Author's response to reviews

Title: Drug-Related Problems in Type 2 Diabetes Mellitus Patients with Dyslipidemia

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Date: 11 December 2013

Author's response to reviews: see over
Response to editorial request

Additional Editorial Request:

1.) Competing Interest

Please be advised that manuscripts must include a "Competing interests? section. This should be placed after the Conclusions/Abbreviations. If there are none to declare, please include the statement "The authors declare that they have no competing interests." Please consider the following questions and include an appropriate declaration of competing interests in your manuscript:

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Non-financial competing interests? Are there any non-financial competing interests (political, personal, religious, ideological, academic, intellectual, commercial or any other) to declare in relation to this manuscript? If so, please specify. For more information please visit the instructions for authors on the journal?s website.

The section of competing interest has been included after the conclusion.

2.) Acknowledgements

By way of a section "Acknowledgements?, please acknowledge anyone who contributed towards the article by making substantial contributions to conception, design, acquisition of data, or analysis and interpretation of data, or who was involved in drafting the manuscript or revising it critically for important intellectual content, but who does not meet the criteria for authorship. Please also include the source(s) of funding for each author, and for the manuscript preparation. Authors must describe the role of the funding body, if any, in design, in the collection, analysis, and interpretation of data; in the writing of the manuscript; and in the decision to submit the manuscript for publication. Please also acknowledge anyone who contributed materials essential for the study. If a language editor has made significant revision of the manuscript, we recommend that you acknowledge the editor by name, where possible. The role of a scientific (medical) writer must be included in the acknowledgements section, including their source(s) of funding. We suggest wording such as 'We thank Jane Doe who provided medical writing services on behalf of XYZ Pharmaceuticals Ltd.' Authors should obtain permission to acknowledge from all those mentioned in the Acknowledgements section.

The acknowledgement section is not applicable for this manuscript.
Response to Reviewer 1

Reviewer's report

Title: Drug-Related Problems in Type 2 Diabetes Mellitus Patients with Dyslipidemia

Version: 1 Date: 11 November 2013

Reviewer: Albert A. Figueras

Reviewer's report:

Dear Authors,

Although the topic is highly prevalent and important, in my opinion the present study, as it is, does not reflect the clinical relevance of the findings from this research.

I would suggest different major revisions in order to improve the text.

Major compulsory revisions

- A general one: when talking about patients, diseases and drugs, the most important are the patients and the consequences of their diseases or the consequences of the drugs they are taking. So... why not consider people (208 patients) instead of drug-related problems? Perhaps this alternative focus could greatly improve the results and the clinical relevance of the results.

The idea of a DRP study is focusing more to drugs as cases. As such this study explored the numbers of DRPs based on patients’ readmission to hospital. It is also interesting to found that most of diabetes patients had frequent hospitalisations.

1) The sample are patients with diabetes and dyslipidemia. In the results sections, the authors state that "more than 70% of subjects were found to have polypharmacy". Shouldn't this figure be 100% or almost 100%? Because most patients should be treated with at least one drug for each clinical condition.

If 70% of polypharmacy is a right figure, then, this would be a first important result: "30% of your study sample (patients with diabetes and dyslipidemia) are not treated at all at present. And this result merits an active intervention in your country.

But I imagine that the 70% of polypharmacy refers to another definition of polypharmacy (excluded treatments for these two diseases? If this is the case, then this would be an inappropriate approach, from my point of view). The study defined polypharmacy based on reference [17] i.e patients taking six or more chronic medications for duration of at least 6 months (inclusive treatment for diabetes and dyslipidemia). In the study, 30% of patients received less than six chronic medications.

2) The Authors found that approximately 25% of patients had their disease "controlled" according to the blood analyses. Is this true? Wouldn't it be interesting to describe more this subset of patients that present a therapeutic failure? Why are not responding to the treatment? Is there a problem of not
taking the medication?

To my opinion, these are the really important approaches when analyzing drur-related problems.

Since the study design was a retrospective type in nature, it was not possible to explore reasons of therapeutic failure. As has been also pointed in question 5, non-adherence only contributed for a small percentage of patient population and thus inferential statistics could have not been performed.

3) "11 subjects were not on any medication except for ant-diabetic agents and LLA"... Perhaps this is the problem of "polypharmacy". Wouldn't it be better to consider the patient as a whole and, then, consider the whole medications? I mean, antidiabetic and LLA agents also produce DRP, interactions, lack of adherence... This indicated that subjects had only diabetes and dyslipidemia without any other comorbidities. This also supported the earlier results where 30% of patients did not experience polypharmacy. In addition results shown there were 5.8% (or 12 subjects) without any co-morbidity.

