

Role of Steroids in COVID-19

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ABSTRACT: In March 2020 covid-19 declared as global pandemic worldwide and threatens the health of people. Covid-19 affects the people of all age groups. It is a positive single strand RNA virus, which have a high ability to modify its structure. Various therapies used for the treatment of corona virus, but does not have any significant effect. In the 2nd wave of covid-19, steroids used for providing the symptomatic relief to the patients by mitigating the inflammatory response, especially in lungs. Steroids help to control the dysregulation of immune system. The main objective of this study is to review on the role of steroids in covid-19 patients. This study includes the mechanism of action of steroids, to control the effect of corona virus, uses of steroids, duration and timing of steroids, their interactions with other drugs and the common ADR's or side effects observed in covid-19 patients. The other main objective of this study is to review the effect of steroids in hospitalized (require oxygen support or ventilators) and mild symptomatic patients.

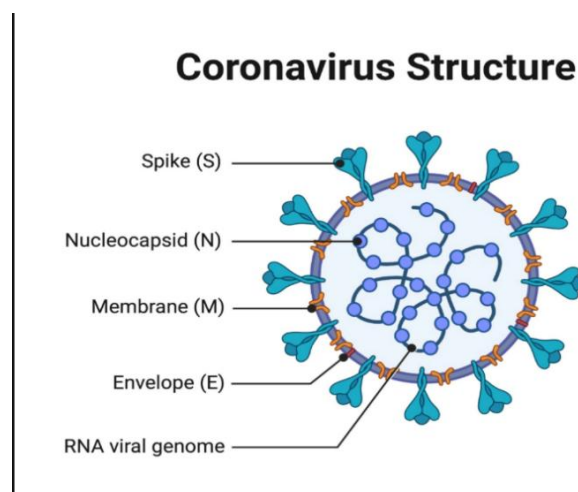
Key words: RNA virus, steroids, inflammatory response, immune system.

INTRODUCTION: In December 2019, a new respiratory virus was introduced to the worldwide. It was first reported in Wuhan, China. In January 9 corona virus was discovered as a causative agent of covid-19 disease. In January 20, 2020 corona virus reached to 3 other countries (Thailand, Japan and Korea). In January 31, 2020 this virus spread 20 more countries. April 28, 2020 29, 54,222 confirmed cases and 2, 02,597 deaths were reported worldwide. In March 2020 it was declared as a global pandemic by world health organization. The international committee on taxonomy of virus named this virus as severe acute respiratory syndrome corona virus 2 (SARS-CoV 2). WHO announced the name COVID-19. COVID stands for corona virus disease.

Corona virus belongs to the family of viruses which affects the respiratory system such as SARS (Severe acute respiratory system) and MERS-CoV (Middle East respiratory syndrome). There are mainly four genera within the subfamily orthocoronavirinae, namely alphacoronavirus, beta coronavirus, gamma coronavirus, delta coronavirus. In 2003-2004 beta coronavirus mainly found in bats named as SARS-CoV spread infection to human and affects 8,422 people and recorded 916 deaths worldwide. Again in 2012 another virus of beta group known as MERS-CoV affects nearly 3,000 humans and 858 deaths. The mortality rate was 34%. The source of corona virus is zoonotic means the virus is first developed in animals before transmitting to humans.

Corona virus belongs to the family Corona viridae. Corona virus contains positive RNA strand and largest RNA virus genome. The structure includes surface glycoproteins, membrane proteins, small

envelop proteins, matrix protein and nucleocapsid. The nucleocapsid protein forms a helical capsid which involve in the packing of genome, and the helical capsid is wrapped within an envelope. A capsid protects the single strand RNA of the virus. There is a presence of spikes on its surface which give crown like appearance to the virus, therefore it is termed as “corona”. These spikes have a ability to attach host cells. SARS CoV-2 virus contains spikes attach to the angiotensin -converting enzyme 2(ACE2) receptor present on the cell surface. SARS-CoV-2 spike is 10 to 20 times more likely to attach with ACE2 as compare to SARS-CoV.



