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Dexamethasone: Therapeutic potential, risks, and future projection during COVID-19 pandemic

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Article Info

ARTICLE INFO

Keywords:
Dexamethasone
Corticosteroid
SARS-CoV-2
COVID-19 therapeutics
Acute respiratory distress syndrome (ARDS)
Immunosuppressant

ABSTRACT

The current outbreak of novel COVID-19 challenges the development of an efficient treatment plan as soon as possible. Several promising treatment options stand out as potential therapy of COVID-19, including plasma-derived drugs, monoclonal antibodies, antivirals, antimalarial, cell therapy, and corticosteroids. Dexamethasone is an approved corticosteroid medication, acting as an anti-inflammatory and immunosuppressant agent. In the current pandemic, dexamethasone is declared a “major development” in the fight against COVID-19. Steroidal dexamethasone was presented as the recent advancement that significantly reduces the mortality rate among severe COVID-19 cases. This review summarizes the preliminary opinion about the dexamethasone outbreak, therapeutic potential, risks, and strategies during the COVID-19 pandemic.

1. Introduction

Since the emergence of COVID-19, researchers and healthcare providers are continually trying to find treatment options for the novel coronavirus (2019-nCoV). COVID-19 is a zoonotic virus that originated from bats with signs and symptoms of persistent fever, dry cough, myalgia, malaise, chills, dyspnea, loss of taste/smell, and headache in humans (Ye, Z.-W. et al., 2020). The World Health Organization issued general guidelines for dealing with SARS-COV-2 disease (COVID-19) on February 11, 2020. COVID-19 is either asymptomatic or includes a high risk of acute respiratory distress syndrome (ARDS), devastating pneumonia with bilateral lung infiltrates, cytokine storm syndrome, shock, and death (News, 2020a, Chen and Li, 2020). Currently, there are very few or no treatment choices to prevent COVID-19 infection (Sahin, A.R. et al., 2020). However, management strategies are functioning, which include palliative care parallel to different viral types of pneumonia: antibiotics for infections, advanced airway, ventilatory support, and supervision of ARDS (Villar, J. et al., 2020a). Since the advancement of treatment scope, additional consideration is directed toward available treatment strategies (Khan, M.M. et al., 2020) besides vaccines (Zhang, W. et al., 2020). Hence poly-pharmacology and drug repurposing open novel avenues to design and identify drugs for the COVID-19 pandemic rationally. Drug repurposing is the identification and testing, whether existing drugs used for other infections could also be useful in treating COVID-19 (Wang, J., 2020). Identification of the crystal structure of COVID-19 triggers the experts to start fundamental research for the therapy of novel corona infection to identify the drugs that might interact with this protein target (Liu, X. et al., 2020; Popov, D., 2020).

Over the last decade, corticosteroids (CS) have emerged as steroidal medicine to reduce inflammation in various disorders, including rheumatoid arthritis, systemic lupus erythematosus, asthma, and certain cancers by mimicking anti-inflammatory hormones produced by the body (Health, N.I.o., 2017; Bethesda, 2012; Rhen, T. and Cidlowski, J. A., 2005). Since 1977, dexamethasone listed on the world health organization (WHO) Model List of Essential Medicines in multiple formulations and presently available in most countries at reasonable cost and off-patent (Broccoli, M.C. et al., 2018). In the fight against corona infection, the body’s immune system is activated and triggers inflammation as the body’s immune response. However, occasionally the immune system becomes overdrive (a cytokine storm), and causes fetal reactions, and starts attacking the body’s cells. Coronavirus further provokes respiratory failure, coagulopathy, and end-organ disease (Gulick, R.M. et al., 2020). CS use is linked to the suppression of the immune system; that is why their use has not been encouraged in the early phase of COVID-19 infection (Isidori et al., 2020, Singh, A.K. et al., 2020).

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https://doi.org/10.1016/j.ejphar.2021.173854
Received 31 August 2020; Received in revised form 12 December 2020; Accepted 5 January 2021
Available online 8 January 2021
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Their use in the early days of infection would result in viral replication, thus compromising the body’s innate immunity (Isidori et al., 2020b). After several clinical trials (Fig. 1) on CS among individuals with COVID-19, it has been concluded that steroidal therapy is supposed to deal with the best possible subsistence for SARS-COV-2 cases that continues to severe disease (Huang, C. et al., 2020; Mahase, E., 2020a; Hasan, S.S. et al., 2020; Villar, J. et al., 2020b; Zha, L. et al., 2020).

