
USO DE ESTEROIDES NO TRATAMENTO DA COVID-19

O Projeto Diretrizes, uma iniciativa da Associação Médica Brasileira, visa combinar informações da área médica para padronizar as condutas, e para auxiliar no raciocínio e na tomada de decisões dos médicos. As informações fornecidas por esse Projeto devem ser avaliadas criticamente pelo médico responsável pela conduta que será adotada, dependendo das condições e do quadro clínico de cada paciente.

Elaboração: julho de 2021.

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QUESTÃO CLÍNICA

Em pacientes com diagnóstico de COVID-19 leve o uso terapêutico de esteroides reduz o risco de hospitalização (enfermaria ou UTI), ventilação mecânica ou mortalidade, e não aumenta o risco de eventos adversos?

MÉTODO

CRITÉRIOS DE ELEGIBILIDADE PARA OS ESTUDOS A SEREM INCLUÍDOS

PICO

Paciente: COVID-19 leve confirmado por PCR

Intervenção: Esteróide (VO, IV, IM) (não associado)

Comparação: Sem esteróide ou placebo

Outcome: hospitalização (enfermaria ou UTI), ventilação mecânica, mortalidade e eventos adversos

Desenho de estudo: Ensaios clínicos randomizados (ECR) fase 3 e Revisões sistemáticas de ECR fase 3 atendendo ao PICO.

Outros critérios: Sem limites de período consultado, de idioma ou de disponibilidade de texto completo.

BASES CONSULTADAS COM AS RESPECTIVAS ESTRATÉGIAS

Medline e EMBASE

#1 = COVID OR COV OR CORONAVIRUS OR SARS

#2 = (Steroids OR Steroid OR Betamethasone OR Dexamethasone OR Flumethasone OR Fluocinolone Acetonide OR Fluocortolone OR Fluorometholone OR Fluoxymesterone OR Fluprednisolone OR Flurandrenolone OR Flurogestone Acetate OR Paramethasone OR Pregnadienes OR Pregnanediol OR Pregnanediones OR Pregnanetriol OR Pregnanolone OR Pregnatrienes OR Pregnenes OR Tetrahydrocortisol OR Triamcinolone)

#3 = #1 AND #2 = 2.389 (13 05 2021)

#4 = #3 AND Random* = 234

EMBASE, Central Cochrane e Clinical Trials

COVID AND Steroids

DADOS EXTRAÍDOS

Serão extraídos dos trabalhos os dados referentes à autoria, ano de publicação, descrição dos pacientes, das intervenções (Esteroides e comparação), dos desfechos e do tempo de seguimento.

RISCO DE VIESES E QUALIDADE DA EVIDÊNCIA

O risco de vieses será avaliado por meio dos itens do Rob 2¹, acrescidos de outros elementos fundamentais, e expresso em muito grave, grave ou não grave. A qualidade da evidência será extrapolada a partir do risco de vieses obtido do(s) estudo(s), se não houver meta-análise, utilizando a terminologia GRADE² em muito baixa, baixa e elevada, e por meio do software GRADEpro² (se houver meta-análise) em muito baixa, baixa, moderada e elevada.

ANÁLISE E SÍNTESE DOS DESFECHOS

Os desfechos quando categóricos serão expressos por grupo (Esteroides e comparação) e por meio do número de eventos e do risco calculado (%) para cada grupo (divisão do número de eventos pelo total de pacientes em cada grupo). Caso a diferença do risco (DR) entre os grupos seja significativa (confiança de 95%) esta será expressa acompanhada do Intervalo de Confiança de 95% (IC95%) e do Número Necessário para tratar (NNT) ou para produzir dano (NNH). Se houver mais de um estudo incluído com desfechos comuns este serão agregados por meio da meta-análise utilizando-se o software RevMan 5.4³.

