**Best Evidence Topic Report – COVID-19 Domus Medica dossier**

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| **Title** | **COVID-19: COPD exacerbatie Medrol opdrijven?** |
| **Original Question** | Wat met COPD patiënten die chronisch onder medrol staan. Bij nieuwe COPD opstoot (dus corona) medrol opdrijven of niet? |
| Report by | Vanlommel Jens, Vanlommel Niels en Apr. Hendrik Vercammen |
| Search checked by | Josefien van Olmen / Hilde Philips / Paul Van Royen |
| Clinical scenario | Wat met COPD patiënten die chronisch onder medrol medicatie staan? Wat zou de aanbeveling zijn bij COVID-19 gemedieerde COPD exacerbatie; medrol opdrijven of niet? |
| Answerable question (PICO/PIRT/PEO/…) | **P**: COPD patiënten die onder onderhoudsbehandeling staan met medrol die een SARS-COV-2 gemedieerde exacerbatie doen (Gold D standard)  **I**: Medrol opdrijven  **C:** Medrol niet opdrijven  **O:** Vermijden complicaties COVID-19 & COPD exacerbaties |
| Search terms | **Pubmed**:((((("Pulmonary Disease, Chronic Obstructive"[Mesh]) OR "Asthma-Chronic Obstructive Pulmonary Disease Overlap Syndrome"[Mesh]) OR "COPD, Severe Early-Onset" [Supplementary Concept]) AND "COVID-19" [Supplementary Concept]) OR "severe acute respiratory syndrome coronavirus 2" [Supplementary Concept]) OR "COVID-19 drug treatment" [Supplementary Concept]  filters: Species; Human and languages: English |
| Search date | 04/04/2020 |
| Search outcome (number of hits) | 375 |
| Relevant papers & guidelines(number of final inclusions) | 11 |
| Expert opinions | Dr. Vercammen E. (Huisartsen team Wiekevortst 05/04/2020) |
| Flow chart | Pubmed  375 zoekresultaten  11 resultaten  Exclusie en inclusie criteria   1. Selection criteria: text: relevant COPD and COVID-19 OR Corticosteroids and COVID-19 |

**Table 1:Evidence tables: scientific studies**

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|  | Title | Author, date and country | Study type | Main risks of bias | characteristics | Key results |
| 1 | COVID-19: what has been learned and to be learned about the novel coronavirus disease (1) | Ye Yi et al.  15/03/2020  China | Review | Selection bias | Steroids as immunosuppressants in severe SARS | “Steroids should be used at low dosage and for a limited time in COVID-19”. |
| 2 | Traditional Chinese Medicine in the Treatment of  Patients Infected with 2019-New Coronavirus  (SARS-CoV-2): A Review and Perspective (2) | Yang et al.  15/03/2020  China | Review | Selection bias | Corticosteroids to supress elevated cytokines levels in patients with SARS-COV and MERS-COV | “Corticosteroids are not suggested to systemically use in SARS-CoV-2 infected patients”. |
| 3 | COVID-19, cytokines and immunosuppression: what can we learn from severe acute respiratory syndrome? (3) | Sarzi-Puttini et al.  21/03/2020  Italië | Review | Lack of adequate clinical trials | Systemic corticosteroids in managing patients with severe viral ARDS | “All these data support the hypothesis that a systemic corticosteroid use would likely exceed any benefit for treatment of viral infections”.  “Methylprednisolone can be used in patients with late-stage ARDS and rapid disease progression as it seems to improve symptoms and lung lesions, but it does not increase overall survival”. |
| 4 | A tug-of-war between severe acute respiratory syndrome coronavirus 2 and host antiviral defence: lessons from other pathogenic viruses (4) | Sin-Yee Fung et al.  14/03/2020  China | Review | Lack of prove of concept ,more clinical studies needed. | High-dose steroids in early phase of infection with SARS-COV-2 | “High dose steroids boost viral replication leading to the shedding of large amounts of virus”. |
| 5 | The origin, transmission and clinical therapies on coronavirus disease 2019 (COVID-19) outbreak – an update on the status (5) | Yan-RongGuo et al.  13/03/2020  China | Review | No Clinical trials, pure hypothetical | systemic corticosteroids as an antiviral treatment | ‘Systemic corticoids such as methylprednisolone is not recommended as a specific antiviral treatment for COVID-19’. |
| 6 | A Review of Coronavirus Disease-2019 (COVID-19) (6) | Tanu Singhal  13/03/2020  Indië | Review | Selection bias | Systemic corticoids as a treatment for COVID-19 ARDS | “The role of corticosteroids is unproven; while current international consensus and WHO advocate against their use, Chinese guidelines do recommend short term therapy with low-to-moderate dose corticosteroids in COVID-19 ARDS”. |
| 7 | What we know so far: COVID-19 current clinical knowledge and research (7) | Mary A Lake  04/03/2020  England | Review | No clinical trials for the use of corticosteroids in the other indications such as exacerbation of asthma in the case of COVID-19 | Corticosteroids as treatment for SARS-COV patients | “There was no definite benefit for corticosteroids in SARS-CoV patients as a group. possible evidence of harm, such as delayed viral clearance, psychosis, diabetes and avascular necrosis. Evidence from management of MERS-CoV also suggests corticosteroids may delay viral clearance.  However, other indications for corticosteroids such as exacerbation of asthma could potentially supervene”. |
| 8 | Do chronic respiratory diseases or their treatment affect the risk of SARS-CoV-2 infection? (8) | Halpin et al  03/04/2020  Engeland | Comment | Lack of representable clinical trials | The effect of corticosteroid on COVID-19 | “The Possibility that inhaled corticosteroids might prevent (at least partly) the development of symptomatic infection or severe presentations of COVID-19.The potential benefits or harms of inhaled corticosteroids and other treatments for people at risk of SARS-CoV-2 infection or patients with COVID-19 are unclear at present, and no changes to the treatment or management of chronic respiratory conditions, including COPD and asthma, should be considered at this stage”. |
| 9 | COVID-19: the new challenge for rheumatologists (9) | Ferro et al.  23/03/2020  Italië | Editorial | Lack of clinical trials for toxicological effects of corticosteroids in COVID-19 patients with COPD exacerbation | Corticosteroid therapy in the management of COVID-19 infected patients | “the effectiveness of adjunctive glucocorticoid therapy in the management of COVID-19 infected patients remains currently controversial. In line with this position, the WHO has recently ad- vised not to routinely give systemic corticosteroids for treatment of viral pneumonia outside of clinical trials unless they were indicated for other reasons (i.e. exacerbation of asthma or COPD, septic shock) “. |
| 10 | Evaluation of SARS-CoV-2 RNA shedding in clinical  specimens and clinical characteristics of 10 patients with  COVID-19 in Macau (10) | Long Lo et al.  15/03/2020  China | Research paper | Small population, selection bias of the included patients | Methylprednisolone in patients with COVID-19 with clinical and radiological exacerbations. | “the use of corticosteroids is controversial; three patients had received methylprednisolone for a short duration due to clinical and radiological exacerbations. We believe that this is still advisable for patients who have severe illness, based on the hypothesis of reducing cytokine storm and inflammation-mediated lung injury. The settlement of this debate still requires further high-quality studies to justify or against the use of corticosteroids, and also to determine the optimal timing, dosage and duration of administration”. |
| 11 | On the use of corticosteroids for 2019-ncov pneumonia (11) | Shang et al  11/02/2020  China | Scientific correspondence | Selection bias | Corticosteroids in 2019-nCoV pneumonia | “Corticosteroid treatment is a double-edged sword. In line with the expert consensus, we oppose liberal use of corticosteroids and recommend short courses of corticosteroids at low-to-moderate dose, used prudently, for critically ill patients with 2019-nCoV pneumonia. Existing evidence is inconclusive, and even systematic reviews and meta analyses on this topic reach differing conclusions”. |

