Reviewer's report

Title: Drug related problems in Neonatal Intensive Care Unit: incidence, characterization and clinical relevance

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Reviewer: Luke Grzeskowiak

Reviewer's report:

The authors have done a reasonable job in responding to previous reviewer comments. I have only a few more additional comments below. A couple have arisen as a result of the new supplemental files attached, while a couple relate to appropriately addressing previously reviewer comments.

The additional of the supplemental files is useful in providing the reader with additional information to interpret and determine the clinical relevance of this paper to their own clinical practice.

I do, however, have some concerns regarding the interpretation/reporting of some of the classifications.

No clinical example has been provided for C1.3. "inappropriate combination of drugs, or drugs and food" - yet under C5.5 the example provided for "Wrong drug administered" is "intravenous drug administered concurrently with another incompatible drug". Wrong drug accounts for 164 DRPs but this example does not fit with the definition. C5.5 would be situations where the completely wrong drug was administered. The example of incompatible drugs being given together actually fits with C1.3. Please amend these.

C3.7 - it is interesting that "pharmacokinetic problems requiring dose adjustment" was considered not applicable for the study, yet a number of medications used in neonatal unit require pharmacokinetic assessment. Does this mean pharmacokinetic evaluation and dosage adjustments of vancomycin, amikacin, gentamicin, theophylline were not taken into consideration?

C6.2 example provided is "vancomycin is prescribed without the infusion time" - presume this is meant to mean that vancomycin was prescribed without a specified administration time - the infusion time would not be something to be expected to be specified on the medication
prescription as it would be standardised as part of the medication administration procedure. Please clarify.

C8.2 "No obvious cause" - no example is listed of DRPs that were classified in this section. Given this accounts for 76 DRPs it would be useful to know what types of things this included as it is completely unclear at this stage what it would include.

I completely disagree with the statement that results can be safely generalised to other NICUs. The reality is that this cannot be assured and therefore a limitation of this study is whether results are generalizable to other units. It is already mentioned that certain medication error prevention strategies are not implemented in this specific neonatal unit, so that factor alone means the distribution and type of DRPs in neonatal units is likely to be different based on support strategies in place. Please amend this as a limitation.

Reference 27 is not adequate as evidence of error prevention strategies - please cite a systematic review on medication safety error prevention strategies specific to the neonatal unit setting. E.g. Nguyen et al (2018). Interventions to Reduce Medication Errors in Neonatal Care: A Systematic Review. Therapeutic Advances in Drug Safety. 9 (2): 123-155. There are also others that could be cited.

"It should be noticed that in our study the DRPs occurred even though the NICU has an institutional clinical practice guideline" - this statement does not make complete sense and does not specifically address the reviewer comment. Please specify whether or not specific dosing guidelines are available for all medications where dosing errors were present.

I agree with the other reviewer regarding the questionable validity of the safety-relevance assessment. This really needs examples around things classified as being minor, significant or high relevance. The additional description provided in the text regarding the limitations associated with this specific part of the method is not adequate. This needs a statement highlighting the limitation that it was only the pharmacist evaluating severity, had clinicians been involved the severity assessments may have been different. There does not appear to be inter-rater agreement evaluated between assessors to see what level of agreement there actually was either in terms of severity assessment. Please amend wording in discussion accordingly.
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.

Yes

Are the conclusions drawn adequately supported by the data shown?
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