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A Systematic Review on Pathogenesis and Treatment of Chronic Pharyngitis

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ABSTRACT
Chronic pharyngitis is a long-term inflammatory condition affecting the pharynx, leading to persistent cough and discomfort. This systematic review explores the pathogenesis, treatment options, and contributing factors related to chronic pharyngitis, drawing insights from recent studies. Characterized by sustained inflammation, the evaluation of treatments for non-infectious causes is limited, largely due to subjective outcome measures and inconsistent diagnostic criteria. While otolaryngologists typically manage initial care, referrals to immunologists are recommended for patients with unsatisfactory results.
The pathogenesis of chronic pharyngitis involves various processes. Infectious agents enter the pharynx through inhalation or ingestion, where toll-like receptors on epithelial cells recognize pathogen-associated molecular patterns (PAMPs). This triggers the immune response, resulting in the release of pro-inflammatory cytokines like IL-1, IL-6, and TNF-α, leading to local inflammation with redness, swelling, and pain. Immune cells, such as neutrophils and lymphocytes, are recruited to facilitate antibody production. Prolonged irritation can cause goblet cells to increase mucus production, resulting in symptoms like sore throat and coughing. Chronic inflammation may ensue from ongoing infection or irritants, leading to complications.
Current research suggests that non-antibiotic therapies for acute sore throat, including analgesics and anti-inflammatories like NSAIDs and corticosteroids, may also be effective for non-infectious pharyngitis.The Anti allergics like levocetrizine and montelukast also foundto be effective treatment. Lifestyle modifications, such as a balanced diet and avoiding irritants, further aid management. Understanding the interplay of infectious agents, immune responses, and environmental factors is essential for guiding treatment and prevention strategies.

KEYWORDS: CP: Chronic Pharyngitis, Treatment, Etiology

I. INTRODUCTION

Pharyngitis refers to the inflammation of the oropharynx, commonly known as a sore throat. However, the term "sore throat" is not precisely defined, leading to potential confusion. While patients may describe their symptom as a sore throat, further examination might reveal inflammation of the nasopharyngeal mucosa, known as nasopharyngitis. Pinpointing the exact site of irritation or inflammation can be challenging, as some studies rely solely on patient-reported diagnoses of a "sore throat." These complexities can complicate the study and treatment of this condition(1).

This review will specifically focus on sore throat as the primary symptom, involving reported irritation and pain due to inflammation and/or irritation of the middle (oro) and lower (hypopharynx) parts of the pharynx. Although overlapping symptoms may occur with nasopharyngitis (affecting the upper part of the pharynx), patients usually receive diagnoses of rhinitis or rhinosinusitis, as sore throat is not their primary symptom.

The origin of a Pharyngitis can be either infectious or non-infectious, and there are instances where these causes may intertwine. The majority of cases stem from infectious sources, with a significant proportion (up to 40%) being attributed to rhinovirus and adenovirus. Additionally, other viruses such as coronavirus, influenza, parainfluenza, Epstein Barr, and herpes simplex have also been linked to the condition. (1)

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While the majority of Pharyngitis cases are caused by relatively harmless infectious or non-infectious factors, it's essential to be aware that pharyngitis can sometimes be a warning sign of severe or even life-threatening illnesses. Viral pharyngitis is the most frequently diagnosed form, but when Group A beta-hemolytic streptococcus (GABHS) is identified as the primary bacterial organism requiring antimicrobial treatment, it often necessitates a visit to the doctor's office. (2)
The following are the common and uncommon causes of pharyngitis, categorized by infectious agents, diseases of unknown cause, and other factors:

Infectious Agents
Viruses
Common agents such as rhinovirus and adenovirus are responsible for 6% to 20% of all cases.
Epstein-Barr virus (EBV), Herpes simplex, Influenza, Parainfluenza, Coronavirus are the less common agents that are responsible for 1% to 5% of all cases.
Enterovirus (poliovirus, coxsackievirus, echovirus), Respiratory syncytial virus, Cytomegalovirus (CMV), Rotavirus, Reovirus, Rubella, Herpes zoster, Rubeola (measles), and HIV-1 are each uncommon agents responsible for less than 1% of all cases.

