Journal for Research in Applied Sciences and Biotechnology

www.jrasb.com

ISSN: 2583-4053

Volume-3 Issue-1 || February 2024 || PP. 305-314

https://doi.org/10.55544/jrasb.3.1.50

Hydrocortisone as Antiallergic Drug

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www.jrasb.com || Vol. 3 No. 1 (2024): February Issue

Received: 20-03-2024	**Revised:** 21-03-2024	**Accepted:** 23-03-2024

ABSTRACT

Glucocorticoids are widely used for the suppression of inflammation in chronic inflammatory diseases such as asthma, rheumatoid arthritis, inflammatory bowel disease and autoimmune diseases, all of which are associated with increased expression of inflammatory genes. The molecular mechanisms involved in this anti-inflammatory action of glucocorticoids is discussed, particularly in asthma, which accounts for the highest clinical use of these agents.

Glucocorticoids bind to glucocorticoid receptors in the cytoplasm which then dimerize and translocate to the nucleus, where they bind to glucocorticoid response elements (GRE) on glucocorticoid-responsive genes, resulting in increased transcription. Glucocorticoids may increase the transcription of genes coding for anti-inflammatory proteins, including lipocortin-1, interleukin-10, interleukin-1 receptor antagonist and neutral endopeptidase, but this is unlikely to account for all of the widespread anti-inflammatory actions of glucocorticoids.[3]

The most striking effect of glucocorticoids is to inhibit the expression of multiple inflammatory genes.[3]

Keywords- Glucocorticoids, Hydrocortisone, antiallergic drug.

I. INTRODUCTION

a- What is hydrocortisone?

Hydrocortisone is a steroid medication that treats inflammation in the body.

The drug comes in an oral form to take by mouth, and a topical form to apply to the skin. It's available over-the-counter (OTC) and with a prescription for higher-strength formulations.

Oral hydrocortisone is typically used to treat certain forms of arthritis, allergies, skin disorders, blood disorders, asthma, kidney disorders, thyroid problems, autoimmune diseases, certain types of cancer, and intestinal problems.

It's also used by some people whose adrenal glands do not produce the normal amount of hydrocortisone that's made in the body.

Topical hydrocortisone is used to treat minor skin irritations, skin allergies, eczema, insect bites, poison ivy, poison oak, mouth sores, poison sumac, hemorrhoids, and other itching in certain parts of the body.

The Food and Drug Administration (FDA) approved hydrocortisone in 1952.

The drug is available under dozens of brand names (Anusol HC, Locoid, Westcort, etc.) and in combinations with other drugs (e.g., antibiotics such as neomycin).

Applying topical hydrocortisone to acne lesions may reduce redness and inflammation. The medicine may also speed up recovery.

You can apply a small amount of cream directly to inflamed pimples or cysts. In some cases, doctors can inject hydrocortisone directly into pimples. [1]

Cortisol is a steroid hormone, in the glucocorticoid class of hormones, and is produced in humans by the zona fasciculata of the adrenal cortex within the adrenal gland. [2] It is released in response to stress and low blood-glucose concentration.

It functions to increase blood sugar through gluconeogenesis, to suppress theimmune system, and to aid in the metabolism of fat, protein, and carbohydrates. [3] It also decreases bone formation. [4]

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Hydrocortisone (INN, USAN, BAN) is a name for cortisol when it is used as a medication. Hydrocortisone is used to treat people who lack adequate naturally generated cortisol. It is on the World Health Organization's List of Essential Medicines needed in a basic [health system. [5]

Oral hydrocortisone may increase your risk of contracting certain illnesses. You should call your doctor if you are exposed to chicken pox, measles, or TB while using this drug.

Also, don't have any type of vaccination or skin test while taking oral hydrocortisone unless your doctor tells you to do so You should report any signs of infection (fever, sore throat, muscle aches) to your doctor right away while taking oral hydrocortisone.

