

2 March, 2015

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name:16561-edited).

Title: Use of biologic agents for rheumatic diseases in pregnancy

Author: Yesim Garip

Name of Journal: *World Journal of Rheumatology*

ESPS Manuscript NO: 16561

1 Format has been updated.

2 Revision has been made according to the suggestions of the reviewer.

Reviewer 1:

It is a well designed paper based on a popular subject. Only key words can be rearranged.

Answer: Key words have been rearranged.

Reviewer 2:

Experience in the management of anti-TNF biologics is perhaps more extensive, but the use of other biologic agents more recently included in therapeutic protocols is limited. Therefore, section concerning the use of other biologic agents during pregnancy is the especial interest. I would recommend broadening this part of the manuscript since it would be very useful for physicians implicated in the management of pregnant women.

Answer: You are absolutely right, however experience with use of other biologic agents during pregnancy is very limited.

Perhaps, addition of a table summarizing the main effect of biologic agents in pregnancy would be useful for having comprehensive overview of the topic of this review.

Answer: A table has been added.

Finally, English needs a review and there are some typos throughout the text that should be corrected.

Answer: Language has been revised and typos have been corrected.

Reviewer 3:

To introduce the discussion on the use of biologics during pregnancy in rheumatic disorders, it could be useful to discuss the relationship between disease activity and pregnancy outcomes. A complement to this point is the fact that biologics may impact on disease activity before pregnancy therefore favoring pregnancy.

Answer: Relationship between disease activity and pregnancy outcomes have been discussed in the introduction.

In the conclusions the author suggests to discontinue TNF inhibitors during late pregnancy. It is unclear on which basis he made this recommendation.

Answer: 'TNF inhibitors do not pass through the placenta during the first trimester, but they cross the placenta during the late second and third trimester' has been added to the conclusions.

A large debate exist on the time required to completely wash out these agents from the body. In general this exceeds three months.

Answer: This had been mentioned in the introduction as 'TNF inhibitors do not actively cross the placenta during the first trimester and organogenesis, but they are transferred across the placenta during the late second and third trimester [12]. These can be found in newborn's cord blood in levels that exceed those of the corresponding maternal serum [16-17]. Additionally, they are detectable in blood of the infant for more than six months after the birth, reducing the safety of vaccination [16]'

On page 9 there is a sentence on abatacept in the middle of the paragraph devoted to kineret that should be moved to the abatacept paragraph.

Answer: Anakinra has been replaced with abatacept.

Reviewer 4: One typo-page 5, middle of page 10% should replace %10

Answer: It has been corrected.

Reviewer 5: The author of this manuscript presents an overview on the use of biologic agents for the treatment of rheumatic diseases in pregnancy. Overall the review is written in a clear and concise manner. However, the rationale and potential side effects for the treatment of rheumatic diseases in pregnancy at the end of the article.

Answer: 'Why the biologics are suggested' and potential side effects from the use of biologic agents for the treatment of rheumatic diseases in pregnancy has been mentioned at the end of the article.

3 References and typesetting have been corrected

Thank you again for publishing our manuscript in the *World Journal of Rheumatology*

Sincerely yours

Yesim Garip, MD

Response to chief editor

First, thank you because of your comments on this manuscript. I have revised the manuscript based on your comments.

Comment 1. Please adopt the criteria of a systematic review; which databases were employed, how many titles and abstracts were screened and how many you final included in the review and why others were excluded.

Answer 1. Search strategy has been added to the manuscript.

Comment 2. The review deals essentially with anti-cytokines and anti cellular agents. I would group the paragraphs according to this subdivision.

Answer 2. The paragraphs have been rearranged according to this subdivision.

Comment 3. Safeness=safety

Answer 3. Safeness has been replaced with safety.

Additional modifications:

1. The description of table 1 has been added following search strategy.
2. Affiliation has been changed as ‘Pinar Physical Therapy and Rehabilitation Center’.

Thank you,

King regards

Dr. Yesim Garip