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CE - LETTER TO THE EDITOR

Adverse drug reactions in SARS-COV-2 hospitalised patients: a case series with a focus on drug–drug interactions—comment

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Dear Editor,

We recently read with great interest the article written by Crescioli et al. with the title "Adverse drug reactions in SARS-CoV-2 hospitalised patients: a case series with a focus on drug–drug interactions" [1]. We agree to the authors when state that "due to the need of early and emergency effective treatments for COVID-19, less attention may have been paid to their safety during the global emergency".

We have some considerations with respect to this article. First of all, it would have been very interesting to know the overall number of patients that have been admitted to the hospital, where the study was carried out during the period of study to consider the prevalence of adverse drug reactions among these inpatients. Besides, knowing the number of patients treated with the different drugs could improve the assessment of burden due to pharmacological treatments in COVID-19 inpatients.

On the other hand, drug–drug interactions (DDIs) have been analysed among these inpatients. According to the authors, "all patients presented at least one DDI" and "among 82 different DDIs, 53 (64.4%) were moderate, and 32 (39%) increased the risk of QT prolongation" [1]. According to our experience in DDIs [2], we prefer the term "potential DDIs (pDDIs)" defined as "drug pairs that could potentially interact and result in an adverse reaction, which had been previously described in an interaction database, drug reference guides or drug compendia" [2]. This consideration is based on the fact that no causality relationship can be established among DDIs and drug-related deaths, because no tool to assess this relationship has been reported yet [2] and, not all interactions are irretrievably associated with adverse drug reactions. In fact, one study recently published showed that not critically ill patients with COVID-19 treated with hydroxychloroquine, azithromycin, and/or antiretrovirals develop a significant, but not clinically relevant, QT interval prolongation [3]; in this research, advanced age, prolonged baseline QTc and low basal potassium levels were independent markers for this prolongation [3].

Finally, besides the difficulty in identifying adverse drug reactions, imputation of the drugs responsible is more challenging in dead patients as previously reported by our research group [4]. Though Naranjo's scale is the most frequently used to assess the causality relationship between the suspected drugs and their related adverse drug reactions, its sensitivity to detect fatal adverse drug reactions in deceased patients is low [4]. In fact, a previous study [5] by our group using this algorithm found a significantly lower prevalence of drug-related deaths compared to another study, based on the same population, in which we used other methodology [4]. The lower sensitivity of Naranjo´s algorithm in deceased patients is because of the lack of information on the response of the individual to the withdrawal, and re-administration of the suspected drug, which are both considered crucial in this scale for the definite imputation of a drug [4]. In their paper, Crescioli et al. show, in Table 3, the features of adverse drug reactions and their outcomes. Among the inpatients with suspected drug-related deaths, the mean age was 83 years (range 70–93), and all of them had severe polypharmacy and multimorbidity. We consider that these deaths may be considered, at least, as "suspected" to be drug-related given the high number of risk factors for death of each patient.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Human and animal rights statement This article does not contain any studies with human and participants or animal performed by any of the authors.

Informed consent For this type of study, formal consent is not required.

References

1. Crescioli G, Brilli V, Lanzi C et al (2020) Adverse drug reactions in SARS-CoV-2 hospitalised patients: a case-series with a focus on drug–drug interactions. Intern Emerg Med. https://doi.org/10.1007/s11739-020-02586-8
2. Pardo-Cabello AJ, Manzano-Gamero V, Del Pozo E et al (2019) Potential drug-drug interactions in deceased inpatients. Intern Emerg Med 14(2):325–328. https://doi.org/10.1007/s11739-018-1972-1
3. Jiménez-Jáimez J, Macías-Ruiz R, Bermúdez-Jiménez F et al (2020) Absence of relevant QT interval prolongation in not critically ill COVID-19 patients. Sci Rep 10:21417. https://doi.org/10.1038/s41598-020-78360-9
4. Pardo Cabello AJ, Del Pozo GE, Gómez Jiménez FJ et al (2016) Drug-related mortality among inpatients: a retrospective observational study. Eur J Clin Pharmacol 72(6):731–736. https://doi.org/10.1007/s00228-016-2026-0
5. Pardo Cabello AJ, González Contreras LG, ManzanoGamero MV et al (2009) Prevalence of fatal adverse drug reactions in hospitalized patients. Int J Clin Pharmacol Ther 47:596–602