**Table 2:Guidelines**

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| --- | --- | --- | --- | --- | --- | --- |
| Organisation | Country | For which context (1st line, hospital, community, …) | For which professional group | Topic | Evidence-base | Key recommendations |
| WHO | / | hospital | clinicians | Clinical management of severe acute respiratory infection when COVID-19 is suspected (12) | Consensus-based | Given the lack of effectiveness and possible harm, routine corticosteroids should be avoided unless they are indicated for another reason. Other reasons may include exacerbation of asthma or COPD, septic shock, and risk and benefit analysis needs to be conducted for individual patients. |
| National Institute for Health and Care Excellence | England | 1ste line, hospital and community | health and care practitioners  health and care staff involved in planning and delivering services  commissioner | COVID-19 rapid guideline: severe asthma (13) | Consensus-based | Tell patients on maintenance oral corticosteroids (for asthma), or their parent or carer, to continue to take them at their prescribed dose because stopping them can be harmful. |

**Table** **3: expert opinions**

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| --- | --- | --- | --- | --- | --- |
| Name person | Organisation | Profession | Date | Communication (email, phone, other, lecture) | Key recommendatations |
| Dr. Vercammen E. | Huisartsen team Wiekevorst | General practitioner | 05/04/2020 | Phone | Er moet benadrukt worden dat patiënten die chronisch oraal medrol innemen zich in een ver gevorderd stadium van COPD ( GOLD C of D) bevinden. Zonder de comorbidditeit COVID-19 in rekening te brengen, is het zeer moeilijk om de dosis medrol af te bouwen zonder het verkrijgen van complicaties. Met dit feit in het achterhoofd noopt dit tot het niet staken van de methylprednisolon therapie. |

