IVIG, PACEMAKER AND ECMO IN ACUTE MYOCARDITIS

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INTRODUCTION

- Definition: Myocarditis is defined by an inflammation of the myocardium diagnosed by established histological, immunological, and immunohistochemical criteria
- Etiology: infections (virus, bacteria, fungi, parasitic and protozoa), drugs, toxic substances, and autoimmune diseases

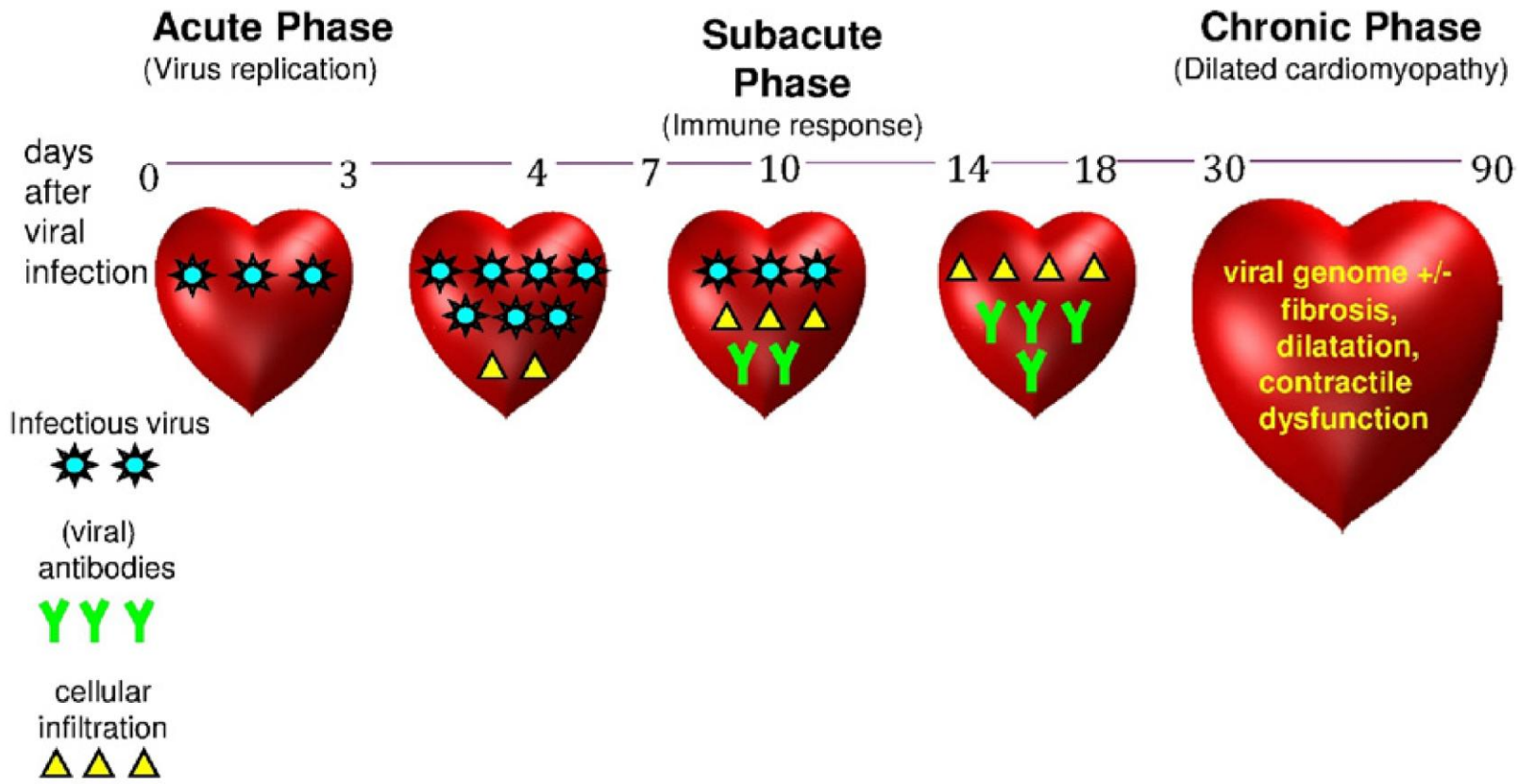

Figure 1 **Time Course of Viral Myocarditis**

Time course of viral myocarditis in 3 phases (derived from murine models). The acute phase of myocarditis takes only a few days, whereas the subacute and chronic phase covers a few weeks to several months. Modified from Kawai (22).

