Reviewer's report

Title: Development of Hypoglycemia in Patients Treated with Tumor Necrosis Factor Alpha Inhibitors: An Observational Case Study.

Version: 1 Date: 26 July 2011

Reviewer: Carlos Wambier

Which of the following following best describes what type of case report this is?: Unreported or unusual side effects or adverse interactions involving medications

Has the case been reported coherently?: Yes

Is the case report authentic?: Yes

Is the case report ethical?: Yes

Is there any missing information that you think must be added before publication?: Yes

Is this case worth reporting?: Yes

Is the case report persuasive?: No

Does the case report have explanatory value?: No

Does the case report have diagnostic value?: No

Will the case report make a difference to clinical practice?: Yes

Is the anonymity of the patient protected?: Yes

Comments to authors:

Dear Dr Czajkowska,

Your series of cases contribute to the better understanding of adverse effects of TNF blockade and therefore it must be published.

However, I would suggest a major revision before acceptance to publication.

As you may know, since 2007 there have been many case reports involving the use of anti-TNF drugs and hypoglycemia in both Rheumatology and Dermatology journals (mainly RA and Psoriasis).

Your publication would be the largest series of cases published to date. That is
the most important aspect of your cases.

To make it more persuasive, I'd suggest some modifications:

1) Title: "series of cases" is more proper than an "observational study". And since the number of cases is important in your report, "Thirteen patients" is an important factor of your title.

2) In your abstract you point to a very important issue: "Under-Publicized" side effect. However, that discussion was lost in the paper itself. Although there are references of this side effect, you should include others, to further compare your findings (you have 13 patients!), with what was already published.

For example, how many other case reports have been published? How about the age group and gender, are they the same from literature or different? The onset of symptoms?

Your series have another particular issue: they were not DM patients. That must be compared with a review of what is already published.

(for example, in my practice, since the reports of severe hypoglycemic events in DM patients, I always advise patients start more frequent glycemic monitoring in the first month of treatment), should that recommendation be expanded?

3) Clinical description of patients: Regarding that metabolic control is an issue of your publication, please include patients weights. If you also have BMI and waist circumference, those would show important issues about prior insulin resistance. Another important aspect: how were those glycemic levels obtained? Capillary? Venous, fasting blood sample?

4) Dosage/posology: Please include the prescribed scheme for each patient. (it is important to know the dosage, and compare with the patients weight.

5) Clinical symptoms or signs: please include if any patient had felt or suffered from those glycemic levels. These levels characterize mild hypoglycemia. Were some of the patients asymptotic?

6) Too much discussion on molecular aspects of TNF action/mechanisms. Your data does not support or add to that discussion. You can keep objectivity if you could shorten those paragraphs on discussion to what you think is the most important aspect of the relationship of TNF blockade and hypoglycemia.

7) Focus your discussion: (MOST IMPORTANT PART OF THE REVIEW) use your discussion to compare your data (series of cases) with case reports in literature, and add more references, try to discuss and support your data. For example, comparing your cases with J Am Acad Dermatol. 2009 May;60(5):883-5 (fast onset (hours), use of insulin, severe hypoglycemia, with convulsions), Endocr Pract. 2011 Mar-Apr;17(2):306-7, (both lead to improved glycemic control after clinical management);

in your references, but not used in your discussion).

Please consider these suggestions and I look forward to revising your revised article.

**Quality of written English:** Acceptable

**Declaration of competing interests:**

I declare that I have no competing interests.