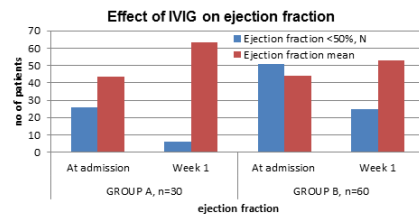
Cardiac dilatation (P value= 0.1525), regional wall motion abnormality (P value 0.1905), regional wall hypertrophy (P= 0.3168) between group A and Group B was compared at the time of admission and at week -1, was found statistically non significant.

Table-2: Effect Of Ivig On Ejection Fraction

EF	Group A (N=30)		Group B (N=30)		P value
	At admission (%)	At week 1 (%)	At admission (%)	At week 1 (%)	
EF <50%	26(86.6)	6(20)	51(85)	25(41.6)	0.0482
MEA N (SD)	43.6(11.53)	63.6(15.25)	44.26(5.68)	52.7(7.9)	at admission-0.7161 week 1-0.0001

At the time of admission left ventricular ejection fraction <50% was present in 86.6% of Group A and 85 % of Group B patients. At week 1, left ventricular ejection fraction <50% was present in 20% of Group A and 41.6 % of Group B patients. P value was 0.0482 which was

significant.



At presentation the mean (SD) ejection fraction in group A and group B was 43.6% (11.53) and 44.26 % (5.68), respectively. At week-1, mean (SD) ejection fraction improved from 43.6% (11.53) to 63.6 % (15.25) in group A, and from 44.26% (5.68) to 52.7 % (7.9) in group B. P value in both group at presentation was 0.7161 which was not significant while at week-1 p value was 0.0001 which was statistically significant. (p=0.0001 between groups A and B).

DISCUSSION

Case materials included two groups of patients, Group A, who had received intravenous immunoglobulin along with standard care and Group B who had received only standard care. We used one of the commonly recommended regimes of administering IVIG. Accordingly, IVIG was administered during five consecutive days by slow infusion at dosage of 400 mg/kg/day[7]. Total 90 patients were taken in which 30 patients were in group A and 60 patients were in group B.

Comparison Of Both Groups

Clinical Presentation

There was no statistically significant difference in the clinical presentation and examination of the two groups at admission.

Echocardiography

Echocardiography remains the most common tool to assess left ventricular structure and function in pediatrics. Previously it has been reported that the most common echocardiographic finding associated with myocarditis is a dilated cardiomyopathy phenotype of left ventricular dilatation and reduced ejection fraction, hypertrophic and restrictive phenotypes have been described in histologically proven myocarditis[8]. Segmental wall motion abnormalities mimicking an ischemic cardiomyopathy can be observed[9]. However, Durani et al[10]. recently showed segmental wall motion abnormalities being the most common findings (hypokinesia, akinesia and dyskinesia).

On echocardiography, reduced ejection fraction was most common finding followed by cardiac dilatation, regional wall motion abnormality and regional wall hypertrophy in our study groups (Table-5)

All the parameters improved after treatment in both groups in our study. Although, we found only ejection fraction to improve significantly. (table-6)

CONCLUSION

In this observational study of IVIG treatment in viral myocarditis in children of age between 1-15 year, treatment with IVIG was associated with recovery of left ventricular function on echocardiography.

These data should be viewed as preliminary in view of several limitations in our study. Our patient selection and exclusion criteria attempted to maximize the percentage of patients with acute myocarditis in the study sample, but discrimination of acute myocarditis from the acute presentation of a cardiomyopathy was necessarily inexact. Also it is difficult to differentiate between children of acute and fulminant myocarditis because they had mixed features of both of these conditions, we differentiate them by clinical and echocardiographic findings, and endomyocardial biopsies which is the gold standard test [11] that might have yielded additional supportive evidence of acute myocarditis were not performed in children for ethical reasons. Finally, we did not have follow-up data for the children with persistent LV dysfunction to see how many improved completely and how many developed complications, such as dilated cardiomyopathy.

In summary, these data suggest that use of IVIG for treatment of acute myocarditis may be associated with improved recovery of left ventricular function. Prospective, randomized, clinical studies are

needed to elucidate the effects of IVIG treatment during the acute myocarditis on ultimate outcomes.

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