COVID 19 affects the people of all age groups, but the following population have higher risk of infection;

- People having severe disease like cardiovascular disease, hypertension, respiratory disease, diabetes, chronic kidney disease, chronic obstructive pulmonary disease, asthma, pulmonary fibrosis.
- Pregnancy
- Old age people
- People who are immunodeficient (on immunosuppressants drugs)

The virus can be transmitted between people who are in close contact with each other, or if the person inhales the infected aerosols or droplets generated by coughing and sneezing from infected person. The virus can enter through the mouth, nose and eyes. The virus can also be transmitted by indirect ways like contact with surface contaminated by covid droplets (floor, furniture and clothes, mobile)

In human's it affects the respiratory tract, gastrointestinal tract, liver and central nervous system. The viruses firstly infect the upper respiratory tract and migrate to lower respiratory tract and reaches to alveolar sac, where it causes the release of various cytokines interleukins and interferons.

SYMPTOMS -One of the most interesting feature about novel corona virus is, in some cases it is asymptomatic.

Most of the corona virus patients have mild symptoms which can be treated at home. The patients who experience severe symptoms like difficulty in breathing should seek medical care immediately.

The most common corona virus symptoms include:

- fever,
- dry cough,
- fatigue,
- loss of taste and odor

Less common symptoms include:

- Aches
- pain
- sore throat,
- diarrhea (not found in SARS and MERS),
- conjunctivitis,
- headache, a rash on skin,
- Discoloration of fingers or toes.

Serious symptoms include:

- difficulty in breathing or shortness of breath,
- loss of speech and movement,
- chest pain or pressure,
- Bluish lips or face.

Serious infection can lead to respiratory failure, heart problem, liver problem and death.

The average incubation period of coronavirus is 2-14 days while in some cases it is 19-27 days. The incubation period of SARS-CoV 2 is longer as compared to MERS (5 days) and SARS (2-7 days).

PREVENTION OF CORONA VIRUS

Vaccination is one of the most important steps to prevent from covid-19, but except this there is certain more steps include:

- Cover mouth and nose in public space.
- Wash hand with soap or using sanitizers.
- maintain social distancing

PATHOPHYSIOLOGY OF CORONAVIRUS

The coronavirus genome is mainly composed of 30000 nucleotides, that encodes four structural proteins, namely Nucleocapsid (N) protein, Membrane protein (M), Spike protein (S), and Envelop (E) protein and other non-structural proteins. The capsid is made up of protein shell, which contains N (nuclear) protein. The nuclear protein bound to the single positive strand RNA which hijack the human cell and use them for the formation of its multiple copies. The N protein coats the viral RNA genome which has a vital role in its replication and transcription.

The M protein is most abundant in viral surface and it is also believed to be the central organizer for the coronavirus assembly. The S protein is integrated over the surface of the virus, which helps in attachment of the virus to the host cell surface receptor and a fusion between the viral and host cell membranes facilitates the viral entry into the host cell. The E protein is a small membrane protein mainly composed of 76-109 amino acids, it plays an important role in the virus assembly, membrane permeability of the host cell and virus host cell interaction.

A lipid envelope encapsulates the genetic material. Hemagglutinin-esterase enzyme located on the surface of virus. This HE protein helps in the entry of virus, not required for the replication but important for the infection of the natural host cell.

COVID-19 VACCINES

Covid 19 vaccines play a very healthy role in reducing the spread of coronavirus infection. Vaccines provide an acquired immunity against the virus. As there is no specific treatment against coronavirus, vaccine is the only way to prevent the transmission of infection. As the rate of transmission was very high and don't have any particular treatment, vaccines were the only way to control the spread of covid 19.

Vaccines should be safe and effective, for which they have to pass through clinical trials. There are mainly 3 phases which help to determine the efficacy and safety of the vaccine. Before starting the manufacturing, manufacturer needs permission from the country's health organization.

