Author's response to reviews

Title: Community acquired bacterial meningitis in Cuba: a follow up of a decade.

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Author's response to reviews: see over
RESPONSE TO THE REVIEWER
We are grateful to reviewer Dr. Annunziata Faustini for their helpful comments and suggestions which we try hard to clarify in this document, as well as in the paper.

Version: 2  Date: 1st March 2010

Reviewer: Annunziata Faustini

Reviewer’s report response:
We are providing all the requested information and improving the manuscript, addressing the comments of the reviewer on the main three points she note.

About the surveillance:
We will try to briefly explain the main changes and improvement achieved in the surveillance of bacterial meningitis in the background.

The surveillance system was modified in 1998 from a special surveillance for invasive meningococcal disease during epidemic (1979-1988). Modifications included: inclusion of all cases of bacterial meningitis (regardless of the bacterial identification), recollection of date of symptoms onset, first medical consultation, admission to hospital (and which hospital), of death and others, some risk factors (attendance to day care and boarding schools), gathering and overcrowding, social categories (worker, unemployed, housewife and others), vaccination status (vaccine and date of the doses), hotbed control and microbiological data about the isolated bacteria, which are described in a previous published paper (Pérez A, Dickinson F, Tamargo I, Sosa J, Quintana I, Ortíz P et al. Resultados y experiencias de la vigilancia nacional de meningitis bacterianas en Cuba. Biotecnología Aplicada 2003; 20:188-22).

Of them, we choose the variables which seem to be the most important to be presented in this paper, taking into account that there are a lot of variables to put in one article.

We consider important to begin the discussion with a concise paragraph describing the analogies of our system with those of developed countries, considering that Cuba is a low income resource country but has a nationwide Public Health System with full access to all citizens.

This time, we modified the first paragraphs of discussion and tried to give a different and brief description of main features of system (complementing the description in the Background).

On the other hand, these data allow assessing some of the objectives of the national immunisation program (variables age, sex, date and number of dose, age of the first dose, inter-dose time interval and other) and the infectious neurological syndrome national program for control and prevention (results showed in the paper and others not shown for conciseness reasons):

"Likewise those of developed countries [9-11], BMSS has been useful and proficient providing and synthesizing critical and multidisciplinary information [16, 17] for more than a decade, fulfilling all suitable surveillance system attributes [17, 18]. Changes implemented in 1998 allowed collecting data which contributed to assess main objectives of both, the
national immunisation program and the infectious neurological syndrome national program for control and prevention”.

**Temporal and spatial distribution:**

In regard with suggestion to standardize rates for comparison, we added to material and methods a paragraph describing that: “A trend to homogenization is among the main demographic characteristics of Cuban population, especially in the last four decades; therefore the age composition of population groups is very similar in all the regions. On the other hand, in Cuban population there are no racial, indigenous, religious or other social groups different to the main population”. This is a statement of the Office for National Statistics in Cuba (which is the governmental structure to study the population in Cuba) based on the studies carried out in the Cuban population, therefore age-standardization to compare populations groups wont be required.

Regarding the temporal trend, it seems that a linear model adjust to our series. We provide all the data we consider essential, but not include the graphic in order to not increase unnecessarily the number of graphics in the paper.

"The time series analysis was done by the best adjusted method (linear trend), choosing the minimum mean square error and minimum interval residuals as appropriate test for trend assumption”

**The association analysis**

In Methods we clarify even more the univariate analysis. We separate host factors from management of BM considering that the information of management was not complete. Nevertheless BM management variables were also analysed by multivariate regression, but neither was found association.

"Univariate analysis was used to elucidate associated factors to mortality comparing deaths versus survival. For the assessment of the timeliness of the medical attention and hospitalization we defined delayed medical consultation as "the time elapsed between the symptoms onset and the first medical consultation greater than one day" and delayed hospitalization as "the time elapsed between the first medical consultation and hospitalization greater than one day".

Also it was assessed by univariate analysis the association of fatal outcome with some host factors (sex, children attending DCC, children at home, student, boarding student, housewife, pensioned, recluse, military, imprisoned, worker, unemployed, S. pneumoniae, H. influenzae type b, N. meningitidis, other identified bacteria and non-identified agent). Association was estimated through Relative Risk (RR) and its confidence interval (CI). Additionally, it was carried out a multiple logistic regression analysis to variables with RR>1. The model was fitted including the selected variables and subsequently dropped one by one until only those that were associated (OR>1.6). ".

Regarding the monthly estimates of incidence, we only describe the monthly number of cases and additionally we used a Holt-Winters multiplicative analysis of seasonality for better understanding: “A Holt-Winters multiplicative analysis was used to analyse the seasonality.”

In Methods we included:

"Age was excluded because it was not possible to rise solid hypothesis allowing dichotomising the rank associated to death".
In regression analysis it was included the precise age and gender. We also included the number of cases deceased and survivor in Table 4.

We hope a good understanding of our answer to reviewer suggestions.

The authors