European Journal of Clinical Pharmacology
https://doi.org/10.1007/s00228-021-03119-8

LETTER TO THE EDITOR

Are adverse drug reactions to anti-diabetic drugs more common in patients whose treatment do not adhere to diabetes management clinical guidelines? Comments on a study report

Zahra Rezaie[1] · Maryam Taghizadeh-Ghehi[2] · Aarefeh Jafarzadeh Kohneloo[3]

Received: 8 December 2020 / Accepted: 2 March 2021

Dear editor,

We have read with great interest the article by Elangwe et al. entitled "Adverse drug reactions to anti-diabetic drugs are commonest in patients whose treatment do not adhere to diabetes management clinical guidelines: cross-sectional study in a tertiary care service in sub-Saharan Africa" [1]. The study evaluated the adherence to clinical guidelines in management of diabetes and reported decreased frequency of adverse drug reactions (ADRs) to anti-diabetic agents in patients who were treated by appropriate regimen. However, we faced some issues with respect to the study methods and results, which need to be highlighted.

The study primary objective was investigation of the pattern of anti-diabetic medication use. However, treatment pattern was not described well. Detailed description of combination therapies using oral hypoglycemic agents and the frequency of dual or triple therapies would have been important to report. Lacked data regarding utilized combinations in addition to the type of insulin preparations has made the drug use picture less informative and the conclusion regarding reported ADRs, specifically hypoglycemia, imprecise [2].

✉ Maryam Taghizadeh-Ghehi
taghizadehgm@sina.tums.ac.ir

Zahra Rezaie
Zrezaei89.zr@gmail.com

Aarefeh Jafarzadeh Kohneloo
Jafarzadeh-aaref@yahoo.com

[1] Department of Clinical Pharmacy, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran

[2] Research Center for Rational Use of Drugs, Tehran University of Medical Sciences, 4th floor, No 92, Karimkhan Zand Ave., Hafte Tir Sq, Tehran, Iran

[3] Department of Epidemiology and Biostatistics, Faculty of Health, Tehran University of Medical Sciences, Tehran, Iran

Considering the study primary objective, comparisons made on patients' characteristics between men and women in Table 1 seem unnecessary and redundant. In addition, some concerns raised here are with respect to the statistical analysis. Chi-square test was used for most statistical comparisons in Table 1. However, for the marital status and professional status, the frequency of certain cells was low, and zero frequency is seen in one cell. In these cells, the problem of "sparse data" exists. In such cases, exact tests which are based on "hypergeometric" distribution should be used, instead of the chi-square test [3].

As the secondary objective, authors assessed the adherence of anti-diabetic treatment to clinical guidelines and compared ADR frequency between treatment adherent and non-adherent groups. However, factors that could affect the occurrence of ADRs in study patients including demographic and clinical characteristics were not taken into account [4]. The frequency of hypoglycemia and weight gain was reported to be different among males and females in previous studies [5]. Moreover, the educational level or professional status of patients could affect the detection and self-report of ADRs. More importantly, data regarding glycemic control of patients and the patients' adherence to anti-diabetic medication in two study groups were necessary to make accurate inferences regarding the association between reported ADRs and the appropriateness of treatment. On the other hand, it was mentioned in the discussion section that the frequency of insulin use alone was less in adherent group than in non-adherent group and the higher hypoglycemia episodes in non-adherent group were explained accordingly. However, the reported values in the Table 2 correspond to total number of patients in each study groups who were treated with insulin, alone or in combination with oral hypoglycemic agents. The frequency of insulin use alone was not reported and compared.

Authors reported that the rate of ADR occurrence was higher in patients who were treated inappropriately. However, the frequency of events was only compared

Published online: 03 April 2021

between two groups, which was not statistically significant. The frequency of patients who developed ADRs was not compared between two groups. Additionally, the frequency of different types of ADRs had to be explored considering the events or the patients who developed ADRs as denominator. The problem of "sparse data" could also be observed in Table 2. For example, comparing the frequency of glibenclamide and lipodystrophy in this table definitely needs a Fisher's exact test. Given the high numbers of covariates, performing univariate analysis and then multiple logistic regression considering a model with influential covariates would have been necessary.

Code availability Not applicable.

Data Availability Not applicable.

Declarations

Competing interests The authors declare no competing interests.

References

1. Elangwe A, Katte J-C, Tchapmi D, Figueras A, Mbanya JC (2020) Adverse drug reactions to anti-diabetic drugs are commonest in patients whose treatment do not adhere to diabetes management clinical guidelines: cross-sectional study in a tertiary care service in sub-Saharan Africa. Eur J Clin Pharmacol 76(11):1601–1605. https://doi.org/10.1007/s00228-020-02949-2
2. Maruthur NM, Tseng E, Hutfless S, Wilson LM, Suarez-Cuervo C, Berger Z, Chu Y, Iyoha E, Segal JB, Bolen S (2016) Diabetes medications as monotherapy or metformin-based combination therapy for type 2 diabetes: a systematic review and meta-analysis. Ann Intern Med 164(11):740–751. https://doi.org/10.7326/M15-2650
3. Agresti A (2003) Categorical data analysis. Wiley
4. Alomar MJ (2014) Factors affecting the development of adverse drug reactions. Saudi Pharmaceut J 22(2):83–94. https://doi.org/10.1016/j.jsps.2013.02.003
5. Schütt M, Zimmermann A, Hood R, Hummel M, Seufert J, Siegel E, Tytko A, Holl R (2015) Gender-specific effects of treatment with lifestyle, Metformin or sulfonylurea on glycemic control and body weight: a German multicenter analysis on 9 108 patients. Exp Clin Endocrinol Diabetes 123(10):622–626. https://doi.org/10.1055/s-0035-1559608