



Maximizing Intubation Comfort: The Benefits of Betamethasone Gel Application on Endotracheal Tube

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Abstract

Background: Steroids like Betamethasone gel usually restricted for application and treatment of skin disorders, but it can also be helpful in preventing postoperative complications of intubation such as cough, sore throat, and hoarseness of voice.

Methods and Results: Multiple case studies including prospective, randomized controlled studies are taken into consideration, various studies, analysed and concluded that Betamethasone gel is superior when compared to other jellies like lignocaine jelly, K Y jelly application on the endotracheal tube optimizes the intubating conditions with ease and prevents post-operative complications.

Conclusion: The maximum benefits of Betamethasone gel outweighs the benefit -risk ratio and superior as compared to other jellies in the market.

Keywords: Complications; Endotracheal intubation; Sore throat; Cough; Larynx; Damage; Pharmacology; Betamethasone gel; Lidocaine; Patient comfort

Introduction

Airway management with endotracheal intubation is an integral part of an anesthesiologist's responsibilities towards patient care. Cuffed endotracheal intubation offers additional safety to the patient by preventing aspiration syndromes. In addition, the wastage of anaesthetic gases and the pollution of the operation theatres are also reduced substantially. However, amongst the sequelae inherent to the usage of the cuffed endotracheal tube, the local irritation and the inflammation of the airway caused by prolonged inflation of the cuff is the prominent one which results in post-intubation morbidities like sore throat, hoarseness of voice, and cough. Many studies have been performed and published exploring the measures to minimize/eliminate post-intubation morbidities, viz,

- Use of high volume-low pressure cuffed endotracheal tubes [1].
- Use of smaller-sized endotracheal tubes [1].
- Inhalation of steroids [2].

- Topical application of lubricant jellies [3].

The use of water-soluble jellies for lubrication of the endotracheal tube is to facilitate smooth insertion of the endotracheal tube and also to reduce trauma to airway mucosa thereby decreasing the overall morbidity. Local anesthetic (2% Lignocaine) jellies along with lubricating properties also limit the potential damage to tracheal mucosa by suppressing the airway reflexes, but the incidence of postoperative morbidities continues to be high (90%) probably due to lack of anti-inflammatory action [4]. Steroids like Betamethasone gel are well known for their anti-inflammatory action and have been claimed to reduce (up to 60%) the incidence of post-intubation morbidities [6]. Other factors were known to correlate with occurrence of these complication, including sex [4,5], age, season, anesthetic drugs and gases, numbers of trials for intubation [4], duration of intubation [4,6], size of endotracheal tube its type and cuff type and size [1], site of the surgery [4,8] and application of lidocaine [2-9] or steroids [3-11].

Pharmacology of Betamethasone

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Betamethasone

Betamethasone [12] (9a-16β-methyl prednisolone) is a synthetic glucocorticoid agent which has been most popular in the treatment of corticosteroid-responsive dermatologic disorders. It is also used systemically for treating inflammatory conditions (Figure 1).

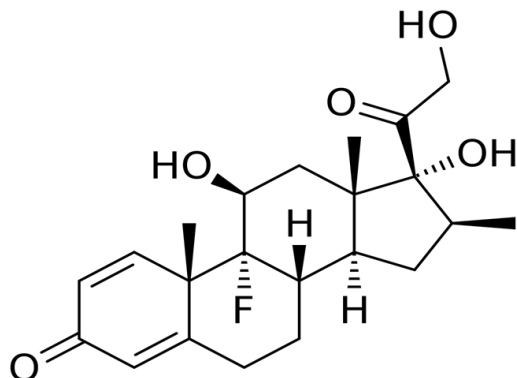


Figure 1: Pharmacology of Betamethasone.

