Effect of steroid-releasing sinus implants after endoscopic sinus surgery (ESS) on postoperative outcomes: A meta analytical study

Meta-Analysis Study

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List of abbreviations

AAO-HNS	American Academy of Otolaryngology – Head and Neck Surgery
ABRS	Acute bacterial rhinosinusitis
AERD	Aspirin-exacerbated respiratory disease
AFRS	Allergic fungal rhinosinusitis
AR	Allergic rhinitis
ARS	Acute rhinosinusitis
AS	Absorbable spacer
CF	Cystic fibrosis
CI	Confidence interval
CRS	Chronic rhinosinusitis
CRSsNP	CRS without (sine) nasal polyposis
CRSwNP	CRS with nasal polyposis
CT	Computerized tomography
DAC	Dimethyl aminopropyl carbodiimide
DESs	Drug eluting stents
DF	Degree of freedom
EP3OS	European Position Paper on Rhinosinusitis
ESS	Endoscopic sinus surgery
EVAC	Ethyl vinyl acetate
FDA	Food and Drug administration
FEM	Fixed- effects method
FESS	Functional endoscopic sinus surgery
GERD	Gastroesophageal reflux
HPLC	High performance liquid chromatography
IG	Immunoglobulin
IL	Interleukin
INCs	Intranasal corticosteroids
LOA	Lysis of adhesions
MF	Mometasone furoate
MCC	Mucociliary Clearance
MRI	Magnetic resonance imaging
MT	Middle turbinate

NAS	Non absorbable spacer
NDGA	Nordihydroguaiaretic acid
NMC	Nasal Mucociliary Clearance
NP	Nasal Polyposis
NSAIDs	Nonsteroidal anti-inflammatory drugs
OMC	Ostiomeatal complex
PA	Polyvinyl acetate
PBS	Phosphate-buffered saline
PEG	Polyethylene glycol
PLA	Polylactic acid
PLG	Polyactide-co-glycolide
PLGA	Polylactic-co-glycolic acid
PVA	Polyvinyl alcohol
Q	Cochran Q statistic
QOL	Quality of life
RCT	Randomized controlled trial
REM	Random-effects method
RR	Relative risk
RS	Rhinosinusitis
SE	Standard error
SEM	Standard error of the mean
SEMD	Standard error of the mean difference
SMD	Standardized mean difference
TH	T helper
TSS	Toxic shock syndrome
VRS	Viral rhinosinusitis

Introduction

Rhinosinusitis (RS) is an extremely prevalent disorder that affects an estimated 14% of the adult population. RS is a significant and increasing health problem which results in a large economic burden, especially when recurs, it has been shown that subsequent episodes cost successively more for diagnostic tests and therapy. It is thought to be more common in childhood than in adults. It affects all races and socioeconomic backgrounds. The incidence is higher in spring, winter, and fall than it is during the summer months **(Anand, 2004)**.

Chronic rhinosinusitis (CRS) is an inflammatory disease of the mucosa of the nose and paranasal sinuses that is present for at least 12 weeks. A diagnosis of CRS is based on the EPOS (European position paper on rhinosinusitis and nasal polyps) criteria both subjective and objective criteria, which are the presence of distinctive symptoms, (e.g. nasal obstruction and nasal discharge) and either endoscopic signs or computed tomography (CT) images showing mucosal changes within the ostiomeatal complex, sinuses, or both **(Fokkens et al., 2012)**.

Multiple factors have been implicated in the development of CRS, including host and environmental factors. Host factors, such as immunodeficiency and eicosanoid dysregulation, also contribute to refractory infections or inflammation and have a significant impact on the severity of CRS. Environmental factors, such as bacteria, biofilms, fungi and allergens, have been described as disease modifying factors that lead to inflammation of the mucosa of the nose and paranasal cavities **(Kennedy, 2004 and Tan et al., 2010)**.

Although medical treatments offer relief for most CRS patients, functional endoscopic sinus surgery (FESS) is commonly performed. Surgical treatment is not considered a curative treatment for CRS; approximately 14% of CRS patients who undergo surgery will require revision ESS **(Bhattacharyya, 2004)**.

There are many reasons for surgical failure including scarring of the sinus ostia, adhesion formation, middle turbinate lateralization and persistent inflammations. Controlling for these postoperative issues may lead to better long-term outcomes **(Otto and DelGaudio, 2010)**.

Sinus stents are devices that are inserted into the nose, sinuses or both following FESS to prevent stenosis of the sinus openings during the postoperative healing period **(Weber et al., 2000)**.

Sinus stents may be composed of non-absorbable alloplastic materials (e.g. silicone, plastic), to be removed in the office setting after a period of several days; or absorbable biomaterials (e.g. bovine gelatin, poly (lactic-co-glycolic acid), which degrade in a controlled fashion over days to weeks following surgery **(Weitzel and Wormald, 2008)**.