Bacteria
Streptococcus pyogenes (group A β-hemolytic, group C β-hemolytic) are the common agent that are responsible for 6-20 % of all cases. Mycoplasma (M. pneumoniae, M. hominis [possibly]) &Arcanobacteriumhaemolyticus are each agent responsible for 1% to 5% of all cases.
Streptococcus pyogenes (group G β-hemolytic, group B β-hemolytic), Chlamydia pneumoniae c) Neisseria (N. gonorrhoeae, N. meningitidis), Corynebacterium (C. diphtheriae, C. ulcerans, C. pyogenes [possibly]) ,Anaerobic bacteria (Peptostreptococcus sp., Fusobacterium sp., Bacteroids sp.) are uncommon and responsible for less than 1% of all cases.
Leptospira species, Actinomyces species, Francisellatularensis, Borrelia (B. burgdorferi, B. recurrentis), Streptobacillus moniliformis, Salmonella typhi, Legionella pneumoniae, Yersinia enterocolitica, Treponema pallidum, Coxiella burnetiid, Klebsiella pneumoniae all are rare causative agents.

Fungi
Candida species, Rhinosporidiumseeberi, Cryptococcus neoformans, Histoplasma capsulatum, Blastomyces dermatitidis, Paracoccidioides brasiliensis are the rare fungi that acts as a infectious agent.

Parasites
Toxoplasma gondii is the rare parasite responsible for the infectious agent.

Diseases of Unknown cause
Kawasaki disease, Stevens-Johnson disease,Behçet's syndrome, Aphthous stomatitis, Systematic lupus erythematosus are the reason for diseases of unknown cause.

Other Infectious Agents
Other infectious agents are such as Allergy, Trauma - Foreign body – Burns, Chemotherapy,Neoplasia - Polyps - Cancer – Leukemia, Radiation, Irritation - Toxin - Inhaled - Swallowed - Dust - Smoke – Dryness, Psychosomatic, Referred pain, Subacute thyroiditis(3)

Overuse syndromes
The vast majority of cases of pharyngitis are attributed to viral or bacterial infections, while parasites or fungi are infrequently responsible. Other contributing factors include trauma, exposure to irritants, various syndromes of unknown origin, and cancer(3,4). The specific cause of pharyngitis can be influenced by factors such as age, time of year, and environmental conditions. Viral agents are more common in young children, whereas GABHS (Group A beta-hemolytic streptococcus) and other bacteria are encountered more often in older children and adolescents. In adults, less invasive bacteria and viruses are found with similar frequency. A study involving 106 adults with acute pharyngitis examined these aspects.(4)

Etiology of non-infectious Pharyngitis
Physico-chemical factors
Pharyngitis can be triggered by a wide range of physico-chemical factors, such as inhaling cigarette smoke, snoring, tracheal intubation, shouting, and the effects of other illnesses or medications. Additionally, smoking is considered a risk factor for developing sore throat(15).Tobacco smoke is commonly mentioned as an irritant that affects the stratified squamous epithelium of the oropharyngeal mucosa (15,16). The study revealed a significant association between passive smoking and sore throat among 46 French non-smokers.

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(17), 382 Australian non-smoking indoor workers and non-smoking Australian nightclub and casino workers (18,19).
Pharyngitis is often linked to snoring, and both conditions share risk factors, including smoking.(20)

Pharyngitis is a frequent occurrence in individuals undergoing general anesthesia, often attributed to tracheal intubation and the use of laryngeal mask airways. (21)

People in professions that demand frequent use (and overuse) of their voice have reported that shouting and voice loading can lead to sore throat, aerobics instructors have reported a higher occurrence of Pharyngitis, unrelated to illness, since they started instructing. (22)

