Reviewer's report

Title: Surfactant Does Not Protect Preterm Infants From Early Deaths In Northeast Brazil

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Reviewer: Nestor Vain

Reviewer's report:

General comments:
This is an interesting study evaluating factors that influence a high early neonatal mortality rate in northern Brazil. Main study strength is to present data about variables affecting neonatal mortality in very low birth weight preterms in a low developmental index setting. This information is relevant to set priorities in public health interventions. However, there are several aspects that need corrections.

The title is misleading: it relates to a collateral unexpected finding rather than being oriented to describe what the study was planned for and its results. The finding that the use of surfactant is associated with an increase in early neonatal mortality in a region where there are many difficulties in the organization of neonatal care should not be surprising: surfactant became available in the USA and the developing world once many general aspects of organization of neonatal intensive care had been solved and were well organized. Without surfactant the mortality of VLBW infants in patient series from the US decreased from over 70% in the 60’s to less than 20% in 1990. The addition of surfactant replacement and high frequency ventilation in the early 90s where associated with a much slower and slighter decrease in mortality.

It is likely that in the analyzed region many aspects of clinical care need to be solved, and before that happens, as the authors recognize, surfactant use is only a marker of the sickest patients whose general clinical care is far from ideal.

The discussion of the paper should also include how the results can be utilized towards the improvement of early care of VLBW infants.

The characteristics of health care facilities, level of training of nursing and medical personnel, are modifiable factors that the authors have the opportunity to show as relevant for their region. Furthermore, there is no clear mentioning of the number of nurses and physicians who is available and actually employed at the participating hospitals which is frequently a problem as important as the level of training, and frequently more important than the quality of the equipment.

It is worth to mention that it can be recognized the effort to obtain and complete a regional and reliable database. The results of the study can be used not only for the specific region but also for improving perinatal care in other regions of the developing world who most likely have similar difficulties as the North East of Brazil.
Specific aspects

Title
Although it is a striking finding, this title does not inform the reader about the specific issue and design of the presented study. Moreover, it seems an overly emphatic statement for one study. The title of the study must be representative of the aims and general findings of the study.

Abstract
The authors evaluate a period of 168 hours. It is unusual to express such a long period in hours. “7 completed days” would be clearer for most readers.

For people who only read the abstract the conclusions have no relationship with the text or the aims described in the abstract. This MUST be corrected.

The end of the sentence:...due to the misuse of medical procedures during childbirth” is not clear. I believe the authors mean that “misuse of medical interventions during pregnancy, or over interpretation of medical test tend to shorten the length of pregnancy”

Introduction:
It is correct that in developed countries the proportion of early to total neonatal mortality is lower than in the areas with poor perinatal care. Average time to death for premature infants deemed to dye is longer in developed countries.

However the proportion between neonatal and infant mortality is higher in the developed world (because there post neonatal infant mortality is extremely low).

The way the introduction is written may induce the reader to understand wrongly this aspect. A brief sentence in this regard should avoid this problem.

There were 24 infants with gestational age #37 weeks among neonates with 500 to 1500 g birth weight. That represents a 2.4%, which sounds as a very high proportion for VLBW infants. This deserves a comment in the discussion.

Methods
• The study appears to this reviewer as a retrospective one, but using a prospectively obtained database. If this is correct it should be clarified in the text.

Results
• It draws attention the fact that the study presented was done 7 years ago. Could these results be considered current data?

• Table 1 is presented at Methods section. If these characteristics were necessary conditions for the institutions to participate in the study, the table should be presented at Methods. However, if as this reviewer believes, the details of the conditions of each hospitals were recorded after the study had started, the table should be presented at the Results section.

• Information regarding to distribution of deaths according to gestational age could be better presented in a Table.
• Was any of the characteristics detailed for each institution considered for the analysis? It is disturbing that some institutions considered as L1 do not have regular clinical staff meetings, do not require neonatal resuscitation training, professional qualification training or neonatal humanized care training. Moreover, it is worrying that despite these characteristics the institution is accredited as a safe maternity. This fact turns the institutional level as a non reliable variable. This deserves a comment in the discussion section.

• There is also a hospital considered reference for high risk gestation, does not require any qualification or training. This issue also deserves a comment at discussion.

• Have the authors any data about the personnel/patient relationship in each institution? Again this is for this reviewer an aspect quite related to survival rates in extremely premature infants.

• It would be interesting to present results of multivariate analysis in a table.

• Is it possible to compare the results between units with low versus units with high patient load?

Discussion:

First paragraph: the authors comment on the results of 4 cohorts, but they mention for 3 of them the survival rates and for the fourth one the mortality rate. To help the reader in the comparison they should either describe survival or mortality for all the cohorts.

Secondly, they mention their own cohort as the survival rate of infants from 23 to 31 weeks gestation. However in their methods they describe that they included only infants within those gestational age limits but between 500 g and 1500 g birth weight. This is different because some infants of 30-31 weeks gestation, and over 1500 g birth weight could have survived more often than the smallest ones. Please clarify.

Data about percentage of patients who survived at the L2 hospitals are presented here, but they should have been presented at the Results section.

In the discussion about the reasons for which surfactant is associated in this series with an increase in the early mortality rate (which is quite appropriate) it should be mentioned for the international reader than the surfactant brands used in Brazil are the same as those used in the developed world. The discussion should insist on the fact that the use of surfactant is a marker of severity and not the cause of an increase in mortality.

The sentence “The use of analgesia in newborn care in worldwide neonatal care units is still inadequate and irregular [30]” is not warranted. Nobody knows what is exactly adequate. I consider the authors should express “controversial and irregular”.

A conclusion sentence at the end of the discussion should be included.

Level of interest: An article of importance in its field
Quality of written English: Needs some language corrections before being published

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

No competing interests