Sinus stents are also known as 'spacers' because they maintain separation between critical areas of healing to prevent synechia formation. For example, middle meatal stents provide a mechanical barrier between the middle turbinate and lateral nasal wall; the goal of stent placement here is to avoid middle turbinate lateralization, a complication that can lead to recurrence and propagation of chronic rhinosinusitis **(Weitzel and Wormald, 2008)**.

Recent advances in biomaterial technology have resulted in the development of corticosteroid-coated sinus stents, which can elute the drug in a controlled fashion via a bioabsorbable core. The drug-eluting stents offer the

potential for the dual benefits of mechanical spacing and anti-inflammatory pharmacotherapy. The slow release of corticosteroid aims to decrease mucosal oedema and expedite wound healing **(Bednarski and Kuhn, 2009)**.

Recent studies have shown that steroid-eluting sinus stents can preserve sinus patency and enhance mucosal wound healing after FESS by reducing inflammation, polyposis and the formation of adhesion **(Han et al., 2014)**.

Aim of the work

The aim of this work is a meta-analysis to evaluate the steroid-releasing sinus implants placement in chronic rhinosinusitis (CRS) patients after functional endoscopic sinus surgery (FESS) in order to assess its efficacy.

Anatomy of the nose

The nose is an important part of the face; it gives the individual his characteristic appearance. The nose is divided into 2 parts: The external nose and the internal nose (nasal cavities). The nasal cavity is divided by midline partition (the nasal septum) into right and left chambers. It extends from the nostrils in front into the choanae behind (where it opens into the nasopharynx) the entrance to the nasal cavity is called the nasal vestibule which ends at the mucocutaneous junction, it is lined by skin and contains skin appendages. The rest of nasal cavity lined by respiratory mucosa (pseudo- stratified columnar ciliated epithelium), and small area lined by olfactory epithelium **(Nouraei et al., 2009)**.

Each cavity has a roof, floor, medial and lateral walls.

The floor is formed by the palatine process of the maxilla and the horizontal process of palatine bone.

The roof is narrow and is formed (from behind forward) by the body of the sphenoid, cribriform plate of the ethmoid which contain numerous tiny perforations which transmit sensory fibers to the olfactory bulbs and the frontal bone.

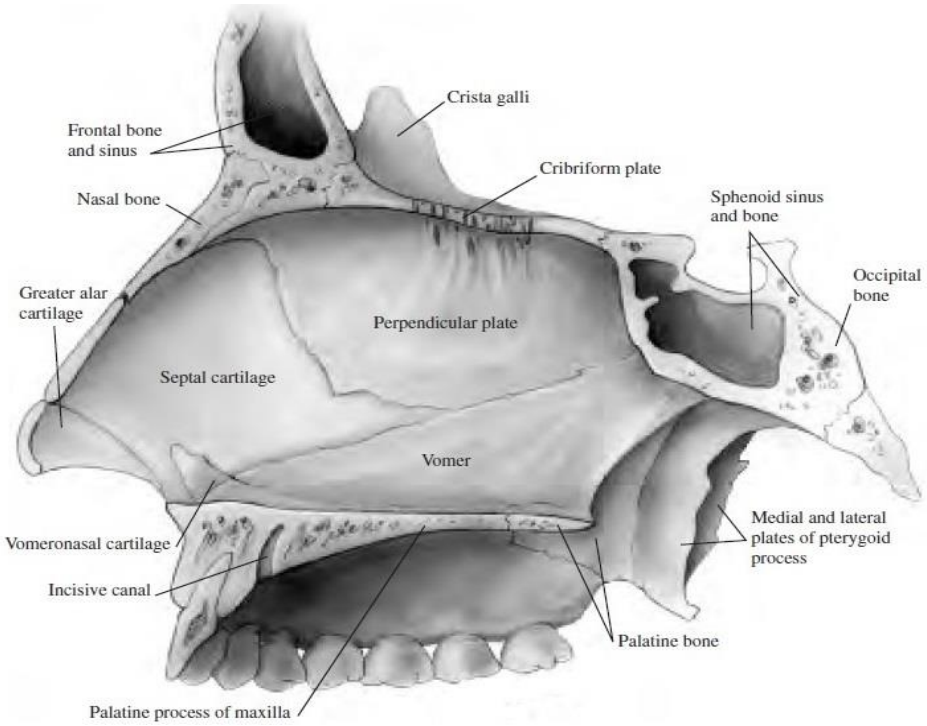

Figure (1): Medial wall of the nose. Quoted from *(Bradoo, 2005).*

The medial wall (the nasal septum) is an osteocartilaginous partition covered by adherent mucoperichondrium and mucoperiostium. The upper part is formed by the perpendicular plate of the ethmoid bone, the posterior part by the vomer and the anterior portion is formed by septal cartilage as shown in figure 1.

The lateral wall is the most complex and variable, it supports the 3 turbinates (inferior, middle, superior and sometimes there is even a supreme) as shown in figure 2. The groove below each turbinate is referred to as a meatus.

Inferior meatus: contain the opening of nasolacrimal duct.

Superior meatus: receives the opening of the posterior ethmoid sinus.

Spheno-ethmoidal recess: is the area above the superior turbinate. It receives the opening of the sphenoid sinus.

