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OPEN PEER REVIEW

Related Factors for Sensitivity to the Initial Dose of Intravenous Immunoglobulin in Children with Kawasaki Disease

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About this report

This open peer review (OPR) report shows the public comments made on this article during peer review, by the reviewers, the associate editor and the editor-in-chief, for every revision round, together with the authors' replies. Comments appear only with the consent of the people who wrote them. Reviewers who chose to sign their report are named; the others are shown as "Referee". Comments are edited for language only, and confidential remarks to the editors are not included.

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1 Original submission

2 comments · 6 Nov 2021 – 11 Nov 2021

Referee 1 Reviewer

MAJOR REVISION 6 Nov 2021

1. Different scoring systems have been previously proposed to predict the IVIG resistance-related risk factors among children with KD from diverse countries and races, including the San Diego, the Egami, and the Kobayashi systems. How does your article differ from the previous article? (1. Kimiyasu Egami, Hiromi Muta, Masahiro Ishii, Kenji Suda, Yoko Sugahara, Motofumi Iemura, Toyojiro Matsuishi. Prediction of resistance to intravenous immunoglobulin treatment in patients with Kawasaki disease. J Pediatr 2006;149:237-240. 2. Tohru Kobayashi, Yoshinari Inoue, Kazuo Takeuchi, Yasunori Okada, Kazushi Tamura, Takeshi Tomomasa, Tomio Kobayashi, Akihiro Morikawa. Prediction of intravenous immunoglobulin unresponsiveness in patients with Kawasaki disease. Circulation 2006;113:2606-2612. 3. Adriana H Tremoulet, Brookie M Best, Sungchan Song, Susan Wang, Elena Corinaldesi, Julia R Eichenfield, Danielle D Martin, Jane W Newburger, Jane C Burns. Resistance to intravenous immunoglobulin in children with Kawasaki disease. J Pediatr 2008;153:117-121.)
2. The manuscript should be read critically by a native English speaker, and corrections should be made accordingly. Punctuation of the manuscript should be reviewed as well.

Reza Sinaei Reviewer

MINOR REVISION 11 Nov 2021

Response:

We have carefully reviewed your valuable article.
Historically, the development of reliable criteria to distinguish non-responders has been linked to previous investigations of clinical features, laboratory parameters, and gene expression in several studies. However, it has emerged that some laboratory and instrumental factors should be evaluated at the time of diagnosis as important prognostic factors.
In this regard, although your article is not a novel work, it deals with an important aspect of KD. Nevertheless, there are several problems in your work that need to be corrected:
1-This article has many grammatical errors and needs a major overhaul. For example, in the abstract, some words should be corrected as follows: non-response, N%, should pay attention, According to, etc.; in the introduction: according to statistics, 5 years, 10-15% (of), etc.
2- The title does not seem appropriate. Moreover, it has several grammatical errors. For example, the structure of the two words (sensitivity & non-response) does not match.
3-The keywords do not seem suitable.
4- This study lacks a proper writing methodology.
5- In Case Presentation: In part 2.1- Exclusion criteria: Since you previously included KD cases, patients who failed to be diagnosed with KD (a) are not suitable as an exclusion criterion. This problem also applies to part b. Regarding part b, you can use a shorter interval or consider other conditions.
6- Regarding study statistics, some items can be completed. For example, you can also state the average item intervals.
7- In the cases of non-responders, you have mentioned "except for secondary infections." However, you did not specify how you identified the secondary infection and what percentage of patients had the secondary infection.
8- Your discussion is not integrated and coherent. Your review will definitely increase the coherence of the

issue.
9- Revise the writing format according to the journal format.
With best regard

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Revision 1

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Manuscript ID: 120214

Title: Related factors for sensitivity or non-response to initial dose of intravenous immunoglobulin in children with Kawasaki disease

Reviewer 1:

The authors aimed to investigate the factors for sensitivity or non-response to initial dose of intravenous immunoglobulin (IVIG) in children with Kawasaki disease. The manuscript is designed well.

Response: Thank you very much for your positive comment.

The results should be discussed in the discussion section in detail. For example, why are not the serum sodium levels between two groups. What is the probable pathophysiology?

Response: We have added the required discussion and related references.

According the conclusion, can be the therapathic approach changed in Kawasaki Disease?

Response: In this study, we conclude that pediatricians should pay attention to possible non-response to the initial dose of IVIG in KD children with N ≥0.725, CRP ≥78.43 mg/L or ALB ≤32.89 g/L. In this case, the initial dose should be adjusted or other treatment methods should be used. For example, IVIG can be given again 36-72 h after such non-response.