Call your doctor if your condition worsens while taking this Medici Avoid using topical hydrocortisone for long periods of time on the face; genital and rectal areas; and in the skin creases of the armpits unless your doctor tells you otherwise.

b- Pregnancy and hydrocortisone

Hydrocortisone is an FDA Pregnancy Category C drug, which means it's unknown how it will affect an unborn baby. This medicine should only be used when clearly needed during pregnancy. [1]-the aim of work:
For showing hydrocortisone history and advantage as drug for allergy and the side effect for it.

II. HEALTH EFFECTS

a- Metabolic response

In the early fasting state, cortisol stimulates gluconeogenesis (the formation of glucose), and activates anti-stress and anti-inflammatory pathways[6]. Cortisol also plays an important, but indirect, role in liver and muscle glycogenolysis, the breaking down of glycogen to glucose-1-phosphate and glucose. This is done through its passive influence onglucagon. [clarification needed] Additionally, cortisol facilitates the activation of glycogen phosphorylase, which is necessary for epinephrine to have an effect on glycogenolysis.[7]

In the late fasting state, the function of cortisol changes slightly and increases glycogenesis. This response allows the liver to take up glucose that is not being used by the peripheral tissue and turn it into liver glycogen stores to be used if the body moves into the starvation state.

Elevated levels of cortisol, if prolonged, can lead to proteolysis (breakdown of proteins) and muscle wasting. [8] Several studies have shown that cortisol can have a lipolytic effect (promote the breakdown of fat). Under some conditions, however, cortisol may somewhat suppress lipolysis. [9]

b- Immune response

Cortisol prevents the release of substances in the body that cause inflammation. It is used to treat conditions resulting from over activity of the B-cell-mediated antibody response. Examples include inflammatory and rheumatoid diseases, as well as allergies.

Low-potency hydrocortisone, available as a non-prescription medicine in some countries, is used to treat skin problems such asrashes, and eczema.

It inhibits production of interleukin (IL)-12, interferon (IFN)-gamma, IFN-alpha and tumor-necrosis-factor (TNF)-alpha by antigen-presenting cells (APCs) and T helper (Th)1 cells, but upregulates IL-4, IL-10, and IL-13 by Th2 cells. This results in a shift toward the immune response rather than general immunosuppression. The activation of the stress system (and resulting increase in cortisol and the shift) seen during an infection is believed to be a protective mechanism which prevents an over activation of the inflammatory response.

Cortisol can weaken the activity of the immune system. Cortisol prevents proliferation of T-cells by rendering the interleukin-2producer T-cells unresponsive to interleukin-1 (IL-1).[10]

c- Other effects

Glucose

Cortisol counteracts insulin, contributes to hyperglycemia-. causing hepatic gluconeogenesis[11] and inhibits the peripheral utilization of glucose (insulin resistance) by decreasing the translocation of glucose transporters (especially GLUT4) to the cell membrane.[12] However, cortisol increases glycogen synthesis (glycogenesis) in the liver. [13] The permissive effect of cortisol on insulin action in liver glycogenesis is observed in hepatocyte culture in the laboratory, although the mechanism for this is unknown.

d- Bone and collagen

Cortisol reduces bone formation, [4] favoring long-term development of osteoporosis (progressive bone disease). It transportspotassium out of cells in exchange for an equal number of sodium ions [14].

This can trigger the hyperkalemia of metabolic shock from surgery.

Cortisol also reduces calcium absorption in the intestine.[15]

Collagen is an important component of connective tissue. It is vital for structural support and is found in muscles, tendons, and joints, as well as throughout the entire body. Cortisol down regulates the synthesis of collagen. [16]

e- Wound healing

Cortisol and the stress response have known deleterious effects on the immune system. High levels of perceived stress and increases in cortisol have been found to lengthen wound healing time in healthy, male adults. Those who had the lowest levels of cortisol the day following a 4 mm punch biopsy had the fastest healing time.[17] In dental students, wounds from punch biopsies took an average of 40% longer to heal when performed three days before an examination as opposed to biopsies performed on the same students during