RESULTADOS

Foram recuperados 226, 28, 92 e 78 estudos na base Medline, Embase, Central Cochrane e Clinical Trials.gov, respectivamente. Eliminando-se as duplicatas e atendendo aos critérios de elegibilidade foram selecionados 18 estudos para que seus textos completos fossem acessados, dos quais se excluiu 18 trabalhos (motivos de exclusão na Tabela 1 – planilha Inclusão/Exclusão motivos)⁴⁻²¹. Então, para sustentar esta avaliação atendendo aos critérios de elegibilidade não foi possível adotar estudos.

SÍNTESE DA EVIDÊNCIA (CONCLUSÃO)

Não há evidência baseada em ensaios clínicos randomizados avaliando o uso de esteroides (VO, IV, IM) em pacientes com quadro de COVID-19 leve.

RECOMENDAÇÃO

O uso de esteroide em pacientes com quadro de COVID-19 leve não deve ser utilizado.

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2600(21)00160-0. doi: 10.1016/S2213-2600(21)00160-0. Epub ahead of print. Erratum in: Lancet Respir Med. 2021 Apr 14; PMID: 33844996; PMCID: PMC8040526.

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ANEXOS

TABELA 1 – ESTEROIDES NA COVID-19 LEVE INCLUSÃO E EXCLUSÃO

PMID	Title	Authors	Citation	First Author	Journal/ Book	Publication Year	Create Date	DOI	INCLUÍDO/EXCLUÍDO (MOTIVOS)
32785710	Methylprednisolone as Adjunctive Therapy for Patients Hospitalized With Coronavirus Disease 2019 (COVID-19; Metcovid): A Randomized, Double-blind, Phase IIb, Placebo-controlled Trial	Jeronimo CMP, Farias MEL, Val FFA, Sampaio VS, Alexandre MAA, Melo GC, Safe IP, Borba MGS, Netto RLA, Maciel ABS, Neto JRS, Oliveira LB, Figueiredo EFG, Oliveira Dinelly KM, de Almeida Rodrigues MG, Brito M, Mourão MPG, Pivoto João GA, Hajjar LA, Bassat Q, Romero GAS, Naveca FG, Vasconcelos HL, de Araújo Tavares M, Brito-Sousa JD, Costa FTM, Nogueira ML, Baía-da-Silva DC, Xavier MS, Monteiro WM, Lacerda MVG; Metcovid Team.	Clin Infect Dis. 2021 May 4;72(9):e373-e381. doi: 10.1093/cid/ciaa1177.	Jeronimo CMP	Clin Infect Dis	2021	2020/08/14	10.1093/cid/ciaa1177	EXCLUÍDO: METILPREDNISONA EM HOSPITALIZADO
33893337	Short term survival of critically ill COVID-19 Egyptian patients on assisted ventilation treated by either Dexamethasone or Tocilizumab	Rashad A, Mousa S, Nafady-Hego H, Nafady A, Elgendy H.	Sci Rep. 2021 Apr 23;11(1):8816. doi: 10.1038/s41598-021-88086-x.	Rashad A	Sci Rep	2021	2021/04/24	10.1038/s41598-021-88086-x	EXCLUÍDO: DEXA vs TCZ (PERDAS > 40%)
33920093	Dexamethasone in Patients Hospitalized with COVID-19: Whether, When and to Whom	Calzetta L, Aiello M, Frizzelli A, Rogliani P, Chetta A.	J Clin Med. 2021 Apr 10;10(8):1607. doi: 10.3390/jcm10081607.	Calzetta L	J Clin Med	2021	2021/04/30	10.3390/jcm10081607	EXCLUÍDO: ANÁLISE POST-HOC
33838657	Methylprednisolone or dexamethasone, which one is superior corticosteroid in the treatment of hospitalized COVID-19 patients: a triple-blinded randomized controlled trial	Ranjbar K, Moghadami M, Mirahmadizadeh A, Fallahi MJ, Khaloo V, Shahriarirad R, Erfani A, Khodamoradi Z, Gholampoor Saadi MH.	BMC Infect Dis. 2021 Apr 10;21(1):337. doi: 10.1186/s12879-021-06045-3.	Ranjbar K	BMC Infect Dis	2021	2021/04/11	10.1186/s12879-021-06045-3	EXCLUÍDO: METILPRED vs DEXA