There are different vaccines which are now available against covid-19 some of them are as follows:

- Pfizer-Bio NTech- people 12 years and older can get this vaccine. Only 2 shots are required. The time interval between 2 shots is 21 days.
- Johnson & Johnson's Janssen – people 18 years and older can get this vaccine. it provides only 1 shot and after 2 weeks person is fully vaccinated.
- Moderna -18 years and older people can get this vaccine. Only 2 shots are required. The time interval between 2 shots is 28 days.
- Covid shield – Also known as Oxford, AstraZeneca vaccine manufactured by serum institute of India. 18 years and old can get this vaccine. it has only 2 shots. The time interval between the 2 shots are 84 days.
- Covaxin- It is inactivated type of vaccine, manufactured by Bharat Biotech. It also has only 2 shots. 18 years and above 18 years people can get this vaccine. The time interval between 2 doses are 4-6 weeks.
- Sputnik V – It is non-replicating viral vector type of vaccine. Manufactured by Gamaleya Research Institute of Epidemiology and Microbiology.

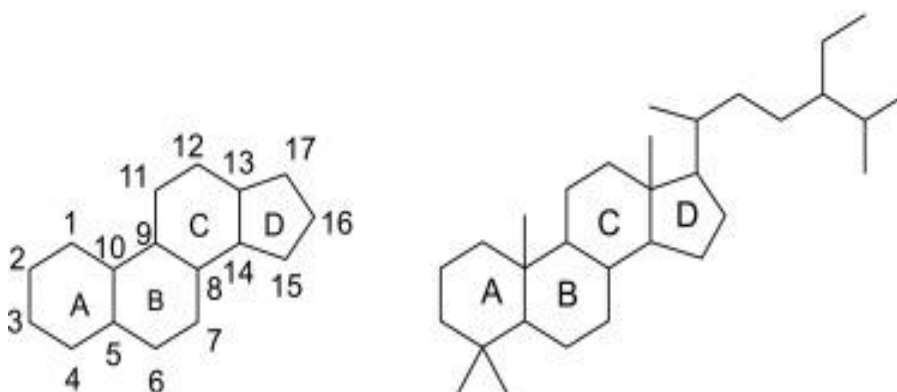
STEROIDS

Corticosteroids are the hormones which is secrete by the cortex of adrenal gland. It mainly secretes Glucocorticoid, mineralocorticoid, and weak androgenic activity. They act as a messenger which help to regulate immune, metabolic and reproductive function in humans.

William Withering was the first scientist who discovered the medicinal use of steroids. He extracted digitalis from the from the leaves of *Digitalis purpurea* to treat edema.

STRUCTURE

Steroids are the biologically active organic compounds. Structurally they are composed of 17 carbon atoms, arranged in four carbon rings which are fused with each other. It contains three six-member cyclohexane rings and one five-member cyclopentane rings. The three six membered rings named as A, B, C and the five membered ring named as D. The 17 carbons numbering is assigned in ascending order starting from ring A to ring D.



Chemical structure of steroid

TYPES

Corticosteroids:

- Glucocorticoids: – it includes cortisol, which act as immunosuppressant.
- Mineralocorticoids: - Aldosterone, helps in regulating blood pressure.