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ISSN: 2583-4053

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https://doi.org/10.55544/jrasb.3.1.50

summer vacation. [18] This is in line with previous animal studies that show similar detrimental effects on wound healing, notably the primary reports showing that turtles recoil from cortisol. [19]

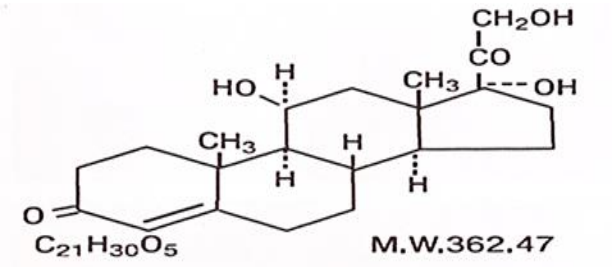
f- Memory

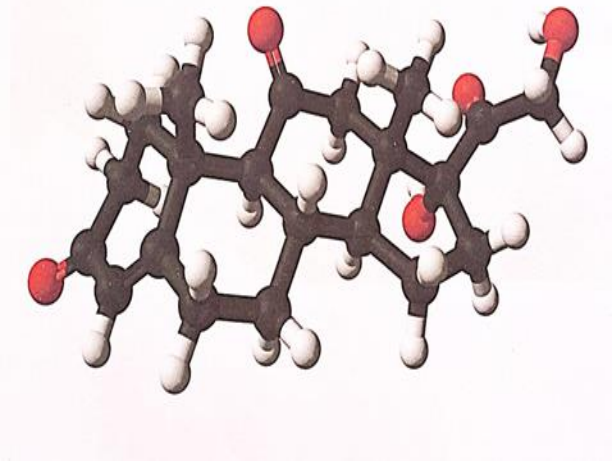
Cortisol works with epinephrine (adrenaline) to create memories of short-term emotional events; this is the proposed mechanism for storage of flash bulb memories, and may originate as a means to remember what to avoid in the future. [20] However, long-term exposure to cortisol damages cells in the hippocampus;[21] this damage results in impaired learning. Furthermore, it has been shown that cortisol inhibits memory retrieval of already stored information. [22]

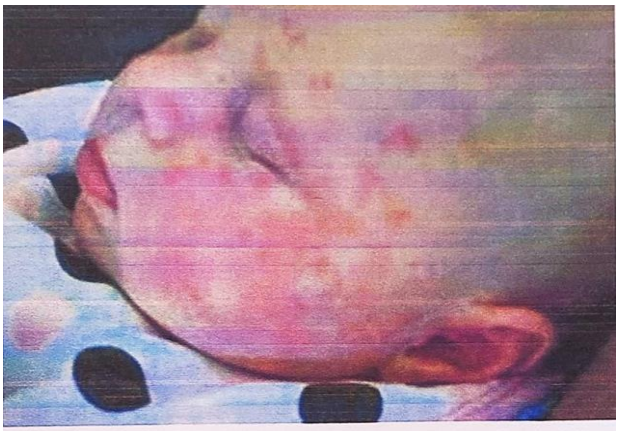
III. DRUG DESCRIPTION

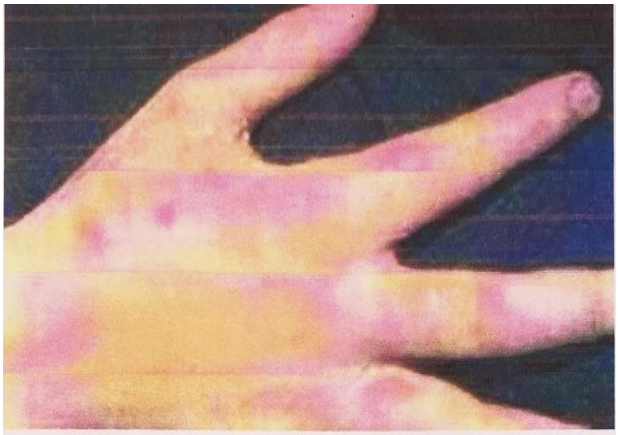
The topical corticosteroids constitute a class of primarily synthetic steroids used as anti-inflammatory and anti-pruritic agents.