Table 3 **Clinical presentations of patients with biopsy-proven inflammatory heart muscle disease**

(1) Acute coronary syndrome-like
- (a) Acute chest pain
  - Frequently starting within 1–4 weeks of a respiratory or gastrointestinal infection
  - Frequently associated with severe and recurrent symptoms
  - In the absence of angiographic evidence of CAD
- (b) ST/T wave changes
  - ST-segment elevation or depression
  - T-wave inversions
- (c) With or without normal global or regional LV and/or RV dysfunction on echocardiography or CMR
- (d) With or without increased TnT/TnI that may have a time course similar to acute myocardial infarction or a prolonged and sustained release over several weeks or months

(2) New onset or worsening heart failure in the absence of CAD and known causes of heart failure
- (a) New onset or progressive heart failure over 2 weeks to 3 months
  - Dyspnoea
  - Peripheral oedema
  - Chest discomfort
  - Fatigue
- (b) Impaired systolic LV and/or RV function, with or without an increase in wall thickness, with or without dilated LV and/or RV on echocardiography or CMR
- (c) Symptoms possibly started after a respiratory or gastrointestinal infection, or in the peri-partum period
- (d) Non-specific ECG signs, bundle branch block, AV-block, and/or ventricular arrhythmias

(3) Chronic heart failure in the absence of CAD and known causes of heart failure (see point 2 above)
- (a) Heart failure symptoms (with recurrent exacerbations) of >3 months duration
- (b) Fatigue, palpitation, dyspnoea, atypical chest pain, arrhythmia in an ambulant patient
- (c) Impaired systolic LV and/or RV function on echocardiography or CMR suggestive of DCM or non-ischaemic cardiomyopathy
- (d) Non-specific ECG signs, sometimes bundle branch block and/or ventricular arrhythmias and/or AV-block

(4) 'life-threatening condition', in the absence of CAD and known causes of heart failure comprising
- (a) Life-threatening arrhythmias and aborted sudden death
- (b) Cardiogenic shock
- (c) Severely impaired LV function

Pediatric myocarditis: presenting clinical characteristics

Yamini Durani, MD, Matthew Egan, MD, Jeanne Baffa, MD, Steven M. Selbst, MD, Alan L. Nager, MD
http://dx.doi.org/10.1016/j.ajem.2008.07.032

Methods

A retrospective cross-sectional study was conducted to identify patients with myocarditis and DCM who presented over a 10-year span at 2 tertiary care pediatric hospitals. Patients were identified based on the *International Classification of Diseases, Ninth Revision*, diagnostic codes.

Results

Common primary complaints were shortness of breath, vomiting, poor feeding, upper respiratory infection (URI), and fever. Common examination findings were tachypnea, hepatomegaly, respiratory distress, fever, and abnormal lung examination result. Sixty-three percent had cardiomegaly on chest x-ray, and all had an abnormal electrocardiogram results.

Conclusions

These data suggest children with acute myocarditis and DCM most commonly present with **difficulty breathing**. Myocarditis and DCM may mimic other respiratory or viral illnesses, but **hepatomegaly** or the finding of **cardiomegaly** and **an abnormal electrocardiogram** result may help distinguish these diagnoses from other more common pediatric illnesses.