PMID	Title	Authors	Citation	First Author	Journal/Book	Publication Year	Create Date	DOI	INCLuíDO/EXCLuíDO (MOTIVOS)
33844996	Inhaled budesonide in the treatment of early COVID-19 (STOIC): a phase 2, open-label, randomised controlled trial	Ramakrishnan S, Nicolau DV Jr, Langford B, Mahdi M, Jeffers H, Mwasuku C, Krassowska K, Fox R, Binnian I, Glover V, Bright S, Butler C, Cane JL, Halner A, Matthews PC, Donnelly LE, Simpson JL, Baker JR, Fadai NT, Peterson S, Bengtsson T, Barnes PJ, Russell REK, Bafadhel M.	Lancet Respir Med. 2021 Apr 9;S2213-2600(21)00160-0. doi: 10.1016/S2213-2600(21)00160-0. Online ahead of print.	Ramakrishnan S	Lancet Respir Med	2021	2021/04/12	10.1016/S2213-2600(21)00160-0	EXCLuíDO: ESTEROIDE INALADO + FASE II
33839489	Effect of nasal corticosteroid in the treatment of anosmia due to COVID-19: A randomised double-blind placebo-controlled study	Rashid RA, Zgair A, Al-Ani RM.	Am J Otolaryngol. 2021 Apr 7;42(5):103033. doi: 10.1016/j.amjoto.2021.103033. Online ahead of print.	Rashid RA	Am J Otolaryngol	2021	2021/04/11	10.1016/j.amjoto.2021.103033	EXCLuíDO: DESFECHO INTERMEDIARIO (ANOSMIA)
33607104	No clinical benefit of high dose corticosteroid administration in patients with COVID-19: A preliminary report of a randomized clinical trial	Jamaati H, Hashemian SM, Farzanegan B, Malekmohammad M, Tabarsi P, Marjani M, Moniri A, Abtahian Z, Haseli S, Mortaz E, Dastan A, Mohamadnia A, Vahedi A, Monjazebi F, Yassari F, Fadaeizadeh L, Saffaei A, Dastan F.	Eur J Pharmacol. 2021 Apr 15;897:173947. doi: 10.1016/j.ejphar.2021.173947. Epub 2021 Feb 16.	Jamaati H	Eur J Pharmacol	2021	2021/02/19	10.1016/j.ejphar.2021.173947	EXCLuíDO: DEXA EM HOSPITALIZADO
33534047	Methylprednisolone in adults hospitalized with COVID-19 pneumonia : An open-label randomized trial (GLUCOCOVID)	Corral-Gudino L, Bahamonde A, Arnaiz-Revillas F, Gómez-Barquero J, Abadía-Otero J, García-Ibarbia C, Mora V, Cerezo-Hernández A, Hernández JL, López-Muñiz G, Hernández-Blanco F, Cifrián JM, Olmos JM, Carrascosa M, Nieto L, Fariñas MC, Riancho JA; GLUCOCOVID investigators.	Wien Klin Wochenschr. 2021 Apr;133(7-8):303-311. doi: 10.1007/s00508-020-01805-8. Epub 2021 Feb 3.	Corral-Gudino L	Wien Klin Wochenschr	2021	2021/02/03	10.1007/s00508-020-01805-8	EXCLuíDO: METILPREDNISONA EM HOSPITALIZADO
33290446	Efficacy of corticosteroid therapy in the treatment of long-lasting olfactory disorders in COVID-19 patients	Vaira LA, Hopkins C, Petrocelli M, Lechien JR, Cutrupi S, Salzano G, Chiesa-Estomba CM, Saussez S, De Riu G.	Rhinology. 2021 Feb 15;59(1):21-25. doi: 10.4193/Rhin20.515.	Vaira LA	Rhinology	2021	2020/12/08	10.4193/Rhin20.515	EXCLuíDO: DESFECHO INTERMEDIARIO (ANOSMIA)
33429174	Corticosteroid nasal spray for recovery of smell sensation in COVID-19 patients: A randomized controlled trial	Abdelalim AA, Mohamady AA, Elsayed RA, Elawady MA, Ghallab AF.	Am J Otolaryngol. 2021 Mar-Apr;42(2):102884. doi: 10.1016/j.amjoto.2020.102884. Epub 2021 Jan 4.	Abdelalim AA	Am J Otolaryngol	2021	2021/01/11	10.1016/j.amjoto.2020.102884	EXCLuíDO: DESFECHO INTERMEDIARIO (ANOSMIA)

