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Use of Steroids in Orthognathic Surgery- A Review on Clinical Aspects

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Abstract:

Corticosteroids are widely used in orthognathic surgeries to control post-operative pain, swelling, inflammation, nausea and vomiting and to provide comfort for patients during the recovery phase. The present article examines several evidence based reports, experimental studies and ratio of dosage risk benefits observations on the use of steroids to reduce post-operative morbidities in orthognathic surgeries. Though, several studies established these steroidal drugs improved the management of post-operative inflammation, pain, swelling and trismus after orthognathic or orthopedic surgeries considerably yet there is a clear lack of evidence and standardized protocol towards its use after surgery. The current regimens are associated with little morbidity and low cost despite more focus were given on the dosage and time of administration pre-operatively thus demanding the need for well-structured multi-centered studies to evaluate the mechanism, outcome and significance of use of steroids post-operatively to enhance the recovery phase and improve the overall quality of life.

Key words : inflammation , trismus ,postoperative pain .

Introduction:

Management of post-operative morbidities associated with orthognathic and oral and maxillofacial surgeries remains one of the most challenging aspects that largely impact the ability of the patient to recuperate back to their routine life activities without compromising the quality and overall health status of an individual [1-2]. Facial pain, edema, inflammation, ecchymosis, limitation of mouth opening and loss of sensory reflexes are the most frequent anticipated sequelae after these surgical interventions [3]. Over the years, corticosteroids are widely used to control post-operative morbidities and to provide comfort for patients. However, there are no definite or standard protocols on doses, frequency, and routes of administration. The term corticosteroids or corticoids includes natural glucocorticoids, mineralocorticoids and their synthetic analogues [4, 5]. Corticosteroids are 21 carbon compound derivative of cholesterol synthesized in adrenal cortical cells. Steroidogenesis takes place under the influence of ACTH which makes the cholesterol readily available for conversion into pregnenolone that further undergoes changes in zona fasciculata into cortisol and corticosterone.

Glucocorticoids such as hydrocortisone, cortisone, prednisolone, methylprednisolone, dexamethasone and betamethasone are often recommended in varying doses pre or perioperatively in oral and maxillofacial surgeries. Though, several studies established these steroidal drugs improved the management of post-operative inflammation, pain, swelling and trismus after orthognathic or orthopedic surgeries considerably yet there is a clear lack of evidence and standardized protocol towards its use after surgery [6-9]. This article briefly discusses the post-operative complications associated with orthognathic surgery and its underlying mechanism with emphasize on the current evidence for the use of steroids in orthognathic surgery.

Methodology:

A structured literature search for publications written in the English language using PubMed/MEDLINE, EBSCO host, Google Scholar, Scopus, and Web of Science databases for articles about steroids or glucocorticoids, oral surgery, orthognathic surgery, orthopaedic surgery and administration of steroids in dental surgical procedures were selected. Original in-vivo, in-vitro experimental studies, and randomized control trials assessing the clinical effectiveness of steroids, and associated clinical complications were included while papers with inconclusive evidences and non-accessible complete article were excluded.

Discussion:

Post-Operative complication and Mechanism of action of steroids:

Inflammation and edema are the normal physiological reaction of the body in response to any injury that occurs with varying severity after every surgical intervention procedures. Following any traumatic procedures enzyme phospholipase A2 catalyze the first step of the arachidonic acid pathway by breaking down the cell membrane phospholipids to arachidonic acid with release of inflammatory mediators such as leukotrienes and prostaglandins. During this process Cyclooxygenase-1 (COX1) and Cyclooxygenase-2 (COX2) enzymes also produces pro-inflammatory mediators' prostacyclins, thromboxane A2 thus inducing overall inflammatory response. Steroidal drugs acts by preventing this catalyzing mechanism, by inhibiting the production of pro-inflammatory mediators and cytokines involved in phagocytosis and leukocyte migration [7-10].

