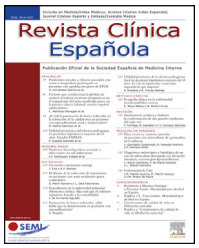
Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Revista Clínica Española 222 (2022) 309–311

Revista Clínica Española

www.elsevier.es/rce



CORRESPONDENCE

Glucocorticoid therapy in patients with COVID-19 and concurrent heart failure☆

Tratamiento con glucocorticoides en pacientes con COVID-19 e insuficiencia cardíaca concurrente

Dear Director:

We read with interest the multicentre, retrospective study performed by Salinas-Botrán et al.[1] to identify the risk factors associated with in-hospital mortality among patients with heart failure hospitalized due to coronavirus disease 2019 (COVID-19).

It was reported from their multivariate analysis that age (adjusted odds ratio [AOR]: 1.03; 95% confidence interval [95% CI] 1.02–1.05), severe dependence (AOR: 1.62; 95% CI 1.19–2.20), baseline tachycardia (AOR: 1.01; 95% CI 1.00–1.01), baseline C-reactive protein level (AOR: 1.004; 95% CI 1.002–1.004), baseline lactate dehydrogenase level (AOR: 1.001; 95% CI: 1.001–1.002), and baseline serum creatinine level (AOR: 1.35; 95% CI 1.18–1.54) were independently associated with in-hospital mortality in their cohort of patients with heart failure hospitalized due to COVID-19. In fact, these identified risk factors of mortality are common in patients with COVID-19, including those without heart failure[2,3].

Nevertheless, based on their findings, it appears that the use of glucocorticoids, which was not incorporated into their multivariate analysis, could also be associated with in-hospital mortality in their cohort of patients. The study reported that the deceased patients had a significantly higher rate of glucocorticoid use than the patients who stayed alive during hospitalization (47.4% vs. 41.7%; $p = .015$). While this may be due to confounding bias, in which the use of glucocorticoids could have selected patients with higher disease severity, we took notice that the deceased patients had a significantly higher rate of development of acute decompensated heart failure than the patients who stayed alive during hospitalization (35.7% vs. 28.6%; $p < .001$).

Apart from their anti-inflammatory activity, glucocorticoids, especially hydrocortisone, prednisone, and prednisolone, can produce an appreciable mineralocorticoid effect, subsequently leading to fluid retention[4]. This may be clinically insignificant in otherwise normal subjects (without heart failure) due to the phenomenon of mineralocorticoid escape that prevents progressive fluid overload. Still, patients with underlying heart disease, particularly those with congestive heart failure, may not be able to tolerate the mineralocorticoid effect of glucocorticoids, which can worsen their pre-existing fluid overload and precipitate acute decompensation of heart failure, as well as subsequent morbidity and mortality. Indeed, a recent study[5] (n = 1155) reported that the use of glucocorticoids was associated with higher rates of in-hospital death, acute decompensated heart failure, need for invasive and non-invasive mechanical ventilation, and in-hospital complications, in patients with heart failure hospitalized for COVID-19. The findings contrast with the widely recognized mortality benefits of glucocorticoid therapy in patients with severe course of COVID-19.

Therefore, pending more investigations, we believe that caution should be exercised in the administration of glucocorticoids in patients with heart failure hospitalized for COVID-19; glucocorticoids with appreciable mineralocorticoid effect such as hydrocortisone should be avoided, while dexamethasone[6] and methylprednisolone[7] with no clinically important mineralocorticoid activity should be preferred when clinically indicated. Indeed, hydrocortisone can also have lower potency compared to dexamethasone in terms of anti-inflammatory activities[8]. In addition, the short-term use of glucocorticoids with minimal mineralocorticoid action, when added to maximum diuretic therapy, can potentiate renal responsiveness to diuretic therapy in patients with congestive heart failure[9]. Alternatively, if glucocorticoids are deemed inappropriate, interleukin-6 antagonists can be administered[10].

We look forward to the authors' reply to report the types of glucocorticoids administered to their cohort of patients with heart failure hospitalized due to COVID-19. In addition, if feasible, the authors should incorporate the use of different types of glucocorticoids in their multivariate analysis to determine if the use of glucocorticoids was associated with in-hospital mortality in their cohort of patients.

References

1. Salinas-Botrán A, Sanz-Cánovas J, Pérez-Somarriba J, Pérez-Belmonte LM, Cobos-Palacios L, Rubio-Rivas M, et al. Características clínicas y factores de riesgo al ingreso de mortalidad en pacientes con insuficiencia cardíaca hospitalizados por COVID-19 en España. Rev Clin Esp. 222:255–65.

☆ Please cite this article as: Kow CS, Ramachandram DS, Hasan SS. Tratamiento con glucocorticoides en pacientes con COVID-19 e insuficiencia cardíaca concurrente. Rev Clin Esp. 2022;222:309–310.