Mechanism of action

For the most part, glucocorticoid effects involve interactions between the steroids and intracellular receptors that belong to the superfamily of receptors that control gene transcription. This superfamily includes the receptors for mineralocorticoids, the sex steroids, thyroid hormones, Vitamin D; and retinoic acid. There are believed to be 10-100 steroid-responsive genes in each cell. The glucocorticoids, after entering the cell, bind to specific receptors (glucocorticoid receptor α {GRα} and glucocorticoid receptor β {GRβ}) in the cytoplasm. These receptors, which have high affinity for glucocorticoids, found in virtually all tissues - about 3000 to 10000 per cell, number varying in different tissues., GRα has been cloned and contains 777 amino acid residues. Becomes 'activated', i.e. it after interaction with the steroid, the receptor becomes 'activated', i.e. it undergoes a conformational change that exposes a DNA-binding domain. The steroid-receptor complexes form dimers, then move to the nucleus and bind to steroid-response elements in the DNA. The effect is either to repress (prevent transcription of) or induce (initiate transcription of) particular genes. Repression is brought about by inhibition of the action of various transcription factors such as AP-1 and NF-κB. These transcription factors normally switch on the genes for cyclooxygenase-2, various cytokines and adhesion factors, as well as the inducible isoform of nitric oxide synthase. Basal and induced transcription of the genes for collagenase is modified and vitamin D; induction of the osteocalcin gene in osteoblasts is inhibited. Induction involves the formation of specific mRNAs, which direct the synthesis of specific proteins. In addition to the enzymes involved in their metabolic actions [cAMP-dependent

kinase]; glucocorticoids induce the formation of annexin-1 (previously called lipocortin-I). Annexin-1 is important in the negative feedback action of glucocorticoids on the hypothalamus and anterior pituitary and has anti-inflammatory actions (possibly by inhibiting phospholipase A). As might be predicted, the anti-inflammatory effect of glucocorticoids takes hours to become evident since the formation of annexin-1 and other active proteins is relatively slow. Glucocorticoids can, however, produce effects over a very much shorter time frame. These rapid effects of glucocorticoids do not involve interaction with the genes but are mediated instead by interacting with specific membrane receptors to Cause changes within the cell (e.g. on intracellular calcium) that are similar to those triggered by neurotransmitters (Table 1).

Table 1: Betamethasone.

Compound	Relative affinity for glucocorticoid receptors	Approximate relative potency in clinical use		Duration of action
		Anti-inflammatory	Sodium-retaining	
Hydrocortisone (cortisol)	1	1	1	S
Betamethasone	5.4	30	Negligible	L
S:- 8-12 hours		L:-36-72 hours		

Pharmacodynamics

General metabolic and systemic effects

The main metabolic effects are on carbohydrate and protein metabolism. It causes both a decrease in the uptake and utilization of glucose and an increase in gluconeogenesis, resulting in the tendency to hyperglycemia. There is a concomitant increase in glycogen storage, which may be a result of insulin secretion in response to the increase in blood sugar. There is decreased protein Synthesis and increased protein breakdown, particularly in the muscle. Glucocorticoids have a permissive effect on the lipolytic response to catecholamines and other hormones, which act by increasing intracellular cAMP concentration. Such hormones cause lipase activation through a cAMP-dependent kinase, the synthesis of which requires the presence of glucocorticoids. The glucocorticoids, in non-physiological concentrations, have some mineralocorticoid actions, causing sodium retention and potassium loss-possibly by occupying mineralocorticoid receptors. They also tend to produce a negative calcium balance by decreasing calcium absorption in the gastrointestinal tract and increasing its excretion by the kidney. Administration of



exogenous glucocorticoids depresses the corticotrophin-releasing factor and adrenocorticotrophic hormone, thus inhibiting the secretion of endogenous glucocorticoids and causing atrophy of the adrenal Cortex.

Anti-inflammatory and immunosuppressive effects

When given therapeutically, glucocorticoids have powerful anti-inflammatory and immunosuppressive effects. They affect all types of inflammatory reactions whether caused by invading pathogens, by chemical or physical stimuli, or by inappropriately deployed immune responses such as are seen in hypersensitivity or autoimmune diseases.