Table 4 Diagnostic criteria for clinically suspected myocarditis

Clinical presentations[a]
Acute chest pain, pericarditic, or pseudo-ischaemic
New-onset (days up to 3 months) or worsening of: dyspnoea at rest or exercise, and/or fatigue, with or without left and/or right heart failure signs
Subacute/chronic (>3 months) or worsening of: dyspnoea at rest or exercise, and/or fatigue, with or without left and/or right heart failure signs
Palpitation, and/or unexplained arrhythmia symptoms and/or syncope, and/or aborted sudden cardiac death
Unexplained cardiogenic shock
Diagnostic criteria
I. ECG/Holter/stress test features
Newly abnormal 12 lead ECG and/or Holter and/or stress testing, any of the following: I to III degree atrioventricular block, or bundle branch block, ST/T wave change (ST elevation or non ST elevation, T wave inversion), sinus arrest, ventricular tachycardia or fibrillation and asystole, atrial fibrillation, reduced R wave height, intraventricular conduction delay (widened QRS complex), abnormal Q waves, low voltage, frequent premature beats, supraventricular tachycardia
II. Myocardiocytolysis markers
Elevated TnT/TnI
III. Functional and structural abnormalities on cardiac imaging (echo/angio/CMR)
New, otherwise unexplained LV and/or RV structure and function abnormality (including incidental finding in apparently asymptomatic subjects): regional wall motion or global systolic or diastolic function abnormality, with or without ventricular dilatation, with or without increased wall thickness, with or without pericardial effusion, with or without endocavitary thrombi
IV. Tissue characterization by CMR
Oedema and/or LGE of classical myocarditic pattern (see text)

Clinically suspected myocarditis if ≥1 clinical presentation and ≥1 diagnostic criteria from different categories, in the absence of: (1) angiographically detectable coronary artery disease (coronary stenosis ≥ 50%); (2) known pre-existing cardiovascular disease or extra-cardiac causes that could explain the syndrome (e.g. valve disease, congenital heart disease, hyperthyroidism, etc.) (see text). Suspicion is higher with higher number of fulfilled criteria.

[a]If the patient is asymptomatic ≥2 diagnostic criteria should be met.

Some recommendations on diagnosis

1. Standard 12-lead ECG should be performed in all patient with clinically suspected myocarditis
2. All patient with clinically suspected myocarditis should undergo a standard trans-thoracic echo at presentation
3. Trans-thoracic echo should be repeated during hospitalization if there is any worsening of hemodynamics.
4. Troponin, VS, CRP should be assessed in all patient

TREATMENT

1. Hemodynamically unstable patients: cardiogenic shock, severe ventricular dysfunction → ECMO?
2. Hemodynamically stable patients: heart failure
3. Arrhythmia: not different from others' causes
4. Avoidance of exercise: physical activity should be restricted during the acute phase and for at least 6 months

IVIG IN MYOCARDITIS

γ-Globulin Treatment of Acute Myocarditis in the Pediatric Population

Nancy A. Drucker, MD; Steven D. Colan, MD; Alan B. Lewis, MD; Alexa S. Beiser, PhD; David L. Wessel, MD; Masato Takahashi, MD; Annette L. Baker, RN, MSN; Antonio R. Perez-Atayde, MD; Jane W. Newburger, MD, MPH

Background Myocardial damage in myocarditis is mediated, in part, by immunological mechanisms. High-dose intravenous γ-globulin (IVIG) is an immunomodulatory agent that is beneficial in myocarditis secondary to Kawasaki disease, as well as in murine myocarditis. Since 1990, the routine management of presumed acute myocarditis at Children's Hospital, Boston, and Children's Hospital, Los Angeles, has included administration of high-dose IVIG.

Methods and Results We treated 21 consecutive children presenting with presumed acute myocarditis with IVIG, 2 g/kg, over 24 hours, in addition to anticongestive therapies. A comparison group comprised 25 recent historical control patients meeting identical eligibility criteria but not receiving IVIG therapy. Left ventricular function was assessed during five time intervals: 0 to 7 days, 1 to 3 weeks, 3 weeks to 3 months, 3 to 6 months, and 6 to 12 months. At presentation, the IVIG and non-IVIG groups had comparable left ventricular enlargement and poor fractional shortening. Compared with the non-IVIG group, those treated with IVIG had a smaller mean adjusted left ventricular end-diastolic dimension and higher fractional shortening in the periods from 3 to 6 months (P=.008 and P=.033, respectively) and 6 to 12 months (P=.072 and P=.029, respectively). When adjusting for age, biopsy status, intravenous inotropic agents, and angiotensin-converting enzyme inhibitors, patients treated with IVIG were more likely to achieve normal left ventricular function during the first year after presentation (P=.03). By 1 year after presentation, the probability of survival tended to be higher among IVIG-treated patients (.84 versus .60, P=.069). We observed no adverse effects of IVIG administration.