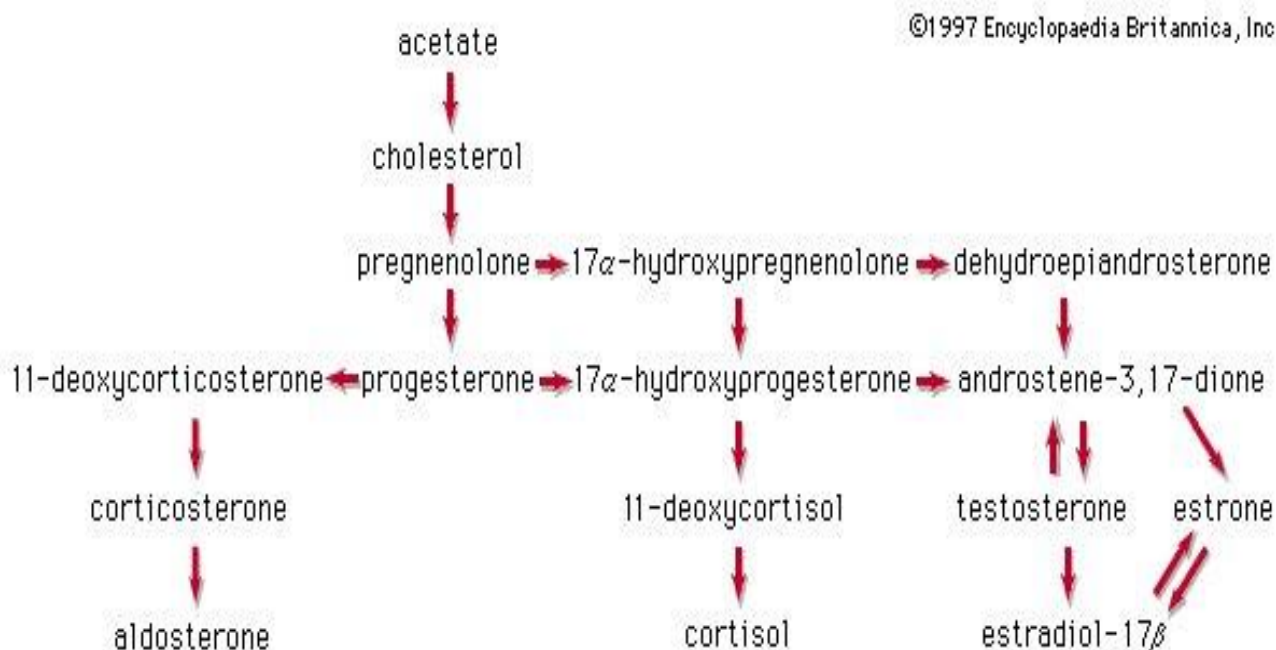
Sex steroids:

- Progestogens: - progesterone, which helps in maintain the pregnancy by regulating the cyclic changes in the endometrium of uterus.
- Androgen: - testosterone, helps in maintaining secondary sexual characteristics in male.
- Estrogen: - estradiol, helps in developing and maintaining female secondary sex characteristics.

BIOSYNTHESIS

Steroids are synthesized in the adrenal cortical cells from cholesterol. Cholesterol stores in large amount in the cytoplasmic vacuole. The process of synthesis of steroid from the cholesterol is known as steroidogenesis. Cholesterol is synthesized from the acetate produce by glycolysis or fatty acid

oxidation and after formation it does not show reverse process. The steroid hormones are primarily synthesized in the liver, ovaries, placenta, testis, adrenal cortex and brain.



ACTION

They help in maintaining fluid electrolyte, homeostasis, fluid electrolyte function of skeletal muscle and nervous system. Corticosteroids shows direct and indirect actions, which means their presence affects the functioning of other hormones. For example, they do not have direct action on blood pressure but their presence affects the release of adrenaline. Glucocorticoid shows effects on carbohydrate, fat and protein metabolism. Mineralocorticoid have effects on Na⁺, k⁺ balance.

Classification of steroids:

Steroids are classified on the basis of their time period

Short acting

- Cortisone
- Hydrocortisone
- Deflazacort

Intermediate acting

- Prednisone
- Prednisolone
- Methylprednisolone
- Triamcinolone

Long acting

- Dexamethasone
- Betamethasone

STERIODS & COVID-19

There are certain drugs which are used to treat the coronavirus infection. Basically, the steroids do not cure the treatment, they only provide relieve from the inflammation which is produce by the body's own immune system. When the virus, bacteria and any foreign biomaterial enters to the human body, the immune system of the body activates and start releasing interleukins, cytokines, interferons and also increase vascular permeability. In the human body steroids reduces the dis-regulation of immune response. The steroids are only effective if they are given in right amount at right time. If they are overdosed, they become dangerous to the body.

MECHANISM OF ACTION OF STEROIDS

MECHANISM OF ACTION=> prednisone reduces the inflammation by decreasing the movement of polymorphonuclear leukocytes and decreases the vasodilation and permeability of the capillaries. Glucocorticoid receptors are the nuclear receptors. During inactivation time they remain in the cytoplasm of the cell. When steroid molecule reached inside the cells by the process of simple diffusion. Receptor present in the cytoplasm receive the molecule and forms drug receptor complex. This drug receptor complex migrates to nucleus and bind with specific part of the DNA molecule and provide signal to messenger RNA for the formation of specific type of protein.

