Author's response to reviews

Title: Evaluation of Seasonal Patterns of Kawasaki Syndrome- and Rotavirus-associated Hospitalizations in California and New York, 2000-2005

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Version: 2 Date: 24 June 2009

Author's response to reviews: see over
To Whom It May Concern:

We would like to thank the editor and reviewers for their comments regarding our manuscript titled "Evaluation of Seasonal Patterns of Kawasaki Syndrome- and Rotavirus-associated Hospitalizations in California and New York, 2000-2005." We have found the comments helpful and have attempted to address all comments. We feel that we have provided an improved version of our manuscript, which we hope will be of strong interest to *BMC Pediatrics* readers.

Please find below a point-by-point response to the editor’s and reviewers’ comments. Thank you for considering our manuscript for publication in *BMC Pediatrics*.

Sincerely,

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Response to reviewer’s comments

Editor’s inquiry about ethical approval.

Because HCUP data is secondary administrative data without clear patient identifiers, it has been determined that the data is exempt from ethical approval.

Reviewer 1.

Reviewers report

In response to the reviewer’s comment with regard to the importance of this study, we have expanded the final paragraph of the introduction to include “Because the etiology of KS remains unknown, and the possibility of an association between KS and rotavirus infection has been raised [7], we sought to further examine the relationship between these diseases. Furthermore, a better understanding of any potential association between KS and natural rotavirus infection could help assess the biologic plausibility of a relationship between rotavirus vaccination and KS.”

With regard to the reviewer’s comment about exploring statistical measure of association, we did explore the usage of an auto-correlation function in time series analysis. However, a correlative analysis of this manner cannot demonstrate a causal association. As we note in the manuscript, Kawasaki syndrome did display a slight seasonality, which naturally will display a statistical correlation with rotavirus seasonality. However, any two diseases that are seasonal (for instance, influenza and rotavirus) will display a correlation. We believe that it is clear from the figures in the manuscript that the year round occurrence of Kawasaki syndrome indicates that its etiology cannot fully be explained by rotavirus, which has a strong seasonal nature, and that applying a measure of temporal correlation to these diseases is not an appropriate display of the causal (or lack thereof) nature of these diseases.

Abstract

We have expanded the abstract, in an attempt to address the reviewer’s comments. In particular, we have reworded the conclusion.

Introduction

As described above, we have expanded the final paragraph of the introduction, to provide further rationale for the study.

Methods

With regard to the representativeness of the population examined in this study, we have added the following statement to the discussion section “Finally, discharge data for this study was from all community hospitals in CA and NY. Community hospitals are
defined as non-Federal, short-term, general, and other specialty hospitals, excluding hospital units of other institutions (e.g., prisons). Community hospitals represent approximately 85% of all U.S. hospitals, including public and private, academic and specialty hospitals. In California, 98% of all community hospitals are included in the HCUP data base, and in New York, 100% of all community hospitals are included.” In addition, we have reworded part of the methods section, to clarify issues raised by the reviewer, with regard to the analysis.

Results

While we understand the reviewer’s comments, we feel that a statistical methodology, such as time series analysis, does not appropriately represent the data in this study. Please see our above comment (under Reviewer 1; Reviewer’s report).

Discussion

In response to the reviewer’s comment, we have expanded the limitations paragraph, to address the potential issue of representativeness.

Illustrations

We have reworded the figure heading, to attempt to make interpretation of the figure easier. In addition, we have modified the figures slightly, to make differentiation of lines and plotted data points, more clear.

Reviewer 2.

Major Compulsory Revisions

1- RotaTeq is one of two rotavirus vaccines currently licensed for rotavirus. While reference 1 does not specifically name RotaTeq, this vaccine is an appropriate vaccine to fill the vaccination recommendation. The reviewer is correct that 2006 is the year of licensing of RotaTeq, but it is important to note that RotaTeq is an appropriate vaccine to be administered as part of the 2009 recommendations. In response to the reviewer’s comment, we have reworded the first paragraph slightly, so as to indicate that vaccination against rotavirus (as opposed to specific administration of RotaTeq) is recommended per reference 1.

2- The reviewer has correctly noted that the incidence of Kawasaki Syndrome is higher in Japanese children. In response to the reviewer’s comment, we now note in the introduction that incidence of Kawasaki Syndrome in Japanese children is higher than in the United States.

Minor Essential Revisions

1- We have modified the figures, slightly, to make it easier to differentiate the lines.
Discretionary Revisions

1- We appreciate the reviewer’s comment, and have added an additional sentence to the discussion section, noting other factors that have been hypothesized to be involved in Kawasaki Syndrome.

2- In response to reviewer’s comment, we have added the following to the conclusion section “appropriate comparison group with similar age, sex, and genetic background”.