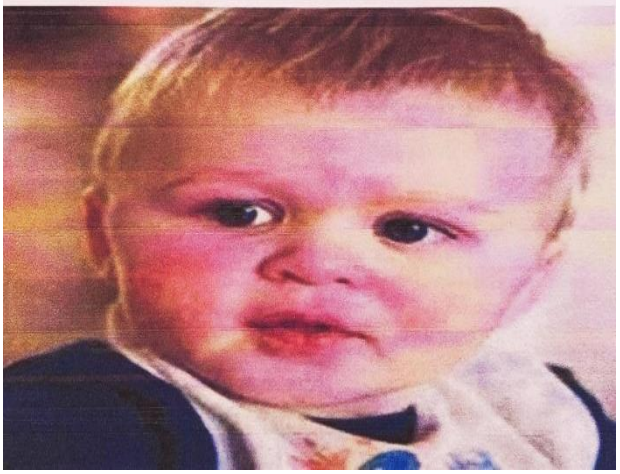
Hydrocortisone Cream 2.5% and Hydrocortisone Ointment 2.5% contain hydrocortisone. Hydrocortisone is a white to pratically white crystalline powder. Chemically, hydrocortisone (hydrocortisone cream and ointment 2.5%) is pregn-4-ene-3,20-dione, 11,17,21-trihydroxy-, (Up)-. The structural formula of hydrocortisone (hydrocortisone cream and ointment 2.5%) is:











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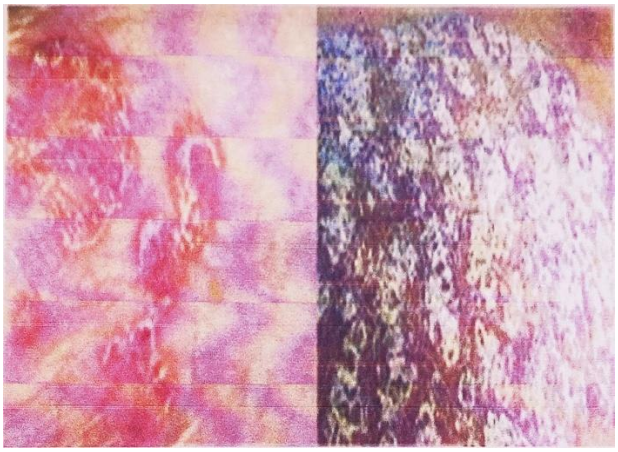

IV. SOME OF THE SIDE EFFECT OF HYDROCORTISONE

a- What are the possible side effect of hydrocortisone:

Get emergency medical help if you have any of these signs of an allergic reaction: hives; difficulty breathing; swelling of your face, lips, tongue, or throat Stop using hydrocortisone topical and call your doctor at once if you have any of these serious side effects:

- blurred vision, or seeing halos around light
- uneven heartbeats
- sleep problems
- insomnia
- weight gain, puffiness in your face; or
- feeling tired.

Less serious side effects may include:

- skin redness
- burning
- itching, or peeling
- thinning

b- Other side effect

- Stomach irritation or upset stomach
- Vomiting
- Headache
- Dizziness
- Insomnia
- Restlessness
- Depression or anxiety
- Acne
- Increased hair growth
- Easy bruising
- Irregular or missed menstrual periods
- Swollen face, legs, or ankles
- Skin rash
- Vision problems
- Muscle weakness
- Cold or infection that lasts a long time
- Black or tarry stools
- Severe skin rash
- Wheezing
- Difficulty breathing or swallowing

V. TYPES OF HYDROCORTISONE

a- Hydrocortisone Sodium Succinate Injection Uses:

This medication is used to treat various conditions such as severe allergic reactions,arthritis, blood diseases, breathing problems, certain cancers, eye diseases, intestinal disorders, and skin diseases. It decreases your body's natural defensive response and reduces symptoms such as swelling and allergic-type reactions. Hydrocortisone is a corticosteroid hormone (glucocorticoid). This injectable form of hydrocortisone is used when a similar drug cannot be taken by mouth or when a very fast treatment is needed, especially in patients with severe medical conditions. Talk to your doctor about the risks and benefits of hydrocortisone, especially if it is to be injected near your spine (epidural). Rare but serious side effects may occur with epidural use.