When virus or bacteria attack to the human cell which is made up of phospholipid, it causes the release of arachidonic acid with the help of enzyme phospholipase A2. This arachidonic acid causes the production of prostaglandin and thromboxane A2 which causes the inflammation. When corticosteroid is given, it causes the activation of protein called annexin-1. This activated protein blocks the release of arachidonic acid from phospholipid by inhibiting the enzyme phospholipase A2.

Steroids works on inhibiting release of prostaglandins, thromboxane and interleukin 4, IL-5, IL-3 which are all involve in the cause of inflammation. Therefore, they are used in the treatment of covid-19. They provide relief to the patients from the coronavirus symptoms. It also helps in reducing mortality rate.

STERIODS IN COVID-19

As there were many therapies used for reducing the severity of inflammation response but they do not show any strong evidence. Corticosteroids are well known for reducing the inflammation and acute respiratory distress syndrome (ARDS). Additionally, they are easily available and affordable treatment option. But on the other hand, they also have some serious side effects which can't be neglectable like, delay viral clearance, high risk of infections and suppression of hypothalamic pituitary gland.

On 2nd September 2020, World Health Organization recommended the use of systemic corticosteroid in the treatment of covid-19. WHO recommends dexamethasone, hydrocortisone or prednisolone to be given orally or intravenously for the severe ill covid-19 patients. According to the WHO guidelines only severe cases can be treated with corticosteroids, they are not for the mild cases. WHO recommends time and duration of steroids should be 7-10 days. Dose should be 6 mg

dexamethasone daily which is equivalent to 160 mg of hydrocortisone (50 mg daily / 8 hour or 100 mg / 12 hour), 40 mg prednisolone, 32 mg methylprednisolone (8mg/6 hour).

Various studies performed during covid-19 shows that steroids should decrease the mortality rate of the patients those are on ventilators or need support. Steroids are mainly used for correcting the dis-regulation of immune system. As in the severe case the body fight with the virus, in response the immune system releases the white blood cells or produce cytokine storm which start damage body tissues. To control the dis-regulation or overcontrol action of immune system steroids are given.

Why WHO recommended steroid only for severe conditions?

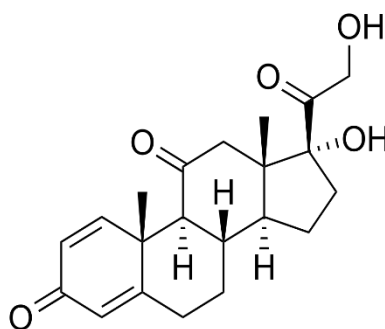
Steroids are well known immunosuppressive and anti-inflammatory agents. They are mainly used in the treatment of various auto immune diseases. If they are giving in the early stage of infection, when the virus is already in it may prolong the residential time of virus in the human body, which later cause more damage. This happens because steroids interfere with the natural defense mechanism of the body which may could develop resistance against the virus. On giving steroid at early-stage cause reduction in defense mechanism which shows prolonged disease.

What happens if the steroids are taking for longer duration?

Steroids are only beneficial to the body if they are taking in a right amount or with required period of time. But if they are taking for longer duration, they show their side effects. Recently in covid cases, various patients develop hyperglycemic conditions, insomnia. If they are using for more time, they suppress the immune system and enhances the chancer of various fungal and bacterial infections that's why there is a rise in black fungus infection in covid patients.

There are some steroidal drugs which are used in Covid-19, are as follows:

PREDNISONE



Prednisone is a synthetic corticosteroid which is synthesized from cortisone. It is an FDA approved delayed release corticosteroid which has anti-inflammatory or immunosuppressive activity. Prednisone is a prodrug which is converted into prednisolone in the liver.

It works on the immune system to provide relief from the from swelling, redness, itching and allergic reactions.

Indication- It is indicated as an immunosuppressive or anti-inflammatory drug for allergic reactions, dermatological, gastrointestinal problems, hematological, ophthalmic problems, nervous system, rheumatological, endocrine and neoplastic conditions and also in organ transplant.