Comun Meatus: vertical slot between all nasal turbinates and septum **(Bradoo, 2005)**.

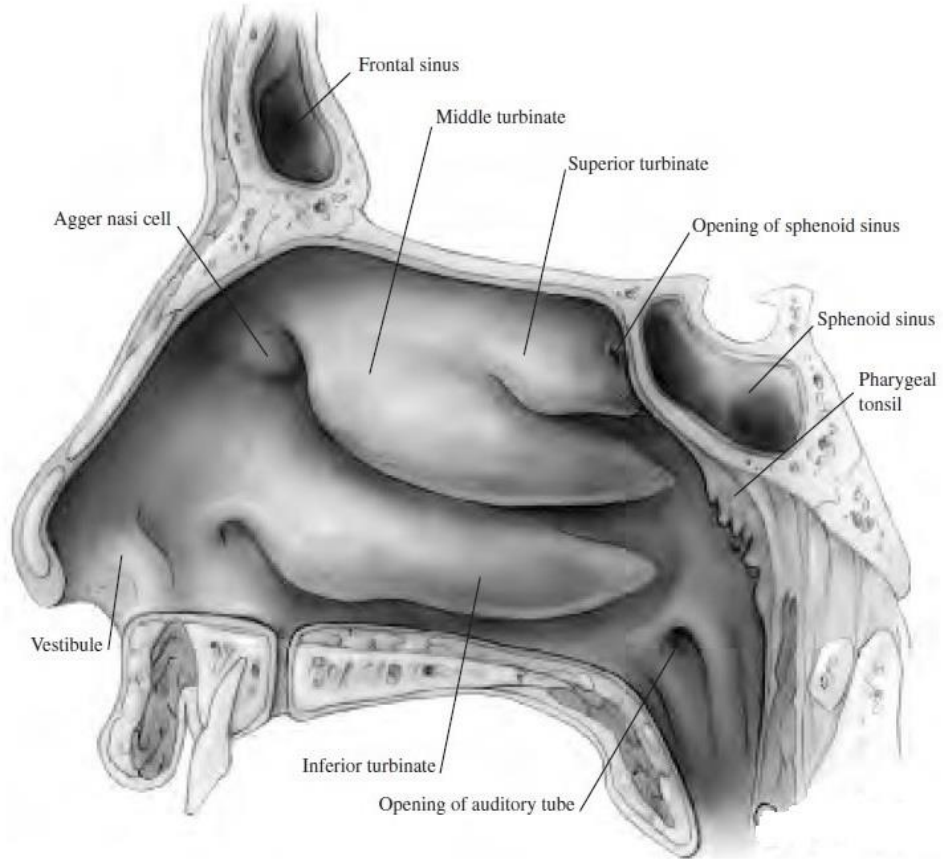

Figure (2): Lateral wall of the nose. Quoted from *(Bradoo, 2005).*

Paranasal Sinuses

Sinuses are hollow spaces in the bones around the nose that connect to the nose through small narrow channels called ostia.

They can be divided into 2 groups:

(1) Anterior group: frontal, maxillary, anterior and middle ethmoidal air sinuses.

(2) Posterior group: posterior ethmoid and sphenoid sinuses. The anterior group drain into the middle meatus of the nose and the posterior ethmoid sinus drain into the

superior meatus and the sphenoid sinus drain into the sphenoethmoidal recess **(Lund, 1997)**.

The frontal sinuses lies at the anterosuperior part of the middle meatus, as a small evagination, the frontal recess develops during the third month. This gradually deepens and by term a small diverticulum is present. The formation of the frontal sinuses occurs with gradual upwards expansion of the diverticulum into the frontonasal region. The sinus may, on rare occasions, develop as an extramural expansion of one of the anterior ethmoidal cells. Medially, the two sinuses come to lie in close proximity, divided by a thin intersinus septum. Situated in the eyebrow area of forehead bone of the skull. Usually asymmetrical, occasionally absent, in about 5% of us **(McLaughlin et al., 2001)**.

Maxillary sinuses is the first to appear as an ectodermal depression just above the uncinate ridge on the inferior turbinate. This pit, which is the site of the eventual maxillary ostium in the central part of the middle meatus, deepens laterally and expands so that by term a cavity measuring 7 x 4 x 4 mm is present in bones of cheeks, one on each side. May grow to be as large as 15ml **(Oneal et al., 1999)**.

Ethmoid sinuses developed during the fifth fetal month, as a small ectodermal evaginations on the lateral nasal wall and grow laterally into the ethmoid bone. By term, these diverticula are globular shaped and they continue to grow until late puberty, usually 6 to 10 per side, situated between the orbits, up to the skull base. Responsible for more complications from sinusitis than other sinuses **(Graney and Rice, 1998)**.

Sphenoid sinus develops during the fourth fetal month, as an ectodermal pit in the posterosuperior aspect of the nasal capsule. At birth, it measures 2 x 2 x 1.5 mm and is still only rudimentary. In the fourth postnatal year, when the nasal capsule resorbs, sphenoid pneumatization