Some medications, such as angiotensin-converting enzyme (ACE) inhibitors, can lead to drug-induced sore throat as a significant adverse effect.(23)

Many individuals taking various other medications often report sore throat as an adverse effect. However, in numerous cases, the symptom may be coincidental, resembling an infectious sore throat and occurring at a similar rate to the placebo group.(1)

Sore throat can directly arise from concurrent illnesses. For instance, Kawasaki disease, a mucocutaneous vasculitis, commonly leads to pharyngitis in both adults and children.(24)

Moreover, chronic pharyngitis is frequently observed as a typical manifestation of gastroesophageal reflux disorder, now referred to as laryngopharyngeal reflux disorder in this context. (25,26)

Environmental Factors

Numerous environmental factors have been identified as potential causes of sore throat. These factors encompass general air pollution, occupation-related or industrial-specific pollution, as well as pollution found in indoor environments. (1)

Sore throat can also be experienced as a secondary symptom by patients with allergic rhinitis, postnasal drip, non-allergic rhinitis, and persistent cough. (27,28)

Sore throat frequently arises from ambient air pollution. This can be attributed to various factors, including ozone, nitrogen oxides, and fine dust.(1)

Reported causes of sore throat related to occupation or hazards include exposure to irritants such as particulates, fumes, chemicals, and odours. Additionally, laryngitis has been identified as another reported cause. (29)

Sore throat has been associated with particulates and fumes originating from diverse industries, including pulp mills (30), woodworking (31), cement works (32), brick kilns (33), and factory exhaust emissions (34)

Various chemicals have been documented to induce sore throat, which includes organic screen-printing solvents (35), boron oxide, boric acid, and borax dust. (36,37)

The newspaper printing industry, which involves the use of multiple chemicals like organic solvents, filler materials, and inks, has reported a higher-than-expected incidence of chronic pharyngitis. (38)

In people with multiple chemical sensitivity syndrome, sore throat is also a commonly reported symptom, with a prevalence of 72%. (39)

The US World Trade Center disaster (9/11) led to unspecified hazardous exposures, which are believed to be responsible for the upper airway inflammation observed in many of the exposed individuals. (40)

Among 10,378 firefighters, the incidence of sore throat was infrequent before the disaster, with only 3.2% reporting frequent sore throat. However, in the year following the disaster, sore throat became the most common respiratory symptom, affecting 62.4% of the firefighters. Subsequently, the prevalence of sore throat decreased and stabilized, reaching 36% after 2 years and 37% after 4 years. Together with cough, sore throat was regarded as the most sensitive initial indicator of respiratory insult. (41)

When volcanoes erupt, they release sulfur dioxide and other gases that can interact with atmospheric elements, leading to sore throat. In Hawaii, volcanic sulfur dioxide and fine sulfate particles were significantly associated with sore/dry throat.(42,43)

Instances of sore throat are commonly reported within communities that have confined animal facilities, wastewater treatment plants, and biosolids recycling operations.(44)

Furthermore, farmers encounter exposure to pesticides, and this factor was linked to the development of pharyngitis in a comparative study conducted between farmers and other workers in the United Arab Emirates. (45)

These research findings demonstrate that sore throat can be attributed to occupational and hazard-related irritants, which encompass

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particulates, chemicals, fumes, gases, and endotoxin.

Sore throat symptoms have been associated with variations in temperature and humidity, which impact mucus membranes.

Nasal pain can result from exposure to heated air (46), while consistent work in cold environments is associated with the development of rhinitis and sore throat, alongside alterations in lung function. (47)

Nonetheless, a study conducted on a population basis demonstrated that cold temperatures and reduced humidity seem to individually contribute to an elevated risk of experiencing sore throat.(48)

Clinical picture of chronic pharyngitis and main mechanisms of its pathogenesis

Chronic pharyngitis presents a distinct clinical picture characterized by sensations of tickling, dryness, discomfort, and pain in the throat, particularly when swallowing. Patients often describe feeling a "lump of mucus" in their throat, leading to a desire to cough. If the inflammation extends to the tubopharyngeal ridges, the pain may radiate to the ears. Palpation of the affected area can elicit pain, and there may be an enlargement of the upper, anterior, and/or posterior lymph nodes.