4) The first sentence in "Drug-related problems" refers to 208 patients... this should be 191.

The correction had been incorporated.

5) Another potentially interesting result is the proportion of patients that are not taking their medicines! Could you analyze this subset? Are the Authors referring to any medications or to any medications in addition to antidiabetics and LLA? 14% of non-adherence is an important proportion. Is it related with the lack of "efficacy" according to blood tests?

In this case we are referring to antidiabetics and LLA. It is not possible to analyse the association between non-adherence and lack of drug efficacy since the data (n=26) is too small to reach statistical significance.

6) Table 6 would improve in clarity if the reference values considered by the Authors or the study centre are given.

The study is the first in the country.

7) Table 6 gives many clues related with inappropriate use of medicines / inappropriate prescription. To my opinion, to highlight these problems is what is clinically relevant for patients and a clue to implement interventions to improve the management of these patients.

For example: in 26% of "cases" there is a drug choice problem. This is very high!

How many individual patients of your sample had one of these problems? This is also a key result.

In 14.3% of "cases", drug was not taken... the same, these are interesting results. Which were the causes?

So, if the Authors try to focus on problems from the patient point of view, the
result would greatly improve and the conclusions and suggested interventions to improve health care would be clear.

Thank you for your great suggestions. As mentioned at the beginning of the responses, the idea of a DRP study is focusing more to drugs as cases. As such this study explored the numbers of DRPs based on patients’ readmission to hospital. It is also interesting to found that most of diabetes patients had frequent hospitalisations.

In addition, some of the causes of DRPs were not able to be documented due to lack of evidence in respect to the retrospective type of study design.

Level of interest: An article of limited interest

Quality of written English: Not suitable for publication unless extensively edited

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I have no competing interests, according to the previous statements. I’m only working at a public university and a World Health Organization Collaborating Centre.

Response to reviewer 2

Reviewer’s report

Title: Drug-Related Problems in Type 2 Diabetes Mellitus Patients with Dyslipidemia

Version: 1 Date: 26 November 2013

Reviewer: Floro Andrés-Rodríguez

Reviewer’s report:
Minor essential revisions

Level of interest: An article of limited interest
Quality of written English: Acceptable
Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests:
I declare that I have no competing interests
Is the question posed by the authors well defined?
Yes, the introduction properly defines the status of patients with DM type 2 and the problem of the pluripathology and associated polypharmacy which leads to the existence of relevants DRPs.

Thank you.

2. Are the methods appropriate and well described?

Study population is well defined and also the procedures and methodology for DRPs identification. Data analysis is appropriate for the research design.

Thank you.

3. Are the data sound?

Yes.

However, as defined study population and sample was calculated, they are only representative of that population, a generalization to wider population is not possible.

Thank you.

4. Does the manuscript adhere to the relevant standards for reporting and data deposition?

The data are properly expressed and clearly reflect the demographic and clinical status of patients.

In the subsection “Medication used in T2DM patients with dyslipidemia”, the most adequate would be to use the ATC classification: http://www.whocc.no/atc/structure_and_principles/.
The medications had been classified based on the pharmacological classes.

5. Are the discussion and conclusions well balanced and adequately supported by the data?

In the Conclusion section the last phrase of the first paragraph, and the second paragraph, are not related with data, and they are not a conclusion. They should be in the discussion section.

The phrases have been moved into the discussion section as per recommended. Although data are evaluated and compared with other similar studies, is not designated to that interpretation of the significance of the identified DRPs has clinical relevance only if it manifests itself as a real health problem.

6. Are limitations of the work clearly stated?

There are several limitations not mentioned in the text, like the fact that are different DRPs classifications which make it difficult to extrapolate data and compare them with others studies.

The lack of representativeness of the sample for the extrapolation of results
outside the specific scope of the study should be noted.

A section of study limitations have been included into the article, before the conclusion.

7. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished? Yes

Thank you.

8. Do the title and abstract accurately convey what has been found?

Yes. The title accurately describes the work and the abstract shows the most relevant aspects of this

Thank you.

9. Is the writing acceptable?

Yes, it’s correct.

In the references section is missing the reference 19

Reference 19 has been incorporated into the manuscript.

Commentaries

This is another observational study about identification of DRPs based in the review of clinical data.

DRPs are only an intermediate step in the whole process of medicine use. The aim of pharmaceutical care is to identify, prevent and resolve negative outcomes associated with medication (NOMs).

I recommend that authors read the paper: Fornos JA, Andrés NF, Andrés JC, Guerra MM, Egea BB.


Sure, thank you.

Conclusion

Methodology of the study is appropriate. It could be published with small changes, but lack of relevance because it’s an observational study with a small population size.