Conclusions These data suggest that use of high-dose IVIG for treatment of acute myocarditis is associated with improved recovery of left ventricular function and with a tendency to better survival during the first year after presentation. (***Circulation*. 1994;89:252-257.**)

Key Words • cardiomyopathy • myocardium • γ-globulin

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A systematic review of intravenous gamma globulin for therapy of acute myocarditis

Joan L Robinson*[1], Lisa Hartling[2], Ellen Crumley[1,2], Ben Vandermeer[1,2] and Terry P Klassen[1,2]

Abstract

Background: Intravenous gamma globulin (IVGG) is commonly used in the management of acute myocarditis. The objective of this study was to systematically review the literature evaluating this practice.

Methods: We conducted a comprehensive search (electronic databases, trials registries, conference proceedings, reference lists, contact with authors) to identify studies evaluating the use of IVGG in adults and children with a clinical or histologically proven diagnosis of myocarditis of possible viral etiology and symptoms of less than six months duration. Two reviewers independently screened the searches, applied inclusion criteria, and graded the evidence.

Results: Results were described qualitatively; data were not pooled because only one randomized controlled trial (RCT) with 62 patients was identified. The RCT showed no benefit with respect to cardiac function, functional outcome, or event-free survival. A small, uncontrolled trial (n = 10) showed significant improvement in LVEF from a mean of 24% to 41% 12 months after IVGG in nine survivors. A retrospective cohort study of pediatric patients showed improvement in cardiac function and a trend towards improved survival in patients receiving IVGG (n = 21) versus historic controls (n = 25). Ten case reports and two case series (total n = 21) described improvement in cardiac function after administration of IVGG; two case reports showed no benefit of IVGG. One case of hemolytic anemia was attributed to IVGG.

Conclusion: There is insufficient data from methodologically strong studies to recommend routine use of IVGG for acute myocarditis. Future randomized studies that take into account the etiology of acute myocarditis will be required to determine the efficacy of IVGG.

Controlled Trial of Intravenous Immune Globulin in Recent-Onset Dilated Cardiomyopathy

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Background—This prospective placebo-controlled trial was designed to determine whether intravenous immune globulin (IVIG) improves left ventricular ejection fraction (LVEF) in adults with recent onset of idiopathic dilated cardiomyopathy or myocarditis.

Methods and Results—Sixty-two patients (37 men, 25 women; mean age ±SD 43.0±12.3 years) with recent onset (≤6 months of symptoms) of dilated cardiomyopathy and LVEF ≤0.40 were randomized to 2 g/kg IVIG or placebo. All

Conclusions—These results suggest that for patients with recent-onset dilated cardiomyopathy, IVIG does not augment the improvement in LVEF. However, in this overall cohort, LVEF improved significantly during follow-up, and the short-term prognosis remains favorable. **(*Circulation*. 2001;103:2254-2259.)**

COMBINED USE OF INTRAVENOUS IMMUNE GLOBULIN AND STEROID FOR ACUTE MYOCARDITIS IN PEDIATRIC POPULATION

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limit of normal for that age group. After establishing the diagnosis of viral myocarditis, a single dose of 2 gm/kg of IVIG was administered over 12-24 hours and corticosteroid was given as per protocol.

Steroids protocol

- Intravenous methylprednisone: 10 mg/kg/day divided in to twice daily doses for 3 days.
- Then oral prednisone: 2 mg//kg/day divided in to twice daily doses for 3 days.
- Then start weaning prednisone by decreasing it 0.2 mg/kg bi-weekly till it's completely weaned off. With this protocol, the total course of steroid would be about 6 weeks. If there is cardiac function improvement but deterioration occurs during weaning period of steroid, then go back to the dose where function got better, keep that dose for one week and then start weaning again. Anti-failure drugs including inotropes, diuretics, afterload reducing agents and anti-platelet agents were given according to the patient's clinical status.

