The use of corticosteroids in the lateral sinus augmentation surgical procedure: a systematic review and meta-analysis

Lorenzo Mordini[1], Giuseppe Pio Patianna[1], Giovanna Laura Di Domenico[1], Zuhair Natto[1], and Nicola Alberto Valente[1]

[1]Affiliation not available

June 8, 2022

Introduction

The maxillary sinus is a pyramidal-shaped cavity and is the largest of the paranasal cavities. The maxillary sinus borders are comprised of 1) the nasal cavity medially, 2) the floor of the ocular orbit superiorly, 3) the maxillary tuberosity posteriorly, 4) the canine fossa anteriorly, and 5) the apical portion of the alveolar process inferiorly. During the aging process, and to a greater degree, after the loss of posterior teeth, the maxillary sinuses progressively increase their volume at the expenses of the superior-posterior alveolar ridge, which can complicate or impede dental implant placement. To overcome this problem, the bone augmentation technique known as sinus lift or maxillary sinus augmentation (MSA) was introduced in 1970. This surgical procedure, and in particular, the lateral approach, has remained essentially unchanged in its execution protocol since it was first described. However, the procedure now exists as a one or two stage variant depending on whether the implants are placed simultaneously or consecutively to augmentation.

The , although rather invasive, appears to be the most successful among the intra-oral bone augmentation techniques, with an implant survival rate comparable to implants placed in native bone. The low frequency of reported post-operative infections, which is reported to be between 2% and 5.6%, contributes to safety and effectiveness of the procedure. However, sinus infections can still occur. An infection of the maxillary sinus can remain localized or spread to neighboring structures, leading to life threatening scenarios if not properly treated. For this reason, it is recommended to follow specific pharmacological protocols to prevent such consequences.

Currently, pre- and post-operative prophylaxis regimens for MSA procedures include the use of antibiotics. However, corticosteroids are less commonly used, and if so, are generally administered only pre- or peri-operatively via oral or intramuscular route. This decision is operator-dependent and is not as standardized as antibiotics.

The use of corticosteroid drugs in oral surgery is much debated; those who use them aim to reduce the direct effects of inflammation on post-operative symptoms such as edema. This is because corticosteroids decrease the activity and migration of inflammatory cells (T helper lymphocytes, monocytes, and macrophages) on the site of trauma and their production of pro-inflammatory substances (histamine, leukotrienes, prostaglandins, and cytokines). Furthermore, the inhibition of enzyme phospholipase A_2 and prostaglandin production makes corticosteroids a potent analgesic substance, which reduces post-operative pain.

A challenging factor regarding MSA-related complications is that the post-operative infections can be either true sinus infections (i.e., acute sinusitis) or bone graft related infections (i.e., bacterial contamination of graft). A sinus infection is distinguished from a bone graft infection in that it occurs within the sinus space surrounded by the Schneiderian membrane (SM) versus a bone graft infection which is found between the inferior aspect of the SM and the apical portion of alveolar process.

In light of these considerations, the purpose of this systematic review is to identify whether the administration of corticosteroids during the MSA surgical procedure operative phase affects post-operative symptoms, including swelling, pain, and infection rate.

Materials and Methods

This review has been registered at the National Institute for Health Research PROSPERO, International Prospective Register of Systematic Reviews and has been assigned the number CRD42020190884.

PICO Criteria Definitions

Population : Partially or fully edentulous atrophic posterior maxillae.

Intervention : Maxillary sinus augmentation surgery with lateral approach with peri-operative prescription of corticosteroids.

Comparison : Maxillary sinus augmentation surgery with lateral approach without peri-operative prescription of corticosteroids.

Outcome : Presence of post-operative inflammatory symptoms (edema, pain, infection, symptoms of acute sinusitis, trismus, and wound dehiscence) within one week post-intervention.

Focused Question

Does the prescribed post or peri-operative corticosteroids reduce the occurrence of complications and patient morbidity after the lateral MSA procedure?

Search Strategy

The data for this systematic review and meta-analysis were obtained and processed following PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) principles (Moher et al., 2010).