PMID	Title	Authors	Citation	First Author	Journal/ Book	Publication Year	Create Date	DOI	INCLUÍDO/EXCLUÍDO (MOTIVOS)
33486496	Early Use of Corticosteroid May Prolong SARS-CoV-2 Shedding in Non-Intensive Care Unit Patients with COVID-19 Pneumonia: A Multicenter, Single-Blind, Randomized Control Trial	Tang X, Feng YM, Ni JX, Zhang JY, Liu LM, Hu K, Wu XZ, Zhang JX, Chen JW, Zhang JC, Su J, Li YL, Zhao Y, Xie J, Ding Z, He XL, Wang W, Jin RH, Shi HZ, Sun B.	Respiration. 2021;100(2):116-126. doi: 10.1159/000512063. Epub 2021 Jan 22.	Tang X	Respiration	2021	2021/01/24	10.1159/000512063	EXCLUÍDO: METILPREDNISONA EM HOSPITALIZADO
32943404	Intravenous methylprednisolone pulse as a treatment for hospitalised severe COVID-19 patients: results from a randomised controlled clinical trial	Edalatifard M, Akhtari M, Salehi M, Naderi Z, Jamshidi A, Mostafaei S, Najafizadeh SR, Farhadi E, Jalili N, Esfahani M, Rahimi B, Kazemzadeh H, Mahmoodi Aliabadi M, Ghazanfari T, Sattarian M, Ebrahimi Louyeh H, Raeeskarami SR, Jamalimoghadamsiahkali S, Khajavirad N, Mahmoudi M, Rostamian A.	Eur Respir J. 2020 Dec 24;56(6):2002808. doi: 10.1183/13993003.02808-2020. Print 2020 Dec.	Edalatifard M	Eur Respir J	2020	2020/09/18	10.1183/13993003.02808-2020	EXCLUÍDO: METILPREDNISONA EM HOSPITALIZADO

PMID	Title	Authors	Citation	First Author	Journal/ Book	Publication Year	Create Date	DOI	INCLuíDO/EXCLuíDO (MOTIVOS)
32876697	Effect of Hydrocortisone on Mortality and Organ Support in Patients With Severe COVID-19: The REMAP-CAP COVID-19 Corticosteroid Domain Randomized Clinical Trial	Angus DC, Derde L, Al-Beidh F, Annane D, Arabi Y, Beane A, van Bentum-Puijk W, Berry L, Bhimani Z, Bonten M, Bradbury C, Brunkhorst F, Buxton M, Buzgau A, Cheng AC, de Jong M, Detry M, Estcourt L, Fitzgerald M, Goossens H, Green C, Haniffa R, Higgins AM, Horvat C, Hullegie SJ, Kruger P, Lamontagne F, Lawler PR, Linstrum K, Litton E, Lorenzi E, Marshall J, McAuley D, McGlothin A, McGuinness S, McVerry B, Montgomery S, Mouncey P, Murthy S, Nichol A, Parke R, Parker J, Rowan K, Sanil A, Santos M, Saunders C, Seymour C, Turner A, van de Veerdonk F, Venkatesh B, Zarychanski R, Berry S, Lewis RJ, McArthur C, Webb SA, Gordon AC; Writing Committee for the REMAP-CAP Investigators, Al-Beidh F, Angus D, Annane D, Arabi Y, van Bentum-Puijk W, Berry S, Beane A, Bhimani Z, Bonten M, Bradbury C, Brunkhorst F, Buxton M, Cheng A, De Jong M, Derde L, Estcourt L, Goossens H, Gordon A, Green C, Haniffa R, Lamontagne F, Lawler P, Litton E, Marshall J, McArthur C, McAuley D, McGuinness S, McVerry B, Montgomery S, Mouncey P, Murthy S, Nichol A, Parke R, Rowan K, Seymour C, Turner A, van de Veerdonk F, Webb S, Zarychanski R, Campbell L, Forbes A, Gattas D, Heritier S, et al.	JAMA. 2020 Oct 6;324(13):1317-1329. doi: 10.1001/jama.2020.17022	Angus DC	JAMA	2020	2020/09/03	10.1001/jama.2020.17022	EXCLuíDO: DEXA EM HOSPITALIZADO

