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SERIES 1: COVID-19 CASE MANAGEMENT - TREATMENT OPTIONS

**NUMBER 001-02: Efficacy of Corticosteroids in Patients with COVID-19
pneumonia**

Based on information as at 12 June 2020

Number 001-02: Efficacy of Corticosteroids in Patients with COVID-19 pneumonia

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1	RAPID POLICY BRIEF NUMBER: 001-02
2	RESEARCH DOMAIN: COVID-19 CASE MANAGEMENT - TREATMENT OPTIONS
3	TITLE: Efficacy of Corticosteroids in Patients with COVID-19 pneumonia
4	DATE OF PUBLICATION: 03/07/2020
5	<p>BACKGROUND</p> <p>There is a growing need to provide COVID-19 evidence, acknowledging the needs of the policy/decision-makers. This rapid policy brief aims to summarize relevant research, in a timely manner and thereby facilitating their use in decision making.</p> <p>The outbreak of the new coronavirus infections COVID-19 become quickly a pandemic and global health emergency. Currently there is no specific anti-viral therapies, and its management is mainly supportive [1], even though several ongoing studies are now under investigation for the treatment of this life-threatening disease and some of them began to show strong findings.</p> <p>The increasing knowledge about the pathophysiology of SARS-CoV-2 infection is leading to consider some steroids drugs as potential treatment options for the management of COVID-19. In this document we will critically summarized the evidences on either positive or negative effect of steroids commonly used to treat other diseases in this particular situation of COVID-19.</p> <p>Death rate among COVID-19 patients is high in patients with risk factors including obesity, older age (>65 years), the male sex, high blood pressure, stroke, coronary heart disease, heart failure, poorly controlled diabetes, chronic obstructive respiratory illnesses, renal chronic disease, and cancer among the key drivers of COVID-19 deaths [2]. Patients with severe COVID-19 pneumonia had markedly increased inflammatory markers such as CRP, IL-6 and FER, which signified occurrence of the inflammatory reaction phase. Meanwhile, most patients developed fever, cough, dyspnea and markedly decline in oxygen saturation, which are the early clinical manifestations of ARDS. This is the indicator for corticosteroid admission to treat these patients [3]. Physicians are concerned whether steroids used in treatment of chronic diseases such as rheumatoid arthritis and asthma affected outcomes of COVID-19 [4]. Sixteen studies have examined the effectiveness of treating COVID-19 patients with anti-inflammatory drugs especially corticosteroids.</p>
6	<p>SEARCH STRATEGY / RESEARCH METHODS</p> <p>The research consisted in using four databases: PUBMED, WHO COVID-19, IRIS (WHO Institutional Repository for Information Sharing) and Google Scholar to pull out papers published from 1 December to 12 June 2020 for relevant studies on (COVID-19 or SARS or MERS or coronavirus) and “corticosteroids”. Randomized controlled clinical trials available for analysis, case–control, cohort studies and case series were eligible for inclusion provided data were available.</p> <p>First inventory was to explore papers on the subject and scoped Africa related evidences. With this search strategy, 106 titles and abstracts of studies were found. All of them were conducted out of Africa. Sixteen publications were retained according to criteria of consistency to assess the efficacy of corticosteroid treatment of patients with coronavirus disease 2019 (COVID-19) that was objective for this rapid policy brief.</p>
7	SUMMARY OF GLOBALLY PUBLISHED LITERATURE RELATED TO THE SUBJECT