Low-dose CS (dexamethasone), a breakthrough against COVID-19, reduces the risk of mortality by one-third for the patients on ventilators and one-fifth for those on oxygen (News, 2020c; Narrandes, N., 2020; Aljazeera, 2020). A different consideration of CS is the convenience of dexamethasone drug, and luckily its mechanism allowing us to conduct this drug repurposing screening. This drug works by dampening down the body’s immune system. Moreover, it helps treat different diseases, including inflammation or swelling in the body, such as in allergic and asthmatic patients where inflammation is in the airways and lungs, or among patients with sore and inflamed joints (Jiang, K. et al., 2020). Other benefits include that dexamethasone has a long-lasting effect, allowing for a once-a-day regimen with the low-cost drug, which already exists and is available in bulk (Meijvis, S.C. et al., 2011).

In this paper, we summarize the life-saving dexamethasone outbreak in treating novel COVID-19 with a particular focus on its mechanism and clinical trials exploring survival at a low dose as well as risks and future projections.

3. Cytokine storm and corticosteroids therapy

Research has identified that the excessive and uncontrolled production of soluble inflammatory markers known as ‘cytokine storm’ is a significant reason for ARDS in COVID-19 patients (Coperchini, F. et al., 2020; Wang, F. et al., 2020). ARDS, the primary cause of mortality in COVID-19 defined by infiltration of immune cells in both lungs and hypoxemia. In ARDS, alveolar-capillary membranes are injured due to inflammation, leading to more lung permeability and exudation of high protein edematous fluid into air sacs (Bhatia, M. et al., 2012). Previous research on SARS and MERS indicated the involvement of pro-inflammatory cytokines (IL-6, IL-12, interferon-gamma) and chemokines (CXCL10, CCL2) in the pulmonary inflammation associated with ARDS (Channappanavar, R. and Perlman, S., 2017). A recent investigation on SARS-CoV-2 by Huang et al. (2020) reported that pro-inflammatory cytokines and chemokines are elevated in infected patients (Huang, C. et al., 2020). Storm of pro-inflammatory cytokines and chemokines leads to the activation of T-helper-1(Th1) immune cells. Th1 cell activation causes recruitment of IL-4 and IL-10, whose primary function is to reduce inflammation. This idea was initiated from the observation that patients seeking ICU admissions have more inflammatory mediators levels compared to patients with less severe infection (Chi Zhang, M. et al., 2020). Another recent study by Wong et al. (2004) described an increase in Th1 cytokine interferon-gamma, IL-1, IL-6, and IL-12 after two weeks of disease onset (Wong, C. et al., 2004). Cytokine storm is immediately followed by immune system activation and attacking the body’s cells, which will ultimately cause ARDS, multi-organ failure, and death in severe cases of infection (Xu, Z. et al., 2020).

Like all other severe respiratory tract infections, there is significant interest and debate regarding the use of corticosteroids to treat severe pneumonia due to coronaviruses. China’s National health commission issued the fifth trial version of diagnosis and treatment for patients suffering from COVID-19 associated pneumonia in February 2020. Systemic corticosteroid therapy for severe cases of COVID-19 associate pneumonia approved for 3–5 days. Methylprednisolone dose of <2–3 mg/kg suggested as adjuvant therapy of COVID-19 (Zhou, W. et al., 2020).