Relevant articles published up to December 30th, 2020 were searched using the relevant keywords and respective Boolean logic operators (AND, OR, NOT) in the above-mentioned databases: PubMed, EMBASE, Ovid MEDLINE, Web of Science. The relevant keywords were combined as follow for the search: ((jaw, edentulous, partially) OR (partially edentulous) OR (partial edentulism) OR (full edentulism) OR (fully edentulous) OR (atrophic maxilla) OR (posterior maxilla)) OR (Lateral AND ("maxillary sinus lift" OR "sinus lift" OR "maxillary sinus floor elevation" OR "sinus floor elevation" OR "maxillary sinus floor augmentation" OR "sinus floor augmentation" OR steroids OR steroid OR corticosteroids OR corticosteroid)) OR (lateral AND ("maxillary sinus lift" OR "sinus lift" OR "maxillary sinus floor elevation" OR "sinus floor elevation" OR "maxillary sinus floor augmentation" OR "sinus floor augmentation")) AND (pain OR pain reduction OR trismus OR swelling OR complications OR inflammation OR outcome).

Four independent reviewers (NAV, GLD, GP and LM) first screened all study titles, then read abstracts, and lastly assessed the full texts of included articles. Disagreements were resolved by discussion among reviewers. The final selections according to the inclusion and exclusion criteria were made by the same authors, as some articles were excluded only after the full text analysis.

Inclusion Criteria

Studies were included if the following criteria were met:

* Studies specifically referring to lateral sinus lift

* RCTs

* Prospective cohort studies

* Case series

* Studies published in the English language

* Explicit reference to the peri-operative (pre and/or post) pharmacological prescriptions (antibiotics, anti-inflammatories, analgesics)

* Details of at least one of the post-operative inflammatory parameters reported (swelling, suppuration, symptoms of acute sinusitis, trismus, pain, wound dehiscence)

Exclusion Criteria

* Crestal/vertical sinus lift

* Less than 20 patients or 20 sinus lift surgeries

* Case reports

* Retrospective studies

* *In vitro* studies

* Animal studies

* Articles with same cohort of patients

* Post-operative inflammatory parameters not considered in the analysis (not mentioned in the materials and methods, or the analysis of the parameters were not clearly identifiable in the results)

* Inflammatory parameters not discernable as values for a meta-analysis

Quality Assessment

Two authors (NAV, LM) independently assessed the studies in terms of the inclusion, relevance, eligibility, and risk of bias following the Cochrane Collaboration tool for RCTs and the Newcastle-Ottawa tool for prospective cohort studies; any disagreement was resolved by consensus of reviewers and statistics researcher (ZN).

Data Extraction and Collection Process

Following the screening process, four reviewers (NAV, GLD, GP and LM) independently extracted the data of the selected articles using data tables. All extracted data were reviewed, and any conflict was resolved among the authors and confirmed by the statistician. The following information was extracted from each included trial: year of publication, study design, number of patients, number of patients at the end of the study, number of implants, dropouts, mean age of patients, age range, mean initial bone height, type of biomaterial used, type of membrane used, single or bilateral sinus augmentation, dosage and timing of antibiotics prescribed, type of antibiotic, timing and dosage of corticosteroids prescribed, other anti-inflammatory medications prescribed, type and number of intra-operative complications, and type and number of post-operative symptoms at one and two weeks.

The primary (swelling, pain, infection) and secondary outcomes (active suppuration, bleeding, wound dehiscence, trismus, hematoma, early implant failure) were classified as present or absent, as clearly reported and numbered by the authors of the selected articles. If an article did not directly provided the number of outcome occurrences, they were extrapolated from the specific scales or tables, by counting the number of patients that still reported that outcome during the first two weeks post-op; as an example, we counted the number of patients that still reported pain in a VAS pain scale after 7 days. In this case, the pain was considered to be medium-high or high.

Statistical Analysis

A meta-analysis was performed using the CMA software (Comprehensive Meta Analysis Version 2.0) for each group separate. A random effects model was performed to estimate the event rate. Heterogeneity was checked based on methods, design, and type of complications.