This drug may also be used with other medications as a replacement for certain hormones.

- How to use hydrocortisone sodium succinate injection

This medication is given by slow injection into a vein or directly into a muscle as directed by your doctor. Dosage is based on your medical condition and response to treatment. Do not increase your dose or use this drug more often than prescribed without consulting your doctor.

If you have been using this medication for a long time, do not suddenly stop using it without your doctor's approval. Your dose may need to be gradually decreased to reduce symptoms such as weakness, weight loss, nausea, or extreme tiredness.

If you are giving this medication to yourself at home, learn all preparation and usage instructions from your health care professional. Before using, check this product visually for particles or discoloration. If either is present, do not use the liquid. Learn how to store and discard medical supplies safely. [1]

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https://doi.org/10.55544/jrasb.3.1.50

b- Hydrocortisone cream

- **Hydrocortisone cream is used for:**

Reducing itching, redness, and swelling associated with many skin conditions.

Hydrocortisone cream is a topical corticosteroid. It works by reducing skin inflammation (redness, swelling, itching, and irritation).

Use hydrocortisone cream as directed by your doctor. Check the label on the medicine for exact dosing instructions.

Apply a small amount of medicine to the affected area.

Gently rub it in until it is evenly distributed. Wash your hands after applying hydrocortisone cream, unless your hands are part of the treated area [38].

- Do NOT use hydrocortisone cream if:

• you are allergic to any ingredient in hydrocortisone cream

Contact your doctor or health care provider right away if any of these apply to you.

Do not bandage or wrap the affected area unless directed otherwise

• by your doctor.

Do not use hydrocortisone cream on your face, groin, or underarms unless your doctor tells you otherwise. [38]

- Before using hydrocortisone cream:

Some medical conditions may interact with hydrocortisone cream.

Tell your doctor or pharmacist if you have any medical conditions, especially if any of the following apply to you:

if you are pregnant, planning to become pregnant, or are breast-feeding

c- Ointment:

For External Use Only

Not For Ophthalmic Use

Hydrocortisone Ointment USP, 1% contains hydrocortisone [Pregn-4-ene-3,20-dione, 11,17,21-trihydroxy-, (11B)-], with the molecular formula C21H3005 and molecular weight 362.47. Each gram contains 10 mg of hydrocortisone in a base containing white petrolatum and mineral oil.

Topical corticosteroids share anti-inflammatory, anti-pruritic and vasoconstrictive actions. The mechanism of anti-inflammatory activity of the topical corticosteroids is unclear. Various laboratory methods, including vasoconstrictor assays, are used to compare and predict potencies and/or clinical efficacies of the topical corticosteroids. There is some evidence to suggest that a recognizable correlation exists between vasoconstrictor potency and therapeutic efficacy in man.

Indications and Usage:

Topical corticosteroids are indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses.

Contraindications:

Topical corticosteroids are contraindicated in those patients with a history of hypersensitivity to any of the components of the preparation.

Precautions:

General: Systemic absorption of topical corticosteroids has produced reversible hypothalamic-pituitary-adrenal (HPA) axis suppression, manifestations of Cushing's syndrome, hyperglycemia, and glucosuria in some patients.