The potential role of corticosteroids in blocking the inflammatory pathway in critical conditions must be carefully monitored due to the chances of secondary infections, untoward effects, and other difficulties associated with corticosteroids usage (McCreary, E.K. and Pogue, J.M., 2020). Pathogenesis of COVID-19 involves pro-inflammatory cytokine production by macrophages in lung alveoli (Armitage, L.C. and Brettell, R., 2020). The use of corticosteroids is to suppress the host inflammatory reactions in the lungs, which may lead to acute lung injury and ARDS (Sanders, J.M. et al., 2020). One small randomized controlled trial has reported improved clinical outcomes in patients with COVID-19 who were given a short course of methylprednisolone (Corral, I. et al., 2020). Dexamethasone (a synthetic glucocorticoid) has previously been used to treat asthma, allergic reactions, arthritis, and other autoimmune diseases. It acts through the blockade of two pathways of inflammation; vasodilation and immune cell migration. Dexamethasone crosses the host cell membrane and binds to glucocorticoid receptors present in the cell cytoplasm, which initiates a series of immune cell responses that lead to pro-inflammatory suppression cytokines IL-1, IL-2, IL-6, IL-8, TNF, and IFN-γ through a decrease in gene transcription (Patel, S.K. et al., 2020). Out of these pro-inflammatory cytokines, five are associated with COVID-19 progression (Yong, S.J., 2020b). It also increases the gene expression of IL-10, which is an anti-inflammatory cytokine mediator (Azimi, S. et al., 2020) and inhibits neutrophil adhesion to endothelial cells, thus preventing the release of lysosomal enzymes and prevent chemotaxis at the site of inflammation (Coutinho, A.E. and Chapman, K.E., 2011). They also inhibit macrophages’ activation, one of the significant perpetrators of cytokine storm in COVID-19 infected individuals (Youssef, J. et al., 2016) (Fig. 2).

4. Dexamethasone; a breakthrough in Covid-19 therapy

A ground-breaking development in the fight against COVID-19 came from the Randomized Evaluation of COVID-19 therapy Trial on June 16, 2020. This randomized trial was started in March 2020 as a randomized
cancerous patients. Dexamethasone is generally recommended as an antiemetic for anticancerous induced severe nausea and vomiting. Dexamethasone induces lymphopenia among those patients by the reduction of B and T cells. As lymphocytes play an essential role in the resistance against COVID-19, for that reason, it is recommended that oncologists should reevaluate the monotonous use of dexamethasone to prevent stimulating lymphopenia (Marinella, M.A., 2020). CS therapy has a direct inhibitory action on β cells and causes lipotoxicity. Potential sequelae of CS treatment are the worsening of latent diabetes, increase insulin resistance, and increased hepatic glucose level by directly interfering with the signaling cascade of the GLUT-4 receptors. Ultimately leads to postprandial hyperglycemia, as well as hepatic glycogenesis (Perez, A. et al., 2014; Tamez-Pérez, H.E. et al., 2015; Lukins, M. B. and Manninen, P.H., 2005). Lastly, work from Youssef et al. (2016) (Youssef, J. et al., 2016) submitted the risk of CS among patients with rheumatic diseases, including severe bacterial infections and opportunistic infections, for example, TB, herpes zoster, and Pneumocystis jiroveci pneumonia. Some well-established risks related to dexamethasone use are summarized in (Table 1).

4.1. Weigh the risks/benefits of corticosteroids

Questions related to the actual practice of steroidal therapy for COVID-19 are gaining considerable debate at the moment among physicians worldwide. Obstetrics Units lacking sufficient data to recommend one steroid regimen over the other. Disparity remains common concerning the dose and period of steroidal therapy to substantially increase the risk (Berton, A. et al., 2020). In this context, the risk-benefit ratio must account for long-term steroidal therapy (≥1–3 months). To achieve the potential benefits of corticosteroids with reduced risk, healthcare providers follow some guidelines (Little, C.P. et al., 2020): Penn Medicine Center clarify about the risks and benefits of CS in a Rapid Guidance Summary for Evidence-based Practice on June 8, 2020 (Matthew D. Mitchell, P.C. and Emilija J. Flores, P., RN (CEP), 2020).

Numbers of side effects are associated with the use of CS. However, if CS utilizes, it alleviates ache, inflammation, and distress caused by many different syndromes and conditions.

The potential risks benefits ratio of steroids varies with:

- The severity of the disease
- Nature of the current infection causing disease
- Availability of other treatment substitutes
- Incidence of other significant medical problems

5. Protection

According to the treatment guidelines established by Russell and colleagues (Shang, L. et al., 2020), patients should be treated based on the following principles when administering corticosteroids: (1) risk to benefit ratio should be calculated before use of corticosteroids; (News,
A. corticosteroids use should be limited to critically ill COVID-19 pa-
tients; (News, A.) patients already using corticosteroids for comorbid-
ities should use with caution; (4) low to moderate dosage should be
administered for a short period.