Prednisone also shows anti emetic effect by blocking the cerebral innervation of the emetic center by the inhibition of prostaglandin.

Common adverse effects: cataracts, easy bruising, fatigue, enhance the risk of infection, depression, psychosis, weakness, mental confusion, immunosuppressant, abdominal pain, peptic ulcer, insomnia, anxiety, black stools, dry mouth, decrease in the amount of urine.

Adverse effects in patients taking high dose of steroids or for longer period of time: skin fragility, weight gain, high chances of infection, hypertension, hyperglycemia, or increase cholesterol level in blood.

Pharmacokinetics: it is absorbed through the gastrointestinal tract. The half-life is 2-3 hour, and the volume of distribution is 0.4-1 L/Kg. prednisone is cleared by the hepatic metabolism process with the help of enzyme cytochrome P450.

Methyl prednisolone is a synthetic corticosteroid, which shows anti-inflammatory and immunosuppressive action in the human body. It is a derivative of prednisolone and have a greater potency as compare to prednisolone. Methyl prednisolone was approved by FDA on 24th October 1957. lower dose of methylprednisolone has anti-inflammatory process while higher dose shows immunosuppressive action. In covid-19 methylprednisolone helps in providing relief to the patients.

Pharmacokinetic- oral methyl prednisolone has 89.9% bioavailability. The plasma half-life is 180 min, and the biological half-life is 24-36 hours. Average volume of distribution is 1.38L/kg. methyl prednisolone shows 76.8% plasma protein binding.

Contradiction- active or inactive tuberculosis, fungal infection, herpes simplex infection in eye, diabetes, high cholesterol, hypokalemia, glaucoma, psychotic disorder, gastritis, seizures, hypertension, cataract, measles, muscle weakness.

Side effects due to its mineralocorticoid activity- fluid retention, swelling of face, Na retention, hypertension, increase chances of chronic heart failure.

Side effects on organs- intestinal bleeding, perforations, ulcerative esophagitis, pancreatitis.

CNS- headache, intracranial pressure, vertigo, convulsion, depression.

Eye- glaucoma, increase intra ocular pressure, cataract.

Skin- thin fragile skin, sweating, facial redness, impaired wound healing.

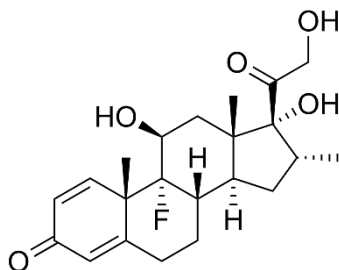
Endocrine system- decrease growth in children, Cushing syndrome (bone loss, moon face), weight gain, hyperglycemia.

Methylprednisolone in COVID-19

According to various researches performed during COVID-19 shows that methylprednisolone has better result as compare to other steroids used for coronavirus treatment. Previous studies on SARS reveals that cytokine dysregulation was the primary cause of organ dysfunction. Therefore, steroids are used as they have a ability to reduce the cytokine storm and provide anti-inflammatory activity. It is a hypothesis that methylprednisolone has is greater lung penetration activity, therefore act as better

immunosuppressive agent in treatment of coronavirus and in improvement of respiratory complications. Methylprednisolone also shows lower mortality rate as compare to those who received dexamethasone.

DEXAMETHASONE



Dexamethasone is long-acting glucocorticoid, which is used to treat various inflammatory diseases. Dexamethasone was approved by FDA on 30th October 1958. Dexamethasone was recommended for the treatment of covid-19 patient.

Chemical formula= C₂₂H₂₉FO₅

Dexamethasone is approximately 30 times more potent than cortisol in terms of anti-inflammatory and immunosuppressive effect. Dexamethasone has 20-30 times more binding affinity towards glucocorticoid receptor as compare to other glucocorticoid drugs. It is one of the most commonly drug used as antiemetics.

Pharmacodynamics- it binds to glucocorticoid receptor. Its duration of action varies according to the route of administration. They have wide therapeutic window.

Absorption- the absorption of dexamethasone via intravenous route is higher as compare to intramuscular route. Its bioavailability is around 70-80%.

