Author's response to reviews

Title: Single-center experience with levosimendan in children undergoing cardiac surgery and in children with decompensated heart failure

Authors:

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Author's response to reviews: see over
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Philippa Harris, PhD  
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Re: Ref. No: 6723480615520347

Dear Dr Harris,

Thank you for your e-mail of July 12, 2011. We were very pleased with the excellent comments your Journal and the peer reviewers provided and to the best of our ability have prepared a revised version of the manuscript for your evaluation.

Detailed responses to the referees’ comments indicating changes made in the manuscript are attached. Unfortunately, reviewer 2 had some suggestions that were not possible to carry out due to the retrospective nature of the survey.

Enclosed please find the revised manuscript. Should further revision of the manuscript be necessary, please do not hesitate to contact me.

Yours Sincerely,

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**Reviewer 1**

1. Thank you for your excellent and informative comments.

2. In patients and methods (page 7, 2nd paragraph) a statement concerning caution when using bolus doses was added. “The bolus dose was omitted in some of the unstable hypotensive patients as recommended in the adult literature [12].

3. After thinking back and fourth at much length about changing the title of the manuscript to “Physicians’ perceptions on. . .” I decide not to do it. This study is a retrospective analysis of all children who had received levosimendan infusions in our institutions during a nine year period. The questionnaire for physicians concerning their clinical perceptions of levosimendan is only part of the article and combining these two topics in the title would have made it too long.

4. The age of the oldest patient was 21.1 years. In some cases children who have been operated on and followed up due to congenital heart defects in our institution, are still operated as young adults. A new table including age distribution and also interquartile range has been added.

5. The phrasing of the sentence in the Results (2nd paragraph) has been corrected, as suggested.

6. The last sentence in the end of the Results has been omitted.
Reviewer 2

1. Thank you for your excellent and helpful comments. You are absolutely right that the age distribution of the patients is valuable information and therefore Table 1 has been included in the results in line with your recommendation.

2. The etiologies of the cardiomyopathy and cardiac failure group have been added to the results (2nd paragraph).

3. Unfortunately, it was not possible to provide a comparison of pre-levosimendan and post-levosimendan measurements of cardiac output, left atrial pressure (LAP), pulmonary artery wedge pressure (PAWP), central venous pressure (CVP) and changes in the severity of heart failure. Repeated cardiac output and PAWP measurements were not available because the Swan-Ganz catheter was and is not used in children. Severity of heart failure classification (AHA) was not used in children in our institution. LAP had been measured in some post cardiac surgery patients and CVP in all them. Cardiac ultrasound evaluations were not routinely done in children before and after levosimendan infusions at specific time points. Therefore regrettably no reliable comparison can be made. On the other hand, levosimendan administration has not been shown to cause changes in blood pressure or heart rate or CVP in children with heart failure (Namachivayam, Pediatr Crit Care Med 2006, 7: 445–448).

4. I fully agree that the information regarding the other vasoactive drugs that these patients were receiving prior to introduction of levosimendan, would have been extremely informative. Unfortunately, the problem is that the patient data in this study are heterogeneous. Indications and timing about when to use levosimendan has been variable and this has been stated in the manuscript (in patients and methods and discussion). Levosimendan was not only used as the last resort therapy in the PICU when the other therapies had failed as in most of the earlier pediatric studies. In our institution levosimendan was also initiated proactively in the OR for some of the higher risk cardiac surgery patients. When the weaning
from CPB failed at the first attempt levosimendan infusion was often initiated in addition to different combinations with the other vasoactive drugs including: epinephrine, norepinephrine, milrinone, vasopressin and inhaled nitric oxide. Moreover, a trend towards the initiation of levosimendan infusion before surgery in the PICU or after induction of anesthesia (for example for patients with HLHS or TGA) has occurred in recent years. Cardiomyopathy patients received levosimendan infusions often as a primary inotrope. Patient treated in mechanical assist devices received levosimendan infusions (no other vasoactive drugs) to enhance weaning from the device or support the right ventricle during the support period. Due to these factors it would be very difficult to make one table for the other vasoactive drugs that these patients were receiving prior to introduction of levosimendan.

5. The author must provide information on impact of levosimendan on discontinuation of other vasoactive drugs.

Please see the information given above. As this study was retrospective and not a placebo controlled study. It would be extremely hard to prove that the other vasoactive drugs could be discontinued or that their dose could be reduced due levosimendan administration in this heterogeneous patient material.

6. How are patients in cardiac failure risk stratified in the author’s institution?

We do not use any specific risk classification for patients in cardiac failure. Evaluations of risk and decisions are made by the anesthesiologist in charge of the patients treatment in the OR or PICU. Therefore levosimendan infusion was started based on the clinical findings of the cardiac failure patient including poor hemodynamic profile, metabolic acidosis, poor tissue perfusion, oliguria and rising serum lactate levels despite escalating inotropic support.

7. Minor Essential Revisions

1. The Questionnaire has been included in the Appendix. This has been done.
2. Page 9, line 3 the spelling error has been corrected.
3. The references in the bibliography are cited according to the Journal requirements.
Although due to the reasons given above I could not make all the changes you suggested, I found your comments very helpful and will bear these in mind for the future.
Reviewer 3
Thank you for your positive and encouraging comments.