Following protections can be followed to catch the maximum ad-
vantages of CS therapy with the minimum side effects (Staff, M.C.,
2020):

- **Use intermittent dosing**: Using the smallest dose to control the
disease risks can be overruled.
- **Use a medical alert bracelet**: Different corticosteroids are available
with varying strengths and intervals of action. So always consult a
health care professional (doctor, pharmacist, nurse), especially when
using corticosteroids for an extended period. Monitor the patient
carefully to detect early signs of severe side effects, and It is advised
wear a medical bracelet or tag.
- **Switch to non-oral forms of corticosteroids**: Oral corticosteroids
cause significant side effects by affecting the whole body rather than
a particular area; therefore, replacing it with a safer route. For
example, in the case of inhaled CS, the drug directly reaches the
lungs’ surfaces, decreasing other body parts’ exposure, ultimately
reduce side effects.
- **Proper follow-up**: When the patients are on long-term CS therapy
(≥1–3 months), routinely monitor blood pressure and blood sugar
often and treat accordingly.
- **Monitor bone density**: Corticosteroids carry a risk of osteoporosis
(bone thinning), consider monitoring and protect the bones through
calcium and vitamin D supplements.
- **Choose a healthy diet plan**: During the long term CS therapy, strict
to a balanced diet plan and physical activities strengthen body
muscles and boost immunity.
- **Watch withdrawal step**: Long term CS therapy alter the average
production of adrenal glands. On sudden withdrawal, the patient
experiences symptoms, including fatigue, body aches, and
headache as adrenal glands lacking sufficient time to recover.
Reduce the dose gradually, giving adrenal glands enough time to
restore their activities.

6. Future projections

With the imposition of current outbreaks, the rising rates of COVID-
19 infections could quickly worsen the situation in the coming years, so
now we need to understand these projections. As we have more powerful
means of fighting against coronavirus, the mortality rate will be below
the estimates. This review offers a comprehensive evaluation of the
dexamethasone outbreak and features a complete assessment by gath-
ering key points from already reported data and trials. In this scenario,
dexamethasone’s current treatment growth rate (cured cases of COVID-
19 from DEXA) started to rise above one threshold. If the current trend
continues, the digit of cured patients expected to reach a peak at the
beginning of August 2020. Based on these assumptions, experts use
different techniques to project the future of game-changer dexametha-
sone among seriously ill COVID-19 patients.

Risk factors associated with the use of corticosteroids are anticipated
to be a key restraint for this forecast period. Risks tend to outweigh the
benefits associated with the use of dexamethasone if used for a pro-
longed period. Further, Long-term use of dexamethasone is projected
to act as an impediment to the global corticosteroids market’s growth
shortly. Researchers are reporting promising results with the role of
steroid dexamethasone and establishing data on a case by case basis.
Ultimately, the clinical utilization of dexamethasone and its role in
COVID-19 management require additional clarity.

7. Conclusion

In this study, research has been reviewed on dexamethasone’s fight
against coronavirus, emphasizing its mechanism to provide the most up-
to-date knowledge into the control and mediation of COVID-19 as
possible. Among steroidal drugs, dexamethasone was identified to have
inhibitory activities against COVID-19 protease. Our review suggests
that drug repurposing screening of dexamethasone is very efficient and
makes a substantial contribution to the treatment of novel COVID-19.

**References**

Alessi, J., de Oliveira, G.B., Schaan, B.D., Telo, G.H., 2020. Dexamethasone in the era
of COVID-19: friend or foe? An essay on the effects of dexamethasone and the potential
risks of its inadvertent use in patients with diabetes. Diabetol. Metab. Syndrome 12
(1), 1.

Aljaeeza, 2020. Dexamethasone reduces death risk in severe COVID-19 cases: Trial.
Aljaeeza.

Armitage, L.C., Brettell, R., 2020. Inhaled corticosteroids: a rapid review of the evidence
for treatment or prevention of COVID-19. https://www.ccmn.nlm.nih.gov/covid-19/inhaled-
corticosteroids-a-rapid-review-of-the-evidence-for-treatment-or-prevention-of-
covid-19/. (Accessed 3 July 2020).

Azimz, S., Sahoebanaz, A., Sharifi, H., Najmeddin, F., 2020. Corticosteroids
administration following COVID-19-induced acute respiratory distress syndrome. Is
it harmful or life-saving? Adv. J. Emerg. Med. 4, e43.

Berton, A., Frecnpe, N., Giurlano, R., Ghigo, E., Grottoli, S., 2020. Systemic steroids in
patients with COVID-19: pros and cons, an endocrinological point of view.
Endocrinol. Invest. 1, Bethesda.