Post-operative edema or swelling often necessitates medications to reduce and control the severity and duration of its recurrence. Postoperative airway obstruction associated with facial edema has been a concern in oral and/or orthognathic surgeries for a long time [11]. Edema occurs due to increased osmotic pressure at the surgical site, altered capillary permeability, fluid transudation through vascular channels into the area of damage, along with obstruction of local lymphatic system by fibrin and fibrinogen clots derived from plasma and adjacent injured tissues. Several mechanisms were proposed by which steroids may decrease edema or post-operative swelling such as fluid extravasation, norepinephrine release, inhibition of prostaglandin synthesis (edema induced by inflammation), altering synthesis of proteins at the endothelial lining, and stabilization of lysosome membranes which decreases the release of proteolytic enzymes and hyaluronidase [12, 13]. However, effectiveness of steroids was more distinct in post-surgical swelling owing to suppressed or modified vascular reactivity, increase capillary permeability, and dilatation on the relatively greater blood supply seen at the maxillofacial region along with greater ease with which edematous fluids can escape the surgical site and movement of fluid into extracellular spaces associated with the soft tissue expansion required to accommodate the fluids. It should be illustrated that administration of steroids in children may not be as effective as seen in adult patients and to recommend steroid management only for soft tissue surgeries (adults) rather than hard tissue procedures owing to substantial prevalence of hemorrhage and edema [14, 15].

Postoperative nausea and vomiting (PONV) remains one of the most common difficulty encountered following orthognathic surgeries that demands short acting drugs and advanced monitoring devices to reduced severe consequences such as aspiration of gastric contents, esophageal rupture, hematoma, and possible decease [16]. It is a complex mechanism that involves number of interrelated pathways, neurotransmitter systems and trigger senses. Chemoreceptors, afferent triggers, cerebral cortex triggers, endocrine environmental triggers, Area Postrema Chemoreceptor Trigger Zone (CTZ) Triggers along with gut and local irritants generate changes at the higher center [17, 18]. The gastrointestinal tract (Gut) activate the vomiting Centre by stimulation of 5- hydroxytryplamine-3 (5-HT3) receptors. Steroids deplete these 5HT3 in neural tissue and prevents its release in the gastrointestinal tract thus bringing about reduced PONV [18, 19].

Pain and sensory loss following orthognathic surgery largely impact the recovery phase, hospitalization and patient's psychology. Inflammatory mediators such as bradykinin and prostaglandins diminishes the pain threshold directly by causing damage to the pain receptors and neural axon fibers, reducing the stimulation of local pain receptors at the surgical site and indirectly by controlling neuropeptide release positive feedback mechanism which further increases inflammation and pain perception [20, 21]. Sensory impairment is a common complication that occurs after orthognathic surgery. Steroids are used in the management of neural injuries, including Bell's palsy and spinal cord injury. Since inflammation, edema-mediated nerve compression, and fascicular damage are possible outcomes of sensory dysfunction after orthognathic surgery, it was hypothesized that steroids have the potential to improve axonal conduction dysfunction and peripheral neural damage by its anti-inflammatory and neurotropic effects [22]. Seo et al also observed significant differences in the accelerated recovery rate and potential reversal effect on the mechanical-touch threshold among individuals with sensory impartment after orthognathic surgery who received steroid treatment following 3weeks and 6weeks of surgery [23].

Steroids and Orthognathic surgery:

Orthognathic surgeries are frequently performed to correct the stomatognathic system and achieve appropriate physiological and facial aesthetics. Due to the risk of postoperative airway obstruction following the intervention, post-surgical pain, nausea, vomiting and inability to eat properly due to facial swelling and upper airway edema, patients undergo a brief phase of hospitalization to attain stabilization and recovery. Concerning orthognathic surgery, several investigations demonstrated that perioperative corticosteroid administration significantly reduced post-operative inflammation and edema. Short-term high doses of corticosteroids were recommended to minimize edema and associated complications, yet there is a clear lack of evidence and standardized protocol towards its use after surgery [1, 2]. Gersema and Baker advocated the use of corticosteroids during oral and maxillofacial surgeries and showed clinical trials largely focused on surgical procedure, duration, dose-specific regime and complications associated with perioperative corticosteroid use and concluded that steroids can be safely administered at its anti-inflammatory equivalent dosage to reduce post-operative swelling pain with no adverse effects [5]. Schaberg SJ et al recommended use of corticosteroids to prevent facial, and parapharyngeal edema causing respiratory complications perioperatively [3]. The most frequently used forms of corticosteroids in oral and orthognathic surgery include oral and intravenous dexamethasone sodium phosphate, dexamethasone acetate, intramuscular Decadron Phosphate, Oral methylprednisolone, intravenous or intramuscular methylprednisolone sodium succinate and methylprednisolone acetate. Cortisol (Hydrocortisone) and cortisone are short acting drugs with biological life of less than 12years whereas dexamethasone and betamethasone are long acting with more than 36 hours up to 54 hours of biological life [3, 4, 24].

