**Reviewer’s report**

**Title:** A systematic review of intravenous gamma globulin for therapy of acute myocarditis

**Version:** 1  **Date:** 27 July 2004

**Reviewer:** Daniel Levi

**Reviewer’s report:**

**General**

Although ivIG remains as a fairly standard treatment for pediatric myocarditis in many centers, its use remains empiric at best and controversial at worst. Because meaningful trials of novel treatments for rare pediatric and adult disorders are very difficult to study, the concept of a literature review/analysis in such cases is very attractive. Unfortunately, the number of prospective clinical studies meeting the author’s inclusion criteria was very limited.

Studying and attempting to draw conclusions about treatment modalities for patients with ‘presumed’ viral myocarditis can be very difficult as there is no well accepted and easily performed diagnostic test. It is possible that many of the patients in the included studies did not have a viral etiology for their myocarditis. Additionally, each virus may act in a unique manner. The pathogenesis of adenovirus is known to be very different than that of the enteroviruses.

While the study design and author’s intentions were excellent, it would have been helpful to see a more in depth analysis of both the prospective, retrospective and observational studies that did meet the inclusion criteria. Which patients responded well to ivIG? Did age make a difference in response rate? Were there other subtypes of patients that appeared to respond favorably to ivIG? For instance, it is possible that biopsy proven myocarditis could respond preferentially to ivIG versus patients with presumptive and potentially incorrect diagnoses. Likewise, patients with proven viral myocarditis could also be sub-selected and also may have a more favorable response to ivIG.

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**Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)**

Is it possible to see more information about the patients included in these studies? Specifically, it would be interesting to include (if available) the characteristics of patients who responded well versus ones who did not?:

1) Ages, weights, BSAs  
2) EMB (biopsy) results  
3) Viral studies (both if attempts were made to identify a virus and what the results were)  
4) ECHO results (Did patients with worse ECHOs have more impressive responses?)  
5) CATH results/hemodynamics if pts were biopsied  
6) Presence of sick contacts or other viral symptoms  
7) Other details of patient history (Did the timing of ivIG make a difference?)

Although the number of patients available for analysis may limit the significance and strength of any conclusions which can be drawn, any trends detected could be the basis for a larger RCT. It is very likely that if a benefit for ivIG is to be detected it will be in a group of carefully selected patients with acute myocarditis.
Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

1) TABLE 2 is very difficult to read in its present format. Some of the columns should be wider or should be divided into more than one column.

2) The conclusion should be that, given the current body of evidence, no solid recommendation can be made for or against the use of ivIG in acute myocarditis. The experience with ivIG has been encouraging enough to justify a larger RCT.

Discretionary Revisions (which the author can choose to ignore)

What next?: Accept after minor essential revisions

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

Statistical review: No

Declaration of competing interests:

None