Pharyngoscopy reveals hyperemia of the posterior wall of the pharynx and palatal arches, along with separate inflamed lymphoid granules. Hyperplasia of the tonsils may also be observed. Notably, typical signs of tonsillar inflammation that are present in tonsillitis may be absent in chronic pharyngitis.

It is important to consider that exacerbations of chronic pharyngitis or acute pharyngitis may be the initial symptoms of certain infectious diseases such as measles, scarlet fever, or rubella. Consequently, in some cases, it becomes necessary to perform a differential diagnosis with Kawasaki disease and Stevens-Johnson syndrome. (5,14)

IMMUNE RESPONSE

Pharyngitis pertains to the discomfort resulting from the inflammation of tissues situated at the back of the throat (50), and up to 80% of instances are attributed to viral origins (such as coronavirus, influenza, and rhinovirus). (51,52)

Globally, reports of sore throat symptoms constitute 1-4% of all primary care cases. (53)

Around 30% of the general population encounters sore throat due to viral infection within a year, and typically, the condition resolves on its own. (54)

Individuals who have a sore throat might also undergo symptoms like redness, swelling, scratchiness, coughing, and hoarseness. (55)

In China, on January 29, 2020, Guan and colleagues detailed the clinical attributes of 1099 patients with COVID-19 within a specific group. (56)

Sore throat was reported by a sum of 153 patients, equating to an approximate incidence rate of 13.9%. (57)

Chronic pharyngitis does not typically manifest with fever or a decline in the general condition, such as weakness and chills. Instead, patients often experience frequent upper respiratory viral infections, nasal congestion, and a prolonged, dry, and occasionally paroxysmal cough. This condition significantly affects their quality of life as they constantly feel discomfort in the throat due to the need to swallow mucus located on the back wall of the pharynx. Breathing becomes more difficult during sleep, leading to irritability and prompting patients to seek medical attention.

The course of the chronic inflammatory process on the posterior pharyngeal wall is influenced by various factors, including the type and virulence of the microflora, the degree of contamination, the overall health of the body, local immunity, and the condition of the mucous membrane. The mucous membrane's innervation, circulation, and hydration also play essential roles in this process. (6).

The pharynx's mucous membrane is a complex structure composed of muscular, nervous, vascular, secretory, and lymphoid components. It serves as a crucial regulator of various reflex stimuli, aiding in the inhibition of the respiratory act and facilitating swallowing delay. The pharynx plays a significant role in several functions, including voice formation, speech, respiration, and the propulsion of food along the oesophagus.

Pain experienced during acute pharyngitis and exacerbation of chronic pharyngitis can be attributed to the abundant innervation of the pharynx. (7).

The pharynx is innervated by sensitive, motor, and vegetative nerve fibers originating from the pharyngeal plexus located on the outer surface of the middle pharyngeal constrictor muscle, beneath the buccopharyngeal fascia. This plexus is formed by branches from the pharyngeal and vagus nerves, along with sympathetic fibers from the upper cervical ganglia. The sensitive innervation of the pharynx is mainly provided by the pharyngeal nerve, although in the pharyngeal ostium of the auditory tubes, there are nerve connections with the

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second branch of the trigeminal nerve. Additionally, the superior laryngeal nerve, considered a "branch of the vagus nerve," also plays a role in the innervation of the hypopharynx. The rich network of nerve connections explains why pain in pharyngeal disorders can sometimes be referred to the ear and lower jaw. (5).

In cases of atrophic pharyngitis, the mucous membrane of the pharynx appears thin, dry, and frequently covered with dried mucus. The shiny surface of the mucous membrane may reveal visible injected vessels. Atrophic changes in the pharyngeal mucous membrane often occur as a result of smoking and tonsillectomy.(8).

