Author's response to reviews

Title: Dalteparin, a Low Molecular Weight Heparin, as Part of Combination Therapy for Patients with Kawasaki Disease: a Retrospective Study

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Date: 3 December 2013

Author's response to reviews: see over
Dear Editor

We have submitted MS ID : 1898384970110248 to the Journal. We rewrote our manuscript according to reviewers’ comments. We corrected words or/and sentences by red color character.

Best regard.
Yasuji Inamo MD., PhD.
Reviewer's report

Title: Dalteparin, a Low Molecular Weight Heparin, as Part of Combination Therapy for Patients with Kawasaki Disease: a Retrospective Pilot Study

Version: Date: 19 October 2013

Reviewer: Jane Burns

Reviewer's report:

Additional comments:

1) Amend title to “retrospective study” and delete “pilot”. This does not seem like a pilot study or a clinical trial. This seems to be a retrospective study of outcomes in patients who received different therapies.

Ans. Thank you for comments. We deleted “pilot”.

2) Design: Retrospective review? [Was this really a clinical trial? The authors seem to be reporting outcomes of patients treated according to clinical judgment, not according to a study protocol. I am still confused on this point]

Ans. Another reviewer also had a same comment. We accepted the proposal.

Design: Change to “Retrospective hospital-based cohort compared to national surveys”.

3) These are males and females, not boys and girls [includes infants]

Ans. We changed to “males and females”.

4) Amend this sentence per above: The aim of this retrospective and pilot study was to investigate whether dalteparin in the initial treatment phase is associated with a lower prevalence of coronary artery outcomes for patients with acute KD. [I believe the authors mean prevalence of CAL, not outcomes.]

Ans. We changed to “CAL”.

5) What were the parents consenting to? The use of dalteparin? Or the use of their data in a review? What did the consent form actually say? Was it describing the experimental use of dalteparin? How many patients declined to participate?

There is no such thing as a clinical trial with 100% enrollment. Were parents
given a choice re: use of dalteparin?  Still very unclear to me.

**Ans.** We were the parents consenting to receive dalteparin.

6) P. 12, line 18: “There were no patients presenting with CAL before the initial treatment in either cohort.” This is simply not possible! Please see Ogata et al. Int. J Cardiol. 2013 For rates of coronary artery lesions at initial echo. It is highly unlikely that ALL patients had a normal echocardiogram on admission. Please explain.

a. The percentage of patients presenting with dilated coronary artery within 24 hours of admission to the hospital was reported 23.4% (34/145 patients) [18].

b. The percentage of presence of coronary artery abnormality at diagnosis was reported 0.5% (12/2014 patients assessed for eligibility) [20].

However, there were really no patients presenting with CAL including dilated coronary artery before the initial treatment in our either cohort.


**Ans.** We amended this sentence as follows.

Although some patients have presented with CAL at diagnosis [18], we did not experience this occurrence before the initial treatment in either cohort.

7) Define fever: give degrees in centigrade that you are calling “fever”.

**Ans.** Define fever: >38°C

8) P. 22, line 1: This study was hypothesis-generating. It did NOT establish anything! It suggests that a proper, randomized, placebo controlled trial
might be
worth pursuing to study the addition of dalteparin to current standard therapy.
**Ans.** We inserted this sentence into the article.

9) *P.23, line 11: Not clear what is meant by “excessive treatment”*
**Ans.** We deleted “excessive treatment”.
Reviewer's report

Title: Dalteparin, a Low Molecular Weight Heparin, as Part of Combination Therapy for Patients with Kawasaki Disease: a Retrospective Pilot Study

Version: 1 Date: 17 October 2013

Reviewer: Parmi Suchdev

Reviewer's report:

Major Compulsory Revisions
None

Minor Essential Revisions
1) Abstract
   a. Design - Change to “Retrospective hospital-based cohort compared to national surveys”.
   Ans. Thank you for comments. We changed to “Retrospective hospital-based cohort compared to national surveys”.
   
   b. Methods - Line 11, Add the phrase “In the first cohort, subjects...” and in Line 16, add the phrase “In the second cohort...”
   Ans. We added the phrases.
   
   c. Conclusion - would change end of sentence to “…in young children with KD.”
   Ans. We corrected it.

2) Methods
   a. Page 10, line 11: There appears to be a grammatical error, since sentence as written is difficult to follow.
   Ans. We corrected English language.
   
   b. Page 15. Paragraph on monitoring parameters of coagulation is a helpful addition. However, some grammatical errors make it difficult to follow.
   Ans. We corrected English language.

3) Results
   a. Page 16, line 13: This paragraph is confusing as written. Incidence of what? As mentioned in first review, it is difficult for the reader to know whether the hospital cohort and national survey represent similar populations. If data on patient characteristics, demographics, disease
severity are not available, this should be stated as a limitation, since the differences in outcomes demonstrated could be due to unmeasured confounding effects.

**Ans.** We stated: “Because the data on patient characteristics, demographics, disease severity are not available in the reference [17], it is a limitation of this study”.

**b. Page 17, line 10:** Similar to comment as above.

**Ans.** We stated as same as above.

**c. Page 20, line 1:** add “(data not shown)”

**Ans.** We added “(data not shown)”.

4) Discussion:

**a. Page 21, line 12:** would change to “…may be more efficacious than IVIG alone.”

**Ans.** We changed it.

**b. Limitations:** list is appropriate, but should also mention that the analysis did not account for potential confounders.

**Ans.** We mentioned: “However, the analysis did not account for potential confounders”.