Conditions which augment systemic absorption include the the application of the more potent steroids, use over large surface areas, prolonged use, and the addition of occlusive dressings. Therefore, patients receiving a large dose of a potent topical steroid applied to a large surface area orunder an occlusive dressing should be evaluated periodically for evidence of HPA axis suppression by using the urinary free cortisol and ACTH stimulation tests. If HPA axis suppression is noted, an attempt should be made to withdraw the drug, to reduce the frequency of application, or to substitute a less potent steroid. Recovery of HPA axis function is generally prompt and complete upon discontinuation of the drug. Infrequently, signs and symptoms of steroid withdrawal may occur, requiring supplemental systemic

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ISSN: 2583-4053

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corticosteroids. Children may absorb proportionally larger amounts of topical corticosteroids and thus be more susceptible to systemic toxicity. If irritation develops, topical corticosteroids should be discontinued and appropriate therapy instituted. In the presence of dermatological infections, the use of an appropriate antifungal or antibacterial agent should be instituted. If a favorable response does not occur promptly, the corticosteroid should be discontinued until the infection has been adequately controlled.

d- Tablet

CORTEF Tablets contain hydrocortisone which is a glucocorticoid.

Glucocorticoids are adrenocortical steroids, both naturally occurring and synthetic, which are readily absorbed from the gastrointestinal tract. Hydrocortisone USP is white to practically white, odorless, crystalline powder with a melting point of about 215° C. It is very slightly soluble in water and in ether; sparingly soluble in acetone and in alcohol; slightly soluble in chloroform.

The chemical name for hydrocortisone is pregn-4-ene-3,20-dione, 11,17,21-trihydroxy-, (11ß)-. Its molecular weight is 362.46

CORTEF (hydrocortisone tablet) Tablets are available for oral administration in three strengths: each tablet contains either 5 mg, 10 mg, or 20 mg of hydrocortisone. Inactive ingredients: calcium stearate, corn starch, lactose, mineral oil, sorbic acid, sucrose.

Hydrocortisone Tablets are indicated for replacement therapy in congenital adrenal hyperplasia in children.

Hydrocortisone Tablets are also used for the emergency treatment of severe bronchial asthma, drug hypersensitivity reactions, serum sickness, angioneurotic oedema and anaphylaxis in adults and children.

VI. PHARMACOLOGY

Hydrocortisone is the pharmaceutical term for cortisol used in oral administration, intravenous injection, or topical application. It is used as an immunosuppressive drug, given by injection in the treatment of severe allergic reactions such as anaphylaxis andangioedema, in place of prednisolone in patients needing steroid treatment but unable take oral medication, and perioperatively in patients on long-term steroid treatment to prevent Addisonian crisis. It may also be injected into inflamed joints resulting from diseases such as gout.

Compared to hydrocortisone, prednisolone is about four times as strong and dexamethasone about forty times as strong, in theiranti-inflammatory effect.For side effects, see corticosteroid and prednisolone.[23]

It may be used topically for allergic rashes, eczema, psoriasis, pruritis (itchyness) and other inflammatory skin conditions.

Topical hydrocortisone creams and ointments are available in most countries without prescription in strengths ranging from 0.05% to 2.5% (depending on local regulations) with stronger forms available by prescription only.

VII. SYNTHESIS AND RELEASE

a- It can be prepared from the bellow starting metals:

Cortisol is produced in the human body by the adrenal gland in the zona fasciculata,[1] the second of three layers comprising theadrenal cortex. The cortex forms the outer "bark" of each adrenal gland, situated atop the kidneys. The release of cortisol is controlled by the hypothalamus, a part of the brain.

The secretion of corticotropin-releasing hormone (CH) by the hypothalamus[49] triggers cells in the neighboring anterior pituitary to secrete another hormone, the adrenocorticotropic hormone (ACTH), into the vascular system, through which blood carries it to the

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ISSN: 2583-4053

Volume-3 Issue-1 || February 2024 || PP. 305-314

https://doi.org/10.55544/jrasb.3.1.50

adrenal cortex. ACTH stimulates the synthesis of cortisol, glucocorticoids, mineralocorticoids and dehydroepiandrosterone (DHEA).

b- Normal levels

Normal values indicated in the following tables pertain to humans (normals vary among species). Measured cortisol levels, and therefore reference ranges, depend on the analytical method used and factors such as age and sex. Test results should, therefore, always be interpreted using the reference range from the laboratory that produced the result.

