Reviewer’s report

Title: Characteristics of Pediatric Adverse Drug Reaction Reports in the Japanese Adverse Drug Event Report Database

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Reviewer: Ugo Moretti

Reviewer's report:

The study aims to evaluate the adverse drug reactions in the Japanese spontaneous reporting database. The study has important critical issues. The most important one is related to the type of data used in the analysis, obtained through the public version of the Japanese database. In this database, the age of the patient is reported only as categorical value expressed in decades. The Authors analyze two decades, including patients not related to the pediatric age (age higher than 16 or 17 years). Moreover it is not possible to analyze the situation for age groups that are very different (eg neonatal or infant vs adolescent).

As stated by the Authors "information on age is essential in discussion about SDRs, especially in pediatric patients". This is an important limitation of the relevance of the study. With these age categories it could at least presented and discussed the comparison between children and adults with respect to the reported drugs and reactions.

Since almost all reports come from drug companies it could be more interesting to analyze Japanese reports through the analyses of the FDA spontaneous reporting database (FAERS), publicly available for download. FAERS include non-US data received by drug companies worldwide and it is possible to select Japanese reports with detailed information for age.

Another important issue is related to serious events. The Authors stated that JADER database includes only serious ADRs. It is not clear how seriousness has been defined, generally serious reports include deaths, life-threatening events, hospitalization, persistent or significant disabilities and congenital abnormalities but it could be possible to define seriousness according to the clinical judgment of the reporter. Table 3 lists among the most frequently reported reactions non-serious events like pyrexia and rash, it is not clear why these reports have been defined serious.

Spontaneous reporting databases include literature reports, cases selected by drug companies in the literature and sent as individual case safety reports. Literature reports include many duplicates since the same case is reported by different drug companies. It should be specified if JADER database include literature data and, if the answer is yes, if duplicates have been deleted.

The list of the most frequently reported drugs seems not related to the drug use. This result should be discussed, specifying if stimulated reporting or other form of active reporting was present for some drugs (like oseltamivir and zanamivir). Moreover among reported reactions the
number of reports of toxic epidermal necrolysis and Stevens-Johnson syndrome associated to paracetamol is very high. This finding should be highlighted and discussed.

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

Yes

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Unable to assess

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

No

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

Not relevant to this manuscript

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Acceptable

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