Protein binding- 77% dexamethasone shows plasma protein binding. Majority of the drug binds with the serum albumin.

Common ADR's include- insomnia, vertigo, weight gain, depression, increase blood pressure, increased risk of infections, vomiting, confusion, nausea, headache, acne, dry skin, dizziness, stomach pain, muscle weakness, peptic ulcer, osteoporosis, glaucoma, fetal abnormalities.

INTERACTION- Drugs such as barbiturates, phenytoin, rifampin is the inducer of hepatic microsomal enzymes can reduce the half-life of dexamethasone.

Volume of distribution of dexamethasone can be increases when given along with oral contraceptives.

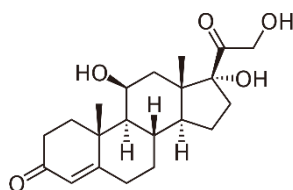
CONTRAINDICATIONS: There are certain conditions in which steroids are contraindicated are as follows:

- Peptic ulcer
- Diabetes mellitus
- Hypertension
- Viral and fungal infection

- Tuberculosis and other infections
- Osteoporosis
- Herpes simplex keratitis
- Psychosis
- Epilepsy
- Chronic heart failure
- Renal failure.

Dexamethasone plays a very important role in the treatment of covid-19. NHS (national health service) and NIH (national institute of health) recommends the use of dexamethasone for the treatment of patients who are on ventilation or need oxygen supplement. IDSA (Infectious Disease Society of America) recommends the use of corticosteroids for patients with SpO₂ <94% on room air. The World Health Organization also suggest the use of steroids only for severe covid-19 patient and not for mild symptomatic covid-19 patient. Various studies from all over the world said that the use of steroids in severe cases decreases the mortality rate. If the steroids are given too early, it may prolong the virus stay in body, the patient may feel better but it becomes more fetal in the days ahead. Or if the steroids are given for longer duration it may lead to cause fungal infection in patients.

HYDROCORTISONE



Hydrocortisone is named on the basis of hormone cortisol. It is a corticosteroid which acts as both glucocorticoid and mineralocorticoid.

Hydrocortisone is 4 times less effective than prednisolone and 40 times less effective against dexamethasone in terms of anti-inflammatory activity.

Pharmacokinetic- only 4% hydrocortisone is bind with the protein and have a 100%bioavailability when given orally.

The plasma half-life of hydrocortisone is about 60-120 minutes, and biological half-life is around 8-2 hours.

Side effects- mood swings, high chances of infection, upset stomach, muscle weakness, osteoporosis, immune suppression.

Uses- hydrocortisone is available in various dosage forms like tablets, creams, ointment and injections.

They are used to trat various skin problems like, rashes, eczema, insect bites, they are used in the forms of suppositories to trat itchy bottom, mouth ulcers, painful joints in case of arthritis.

MEDICINAL USES OF STEROIDS

- Rheumatoid arthritis
- Osteoarthritis
- Rheumatic fever
- Gout
- Severe allergic reactions
- Autoimmune diseases
- Bronchial asthma
- Lung diseases (pneumonia & pulmonary edema)
- Eye diseases
- Infective diseases
- Skin diseases
- Intestinal diseases
- Cerebral edema
- Organ transplant
- Septic shock
- Thyroid storm

ADVERSE DRUG REACTIONS OF STEROIDS:

Cushing's syndrome- it is also called hypercortisolism. It mainly occurs due to the over use of steroids. It includes weight gain, round face, narrow mouth and obesity of trunk with thin limbs.

Purple Striae (stretch marks), fragile skin- if the steroids are used for longer duration, they may develop pink or purple stretch marks on skin mainly on the abdomen, thighs and arms, hirsutism. Steroids may also show degradation or thinning of epidermal or dermal layer of skin with topical use.

Hyperglycemia- steroids increase the blood sugar level. Steroids stimulate gluconeogenesis in liver and oppose insulin action.