Time Upper limit	Lower limit	Unit
700	140	nmol /L
09.00 am		
25	5	ug /dL nmol /L
Midnight		
13	2.9	ug /dL

Reference ranges for blood plasma content of free cortisol

VIII. REGULATION

The primary control of cortisol is the pituitary gland peptide, adrenocorticotropic hormone (ACTH). ACTH probably controls cortisol by controlling the movement of calcium into the cortisol-secreting target cells. [25] ACTH is in turn controlled by the hypothalamic peptide corticotropin-releasing hormone (CRH), which is under nervous control. CRH acts synergistically witharginine vasopressin, angiotensin II, and epinephrine. (In swine, which do not produce arginine vasopressin, lysine vasopressin acts synergistically with CRH.

IX. FACTORS REDUCING CORTISOL LEVELS

a- Magnesium: supplementation decreases serum cortisol levels after aerobic exercise,[27][28] but not after resistance training[29]

b- Omega-3 fatty acids: have a dose-dependent effecti301 in slightly reducing cortisol release influenced by mental stress, suppressing the synthesis of interleukin-1 and -6 and enhancing the synthesis of interleukin-2; the former promotes higher CRH release. Omega-6 fatty acids, on the other hand, have an inverse effect on interleukin synthesis. [31]

Music therapy: can reduce cortisol levels in certain

c- situations. [32]

X. FACTORS INCREASING CORTISOL LEVELS

- Viral infections increase cortisol levels through activation of the HPA axis by cytokines.[33]
- Caffeine may increase cortisol levels.[34]
- Sleep deprivation. [35]
- Intense (high VO2 max) or prolonged aerobic exercise transiently increases cortisol levels to increase gluconeogenesis and maintain blood glucose; however, cortisol declines to normal levels after eating (i.e., restoring a neutral energy balance).
- The Val/Val variation of the BDNF gene in men and the Val/Met variation in women are associated with increased salivary cortisol in a stressful situation. [36]

XI. HYDROCORTISONE WARNINGS

a- Oral Hydrocortisone

Before taking oral hydrocortisone, you should tell your doctor if you have or have ever had:

- Liver disease
- Kidney disease
- A mental illness
- An underactive thyroid gland
- Osteoporosis
- Herpes eye infection
- Seizures
- Malaria
- Tuberculosis (TB)
- Ulcers

Myasthenia gravis (a condition that causes muscles to)

- weaken
- Intestinal disease
- Heart disease
- Diabetes
- High blood pressure

You should also tell your physician if you have a fungal infection before taking this drug. Tell your doctor you are taking oral hydrocortisone before having any type of surgery, including dental procedures. [1]

XII. ORAL HYDROCORTISONE INTERACTION

Tell your doctor about all prescription, non-prescription, illegal, recreational, herbal, nutritional, or dietary drugs you're taking, especially:

Anticoagulants (blood thinners) such as warfarin

- (Coumadin)
- Arthritis medications
- Aspirin
- Cyclosporine (Neoral, Sandimmune)

ISSN: 2583-4053

Volume-3 Issue-1 || February 2024 || PP. 305-314

https://doi.org/10.55544/jrasb.3.1.50

- Digoxin (Lanoxin)
- Diuretics (water pilis)
- Estrogen (Premarin)
- Ketoconazole (Nizoral)
- Oral contraceptives
- Phenobarbital
- Phenytoin (Dilantin)
- Rifampin (Rifadin)
- Theophylline (Theo-Dur)
- Vitamins
- Chemotherapy drugs
- Other topical medications

- ***Hydrocortisoneand Alcohol***

You should limit the amount of alcohol you consume while taking oral hydrocortisone if you have a history of stomach ulcers or take large doses of aspirin or other arthritis medicines. [1]

XIII. HYDROCORTISONE DOSAGE

a- Oral Hydrocortisone

Oral hydrocortisone comes as a tablet and a suspension to take by mouth. Your doctor will prescribe a dose for your particular condition.

