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caciones se relaciona en mayor medida con la técnica que con la vía de acceso^{2,3}. La obtención de accesos vasculares guiada por ultrasonidos ha simplificado la técnica, minimizando las complicaciones. El acceso yugular interno ecoguiado permite una rápida canulación, reduciendo complicaciones pulmonares como pneumo o hemotórax, en comparación con el acceso subclavio, y minimizando complicaciones vasculares, en contraposición a la punción guiada por escopia o anatomía^{2,3}. Asimismo, el acceso yugular facilitaría el acceso de los electrocatéteres al ventrículo derecho y con ello los procedimientos.

2. *Preservación de accesos venosos:* la gran mayoría de los implantes de dispositivos definitivos se realiza habitualmente por vía subclavia izquierda, incluso en pacientes que requieren previamente marcapasos temporal. Aunque el acceso femoral evitaría la trombosis de las venas del hemicuerpo superior, el previsible efecto a gran escala sería marginal como demuestra el hecho de que a la mayoría pacientes, incluidos en las series con acceso yugular, se les implanta un marcapasos definitivo².
3. *Infecciones y tromboembolias:* Es bien conocido que los electrodos femorales se asocian con infección local y sepsis, así como con trombosis venosa profunda y embolia pulmonar. Los autores reportan una limitada aparición de infecciones y una ausencia de eventos trombóticos. Aportar información acerca de si fue empleada profilaxis infecciosa o tromboembólica podría aportar una valiosa información para comprender mejor el estudio^{4,5}.
4. *Demora hasta el implante definitivo:* finalmente, queríamos destacar que la mayoría de las complicaciones aumenta a medida que se dilata el tiempo hasta el implante definitivo. Aunque la causa de la bradiarritmia pueda ser reversible, el grueso de los pacientes acabará siendo subsidiario de marcapasos definitivo. En este estudio, 32 de 35 pacientes (91,4%) recibieron marcapasos definitivo con una media hasta el implante de $4,9 \pm 4,6$ días. Aunque los autores refieren que es un tiempo de espera corto, reducir estos tiempos, en caso de bradiarritmias previsiblemente no reversibles, podría conllevar una reducción relevante en las complicaciones al generalizar los procedimientos.

En conclusión, concordamos con los autores en la utilidad del empleo de electrodos de fijación activa para prevenir la dislocación de los electrodos. Sin embargo, con base en la información disponible actualmente, consideramos que el acceso yugular ecoguiado y la pronta implantación de los dispositivos definitivos debería considerarse la estrategia de elección.

Bibliografía

1. Keituqwa Yáñez I, Navarro Martínez J, García Valiente M, Rodríguez González FJ, Nicolás Franco S. Outcomes of temporary pacing via transfemoral externalize active fixation leads. *Med Intensiva*. 2021; <http://dx.doi.org/10.1016/j.medint.2020.11.005>. Online ahead of print. S0210-5691(20)30346-6.
2. Suarez K, Banchs JE. A review of temporary permanent pacemakers and a comparison with conventional temporary pacemakers. *J Innov Card Rhythm Manag*. 2019;10:3652–61.
3. Ferri LA, Farina A, Lenatti L, Ruffa F, Tiberti G, Piatti L, et al. Emergent transvenous cardiac pacing using ultrasound guidance: A prospective study versus the standard fluoroscopy-guided procedure. *Eur Heart J Acute Cardiovasc Care*. 2016;5: 125–9.
4. Peters G, Saborowski F, Locci R, et al. Investigations on staphylococcal infection of transvenous endocardial pacemaker electrodes. *Am Heart J*. 1984;108:359–65.
5. Nolewajka AJ, Goddard MD, Brown TC. Temporary transvenous pacing and femoral vein thrombosis. *Circulation*. 1980;62:646–50.

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<https://doi.org/10.1016/j.medint.2021.03.003>
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Dexametasona en COVID-19: ¿un medicamento para todos?



Dexamethasone in COVID-19: does one drug fit all?

Dear Editor,

The COVID-19 pandemic challenged clinicians worldwide to treat a new and unknown disease. With more than 95 million confirmed cases since its beginning¹, a lot of effort has been made to identify the best possible treatments.

The RECOVERY trial² provides strong evidence in favor of the administration of 6 mg of dexamethasone for ten days once a day in COVID-19 patients, if requiring at least oxygen

supplementation (the incidence of death in the dexamethasone group compared to the usual care group was 23.3% vs 26.2% for patients receiving oxygen, and 29.3% vs 41.4% for patients under mechanical ventilation at the time of randomization). This finding changed the WHO therapeutic guidelines for patients with COVID-19³ and triggered into clinicians the automatic binomial prescription: oxygen therapy-dexamethasone. In the current pandemic era, where everyone is searching for the magic bullet, and no clear evidence is available on any therapeutic agent capable to reduce mortality, having this option with such a familiar drug gave back to clinicians the feeling of having at least a weapon.