Results

Risk of Bias

According to the Revised Cochrane risk-of-bias tool for randomized trials (RoB 2), regarding the randomized controlled trials included, only some concern was found in some studies. No study reported another risk of bias for our outcome variables (Figure 2).

Regarding the non-RCT studies, according to the Newcastle-Ottawa Scale (NOS) for Assessing the Quality of Nonrandomized Studies in Meta-Analysis, no high risk of bias was found for any study, especially for the parameters relating to outcomes (Table 1).

Among the studies initially included in the "corticosteroid group" (Cort), 5 used dexamethasone, 5 used betamethasone, one used methylprednisolone, and one used deflazacort. In 7 studies corticosteroids were administered post-operatively, in 3 studies pre-operatively, in one study both pre- and post-operatively, and in one study they were administered intra- and post-operatively. Corticosteroids were administered orally (7 studies), intramuscularly (3 studies), intravenously (3 studies), and both orally and intramuscularly (one study).

Antibiotic Use

Amoxicillin was used in 3 studies of the Cort group and in 12 studies of the no corticosteroid group (No-Cort). Amoxicillin plus clavulanate was used in 5 Cort and 4 No-Cort studies. Antibiotic choice was unreported in 4 studies, including one study of the Cort group. In most studies clindamycin was used for patients who were intolerant to amoxicillin, however one Cort group used Clindamycin as the first line of antibiotics and amoxicillin as the second. Ceftriaxone, Phenoxymethylpenicillin, and penicillin V were used in only one study each. In the majority of the studies antibiotics were prescribed for a total of 7 days.

Sinus Lift Procedures

In 5 studies of the Cort group and in 7 of the No-Cort group, unilateral sinus lifts were performed. In 2 Cort and 2 No-Cort studies, bilateral sinus lifts were executed. In the remaining studies, the authors did not specify whether the performed uni- or bilateral MSA on the participating subjects.

The most commonly used biomaterial was bovine xenograft and it was most often combined with other autologous or synthetic biomaterials. In 6 studies of the Cort group and in 7 of the No-Cort group, the implants were placed at the same time as the MSA. In 6 No-Cort studies and in one Cort study the implants were placed simultaneously or in two stages depending on the clinical scenario. In all other studies, only the MSA was performed.

Post-operative Complication Rates

The cumulative rates of events related to the immediate post-operative phase and the results for each type of event in the two groups are described by the forest plots in Figures 3-12

The basic characteristics of the studies, the descriptive factors of the MSA procedures, the pharmacological therapies, and the outcomes are illustrated in tables 2, 3A-B, and 4.

In the absence of studies comparing the outcomes of MSA with prescribed corticosteroids versus MSA without corticosteroids, a comparative meta-analysis could not be carried out.

In the 37 studies included, a total of 1599 patients (378 Cort, 1221 No-Cort) were analyzed.

Overall, the complication rates post-operatively were comparable between the two study groups, however slight differences existed in the incidence of active suppuration (1.7% Cort vs. 3.2% No-Cort), wound dehiscence (3.9% Cort vs. 2.1% No-Cort) and trismus (2.7% Cort vs. 1.4% No-Cort). Trismus complications were surprisingly unfavorable to the Cort group, perhaps due to the fact that this complication occurred only in a single study. Otherwise, the parameters of swelling (9.3% Cort vs. 10.8% No-Cort) and pain (6.2%

Cort vs. 4.9% No-Cort), namely the two for which a corticosteroid effect could have been expected, showed no substantial differences.

The total number of complications could not be calculated or meta-analyzed because different types of complications occurred at varying levels (patient level, sinus level, and implant level).

Discussion

The scientific literature lacks clinical studies directly comparing the use of corticosteroids and the outcomes of lateral MSA procedures. To the authors' knowledge, this is the first systematic review providing data with the use of corticosteroids during MSA procedures to help clinicians to reduce MSA post-operative sequelae.

