An urgent study on NSAIDs use is needed in Mexico | 27 May 2009

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Send response
to journal:
Re: An urgent
study on
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Mexico

Shimazu's comments are very important [1] in considering the high case mortality ratio in Mexico in the 2009A/H1N1 epidemic [2].

According to the data reported from WHO [2], case fatality ratios in adults were 3.7 % for all adults (20-29y: 2.8 %, 30-49y: 4.0 %, >=50y: 5.6 %), while 0.6 % in children aged less than ten and 0.4 % in teenagers (combined: 0.5 %).

Mortality ratio in those in each ten years of age from 20-59 and in those 60 years old or more is significantly higher than each ten years of age in those less than twenty years old. According to my reanalysis of the WHO's data, odds ratio (OR) of case fatality of combined adults compared with combined children and teenagers (0-19 yeas) is 7.63 (95% confidence interval (CI): 3.78-15.85, p=0.0000000). The authors say "Reasons to be determined".

Several cases experiencing cardiopulmonary arrest shortly after arrival at hospital, rapid progression to acute respiratory distress syndrome (ARDS) and renal or multi-organ failure are reported in 24% of fatal cases [2]. Both leukocytosis and leucopenia are reported [2] and both are the fundamental diagnostic criteria of sepsis: i.e. systemic inflammatory response syndrome (SIRS) due to infection. Bacterial co- infections were rarely documented (only in 3 among 45 fatal cases).

Laboratory findings such as high levels of aminotransferases and creatinine phosphokinase, skeletal muscle necrosis, renal insufficiency, hypotension and even myocarditis often reported as clinical or autopsy findings in fatal cases in this report [2] are also the common findings in sepsis-multiorgan failure syndrome with or without shock induced by the systemic cytokine storm in viral infections.

Mizuguchi et al [3] reviewed acute encephalopathy as one of the most serious complications of pediatric viral infections. Of the three major groups, the second group which is characterized by a systemic cytokine storm and vasogenic brain edema, includes Reye-like syndrome, hemorrhagic shock and encephalopathy syndrome, and acute necrotizing encephalopathy [3]. Non-steroidal anti-inflammatory drugs, such as diclofenac sodium and mephenamic acid, may aggravate these syndromes [3]. Severe cases are complicated by multiple organ failure and disseminated intravascular coagulation [3].

These clinical and epidemiological evidences are consistent with the results of meta-analysis of experimental studies using infected animals [4,5].

The authors of WHO warned "Salicylates (such as aspirin and aspirin- containing products) should not be used in children and young adults because of the risk of Reye syndrome."

However use of salicylates is neither restricted in adults nor use of other NSAIDs including ibuprofen is restricted in any age, though they warned of the use of corticosteroids referring the experience of SARS (severe acute respiratory syndrome) and increased mortality in avian influenza A (H5N1) disease [6].

The authors of WHO [2] discussed about the risk factors for severe or complicated diseases. They mentioned relatively common but unspecific risk factors such as smoking, air pollution, high altitude (Mexico City at >2200 m). However the possibility of harmful effects of NSAIDs is not discussed.

Washington Post [7] reported that the uninsured, about 50 percent of the population, include the unemployed and those who work in the informal economy. They also reported a doctor's comments saying "In Mexico, we are very unaccustomed to going to the hospital. Here, if someone has a cold or anything else, they buy something in the pharmacy, or they leave it be,"

Doesn't something in the pharmacy mean aspirin and/or NSAIDs antipyretics, and/or drugs containing these?

I strongly propose first of all, an urgent retrospective study to reveal whether NSAIDs were used or not in severe and fatal cases before they deteriorated.

If NSAIDs are highly used before deterioration, then a case- controlled study to confirm the relation of NSAIDs to the high fatality should be carried out.

Errata:

In my previous response [1], the 2 parts should be read as follows:

#1 The 12th line from the bottom of the text:

restricted to the treatment-->restricted in the treatment

#2 The 7th line from the bottom of the text:

restricted to children-->restricted in children .

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Competing interests: None declared