Conclusion: Our data suggest that use of high dose IVIG in combination with corticosteroid is an effective treatment for acute viral myocarditis in pediatric population. ***Heart Views 2008;9(4):137-141.***

IVIG IN MYOCARDITIS

- Insufficient data
- Because of the risk of death and significant morbidity associated with myocarditis, we administer high dose IVIG (2 g/kg over 24 hours) for children with acute myocarditis, which is confirmed by endomyocardial biopsy, or when clinical suspicion is high

Treatment and prognosis of myocarditis in children- Uptodate 2016

PACEMAKER IN MYOCARDITIS

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STATE-OF-THE-ART PAPER

Update on Myocarditis

Ingrid Kindermann, MD,* Christine Barth,* Felix Mahfoud, MD,* Christian Ukena, MD,* Matthias Lenski, MD,* Ali Yilmaz, MD,† Karin Klingel, MD,‡ Reinhard Kandolf, MD,‡ Udo Sechtem, MD,† Leslie T. Cooper, MD,§ Michael Böhm, MD*

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Pacemaker and implantable cardiac defibrillator. Temporary pacemaker insertion is indicated for patients with acute myocarditis who present with symptomatic atrioventricular (AV) block II or III. Lyme carditis patients can have varying degrees of AV conduction abnormalities (75). Persistent AV block III is rare, but necessitates permanent pacing. In Chagas disease, conduction defects with a progression to complete heart block, and life-threatening ventricular arrhythmias are common (11). Because of dyssynchrony, chronic right ventricular pacing should be avoided in patients with restricted LV function, and implantation of a biventricular pacemaker should be considered (76). Insertion of an implantable cardiac defibrillator (ICD) in patients with myocarditis is indicated after cardiac arrest due to ventricular fibrillation or after symptomatic ventricular

ECMO IN MYOCARDITIS

Extracorporeal membrane oxygenation for the support of infants, children, and young adults with acute myocarditis: A review of the Extracorporeal Life Support Organization registry*

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Objective—To describe survival outcomes for pediatric patients supported with extracorporeal membrane oxygenation for severe myocarditis and identify risk factors for in-hospital mortality.

Design—Retrospective review of Extracorporeal Life Support Organization registry database.

Conclusion—Extracorporeal membrane oxygenation is a valuable tool to rescue children with severe cardiorespiratory compromise related to myocarditis. Female gender, arrhythmia on extracorporeal membrane oxygenation, and need for dialysis during extracorporeal membrane oxygenation were associated with increased mortality.

Crit Care Med. 2010 February ; 38(2): 382–387. doi:10.1097/CCM.0b013e3181bc8293.

Indication and timing of extracorporeal life support

The following criteria were indications for ECLS therapy

(i) cardiac and pulmonary failure refractory to medical therapy,

(ii) uncontrolled arrhythmia including ventricular tachycardia or ventricular fibrillation,

(iii) cardiac arrest, and

(iv) low left ventricular ejection fraction (LVEF) <20%.

All ECLS procedures were started within 2–4 h if the patients arrived via emergency room. If the patients were already admitted to another department, and an order for ECLS therapy was delivered to our team, the ECLS procedure was performed immediately.

Extracorporeal life support can be a first-line treatment in children with acute fulminant myocarditis

Se Yong Junga, Hong Ju Shinb,c,*, Jo Won Junga, Han Ki Parkb, Yu Rim Shinb, Young Hwan Parkb, Nam Kyun Kima and Jae Young Choia

INDICATION OF ECMO IN MYOCARDITIS

- Sốc tim thất bại với điều trị nội khoa:
  - đã dùng liều adrenalin > 0,2 mcg/kg/phút hoặc
  - dobutamin > 20 mcg/kg/phút ± noradrenalin 0,2 mcg/kh/phút
  - và tối ưu tiền tải;
  - siêu âm tim CI < 2,2 L/phút/m^2; hoặc EF < 20 %,
  - lactate máu > 5 mmol/L

(ICU BV Chợ Rẫy)

THANK YOU FOR YOUR LISTENING