Pathophysiology of Chronic Rhinosinusitis without Nasal Polyp and Met-analysis of its Pharmaceutical Options

A Meta-analysis Study

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List of Abbreviations

Abbr.	Full-term
AAAAI	American academy of allergy, asthma and immunology
AAOA	American Academy of Otolaryngic Allergy
ACAAI	American College of Allergy, Asthma and Immunology
ACTH	Adrenocorticotrophic hormone
ANS	Autonomic nervous system
BSACI	British society for allergy and clinical immunology
CF	Cystic fibrosis
CGRP	Calcitonin gene-related peptide
CI	Confidence interval
CNS	Central nervous system
CRH	Corticotrophin releasing hormone
CRS	Chronic rhinosinusitis,
CRSsNP	Chronic rhinosinusitis without nasal polyp
CRSwNP	Chronic rhinosinusitis with nasal polyp
EPOS	European position paper on rhinosinusitis and nasal polyp
FDA	Food and drug administration
FEM	Fixed effect model
GABA	γ-amino butyric acid
HPA	Hyphophyseal-pituitary - adrenal
IL	Interleukin
JCAAI	Joint council of allergy, asthma and immunology

LTD4 : Leukotriene receptor antagonist 4

MMPI : Minnesota Multiphasic Personality Inventory profiles

NGF : Neuron growth factor

NO : Nitric oxide

OMC : Osteomeatal complex

pSmad : Phosphorylated smad cells

REM : Random effect model

SNOT : Sinonasal outcome treatment score

SP : Substance p

TGF-b : Tissue growth factor b

TH-1 : T -helper 1 cell

TH2 : T-helper 2 cell

TNFα : Tumor necrosis factor alpha

VAS : Visual analog scale

VIP : Vasoactive intestinal peptide

V1 : Ophthalmic branch of trigeminal

V2 : Maxillary branch of trigeminal

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Introduction

Chronic sinusitis is defined as sinusitis with symptoms of nasal obstruction, discharge, facial pain and pressure together with hyposmia supported by subjective endoscopic and CT findings persisting for at least 8 to 12 weeks, despite appropriate medical therapy. Alternatively, rhinosinusitis may be considered chronic in a patient experiencing four or more episodes annually of recurrent acute sinusitis, each lasting at least 10 days, in association with persistent changes on CT scan for 4-6 weeks following medical treatment. The cause of chronic sinusitis is poorly understood, the most widely held view being that it is established as a result of interference with normal sinus clearance mechanisms, leading to colonization with bacteria normally resident in the nose and nasopharynx and their subsequent proliferation (Meltzer et al., 2004).

Allergic rhinitis is a variant of chronic rhinosinusitis without nasal polyp and is mediated with immunoglobulin E, thought to occur after exposure to indoor and outdoor allergens such as dust mites, insects, molds, animal danders and pollens. Symptoms include rhinorrhea, nasal congestion, obstruction, and itching. Optimal treatment includes avoidance of the allergen, targeted symptom control and immunotherapy (Nelson, 2000).

Chronic rhinosinusitis has two types, chronic rhinosinusitis with nasal polyp and without nasal polyp. This study is focused on chronic rhinosinusitis without nasal polyp so as to narrow and focus the study, also incidence of chronic rhinosinusitis without nasal polyp versus chronic rhinosinusitis with nasal polyp is 1048 versus 83 per 100000 patient between 2007 and 2009 respectively in Geisinger Clinic in central Pennsylvania in United States (Tan et al., 2013).

In 2012 national health survey Lethbridge-Cejku reported 12% of the US population (nearly 1 in 8 adults) being diagnosed with chronic rhinosinusitis (Lethbridge-Cejku M; et al., 2006).

National ambulatory care data from 2006 to 2010 conducted annually by the United States Department of Health and Human Services revealed that rhinosinusitis accounted for more prescriptions of antibiotic than any other diagnosis and accounted for 11% of all antibiotic visits of the primary care patients with chronic rhinisinusitis (Smith et al., 2013).

CRS can also have a significant impact on health-related quality of life. Patients with CRS referred to otolaryngologists score significantly lower values on measures of bodily pain and social functioning than do those with angina, back pain, congestive heart failure, and chronic

obstructive pulmonary disease. Similarly, patients with CRS have health utility scores that are worse than many chronic diseases, including heart failure, coronary artery disease, and chronic obstructive pulmonary disease. Moreover, treatment of chronic rhinosinusitis can improve health state score values and significantly reduce fatigue and bodily pain (Bhattacharyya, 2011).

Aim of the Study

A meta-analysis study to provide an evidence based approach for the use of different pharmaceutical agents in the management of chronic rhinosinusitis without nasal polyp with an overview of the pathophysiology of chronic rinosinusitis without nasal polyp.

Chapter 1
Anatomy of Paranasal Sinuses

Understanding the normal anatomy and physiology of the paranasal sinuses is important to understand the pathogenesis of sinus disease. There are four pairs of sinuses named for the bones of the skull they pneumatize. They are the maxillary, ethmoid, frontal and sphenoid sinus air cells and they are lined by pseudostratified columnar epithelium bearing cilia. The mucosa contains goblet cells that secrete mucus, which aids in trapping inhaled particles and debris. The uncinate process is a sickle-shaped bone extension of the medial maxillary wall that extends anterosuperiorly to posteroinferiorly. The uncinate process is rarely pneumatized. The hiatus semilunaris, situated immediately superior to the uncinate process, is a slit like air-filled space anterior and inferior to the largest ethmoid air cell, the ethmoidal bulla. It is clinically significant because disease located here results in obstruction of the ipsilateral maxillary antrum, anterior and middle ethmoid air cells and frontal sinus, whereas disease in the infundibulum results in isolated obstruction of the ipsilateral maxillary sinus alone (Arash et al., 2007).

The ethmoid sinuses are paired, discrete cells that may number 18 or more. They are anatomically divided into anterior and posterior groups according to the location of the draining