Actions on inflammatory cells include

- Decreased egress of neutrophils from the blood vessels and reduced activity of neutrophils and macrophages owing to decreased transcription of the genes for cell adhesion factors and the relevant cytokines.
- Decreased action of T helper, cells and reduced clonal proliferation of T cells, mainly through decreased transcription of the genes for interleukin-2 (IL-2) and its receptor.
- Decreased fibroblast function and, therefore, less production of collagen and glycosaminoglycans; the contribution of these events to chronic inflammation is reduced but also in healing and repair.
- Reduced function of osteoblast and increased activity of osteoclasts.

Action on the mediators of inflammatory and immune responses include

- Decreased production of prostanoids owing to decreased expression of cyclooxygenase-2.
- Decreased generation of cytokines- IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-8, TNE-Y and cell adhesion factors, granulocyte-macrophage colony-stimulating factor-through inhibition of transcription of relevant genes.
- Reduction in the concentration of complement components in the plasma.
- Decreased generation of induced nitric oxide.
- Decreased histamine release from basophils.
- Decreased IgG production.

Pharmacokinetics

Absorption

Betamethasone may be given by a variety of routes. It can be given oral, intramuscular, intravenous, intraarticular, and topical. There is much less likelihood of systemic toxic effects after

topical administration unless large quantities are used. Betamethasone 0.6 milligram is equivalent to Triamcinolone 4 milligrams, Methylprednisolone 4 milligrams, Dexamethasone 0.75 milligram, and Hydrocortisone 20 milligrams.

Distribution

The endogenous glucocorticoids are carried in plasma, bound to corticosteroid-binding globulin and to albumin. Corticosteroid-binding globulin does not bind to synthetic steroids but albumin binds both natural and synthetic steroids. Peak serum concentrations of betamethasone occur within 10 to 36 minutes with intravenous doses; systemic absorption from topical therapy is 12% to 14% of a dose; protein binding is 64%; volume of distribution is 75 to 90 L; elimination half-life is 56 hours.

Metabolism and excretion

Betamethasone has a double bond in the 4, 5 positions and a ketone group Metabolism involves sequential additions of oxygen or hydrogen atoms, Followed by conjugation to form water-soluble derivatives. Reduction of the 4,5 double bond occurs at hepatic sites yielding inactive compounds. Subsequent reduction of the 3-ketone substituent to the 3-hydroxyl derivative, forming tetrahydrocortisol. Most of these are conjugated through the 3-hydroxyl group with sulfate or glucuronide by enzymatic reactions that take place in the liver and, to a lesser extent, in the kidney. The resultant sulfate esters and glucuronides are water-soluble and are the predominant forms excreted in the urine.

Interactions

The concomitant use of corticosteroids with neuromuscular blocking agents has been reported to antagonize neuromuscular blockade. In addition, prolonged coadministration of these agents may increase the risk and/or severity of myopathy resulting in prolonged flaccid paralysis following discontinuation of the neuromuscular blocking agent. Concomitant corticosteroid and phenobarbital therapy has been reported to result in enhancement of the metabolism of corticosteroids due to hepatic microsomal enzyme induction. It may be necessary to increase the dosage of corticosteroids if barbiturates or other enzyme inducers are used concomitantly.