PMID	Title	Authors	Citation	First Author	Journal/Book	Publication Year	Create Date	DOI	INCLUÍDO/EXCLUÍDO (MOTIVOS)
32876695	Effect of Dexamethasone on Days Alive and Ventilator-Free in Patients With Moderate or Severe Acute Respiratory Distress Syndrome and COVID-19: The CoDEX Randomized Clinical Trial	Tomazini BM, Maia IS, Cavalcanti AB, Berwanger O, Rosa RG, Veiga VC, Avezum A, Lopes RD, Bueno FR, Silva MVAO, Baldassare FP, Costa ELV, Moura RAB, Honorato MO, Costa AN, Damiani LP, Lisboa T, Kawano-Dourado L, Zampieri FG, Olivato GB, Righy C, Amendola CP, Roepke RML, Freitas DHM, Forte DN, Freitas FGR, Fernandes CCF, Melro LMG, Junior GFS, Morais DC, Zung S, Machado FR, Azevedo LCP; COALITION COVID-19 Brazil III Investigators.	JAMA. 2020 Oct 6;324(13):1307-1316. doi: 10.1001/jama.2020.17021	Tomazini BM	JAMA	2020	2020/09/03	10.1001/jama.2020.17021	EXCLUÍDO: DEXA vs STANDARD (PERDAS > 4,0%)
32876689	Effect of Hydrocortisone on 21-Day Mortality or Respiratory Support Among Critically Ill Patients With COVID-19: A Randomized Clinical Trial	Dequin PF, Heming N, Meziani F, Plantevèze G, Voiriot G, Badié J, François B, Aubron C, Ricard JD, Ehrmann S, Jouan Y, Guillon A, Leclerc M, Coffre C, Bourgoin H, Lengellé C, Caille-Fénérol C, Tavernier E, Zohar S, Giraudeau B, Annane D, Le Gouge A; CAPE COVID Trial Group and the CRICS-TRIGGERSep Network.	JAMA. 2020 Oct 6;324(13):1298-1306. doi: 10.1001/jama.2020.16761	Dequin PF	JAMA	2020	2020/09/03	10.1001/jama.2020.16761	EXCLUÍDO: HIDROCORTISONA EM HOSPITALIZADO
32828135	Hydroxychloroquine in the Treatment of COVID-19: A Multicenter Randomized Controlled Study	Abd-Elsalam S, Esmail ES, Khalaf M, Abdo EF, Medhat MA, Abd El Ghafar MS, Ahmed OA, Soliman S, Serangawy GN, Alborai M.	Am J Trop Med Hyg. 2020 Oct;103(4):1635-1639. doi: 10.4269/ajtmh.20-0873.	Abd-Elsalam S	Am J Trop Med Hyg	2020	2020/08/24	10.4269/ajtmh.20-0873	EXCLUÍDO: HCQ
33447376	Effects of rapid recruitment and dissemination on Covid-19 mortality: the RECOVERY trial	Knowlson C, Torgerson DJ.	F1000Res. 2020 Aug 21;9:1017. doi: 10.12688/f1000research.25842.2. eCollection 2020.	Knowlson C	F1000Res	2020	2021/01/18	10.12688/f1000research.25842.2	EXCLUÍDO: FOCO NO RECRUTAMENTO/DISSEMINAÇÃO
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