Glucocorticoids have a minimal effect on acute inflammation, involving primarily of increased vascular permeability and diminished leukocyte migration. Cortisol and its analogs (dexamethasone, cortisone) decreases tissue levels of bradykinin and suppresses circulating levels of cortisol and beta-endorphin. It is evident that bradykinin and kallidin acts synergistically with products of the arachidonic acid pathway to increase vascular permeability and induce hyperalgesia [25, 26]. These steroids inhibit the local inflammation and also produces neuromodulatory effect to reduce peripheral and central pain sensation associated with inflammatory response. Several studies hypothesized that glucocorticoids do not produce changes in the pain intensity in the absence of inflammatory response and tissue edema. Cortisol and its analogs (dexamethasone, cortisone) also suppresses the inflammatory responses by reducing prostaglandins biosynthesis [27]. Chegini S and Dhariwal DK evaluated several evidence based literature studies for the use of steroids following orthognathic surgery and put forwarded that glucocorticoids are effective in reducing postoperative pain, swelling, trismus and nausea by providing analgesic and antiemetic cumulative effect and also emphasized the need for establishing therapeutic dose, duration and short- term beneficial action of steroids preoperative and postoperatively in orthognathic surgery patients [1].

Various corticosteroids have been used in previous studies, but dexamethasone had shown beneficial effects because of its highest anti-inflammatory activity, no mineralocorticoid activity, and a longest available biologic half-life of 36 to 54 hours. It has a longer duration of action than methylprednisolone and is considered more potent. Munro et al in a randomized double blind study among pediatric patients undergoing maxillary or mandibular osteotomies administered with dexamethasone (steroids) immediately (0.5mg/kg) and 48 hours postoperatively (0.25mg/kg) showed reduction in post-operative facial swelling [4]. Dexamethasone enhances the effect of diclofenac and extends the coverage up to 54 hours by increased bioavailability when administered intravenously compared to oral administration [6]. Weber and Griffin [7] performed a randomized double blind prospective study to determine the efficacy of intravenous dexamethasone in reducing edema and inflammatory reaction among bilateral sagittal split osteotomy patients observed a significant reduction in swelling and inflammatory markers (C - reactive protein) on the postoperative day (24hours) among patients who received pre-operative intravenous dexamethasone (16mg preoperatively and 8mg postoperatively every 6hours for one day). It was revealed that dexamethasone reduces edema by decreasing permeability of capillary endothelium and thus reducing the amount of fluid, protein, macrophages, and other inflammatory cells entering areas of tissue injury. Bamgbose et al in a prospective randomized blind study on patients requiring surgical removal of unilateral or bilateral impacted mandibular third molars evaluated the analgesic and postoperative efficacy of Prophylactic dose of Dexamethasone 8mg and postoperative dose of 4mg IV given with Diclofenac K 50mg orally before and after the surgical procedure [11].

Methylprednisolone effectively aids in control and management of post-operative swelling during the initial 24hours up to 72hours attributed to rich blood supply, relatively high anti-inflammatory reaction and low sodium-retaining properties with fluid exchange necessary for the reduction of postoperative facial edema. Schaberg et al assessed the effectiveness of methylprednisolone after LeFort I osteotomy or tans-oral vertical osteotomy orthognathic surgery in reducing post-operative facial swelling using computed tomography (CT) scans [3]. Various steroid preparation showed changes in potency and duration of action in corresponding to biological half-life. 100mg of cortisone is equivalent to 80 mg of hydrocortisone, 16 mg of methylprednisolone, and 3 mg of dexamethasone or betamethasone. Administration of methylprednisolone 1mg/kg 12hours preoperatively and 0.5 to 1mg/kg every 4 hours intra-operatively and postoperatively for 36 hours demonstrated up to 61% facial edema reduction in LeFort surgeries and 38% in vertical osteotomies at 24hours respectively with no marked side effects suggesting clinical effectiveness of post-operative methylprednisolone therapy [6, 7, 24, 25, 26]. Peillon et al also showed significant decrease in postoperative inflammation and facial edema among maxillary osteotomy cases who received methylprednisolone intravenously at the beginning of surgery and after surgery (1.5mg/kg/-1) for three consecutive days [8]. Jodeh et al examined the association between the use of corticosteroids and its outcome following orthognathic surgery and established a significant association between duration of hospital stay, post-operative pain, and swelling among patients under steroid exposure before and after the surgical procedure. In orthognathic surgery, the threshold dose value of 1 intravenous methylprednisolone is expected to be around 85 mg, above which any single dose administered will result in a significant decrease in edema [21].