In the hypertrophic form of chronic pharyngitis, pharyngoscopy reveals scattered pockets of hyperplastic lymphoid tissue at the back of the throat, or enlarged tubopharyngeal ridges located behind the rear palatine arches. During exacerbations of chronic pharyngitis, these changes are accompanied by hyperemia and edema of the mucous membrane. However, in some cases of chronic pharyngitis, objective changes observed during pharyngoscopy may be less pronounced than the symptoms experienced by patients.

The development of chronic pharyngitis can be influenced by constantly difficult nasal breathing. This difficulty in breathing through the nose can be caused not only by a transition to mouth breathing but also by the excessive use of vasoconstrictor nasal drops. These nasal drops may flow down from the nasal cavity into the throat and have an excessive anematizing effect, contributing to the development of chronic pharyngitis. (5).

The development of chronic pharyngitis can be attributed to persistent difficulty in nasal breathing. Chronic pharyngitis may arise not only from the shift to mouth breathing but also from the misuse of vasoconstrictor nasal drops. These drops can flow down from the nasal cavity into the throat, leading to an excessive anematizing effect, thus contributing to the onset of chronic pharyngitis.(9)

Symptoms of pharyngitis may manifest due to postnasal drip. In such instances, the discomfort in the throat is linked to the flow of abnormal secretions from the nasal cavity or paranasal sinuses along the back wall of the pharynx. This condition can lead to persistent coughing and, more frequently in children, wheezing, which necessitates distinguishing it from bronchial asthma through differential diagnosis.

Chronic pharyngitis can be influenced by various factors, including:

• Constitutional features of pharyngeal and gastrointestinal (GIT) mucous membrane structure.
• Prolonged exposure to external factors like dust, hot dry or smoky air, and chemicals.
• Difficulty in nasal breathing, which can occur due to mouth breathing or excessive use of decongestants.
• Smoking and alcohol abuse.
• Allergic conditions such as pollinosis and food allergies.
• Endocrine disorders like menopause, hypothyroidism, and metabolic syndrome.
• Vitamin deficiency, particularly a lack of Vitamin A.
• Diabetes.
• Heart and lung failure.
• Renal failure.
• Disruptions in the intestinal microenvironment system, such as dysbiosis, irritable bowel syndrome (IBS), and other related disorders.

Notably, the development and persistence of chronic inflammatory processes in the posterior pharyngeal wall are significantly influenced by imbalances in the pharyngeal and intestinal microenvironments (dysbiosis). (5,10).

In a healthy individual, the normal microflora's quantitative and qualitative composition remains quite stable in various areas like the oral cavity, upper respiratory tract, and intestines. The person's microenvironmental phenotype is influenced by both genotypic characteristics and environmental factors.

In cases of chronic pharyngitis (CP), disruptions in the pharyngeal microenvironmental mucosa were observed. Under normal circumstances, the microorganisms residing on the mucous membrane of the oropharynx cannot penetrate the deeper tissue layers and cause an infectious and inflammatory process. However, in cases of mucosal dysbiosis, there can be an invasion facilitated by enzyme synthesis, which is linked to the suppression of specific and nonspecific factors of the body's natural reactivity.

This invasion leads to a local impairment of the mucociliary barrier, blood circulation, and increased vascular wall permeability. In the initial stages of inflammation, there is an increase in the levels of neutrophils, lymphocytes, and phagocytic cells. Subsequently, these levels decrease, leading to local and general immunosuppression. The transient and opportunistic pathogenic resident microflora becomes activated, eventually leading to the development of chronic inflammation in the

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tissues of the posterior pharyngeal wall and tonsils. (11).

Chronic inflammation in the mucous membrane of the nasal cavity, paranasal sinuses, larynx, and trachea can lead to focal or diffuse metaplasia of the multirowed columnar epithelium. This results in the formation of a multilayer epithelium without cilia. Such a modifiedepithelium loses its ability to actively remove bacteria and viruses from its surface through mucociliary transport. (5).