	<p>Dexamethasone is first drug shown to save lives, in the RECOVERY (Randomized Evaluation of COVID-19 thERapY) a randomized clinical trial to test a range of potential treatments for COVID-19, the effect of dexamethasone was most striking among critically ill patients on ventilators. Dexamethasone reduced deaths by one-third in ventilated patients (rate ratio 0.65 [95% confidence interval 0.48 to 0.88]; p=0.0003) and by one fifth in other patients receiving oxygen only (0.80 [0.67 to 0.96]; p=0.0021). There was no benefit among those patients who did not require respiratory support (1.22 [0.86 to 1.75]; p=0.14) [5]. There is currently paucity of evidence on effectiveness of ICS in treatment of COVID-19 patients [6].</p> <p>In all analyzed studies, systemic steroid treatment has not been recommended for COVID-19. Three reported cases of the COVID-19 pneumonia successfully treated with ciclesonide inhalation. Rationale of the treatment is to mitigate the local inflammation with inhaled steroid that stays in the lung and to inhibit proliferation of the virus by antiviral activity. Larger and further studies are warranted to confirm the result of these cases [7]. Conventional therapeutics for asthma, including inhaled corticosteroids, allergen immunotherapy (AIT), and anti-IgE monoclonal antibody, might also reduce the risks of asthmatics suffering infection of the virus through alleviating inflammation or enhancing antiviral defense.</p> <p>Research indicate that in patients with severe COVID-19 pneumonia, early, low-dose and short-term application of corticosteroid was associated with a faster improvement of clinical symptoms and absorption of lung focus [8,9,10].</p> <p>In people with COVID-19, corticosteroids may theoretically modulate the inflammatory response and reduce the risk of developing ARDS [11]. From a systematic review quality assessment, there is currently very low-quality evidence from a case series report from Japan of improvement in three patients with COVID-19 requiring oxygen, but not ventilatory support, after being given inhaled ciclesonide [12].</p>
<p>8</p>	<p>SUMMARY OF AFRICA-SPECIFIC LITERATURE ON THE SUBJECT</p> <p>Not found</p>
<p>9</p>	<p>POLICY FINDINGS</p> <ul style="list-style-type: none"> ✚ Critically ill patients on ventilators and those who receive oxygen therapy but not on ventilators, these can receive dexamethasone at a low or moderate dose of six milligrams per day (either by mouth or by intravenous injection) for ten days [5]. ✚ Corticosteroids may reduce mortality for patients with COVID-19 and ARDS. For patients with severe COVID-19 but without ARDS, evidence regarding benefit from different bodies of evidence is inconsistent and of very low quality [13]. ✚ During inflammatory reaction phase, most patients developed early clinical manifestations of ARDS and markedly decline in oxygen saturation. corticosteroid admission is indicated to treat these patients and Early application of low-dose corticosteroid could improve the treatment effect, presenting as improvement of hypoxia and fever symptom, shorten the disease course, and accelerating focus absorption. Benefited from condition monitoring and refined management, no serious complications caused by corticosteroid happened in these patients. The corticosteroid formulation used in a cohort study was methylprednisolone, a median effect corticosteroid with a half-life of 12-36, which has been proved to be associated with a better intensity of immunosuppression [14]. The dosage, duration and route of methylprednisolone administration can be 1-2mg/kg/d for 5-7 days via intravenous injection. Nevertheless, the specific dosage and duration for individual patient must be determined on the clinical manifestations, leucocyte and lymphocyte count, inflammatory index and lesion range [8].

- ✚ The Chinese Thoracic Society has issued the following expert consensus on the use of corticosteroids in CoV-2 SARS pneumonia [15,16]:
 - ✓ The benefits and risks must be carefully weighed before using corticoids;
 - ✓ Corticosteroids should be used with caution in critically ill patients with CoV-2 SARS pneumonia;
 - ✓ In patients with hypoxemia caused by underlying disease or who regularly use corticosteroids for chronic diseases, the use of extra steroids should be used with caution;
 - ✓ Dosage should be low to moderate (equivalent to $\leq 0.5-1$ mg/kg/day of methylprednisolone) and the duration should be short (≤ 7 days).

✚ In the current pandemic situation, corticosteroid therapy is not recommended for bacterial Ears, Nasal and Throat infections.

✚ In rhinology, there is no indication for systemic corticosteroid therapy in the current COVID-19 situation, especially in cases of nasosinus polyposis or infectious or very painful sinusitis. However, patients are advised to continue with their usual local corticosteroid therapy as a nasal spray or by inhalation. Treatments with corticosteroid nasal sprays can still be prescribed if there is no other therapeutic alternative. However, treatment with corticosteroid aerosols should be avoided due to the risk of spreading the virus to people around the patient.

In Grade V and VI Bell's palsy according to the House-Brackmann grading system, a week's course of oral corticosteroids is recommended. Corticosteroid therapy is also recommended in cases of sudden hearing loss of more than 60 dB, either in the form of intratympanic injections or a week's course of oral medication. Finally, systemic or local corticosteroid therapy is not indicated for bacterial Ears, Nasal and Throat infections. [4]

- ✚ Pneumonia in confirmed COVID-19 positives this treatment can be indicated
 - ✓ A: Ciclesonide (Alvesco) 200 µg Inhaler (56 puffs/kit), 2 times a day, 2 inhalations each time
 - ✓ B: Ciclesonide (Alvesco) 200 µg Inhaler (56 puffs/kit), 3 times a day, 2 inhalations each time

Take A as a basis, consider changing to B. for severe cases and cases where the effect is not sufficient. Considering that the drug must reach the infected area, "deep inhalation" is the most reasonable method of administration at present [16].

10 ONGOING RESEARCH IN THE AFRICAN REGION

Not found

11 AFRO RECOMMENDATIONS FOR FURTHER RESEARCH

WHO/AFRO invites all researchers to scientifically document the corticosteroid efficacy in patients with COVID-19 Pneumonia; Also interactions between COVID-19 and lung chronic disease such as asthma deserve further attention and clarification in the African Region.

WHO/AFRO encourages sharing scientifically research and knowledge related to the use of corticosteroids in patients with COVID-19 pneumonia.

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