The most unfavorable side effects of corticosteroid use in oral surgery are avascular osteonecrosis, adrenal suppression, impaired healing, and increased risk of infections. Avascular osteonecrosis occurs more often when high doses of corticosteroids are taken for a long duration, which results in an inhibition of micro vascularity in the bone and necrosis. There are no studies reporting avascular osteonecrosis after low dose and short terms use of corticosteroid use in oral surgery procedures. Corticosteroid related adrenal suppression involves a reduced production of cortisol resulting from exposure of the hypothalamic-pituitary-adrenal axis to exogenous glucocorticoids and can have serious consequences including coma and death. However, the dosage and time required to reach these serious consequences are beyond those used in oral surgery. To avoid these side effects, it would be advisable not to administer corticosteroids in patients who are concurrently taking steroid doses for other pathologies, moreover, the most recent evidence-based guidelines advise against this practice .

Corticosteroids administration may also inhibit fibroblasts activity and proliferation causing delayed wound healing and increased rate of infections. The current review this hypothesis, reporting the highest number of wound dehiscences in the study with the longest duration of corticosteroid therapy. Infections can be a side effect of corticosteroids as they limit the inflammatory response by decreasing lymphocytes, monocytes, and macrophages migration and activity. However, Dan et al. support the use of corticosteroids in oral surgery, reporting a nonsignificant increase in the rate of infections compared to placebo. The authors mention that it is important to consider the combination of corticosteroids with antibiotics, which can lead to superinfections, when bacteria is not covered by the spectrum of action. It is not recommended, according to Dan et al. they be used in combination unless other indications are present. low or medium risk patients, antibiotics can be avoided or limited to a short pre-operative prophylaxis, pre- and post-operative prophylaxes are strongly recommended for guided bone regeneration procedures and especially for bone grafts in the maxillary sinus. Finally, the current review showed that the two studies reporting the longest duration of corticosteroid therapy (5 days) showed the absolute highest rates of postoperative swelling. This event was not confirmed by Dan et al.

The limitations of this systematic review are the absence of comparative studies specifically designed to investigate the use of corticosteroids in lateral MSA procedures, the extreme heterogeneity of reported complication outcomes, and the subjectivity of parameters such as pain.

Conclusions

In general, the event rate of the one-to-two-week postoperative complications analyzed in this systematic review did not differ between the two groups. In light of this observation, and within the limits of this analysis, we can conclude that the use of corticosteroids in the lateral sinus augmentation procedure needs further investigation in order to determine whether or not they have an impact on the post-operative course of lateral MSA. This can only be confirmed or denied through randomized clinical trials with the main purpose of investigating the use of corticosteroids in the lateral maxillary sinus augmentation procedure.

The data sets used and/or analyzed during the current study are available from the corresponding author on reasonable request

References

Tables legend

Figures Legend

Figure 1. PRISMA flow diagram of the study selection process.

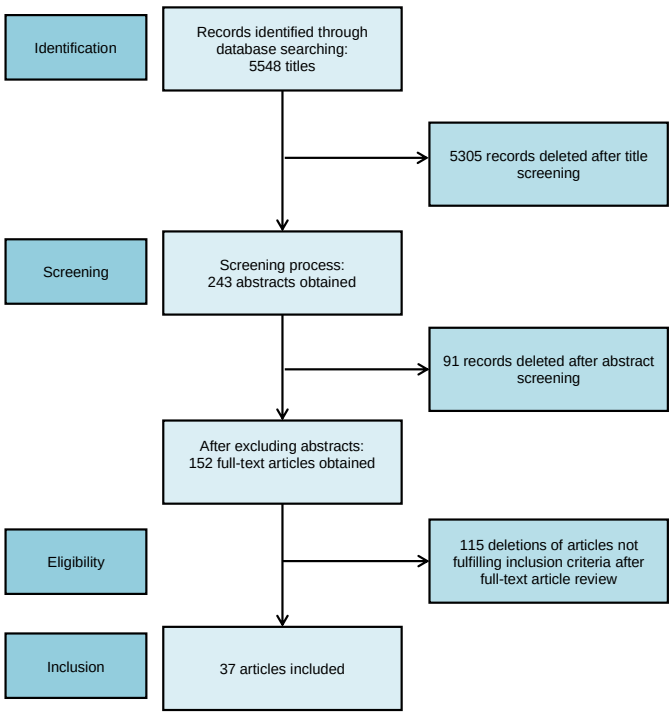

Figure 1: This is a caption