**Table 4: extra information**

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| --- | --- | --- | --- |
| Title | Author and publication date | Key results | conclusie |
| COVID-19: what has been learned and to be learned about the novel coronavirus disease (1) | Ye Yi et al.  15/03/2020 | a cytokine storm results from an overreaction of the immune system in SARS and MERS patient. Corticosteroids have been used to treat cytokine storm Steroids, as immunosuppressants, were widely used in the treatment of SARS to reduce the severity of inflammatory damage | *Algemeen kan een cytokine storm ervoor zorgen dat er een enorme hoeveelheid vrije radicalen vrijkomen wat ARDS en orgaanfalen in de hand kan werken. COVID-19 kan deze systemische inflammatoire respons veroorzaken waardoor corticosteroiden in theorie gebruikt worden om de graad van inflammatoire schade te beperken. Hierdoor kunnen corticosteroiden in theorie gebruikt worden bij COVID-19 patiënten in kritieke toestand. Echter ontbreken er nog onvoldoende klinische studies die deze hypothese staven.* |
| Coronavirus disease 2019 (COVID-19): Critical care issues(14) | Anesi et al.  Last update  04/04/2020 | glucocorticoids should not be routinely administered to patients with COVID-19, unless there is a separate evidence-based indication (eg, asthma or chronic obstructive lung disease exacerbation, refractory septic shock, and adrenal insufficiency).  methylprednisolone administration reduced the risk of death in patients with COVID-19 compared with patients who did not receive methylprednisolone treatment. | *Het WHO en CDC zijn het eens dat er geen sprake mag zijn van het routinematig behandelen van COVID-19 patiënten met glucocorticoïden TENZIJ er een ‘seperate evidence-based’ ziektebeeld kan vastgesteld worden zoals frequente COPD exacerbaties. Het SCCM brengt echter wel het feit naar de voorgrond dat er bij patiënten die naar een terminale ARDS dreigen te gaan (zeer slechte zuurstofsaturatie) er corticoïden kunnen worden toegedien, al moet men in het achterhoofd houden dat er nog onvoldoende bewijs is qua veiligheid van deze behandeling bij terminale COVID-19 patiënten* |
| Coronavirus disease 2019 (COVID-19) (15) | McIntosh et al.  05/04/2020 | The WHO and CDC recommend glucocorticoids not be used in patients with COVID-19 pneumonia unless there are other indications (eg, exacerbation of chronic obstructive pulmonary disease) | *Aanbevelingen van de WHO en CDC : het gebruik van corticosteroiden wordt niet aanbevolen bij COVID-19 patiënten TENZIJ, er sprake is van COPD met frequente exacerbaties als comorbiditeit.* |
| COVID-19: Prevention & Investigational Treatments (16) | Stewart et al.  05/04/2020 | methylprednisolone is being studied for safety and effectiveness in the treatment of novel coronavirus pneumonia in a number of hospitals in the Hubei province of China | *Het gebruik van methylprednisolon wordt momenteel onderzocht als therapie in COVID-19. Dit impliceert dat tot op het heden er nog geen reden is om te staken met methylprednisolone bij COVID-19 gemedieerde COPD exacerbaties.* |

Add conclusions of overall body of evidence here:

* Main results:

Samenvattend wordt het niet aangeraden om patiënten zonder pre-existent longlijden zoals astma of COPD met COVID-19 specifiek te behandelen met corticosteroïden aangezien dit geen positieve invloed zou hebben op de mortaliteit. Patiënten **met COPD** vormen echter een uitzondering op deze regel. Er wordt aangeraden dat patiënten die op een onderhoudsbehandeling staan van orale corticosteroïden (medrol) die een COVID-19 gemedieerde exacerbatie ondergaan om de dosis van de onderhoudsbehandeling op te drijven met als doel de exacerbatie te behandelen. Dit is conform aan de huidige richtlijnen van het WHO.(12)

* Risks of bias:

De data van de meeste studies gaan concreet over het gebruik van corticosteroiden als behandeling voor COVID-19. Er is geen enkel clinical trial die aantoont dat het gebruik van corticosteroïden op een COVID-19 gemedieerde exacerbatie van COPD/Astma een goede outcome bewerkstelligd. Momenteel wordt de evidence grotendeels gestaafd door bevindingen van SARS-COV en MERS. Nieuwe clinical trials moeten het nut of onnut van corticosteroïden (medrol) gebruik in COPD Patiënten, gediagnosticeerd met COVID-19 nog aantonen.

* Heterogeneity: statistical and/or clinical

Er is geen heterogeniteit: alle geïncludeerde studies raden aan om corticosteroiden niet te gebruiken als specifieke behandeling in COVID-19. Verder heerst er een consensus om geen wijzigen uit te voeren in het COPD behandelingsschema vanwege COVID-19.

Add clinical bottom line here:

* What is your response rephrased for Domus Medica?

Aangezien er momenteel geen evidence is dat het toedienen van Medrol bij een patiënt die lijdt aan COVID-19 nefast is, raad men aan om het huidige COPD behandelingsschema toe te passen. Dit impliceert dat er bij een COVID-19 gemedieerde exacerbatie van COPD wordt geopteerd voor een opdrijving van medrol om de exacerbatie te onderdrukken. Dit wordt ook gestaafd door huidige guidlines van de WHO (12, 13). Aangezien er uit dit literatuur onderzoek voortvoloeit dat er clinical trials aan de gang zijn over het gebruik van corticosteroiden specifiek tegen COVID-19, kan er geimpliceerd worden dat het gebruik van bv. Medrol niet nefast is voor de patiënt in het kader van COVID-19. (16)

References for Domus Medica Website

**Referenties**

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