Contraindications

- Hypersensitivity to betamethasone
- Systemic fungal infection

Precautions

- Application to the groin, axillae, or facial areas (increased risk of side effects)
- Cirrhosis

- Compromised intestinal conditions (eg, active or latent peptic ulcer disease, nonspecific ulcerative colitis, diverticulitis, fresh intestinal anastomoses)
 - Emotional instability or psychotic tendencies (may be aggravated by corticosteroids)
 - Exposure to viral illnesses, such as chickenpox or measles (may increase risk of serious or fatal infection) (systemic or local steroid treatment)
 - Hypertension
 - Hypothyroidism
 - Infection (may impair the ability to localize the infection and/or decrease immunoprotection against infection)
 - Myasthenia gravis
 - Osteoporosis
 - Periods of stress
1. Dosage need of steroid may be increased before, during, and after stressful situations.
 - Previously infected joints or unstable joints (intra-articular injections)
 - Renal insufficiency
 - Strongyloides (threadworm) infestation, known or suspected
 - Tuberculosis (TB), latent or active
 1. Observe latent cases closely for disease reactivation.
 2. Use in active tuberculosis (TB) should be restricted to cases of fulminating or disseminated disease where the corticosteroid is used for management along with an appropriate anti-tubercular regimen.

Available Topical Preparation and Its Storage

Topical betamethasone dipropionate is only available in a vehicle that augments the penetration of this product. BETAMETHASONE DIPROPIONATE cream, ointment, and lotion should be stored at 36 to 86 degrees F (2 to 30 degrees C), the gel should be stored at 36 to 77 degrees F (2 to 25 degrees C).

Adverse effects

1. Cushing habitus
2. Fragile skin, purple striae
3. Hyperglycemia
4. Muscular weakness
5. Susceptibility to infection
6. Delayed healing
7. Peptic ulceration
8. Osteoporosis
9. Posterior sub capsular cataract
10. Glaucoma
11. Growth retardation

12. Psychiatric disturbances
13. Suppression of hypothalamus-pituitary-adrenal axis.

Discussion

In the year 2003, Levy B [1] conducted a study on 60 patients, divided into 2 groups, one group received topical lidocaine 5% (15 puffs) and the other group aerosolized methylprednisolone (80mg) before endotracheal intubation and showed that the incidence of sore throat and cough were less in the methylprednisolone group compared to lidocaine group. El Hakim [10] showed that beclomethasone reduced the incidence of postoperative sore throat by 45% in comparison to 10% with lignocaine but its cost precludes its use.

Though Stride P C [3] (1990) concluded that 1% hydrocortisone water soluble cream applied to the tip and cuff of the endotracheal tube was ineffective in reducing the incidence of postoperative sore throat, Ayoub M Cand Selvaraj [11] Showed that wide spread application of betamethasone accounted for decrease in incidence of post-operative Sore throat, hoarseness of voice and cough. Asif Kazemi and Afshin Amini [15] concluded that betamethasone gel, when used for lubrication of endotracheal tubes reduced the incidence of postoperative sore throat, cough and hoarseness of voice.

P A Sumathi, T Shenoy, M Ambareesha, H M Krishna [14,15] {2008 } randomized controlled trial study has found that widespread (15 cm) application of steroid gel markedly reduced the incidence of sore throat, hoarseness of voice and cough. The scores for sore throat, hoarseness of voice and cough were significantly very low in steroid group at 1hr, 6hrs, 12hrs and 24hrs, though the duration of endotracheal intubation is significantly more in betamethasone group. It also shows that betamethasone gel is superior to lignocaine jelly and normal saline in reducing post intubation morbidities.

This study confirms that pharyngotracheal sequelae after endotracheal intubation are due to local inflammation and not irritation, as steroid gel proved far superior to local anesthetic jelly in decreasing their incidence. The beneficial effect was observed because of the application of steroid gel to all portions of the tube that come in contact with the posterior pharyngeal wall, vocal cords, and tracheal mucosa and not just confined to the tip and cuff of the endotracheal tube as observed by Stride P C's [3] study (1990) where the percentage and the total quantity of the gel applied was high.

Conclusion

Considering the pros and cons of Betamethasone gel application on endotracheal tube is an added advantage for effective airway management. Since betamethasone gel is cost-effective and easily available, it can be used routinely as an applicant on the



endotracheal tubes in the preemptive methods to mitigate the postoperative sore throat, hoarseness of voice and cough.

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