Reviewer 2:

1. Different scoring systems have been previously proposed to predict the IVIG resistance-related risk factors among KD children from diverse countries and races, including the San Diego, the Egami, and the Kobayashi systems. What is the reason why your article is different from the previous article? (1. Kimiyasu Egami, Hiromi Muta, Masahiro Ishii, Kenji Suda, Yoko Sugahara, Motofumi Iemura, Toyojiro Matsuishi.Prediction of resistance to intravenous immunoglobulin treatment in patients with Kawasaki disease. J Pediatr 2006;149:237-240. 2. Tohru Kobayashi, Yoshinari Inoue, Kazuo Takeuchi, Yasunori Okada, Kazushi Tamura, Takeshi Tomomasa, Tomio Kobayashi, Akihiro Morikawa.Prediction of intravenous immunoglobulin unresponsiveness in patients with Kawasaki disease. Circulation 2006;113:2606-2612. 3. Adriana H Tremoulet, Brookie M Best, Sungchan Song, Susan Wang, Elena Corinaldesi, Julia R Eichenfield, Danielle D Martin, Jane W Newburger, Jane C Burns.Resistance to intravenous immunoglobulin in children with Kawasaki disease. J Pediatr 2008;153:117-121.

Response: Thank you very much for your valuable comment. Previous studies only analyzed the risk factors, and the included indicators were not sufficiently comprehensive. In this study, more comprehensive indicators were involved, including general data, clinical characteristics and laboratory indicators. Besides, this study also compared the incidence rates of non-response to different IVIG administration methods.

2. The manuscript should be read critically by a native English speaker, and corrections should be made accordingly. Punctuation of the manuscript should be reviewed as well.

Response: We have asked a native speaker to revise the English language throughout the manuscript.

Reviewer 3:

We have carefully reviewed your valuable article.

Historically, developing reliable criteria to discriminate non-responders linked to previous

investigations of clinical features, laboratory parameters, and gene expression in several studies. However, it has emerged that some laboratory and instrumental factors should be evaluated at the time of diagnosis, as important prognostic factors.
In this regard, though, your article is not a novel work, it deals with an important aspect of KD. Nevertheless, there are several problems in your work that need to be corrected:
1- This article has many grammatical errors, which needs a major overhaul. For example, in abstract some words should be corrected as: non-response, N%, should pay attention, According to, etc., or in introduction: according to statistics, 5 years, 10-15% (of), etc.
Response: We have asked a native speaker to revise the English language throughout the manuscript.

2- The title does not seem appropriate. Moreover, it has several grammatical errors. For example, the structure of two words (sensitivity & non-response) does not match.
Response: We have revised the title according to your requirement.

3- The key words do not seem suitable.
Response: We have revised the key words according to your requirement.

4- This study lacks a proper writing methodology.
Response: We have tried our best to revise the manuscript according to your requirement.

5- In Case Presentation: In part 2.1- Exclusion criteria: When you included KD cases previously, the patients who failed to be diagnosed with KD (a), do not suitable as an exclusion criterion. This problem also applies to part b. Regarding part b, you can use a less interval or consider other conditions.
Response: We are really sorry for the mistake and have made corresponding revision.

6- Regarding study statistics, some items can be completed. For example, you can also state the average item intervals.
Response: We have added the required description.

7- In the cases of non-responders, you have mentioned "except for secondary infections. ” However, you did not specify how you identified the secondary infection and what percentage of patients had the secondary infection.
Response: Actually, the description originates from the diagnostic guideline. In this study, no patients suffered from secondary infections.

8- Your discussion is not integrate and coherent. Your review will definitely increase the coherence of the issue.
Response: We have added the required discussion and related references.

9- Revise the writing format according to the journal format.
Response: We have reformatted the manuscript according to the journal guideline.

Associate Editor 1:
Your manuscript was reviewed by our reviewers. The reviewers have raised concerns regarding the manuscript, and therefore, your paper is not acceptable for publication in this format. However, since the reviewers do find some merit in the paper, I would be willing to reconsider if you wish to undertake major revisions and re-submit, addressing the referees'

concerns.
Please note that resubmitting your manuscript does not guarantee acceptance, and that your resubmission will be subject to a re-review before a decision is rendered.
Response: We have thoroughly revised the manuscript according to the reviewers' comments and responded to all comments point-by-point.

Associate Editor 2:
The reviewer was interested in your work. He however had a few minor concerns regarding your manuscript, as detailed in his attached review.
Response: We have thoroughly revised the manuscript according to the reviewers' comments and responded to all comments point-by-point.

EIC Decision:
Thank you for submitting your manuscript to Iran J Pediatr. Your manuscript has now been reviewed by three reviewers and two Associate Editors. I now have the reports of the Referees, which suggest that your manuscript might be suitable for publication following a number of revisions. I attach some reviewer comments and invite you to submit a revised version of your manuscript addressing the points made.
Response: We have thoroughly revised the manuscript according to the reviewers' comments and responded to all comments point-by-point.

2 Revision 1

0 comments

No public comments in this round.