Typical dosages range from 10 milligrams (mg) to 300 mg a day.

These are usually given in three to four divided doses. You should take this medicine exactly as directed; don't take more or less of the drug than prescribed.[1]

b- Topical Hydrocortisone

Topical hydrocortisone comes as an ointment, lotion, cream, liquid, gel, medicated towel, and spray. [1]

c- Hydrocortisone Overdose

If you suspect an overdose, contact a poison control center or emergency room immediately. You can get in touch with a poison control center at (800) 222-1222.[1]

d- Missed Dose of Hydrocortisone

If you miss a dose of topical hydrocortisone, apply it as soon as you remember.

However, if it's almost time for your next dose, skip the missed dose and continue on your regular dosing schedule. Don't take extra medicine to make up for a missed dose.

When you start taking oral hydrocortisone, ask your doctor what to do if you miss a dose. Write down the instructions, so you can refer to them later.[1]

XIV. SUGGESTIONS AND RESULTS

We take about 100 cases for patients treated by hydrocortisone in the hospital and notice:

- About 70% of patients that use hydrocortisone vial, healing rate for them was about 95%.
- About 20% of patients that use hydrocortisone cream, healing rate for them was about 80%.
- About 10% of patients that use hydrocortisone ointment, healing rate for them was about 85%.
- We notice that most of the patients don't come back to the hospital again, because healing rate for them was high.

XV. SUGGESTION AND IMPORTANT SAFETY

- Hydrocortisone cream is for external use only. If you get hydrocortisone cream in your eyes, immediately flush them with cool tap water.
- Do NOT use more than the recommended dose or use for longer than 2 weeks without checking with your doctor.
- Do not apply hydrocortisone cream over large areas of the body, to open wounds, or to scraped, infected, or burned skin without first checking with your doctor.
- If your symptoms do not get better within 2 weeks or if they get worse, check with your doctor.
- Talk with your doctor before you use any other medicines or cleansers on your skin.
- Do not use hydrocortisone cream for other skin conditions at a
- later time.
- If hydrocortisone cream was prescribed to treat the diaper area of a child, avoid using tight-fitting diapers or plastic pants.
- Hydrocortisone cream has a corticosteroid in it. Before you start any new medicine, check the label to see if it has a corticosteroid in it too. If it does or you are not sure, check with your doctor or pharmacist.
- Tell your doctor or dentist that you use hydrocortisone cream before you receive any medical or dental care, emergency care, or surgery.
- Check with your doctor before having vaccinations while you are using hydrocortisone cream.
- Corticosteroids may affect growth rate in CHILDREN and teenagers in some cases. They may need regular growth checks while they use hydrocortisone cream.
- Hydrocortisone cream should not be used in CHILDREN; safety and effectiveness in children have not been confirmed. [38]
- Do not use hydrocortisone cream for other skin conditions at a
- later time.

XVI. GENERAL INFORMATION

- If you have any questions about hydrocortisone cream, please talk with your doctor, pharmacist, or other health care provider.
- Hydrocortisone cream is to be used only by the patient for whom it is prescribed. Do not share it with other people.
- If your symptoms do not improve or if they become worse,

ISSN: 2583-4053

Volume-3 Issue-1 || February 2024 || PP. 305-314

https://doi.org/10.55544/jrasb.3.1.50

- check with your doctor.
- Check with your pharmacist about how to dispose of unused
- Medicine.

This information should not be used to decide whether or not to take hydrocortisone cream or any other medicine. Only your health care provider has the knowledge and training to decide which medicines are right for you. This information does not endorse any medicine as safe, effective, or approved for treating any patient or health condition. This is only a brief summary of general information about hydrocortisone cream. It does NOT include all information about the possible uses, directions, warnings, precautions, interactions, adverse effects, or risks that may apply to hydrocortisone cream. This information is not specific medical advice and does not replace information you receive from your health care provider. You must talk with your healthcare provider for complete information about the risks and benefits of using hydrocortisone cream. [38]

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