Bhatia, M. Zemans, R.L., Jayaseelan, S., 2012. Role of chemokines in the pathogenesis of
acute lung injury. Am. J. Resp. Cell Mol. 46, 566–572.

Broadbent, C., Pfeffer, P., Steed, L., Walker, S., 2018. Patient-reported side effects of oral
corticosteroids. Eur. Respir. Soc.

Brogcol, M.C., Pigpoper, J.L., Nyidida, M., Wallis, L., Hynes, E.C., 2012. Essential
medicines for emergency care in Africa. Afr. J. Emerg. Med. 8, 110–117.

Channappanavar, R., Perilmar, S., 2017. Pathogenic Human Coronavirus Infections:
Causes and Consequences of Cytokine Storm and Immunopathology. Semin
Immunopathol. Springer, pp. 329–339.

Chen, Y., Li, L., 2020. SARS-CoV-2: virus dynamics and host response. Lancet Infect.
Dis. 20, 515–516.

Chi Zhang, M., Zhou Wu, P., Jia-Wen Li, M., 2020. The cytokine release syndrome (CRS)
of severe COVID-19 and Interleukin-6 receptor antagonist Tocilizumab may be the
key to reduce mortality. Int. J. Antiinmicob. Agents. 105954.

Chu, C., Cheng, V., Hung, I., Wong, M., Chan, K., Chan, K., Kao, R., Poon, L., Wong, C.,
Guu, Y., 2004. Role of lopinavir/ritonavir in the treatment of SARS initial
virological and clinical findings. Thorax 59, 252–256.

Coperchini, F., Chiavato, L., Croce, L., Magni, F., Rotondi, M., 2020. The cytokine storm
in COVID-19: an overview of the involvement of the chemokine/chemokine-receptor
system. Cytokine Growth Factor Rev. 53, 25–32.

Corrol, L., Bahamonde, A., Delas Reviillas, F.A., Gomez-Banquero, J., Abada-Otero, J.,
Garcia-Blabia, C., Mora, V., Hernandez, J.L., Lopez-Muniz, G., Hernandez-
Blanco, F., 2020. GLUCOCOVID: a controlled trial of methylprednisolone in adults
hospitalized with COVID-19 pneumonia. MedRxiv.

Coutinho, A.E., Chapman, K.E., 2012. Corticosteroids. https://www.ncbi.nlm.nih.gov/books/NBK548400/
2020.

Curtis, J.R., Patkar, N., Xie, A., Martin, C., Allison, J.J., Saag, M., Shatin, D., Saag, K.G.,
David, Z., 2020. Steroid injections. WebMD Med. Ref.

David, Z., 2020. Steroid injections. WebMD Med. Ref.

Fields, T., 2009. Steroid side effects: how to reduce corticosteroid side effects. Hosp.
Spec. Surg. 2.

Group, R.C., 2020. Dexamethasone in hospitalized patients with covid-19—preliminary
report. N. Engl. J. Med.

Galicik, H.M., Sobieszczuk, M.E., Landry, D.W., Hollenberg, A.N., 2020. Prioritizing
clinical research studies during the COVID-19 pandemic: lessons from New York
City. J. Clin. Invest. 130 (9).