The pathogenesis of chronic pharyngitis is indeed multifaceted and involves several key processes:

Entry of Infectious Agents: Pathogens such as bacteria, viruses, or fungi enter the pharynx through inhalation or ingestion. These pathogens are recognized by toll-like receptors (TLRs) on the epithelial cells of the pharynx. TLRs identify pathogen-associated molecular patterns (PAMPs), which are unique to microbial invaders.

Immune Response Activation: The recognition of PAMPs by TLRs triggers the immune response. This leads to the release of pro-inflammatory cytokines, including interleukin-1 (IL-1), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α). These cytokines play a crucial role in mediating inflammation, causing symptoms such as redness, swelling, and pain in the pharyngeal tissues (79).

Recruitment of Immune Cells: The inflammatory response attracts immune cells like neutrophils and lymphocytes to the site of infection. Neutrophils are the first responders and help in phagocytosing (engulfing and digesting) pathogens. Lymphocytes, particularly B cells, are involved in antibody production, which helps in neutralizing the pathogens(80).

Mucus Production: Prolonged irritation and inflammation stimulate goblet cells in the pharyngeal mucosa to increase mucus production. This results in symptoms such as a sore throat and coughing, as the body attempts to clear the pathogens and debris.

Chronic Inflammation: If the infection or irritation persists, chronic inflammation can develop. This ongoing inflammatory state can be due to continuous exposure to infectious agents, environmental irritants (like smoke or pollutants), or conditions such as acid reflux. Chronic inflammation can lead to tissue damage and complications, including fibrosis or the formation of granulomas.

Understanding these process of pathogenesisis crucial for developing effective treatments and management strategies for chronic pharyngitis.

Sign and Symptoms

The following are the sign and symptoms for
Chronic pharyngitis is a persistent inflammation of the pharyngeal mucosa, submucosa, and lymphoid tissues. Here are the common signs and symptoms, including continuous coughing, with references from research papers and reviews:
Continuous Coughing: Persistent cough is a frequent symptom, often exacerbated by irritants or allergens.(76)
Sore Throat: Ongoing throat pain or discomfort, which may worsen with swallowing.(77)
Foreign Body Sensation: A feeling of something being stuck in the throat. (76)
Hoarseness: Changes in voice quality, such as hoarseness or a muffled voice.(77)
Dry Throat: Persistent dryness in the throat.(77)
Burning Sensation: A burning feeling in the throat.(76)
Difficulty Swallowing: Pain or discomfort when swallowing.(76)
Fatigue: General tiredness or weakness.(76)
Skin Rashes: Occasionally, skin rashes may appear.(77)

Diagnosis of chronic pharyngitis

The diagnosis of chronic pharyngitis (CP) involves employing a set of modern methods:
Survey: This includes identifying patient complaints and clinical symptoms such as sore throat, tickling sensation, mucus drainage on the back of the pharynx, and additional symptoms like dry mouth and paroxysmal cough.
Physical examination: A thorough examination is conducted, which involves inspecting the posterior pharyngeal wall using pharyngoscopy, palpation, and ultrasound examination of neck lymph nodes (submandibular, anterior, and posterior cervical). Common findings in CP include hyperemia, edema, and mucosal atrophy in the posterior pharyngeal wall, as well as the presence of granulomas of various sizes (mucosal hyperplasia).
Laboratory tests: The standard for laboratory diagnosis in CP is to culture a smear taken from the posterior pharyngeal wall to identify etiologically significant microflora (bacterial, fungal). Additionally, PCR (polymerase chain reaction) is used to diagnose chlamydia, mycoplasma, and various viral microflora such as herpes viruses (types 1, 2, and 6), cytomegalovirus, and Epstein-Barr virus. (12)

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In cases of chronic pharyngitis (CP), determining etiologically significant microorganisms based on patients' constant complaints can often be challenging. As a result, the introduction of new diagnostic methods for CP becomes highly crucial. Over 20 years ago, the method of mass spectrometry of microbial markers (MSMM) was developed and recommended for diagnostic use. This method allows the detection of 57 markers of microorganisms in the smear from the pharynx, which is a significant improvement compared to culture-based methods that can only detect 12-15 microorganisms.