The trial findings were confirmed also in a recent meta-analysis⁴ including more than seven thousand patients: overall mortality was significantly lower in the corticos-

teroids group (26% vs 28%, relative risk {RR} = 0.89 [95% confidence interval {CI} 0.82-0.96], p=0.003). However, for COVID-19 patients not requiring oxygen the meta-analysis suggested an increase in mortality in patients receiving corticosteroids (17% vs 13%, RR = 1.23 [95% CI 1.00-1.62], p = 0.05).

The rationale for the use of dexamethasone is the mitigation of the inflammatory organ injury that may occur during SARS-CoV-2 infection. In the RECOVERY Trial the benefit of dexamethasone was indeed clear when inflammatory lung damage was more likely to be common, that is supposed to be in those patients treated "more than 7 days after symptom onset". However, as mentioned by the authors of the trial, only a subgroup of severe COVID-19 patients showed significant elevation in inflammatory biomarkers (such as C-reactive protein and ferritin), and unfortunately the "inflammatory lung damage" was advocated but not assessed.

Beside the desired anti-inflammatory effect, dexamethasone is also known for its immunosuppressive properties, that can lower resistance to bacterial and viral infections through a cell-mediated mechanism. Although steroids were recently found not to affect time to negativization of nasopharyngeal swab in a cohort of 280 Italian patients⁵, the development of secondary opportunistic infections certainly remains a major issue, affecting patients' outcome.

Furthermore, as well as corticosteroids increase mortality in patients not requiring oxygen therapy⁴, it is reasonable to think that their effect among patients requiring low flow oxygen could be mixed. As in a previous study⁶ that identified two different subphenotypes of acute respiratory distress syndrome, one of which was categorised by more severe inflammation, it is likely that also in COVID-19 patients different inflammatory patterns may occur. In support to this previous finding, a recent review and meta-analysis of COVID-19 studies focused on the role of cytokines and inflammatory biomarkers and found different mean levels of C-reactive protein between severe and critical COVID-19 patients (55.9 µg/mL [CI 23.1-88.8 µg/mL

Beyond the initial enthusiasm after the trial results, leading to an almost indiscriminate adoption of dexamethasone in COVID-19 patients, we suggest that a more personalized prescription would lead to further improvements in patients' outcome. We think that, beside avoiding corticosteroids for patients not on oxygen, COVID-19 patients requiring oxygen should be screened for high or normal inflammatory biomarkers thresholds. Furthermore, for those patients who may benefit from corticosteroid treatment it is reasonable to investigate whether a higher or a lower dose of dexamethasone is most beneficial, and a clinical trial is currently ongoing randomising patients with severe hypoxia to receive either 6 or 12 mg of dexamethasone.⁷

This would serve to target inflammation only in those patients who would probably benefit from its modulation, while removing the burden of corticosteroids side effects in those patients without an inflammatory pattern who would probably not benefit from this therapy.

Authors' contributions

All the authors have substantially contributed to the conception of the work, and to the drafting or revision; all the authors have approved the final version and agree to be accountable for all the aspects of the work.

Conflict de intereses

Los autores declaran no tener ningún conflicto de intereses.

Bibliografía

- WHO Coronavirus Disease (COVID-19) Dashboard, <https://covid19.who.int>. [accessed 10 February 2021].
- RECOVERY Collaborative Group; Horby P, Lim WS, Emberson JR, Mafham M, Bell JL, Linsell L, et al. Dexamethasone in Hospitalized Patients with Covid-19. *N Engl J Med.* 2021;384:693-704, <https://doi.org/10.1056/NEJMoa2021436>. Epub Jul 17 2020.
- Therapeutic Management | COVID-19 Treatment Guidelines (nih.gov) <https://www.covid19treatmentguidelines.nih.gov/therapeutic-management/>. [accessed 10 February 2021].
- Pasin L, Navalesi P, Zangrillo A, Kuzovlev A, Likhvantsev V, Hajjar LA, et al. Corticosteroids for Patients With Coronavirus Disease 2019 (COVID-19) With Different Disease Severity: A Meta-Analysis of Randomized Clinical Trials. *J Cardiothorac Vasc Anesth.* 2021 Feb;35:578-84, <http://dx.doi.org/10.1053/j.jvca.2020.11.057>.
- Spagnuolo V, Guffanti M, Galli L, Poli A, Rovere Querini P, Ripa M, et al., COVID-BioB study group. Viral clearance after early corticosteroid treatment in patients with moderate or severe covid-19. *Sci Rep.* 2020 Dec 4;10:21291, <http://dx.doi.org/10.1038/s41598-020-78039-1>.
- Calfee CS, Delucchi K, Parsons PE, Thompson BT, Ware LB, Mattay MA. NHLBI ARDS Network Subphenotypes in acute respiratory distress syndrome: latent class analysis of data from two randomised controlled trials. *Lancet Respir Med.* 2014 Aug;2:611-20, [http://dx.doi.org/10.1016/S2213-2600\(14\)70097-9](http://dx.doi.org/10.1016/S2213-2600(14)70097-9). Epub May 19 2014.
- Higher vs. Lower Doses of Dexamethasone for COVID-19 and Severe Hypoxia (COVIDSTEROID2). <https://clinicaltrials.gov/ct2/show/NCT04509973>.

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<https://doi.org/10.1016/j.medir.2021.03.008>

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