Hasan, S.S., Capstic, T., Ahmed, R., Kow, C.S., Mazhar, F., Merchant, H.A., Zaidi, S.T.R.,
2020. Mortality in COVID-19 patients with acute respiratory distress syndrome
and
corticosteroids use: a systematic review and meta-analysis. Expert Rev. Respir. Med. 14 (11), 1149-163.
Health, N.I.O., 2017. LiverTox: clinical and research information on drug-induced liver injury. Nih. gov. https://livertox.nih.gov.
Hersh, E., 2019. Everything you need to know about steroid injections. Healthline.
Horby, P., Lim, W.S., Emberson, J., Matham, M., Bell, J., Linsell, L., Staplin, N., Brightling, C., Ustianowski, A., Elmdahl, E., 2020. Effect of dexamethasone in hospitalized patients with COVID-19: preliminary report. MedRxiv.
Huang, C., Wang, Y., Li, X., Ren, L., Zhao, J., Hu, Y., Zhang, L., Fan, G., Xu, J., Gu, X., 2020. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 395, 497-506.
Isidori, A., Arnaldi, G., Bocaro, M., Falorni, A., Giordano, C., Giordano, R., Pivonello, R., Pofi, R., Hasenmayer, V., Venneri, M., 2020a. COVID-19 infection and glucocorticoids: update from the Italian Society of Endocrinology Expert Opinion on steroid replacement in adrenal insufficiency. J. Endocrinol. Invest. 1.
Isidori, A.M., Arnaldi, G., Bocaro, M., Falorni, A., Giordano, C., Giordano, R., Pivonello, R., Pofi, R., Hasenmayer, V., Venneri, M., A., B., E., F., G., C., R., 2020b. COVID-19 infection and glucocorticoids: update from the Italian Society of Endocrinology Expert Opinion on steroid replacement in adrenal insufficiency. J. Endocrinol. Invest.
Jiang, K., Weaver, J.D., Li, Y., Chen, X., Liang, C., Stabler, C.L., 2017. Local release of dexamethasone from macroporous scaffolds accelerates islet transplant engraftment by promotion of anti-inflammatory M2 macrophages. Biomaterials 114, 71-81.
Khan, M.M., Noor, A., Madni, A., Shafig, M., 2020. Emergence of novel coronavirus and progress toward treatment and vaccine. Rev. Med. Virol. 30 e2116.
Little, C.P., Bicks, M.E., Horwitz, M.D., Ng, C.Y., Warwick, D., 2020. COVID-19: a rethink of corticosteroid injection? Bone Joint J. 1, 253-256.
Liu, X., Zhang, B., Jin, Z., Yang, H., Rao, Z., 2020. The Crystal Structure of COVID-19 Main Protease in Complex with an Inhibitor N3. Protein Databank.
Lukino, M.B., Mannheimer, N., 2005. Hyperglycemia in patients administered dexamethasone for cranioectomy. Anesth. Analg. 100, 1129-1133.
Mahave, E., 2020a. COVID-19: Demand for Dexamethasone Surges as RECOVERY Trial Publishes Preprint. British Medical Journal Publishing Group.
Mahave, E., 2020b. COVID-19 Low Dose Steroid/Death in Ventilated Patients by One Third. Trial Finds. British Medical Journal Publishing Group.
Mansson, S.C., Brown, R.E., Cerulli, A., Vidaurre, C.F., 2009. The cumulative burden of glucocorticoids: update from the Italian Society of Endocrinology Expert Opinion on steroid replacement in adrenal insufficiency. J. Endocrinol. Invest.
Marinella, M.A., 2020. Routine antipyretic prophylaxis with dexamethasone during 2019-nCoV. Lancet Resp. Med. 8, 267-276.
Miller, D., Mitchell, P.C., Emilja, J., Flores, P., Rn, (Cep), 2020. COVID-19: CORTICOSTEROIDS for HOSPITALIZED PATIENTS(as of 8 June 2020). Center for Evidence-based Practice.
Matsos, T., Paula, F., Nathane, S.S., Pedro Leme Robbo, L.R., Chibra, B., Denise, Pelosi, Paolo, R., Patricia Rieken, M.C., Fernanda, F., 2020. Pros and cons of corticosteroids therapy for COVID-19 patients. Respir. Physiol. Neurobiol. 280 https://doi.org/10.1016/j.resp.2020.103492.
MayoClinic, 2019. Cortisone Shots. Mayo Foundation for Medical Education and Research.
McCreary, E.K., Pogue, J.M., 2020. Coronavirus disease 2019 treatment: a review of early and emerging options. Open Forum Infectious Diseases. Oxford University Press US, 1-9.