Muscular weakness- steroids mainly wasting shoulder, arm, pelvis and thigh muscle also known as proximal myopathy. It mainly occurs after withdrawing corticosteroids. Hypercortisolism and hypocortisolism both show muscle weakness. Hypokalemia is the main cause in hypercortisolism.

Risk of infection- longer use steroids may develop immunosuppressive actions, due to which the body becomes more prone to bacterial and fungal infections.

Peptic ulceration- as the steroid has anti-inflammatory action, they inhibit the prostaglandins, which help in protecting the stomach lining. Due to lack of prostaglandin production, acid irritates the stomach lining and leads to peptic ulcer.

Osteoporosis- it mainly affects vertebrae and flat bones. Compression fracture of vertebrae and spontaneous fracture of long bones may occur, it is mainly found after withdrawing of steroids. Steroids producing osteoporosis can be prevented by calcium supplements with vitamin D, androgen replacement in male, estrogen/raloxifene in female.

Posterior subcapsular opacities of the lens may be found, by using steroids for several years. It mainly occurs in children.

Glaucoma- glaucoma may be develop insensitive individuals after prolonged topical use.

Growth retardation- the longer use of steroids may develop growth retardation in children even with a small dose. Larger dose inhibits the growth hormone secretion.

Psychiatric disorder- corticosteroids disturb the circadian rhythm which cause insomnia. Anxiety, nervousness and mild euphoria are the side shown by using high dose of steroids.

Suppression of hypothalamus-pituitary-adrenal axis- using high dose and longer duration therapy both are the main cause of adrenal suppression. When there is suppression of HPA axis, the body is unable to regulate stress and energy levels, shows symptoms such as fatigue, depression, anxiety, weakness, pain in muscles, joints.

To avoid suppression of HPA axis, there are some measures:

- Use steroids for shorter duration of time.
- Use shorter acting steroids.
- give entire daily dose in the morning
- switch to alternate treatment if possible.

DISCUSSUON

As covid-19 is a new viral disease, there is no specific anti-viral drug for its treatment. Coronavirus is single positive stranded RNA virus which have an ability to perform mutation for its structure. Patients infected with SARS-CoV-2 were treated with symptomatic therapy. Steroids mainly used to prevent the lung fibrosis in severe covid-19 patients. Corticosteroids mainly used for symptomatic treatment.

Some studies claimed that corticosteroids should not be used in covid-19 treatment, as they cause lung injury or shock. But on the other hand, some studies had different prospective, use of steroids for shorter duration, with low dose for critically ill patients show beneficial results.

According to the data published in the PubMed, Scopus, google scholar etc. suggest that patients with severe conditions were more require steroid treatment. In some study it was observed that the patient with SARS-CoV-2 had more concentration of cytokines (such as IL 7, IL 8, IL 9, IL 10) in the serum as compared to healthy person. Concentration of IL 2, IL 7 and IL 10 was higher in ICU patients as compared to non-ICU patients. due to release of all these chemicals, inflammation developed in lungs and leads to lung fibrosis.

Corticosteroids do not have direct role on viral inhibition, their main role is anti-inflammatory and immunosuppressive action. In the beginning phase of inflammation, steroids decrease capillary dilation, inflammatory cell exudation, phagocytosis and leucocyte infiltration. In the delay stage, glucocorticoids can hinder the expansion of vessels and fibroblast. Moreover, corticosteroids binding to their receptors block nuclear transcription factor -KB (NF-KB) signaling and further repress the

transcription and translation of inflammation factors. These clarified why corticosteroids treatment was more required in seriously sick patients with covid infection.

CONCLUSION

Corticosteroids only help to provide symptomatic relief to the severe critically ill patients of covid-19 required oxygen support or mechanical ventilators. If steroids not given to such patients, virus may develop lung fibrosis and ultimately leads to death. Steroids are only effective when they are given in right amount at right time. If steroids are given too early stage of infection, it causes prolong stay of the virus in body and cause more damage to the body in the days ahead. If steroids are given for longer duration than required, it may cause fungal infection like black fungus, hyperglycemia, suppress natural immune response, which make patient more vulnerable towards bacterial and other infections, hypokalemia, weakens bones and muscles and other effects include kidney damage and cardiovascular diseases.

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