Methylprednisolone suppresses inflammation by its anti-inflammatory action on mediators and reduces post-operative bleeding by initiating thromboxane synthesis pathway. Steroids inhibit mast cell production and secretion of cytokines, kinins, and histamine that subsequently promote an inhibition of thromboxane and bradykinin resulting in reduced vasodilatation and decreased permeability [6, 11]. In combination with diclofenac it reduces postoperative bleeding caused by diclofenac induced thromboxane synthesis inhibitory reaction producing prolonged bleeding time following surgical procedures like third molar extraction, orthognathic surgeries. Prednisolone deplete 5HT3 (Receptor blockers) in neural tissue and prevents its release in the gastrointestinal tract thus bringing about reduced PONV [27]. Silva et al conducted a retrospective cross sectional analysis among patients who had maxillary and/or mandibular osteotomies and reported an overall 30% to 40% experienced post-operative nausea and vomiting within 24hours after surgery [18]. It was observed that patients who had received prophylactic dose of methylprednisolone (125 mg) and penicillin G (1,000,000 units and cephalosporin 1g) before the procedure showed lesser post-operative complications [28].

Complications associated with steroids:

Use of systemic steroids following surgeries is absolutely contraindicated for patients with inactive or active, incompletely healed or rehabilitated cases of tuberculosis. Herpes simplex infections, primary glaucoma, and acute psychosis are often considered as absolute contraindications [1, 2, 5]. Relative contraindications include peptic ulcers, Cushing's syndrome, adrenal insufficiency, hypertension, osteoporosis, diabetes mellitus as well as first trimester of pregnancy. Complications can be categorized based on dose and duration as long term and short term effects. One of the most serious complication associated with long term use of steroids is the potential suppression of the hypothalamic-pituitary adrenal axis leading to adrenal atrophy. Studies have shown administration of 20mg hydrocortisone for 5days or longer may induce this effect and lead to acute stress over a period of time. Alternative use of

low doses, intermediate duration use of analogues, and short-term high dose glucocorticoids however, does not cause significant adrenal suppression [9, 21, 29].

In Orthognathic surgery, complications are rare despite higher doses following surgery since normal serum cortisol concentrations were restored by seventh day after administration. In accordance with the several studies and recommendations to administer oral doses at least 3 to 4 hours before surgery, a preoperative dose of two 8-mg methylprednisolone tablets or two 4-mg dexamethasone tablets can be considered beneficial however follow-up doses of dexamethasone and betamethasone are not required because of their longer half-lives [29, 30]. The most common encountered side effects being increased serum glucose concentration specifically among patients with poor glycemic control, impaired glucose tolerance resulting in difficult to control and restore normal concentration. In addition, studies have shown increased tendency towards drug dependent mineralocorticoid effects manifesting as increased fluid retention with reduced fluid intake [1, 2, 26, 29, 30].

Various other complications includes delayed wound healing, avascular osteonecrosis, steroid-induced acne, gastrointestinal bleeding, gastric ulcers, hematomas, increased intraocular pressure, immunosuppressive infection and stress-induced psychosis very rarely. Salerno and Hermann in a recent update on efficacy and safety of steroid use as an analgesic agent revealed a strong evidence supporting the safe and effective use of corticosteroids only at optimal dose as a short-term regimen for reducing postoperative pain however larger doses for long-term resulted in severe complications such as adrenal suppression, poor wound-healing and necrosis of the bone at the surgical site [20]. Dan AE et al in a systematic review and meta-analysis showed significant reduction in post-operative edema and pain following administration of methylprednisolone (>25mg) and suggested an overall administration dose of 85mg IV for orthognathic surgery patients to reduce post-operative pain, swelling and trismus with minimal to higher risk of adrenal suppression, avascular osteonecrosis, and steroid induced psychosis [12]. Nonetheless, these symptoms are short-lived and recovery can take few days to a week after the stoppage of medication.

Conclusion:

Corticosteroids either in a single dose or in combination form with other drugs have shown great benefits in the management of post-operative edema and inflammation despite carrying significant risk potential. Though the effects of corticosteroids on post-operative morbidities after orthognathic surgeries have been widely investigated in the literature, several methodological dissimilarities, discrepancy in steroidal agents, doses, and routes of administration have compromised their clinical implication conclusions. Further studies are recommended focusing on the benefits rather than risk potential alone with emphasizing on prescribing short-term, less potent and minimal dose steroids with simultaneous use of other non-steroidal agents to produce appropriate therapeutic effect not associated with severe and life threatening complications.

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