Meijvis, S.C., Hardeman, H., Remmelts, H.H., Heijligenberg, R., Rijkers, G.T., Van De Garde, E.M., Endeman, H., Grutters, J.C., 2011. Biodegradable dexamethasone from macroporous scaffolds accelerates islet transplant engraftment by promotion of anti-inflammatory M2 macrophages. Biomaterials 114, 71-81.
Mejívars, C.C., Hardeman, H., Remmelts, H.H., Heijligenberg, R., Rijkers, G.T., Van Velzen-Blad, H., Voorn, G.P., Van De Garde, E.M., Endeman, H., Grutters, J.C., 2011. Dexamethasone and length of hospital stay in patients with community-acquired pneumonia: a randomised, double-blind, placebo-controlled trial. Lancet 377, 422-427.
Xu, Z., Shi, L., Wang, Y., Zhang, C., Liu, S., Zhao, P., Liu, H., Zhu, L., 2020. Pathological Findings of COVID-19 associated with acute respiratory distress syndrome. Lancet Resp. Med. 8, 420-422.
Ye, Z.W., Yuan, S., Yuen, K.S., Fung, S.Y., Chan, C.P., Jin, D.V., 2020. Zoonotic origins of human coronaviruses. Int. J. Biol. Sci. 16, 1686.
Yong, S.J., 2020a. Biology of dexamethasone: the first lifesaving drug for covid-19. https://medium.com/@shinjeyong/biology-of-dexamethasone-the-first-lifesaving-drug-for-covid-19-357e9ddaf7a7.
Yong, S.J., 2020b. Biology of dexamethasone: the first lifesaving drug for covid-19. https://medium.com/@shinjeyong/biology-of-dexamethasone-the-first-lifesaving-drug-for-covid-19-357e9ddaf7a7.
Yousef, N., Novosad, S.A., Winthrop, K.L., 2016. Infection risk and safety of corticosteroid use. Rheum. Dis. Clin. 42, 157-176.
Yu, W.C., Hui, D.S.C., Chan-Yeung, M., 2004. Antiviral agents and corticosteroids in the management of severe acute respiratory syndrome (SARS). Thorax 59, 643-645.
Zha, L., Li, S., Pan, L., Tefsen, B., Li, Y., Chinese, N., Chen, Y., Yang, Z., Xu, J., Zhou, X., Chen, D., Xiong, W., Xu, L., Zhou, F., Jiang, J., Bae, J., Zheng, J., Song, Y., 2020. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in wuhan, China. JAMA Intern. Med. 180 (7), 934-943.
Xu, Z., Shi, L., Wang, Y., Zhang, J., Huang, L., Zhang, C., Liu, S., Zhao, P., Liu, H., Zhu, L., 2020. Characteristics of peripheral lymphocyte subset alteration in COVID-19 pneumonia. J. Infect. Dis. 221, 1762-1769.
Walshe, L.J., Wong, C.A., Oborne, J., Cooper, S., Lewis, S.A., Pringle, M., Hubbard, R., Tattersfield, A.E., 2001. Adverse effects of oral corticosteroids in relation to dose in patients with lung disease. Thorax 56 (4), 279-284.
Wang, J., 2020. Fast identification of possible drug treatment of coronavirus disease-19 (COVID-19) through computational drug repositioning study. J. Chem. Inf. Model. 60 (6), 3277-3286.
WHO, 2020. Coronavirus Disease (COVID-19): Dexamethasone. Who.int.
Wong, C., Lam, C., Wu, A., Ip, W., Lee, N., Chan, I., Lit, L., Hui, D., Chan, M., Chung, S., 2004. Plasma inflammatory cytokines and chemokines in severe acute respiratory syndrome. Clin. Exp. Immunol. 934, 994-1073.
Wright, K., 2020. Corticosteroids: Weigh the Benefits and Risks of Corticosteroids. Open Forum Infectious Diseases. Oxford University Press US, 1-9.
Youssef, N., Novosad, S.A., Winthrop, K.L., 2016. Infection risk and safety of corticosteroid use. Rheum. Dis. Clin. 42, 157-176.
Yu, W.C., Hui, D.S.C., Chan-Yeung, M., 2004. Antiviral agents and corticosteroids in the management of severe acute respiratory syndrome (SARS). Thorax 59, 643-645.
Zha, L., Li, S., Pan, L., Tefsen, B., Li, Y., Chinese, N., Chen, Y., Yang, Z., Xu, J., Zhou, X., Chen, D., Xiong, W., Xu, L., Zhou, F., Jiang, J., Bae, J., Zheng, J., Song, Y., 2020. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in wuhan, China. JAMA Intern. Med. 180 (7), 934-943.
Xu, Z., Shi, L., Wang, Y., Zhang, J., Huang, L., Zhang, C., Liu, S., Zhao, P., Liu, H., Zhu, L., 2020. Pathological Findings of COVID-19 associated with acute respiratory distress syndrome. Lancet Resp. Med. 8, 420-422.
Ye, Z.W., Yuan, S., Yuen, K.S., Fung, S.Y., Chan, C.P., Jin, D.V., 2020. Zoonotic origins of human coronaviruses. Int. J. Biol. Sci. 16, 1686.