2. Dessie ZG, Zewotir T. Mortality-related risk factors of COVID-19: a systematic review and meta-analysis of 42 studies and 423,117 patients. BMC Infect Dis. 2021;21:855.
3. Zhang L, Hou J, Ma FZ, Li J, Xue S, Xu ZG. The common risk factors for progression and mortality in COVID-19 patients: a meta-analysis. Arch Virol. 2021;166:2071–87.
4. Becker DE. Basic and clinical pharmacology of glucocorticosteroids. Anesth Prog. 2013;60:25–32.
5. Pérez-Belmonte LM, Sanz-Cánovas J, Salinas A, Sagastagoitia Fornie I, Méndez-Bailón M, Gómez-Huelgas R, et al. Corticosteroid therapy in patients with heart failure hospitalized for COVID-19: a multicenter retrospective study. Intern Emerg Med. 2021;16:2301–5.
6. Horby P, Lim WS, Emberson JR, Mafham M, Bell JL, Linsell L, et al. RECOVERY Collaborative Group. Dexamethasone in hospitalized patients with Covid-19. N Engl J Med. 2021;384:693–704.
7. Hasan SS, Kow CS, Mustafa ZU, Merchant HA. Does methylprednisolone reduce the mortality risk in hospitalized COVID-19 patients? A meta-analysis of randomized control trials. Expert Rev Respir Med. 2021;15:1049–55.
8. Kow CS, Hasan SS. Dexamethasone or hydrocortisone in COVID-19? Cleve Clin J Med. 2020;87:715.
9. Liu C, Liu K. Effects of glucocorticoids in potentiating diuresis in heart failure patients with diuretic resistance. J Card Fail. 2014;20:625–9.
10. Kow CS, Zaihan AF, Ramachandram DS, Hasan SS. IL-6 antagonists to replace systemic corticosteroids as the preferred anti-inflammatory therapy in patients with COVID-19? Cytokine. 2022 Jan;149:155730.

C.S. Kow[a,*], D.S. Ramachandram[b], S.S. Hasan[c,d]

[a] *School of Postgraduate Studies, International Medical University, Kuala Lumpur, Malaysia*
[b] *School of Pharmacy, Monash University Malaysia, Bandar Sunway, Subang Jaya, Selangor, Malaysia*
[c] *School of Applied Sciences, University of Huddersfield, Huddersfield, United Kingdom*
[d] *School of Biomedical Sciences & Pharmacy, University of Newcastle, Callaghan, Australia*

* Corresponding author.
E-mail address: chiasiang_93@hotmail.com (C.S. Kow).

Answer to the ''Glucocorticoid therapy in patients with COVID-19 and concurrent heart failure'' correspondence☆

Respuesta a la carta «Tratamiento con glucocorticoides en pacientes con COVID-19 e insuficiencia cardíaca concurrente»

Dear Director,

We are grateful for the comments on our article ''Clinical characteristics and risk factors for mortality upon admission in patients with heart failure hospitalized due to COVID-19 in Spain.''[1] Indeed, glucocorticoid (GC) use was greater in patients with heart failure (HF) hospitalized for COVID-19 who died. This can be explained by the effects of the mineralocorticoid and sodium and water retention, as the letter's authors correctly indicate.[2]

Unfortunately, we do not have specific data regarding the type of GC used; the only data recorded were whether they were used or not, the dose used, and the duration of treatment (SEMI-COVID-19 Registry).[3] However, the following considerations should be noted:

First, the most used GC during the first wave of the epidemic in Spain was methylprednisolone, as a recent article indicated.[4] Evidence on the reduction in mortality associated with the use of dexamethasone was not reported until later on[5] and as such, it was used less in our country during the first wave.

Second, the initial multivariable analysis conducted in our study included patients' baseline clinical variables at the time of admission and did not include variables regarding treatment administered. We are currently working on a larger, more focused database in order to discern the effect of treatment, including the use of GC (especially dexamethasone) on this profile of patient.

Lastly, and in contrast to the possible deleterious effect of GC in patients with HF, it should be noted that some recent works have demonstrated the utility of other drugs in patients with HF during hospitalization for COVID-19. Patients with HF who continued treatment with renin-angiotensin-aldosterone system inhibitors during hospitalization had lower in-hospital mortality rates than those who did not receive them or in whom they were suspended.[6]

In conclusion, according to our results, GC should be used with caution in patients with HF, weighing their risks and benefits. More prospective, controlled studies on the use of GC in patients with HF and COVID-19 are needed to confirm these results.

References

1. Salinas-Botrán A, Sanz-Cánovas J, Pérez-Somarriba J, Pérez-Belmonte LM, Cobos-Palacios L, Rubio-Rivas M, et al. Características clínicas y factores de riesgo de mortalidad al ingreso en pacientes con insuficiencia cardíaca hospitalizados por COVID-19 en España. Rev Clin Esp. 2022;222:255–65.
2. Kow CS, Ramachandram DS, Hasan SS. Tratamiento con glucocorticoides en pacientes con COVID-19 e insuficiencia cardíaca concurrente. Rev Clin Esp. 2022;222:309–10.
3. Casas-Rojo JM, Antón-Santos JM, Millán-Núñez-Cortés J, Lumbreras-Bermejo C, Ramos-Rincón JM, Roy-Vallejo E, et al. Características clínicas de los pacientes hospitalizados con COVID-19 en España: resultados del Registro SEMI-COVID-19. Rev Clin Esp. 2020;220:480–94.

☆ Please cite this article as: Salinas-Botrán A, Pérez-Belmonte LM, Méndez-Bailón M. Respuesta a la carta «Tratamiento con glucocorticoides en pacientes con COVID-19 e insuficiencia cardíaca concurrente». Rev Clín Esp. 2022;222:310–311.