Revista de Gastroenterología de México 88 (2023) 453–459

REVISTA DE GASTROENTEROLOGÍA DE MÉXICO

www.elsevier.es/rgmx

LETTER TO THE EDITOR

The Roussel-Uclaf hepatotoxicity causality assessment method in the context of diagnostic suspicion of drug-induced liver damage: Is it still valid?☆

El método de evaluación de causalidad de hepatotoxicidad de Roussel-Uclaf en el contexto de sospecha diagnóstica de daño hepático inducido por medicamentos: ¿es aún vigente?

Dear Editors,

I have carefully read the interesting study ''Drug-induced liver injury: Relation between the R ratio and histopathology'' by O.M. Ardila-Suárez et al., published in this journal. The authors state that the diagnosis of drug-induced liver injury (DILI) is based on the ruling out of other potential causes and on the clinical capacity to establish causality between the potentially hepatotoxic substance and abnormal liver biochemical profile results and that neither the Roussel-Uclaf hepatotoxicity causality assessment method (RUCAM) nor other methods were applied because of their limitations for use in retrospective studies.[1]

The RUCAM emerged from a consensus meeting on adverse reactions to drugs, at which it was proposed as a method for evaluating causality. It scores different criteria for studying the probability of causality of a drug: time to onset and course of the reaction; risk factors, such as age, alcohol use, or pregnancy; the search for other causes or concomitant medications; prior knowledge of toxicity; response to rechallenge; serum levels of the medication; and validated laboratory tests. In practice, the overall scoring range would be from −5 to +13, signifying the total of arguments for or against the drug as the cause of liver injury. A score of 0 or less excludes causality probability, it is unlikely with a score of 1-2, possible with a score of 3-5, probable with a score of 6-8, and highly probable with a score over 9. Table 1 shows a model of the RUCAM, adapted from the original publication by Danan and Benichou[2] (Annex. Supplementary material).

Articles analyzing the use of the RUCAM conclude that the causality assessment method adapts to prospective and retrospective studies and is a reliable tool in the context of DILI and herb-induced liver injury (HILI) for establishing the association of the cases with the suspected offending drug or herb. Thus, RUCAM should be systematically implemented and included in the clinical history of patients suspected of presenting with DILI.[3]

RUCAM is a validated method that is useful as a diagnostic algorithm for attaining a probable or highly probable causality score for the suspected drug. It provides a solid causality assessment of drugs suspected of involvement in DILI, which is of particular significance, given that the management of idiosyncratic DILI is considered a therapeutic challenge.[4]

The RUCAM appeared in 1993 and is a widely used tool worldwide for diagnosing DILI and HILI in a large number of epidemiologic studies, case reports, and case series. The RUCAM has been shown to have high sensitivity (86%) and specificity (89%), with elevated positive predictive values (93%) and negative predictive values (78%). In addition, it has shown good reproducibility results and low interobserver variability. At present, the RUCAM continues to be the main standard for causality assessment methods when drug-induced or herb-induced liver injury is suspected.[5]

Financial disclosure

No financial support was received in relation to this letter to the editor.

Conflict of interest

The author declares that there is no conflict of interest.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.rgmxen.2023.04.016.

References

1. Ardila-Suárez OM, Oriz-Benjumea L, Arteta AA, et al. Daño hepático inducido por medicamentos: relación entre el índice R y la histopatología. Rev Gastroenterol Mex. 2023;88:19–27, http://dx.doi.org/10.1016/j.rgmx.2021.03.008.
2. Danan G, Benichou C. Causality assessment of adverse reactions to drugs — I. A novel method based on the conclusions of International Consensus Meetings: application to drug-

☆ Please cite this article as: Sánchez Luque CB. El método de evaluación de causalidad de hepatotoxicidad de Roussel-Uclaf en el contexto de sospecha diagnóstica de daño hepático inducido por medicamentos: ¿es aún vigente? Rev Gastroenterol Mex. 2023;88:453–454.

induced liver injuries. J Clin Epidemiol. 1993;46:1323–30, http://dx.doi.org/10.1016/0895-4356(93)90101-6.
3. Danan G, Teschke R. Roussel Uclaf causality assessment method for drug-induced liver injury: present and future. Front Pharmacol. 2019;29:853, http://dx.doi.org/10.3389/fphar.2019.00853.
4. Teschke Rolf. Treatment of drug-induced liver injury. Biomedicines. 2023;11:15, http://dx.doi.org/10.3390/biomedicines11010015.
5. Danan G, Teschke R. Drug-induced liver injury: why is the Roussel Uclaf Causality Assessment Method (RUCAM) still used 25 years after its launch? Drug Saf. 2018;41:735–43, http://dx.doi.org/10.1007/s40264-018-0654-2.

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Answer to Sánchez-Luque et al. regarding ''The Roussel-Uclaf hepatotoxicity causality assessment method in the context of diagnostic suspicion of drug-induced liver damage: Is it still valid?''☆

Respuesta a Sánchez-Luque et al.: «El método de evaluación de causalidad de hepatotoxicidad de Roussel-Uclaf (RUCAM) en el contexto de sospecha diagnóstica de daño hepático inducido por medicamentos DILI: ¿es aún vigente?»

We have attentively read the letter to the editor by Dr. Sánchez Luque, with respect to the absence of the Roussel-Uclaf hepatotoxicity causality assessment method (RUCAM) in our study. Unfortunately, all the variables required for completing the latest version of that scoring method were not available in all the cases we studied.[1] We compiled our study population from a database of histopathologic reports of liver samples, not from the viewpoint of the treating clinicians. Thus, added to the limitations inherent in retrospective studies, data, such as the course of ALT levels at 180 days of follow-up and all the tests for determining alternate causes, were not available for the majority of cases. Likewise, the specific question about previous reactions to a given drug or substance, involving liver damage, or re-exposures to those agents, were not reported in the clinical histories of each patient.

Therefore, had we calculated the score of the RUCAM in our cases, the result would inevitably have been erroneous and most likely lower than the hypothetically real one, in turn, leading to disinformation about the accuracy of the tool for analyzing such cases. As Dr. Sánchez Luque correctly pointed out, the accuracy of the RUCAM is very high, but requires a level of quality and checklist that are not always available in retrospective studies.

☆ Please cite this article as: Ardila-Suárez OM, Oriz-Benjumea L, Arteta AA, Guevara-Casallas LG. Respuesta a Sánchez-Luque et al.: «El método de evaluación de causalidad de hepatotoxicidad de Roussel-Uclaf (RUCAM) en el contexto de sospecha diagnóstica de daño hepático inducido por medicamentos DILI: ¿es aún vigente?» Rev Gastroenterol Mex. 2023;88:454.

Financial disclosure

No financial support was received in relation to this letter.

Conflict of interest

The authors declare that there is no conflict of interest.

Reference

1. Sánchez-Luque AB. El método de evaluación de causalidad de hepatotoxicidad de Roussel-Uclaf (RUCAM) en el contexto de sospecha diagnóstica de daño hepático inducido por medicamentos DILI: es aún vigente? Rev Gastroenterol Mex. 2023;88.

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