During MSMM, the content of genetically stable biomarkers of microorganisms, including anaerobic cocci, actinomycetes, gram-negative microorganisms, enterobacteria (HP, Campylobacter), fungal markers, and viral markers, is determined. The test result and conclusion show the quantity of each microorganism per 1 ml of the biological sample. The test results can be obtained within 2 hours after transferring the biomaterial to the laboratory. (13).

Complications in Chronic Pharyngitis

The most common accompanying conditions and illnesses seen in cases of recurrent chronic pharyngitis include cervical lymph node lymphadenopathy (in 80% of cases), chronic tonsillitis, conjunctivitis, otitis media, sinusitis, maxillary sinusitis, labial herpes virus infection, Epstein-Barr virus infection (EBVI), laryngitis, tracheitis, bronchitis, pneumonia, and paratonsillar abscess (often due to streptococcal infection). (5) Continuous Coughing is the major issue in chronic pharyngitis that is not infectious. Person's Psychology could also be the reason for building long term coughing problem indirectly Chronic Pharyngitis (PSYCHOSOMATIC) .

When chronic pharyngitis is accompanied by chronic tonsillitis, it can lead to severe systemic complications such as rheumatic fever, rheumatic heart disease. glomerulonephritis (often associated with gram-negative bacteria), hematuria, psoriasis, urticaria, insomnia, and arthritis and this condition is more . (49)

Treatment & Management of Pharyngitis

There has been limited organized evaluation of treatments for non-infectious causes of Pharyngitis, and the field faces challenges due to the absence of concrete outcomes. Most studies depend on subjective (self-reported) endpoints. In cases where the chronic pharyngitis is non-infectious or viral, antibiotics would not be appropriate.

The treatment of chronic pharyngitis with antibiotics is generally focused on cases where there is a confirmed bacterial infection. Common antibiotic options include:

Penicillin: Often the first choice for bacterial infections, especially for Streptococcus pyogenes (Group A strep).

Amoxicillin: A broader-spectrum option that is effective against various bacteria.

Azithromycin or Clarithromycin: Macrolide antibiotics useful for patients allergic to penicillin.

Cephalexin: A cephalosporin antibiotic that may be used for certain bacterial infections.

It's essential to conduct a throat culture or rapid antigen test to confirm a bacterial cause before initiating antibiotic therapy.

In cases where the chronic pharyngitis is non-infectious or viral, antibiotics would not be appropriate

During the initial phases of the illness, otolaryngologists handle the treatment, and if patients don't achieve satisfactory clinical outcomes despite repeated courses of therapy, they should turn to immunologists for assistance.

Examinations of non-antibiotic therapies often face comparable challenges due to the incorporation of inclusion criteria such as 'acute pharyngitis' or 'chronic pharyngitis,' which are likely to encompass a blend of different causes.

A group of individuals experiencing sore throat as a result of functional dysphonia could potentially offer a more accurate representation of non-infectious causes, although studies in this regard are limited. Thus, there is a need for well-defined study populations focusing on non-infectious factors.

In cases where the chronic pharyngitis is non-infectious or viral, antibiotics would not be appropriate.

The effectiveness of non-antibiotic treatments, as observed in cases of acute sore throat (mostly infectious), is likely to extend to non-infectious sore throat as well.

This inference is grounded on the presumption that basic pain relief and anti-inflammatory effects are expected to be efficacious regardless of the cause, particularly when neurogenic inflammation is implicated.

In a comprehensive analysis of acute sore throat, it was observed that interventions yielding positive results within the initial 24 hours encompassed steroids, non-steroidal anti-

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inflammatory drugs (NSAIDs), caffeine, and paracetamol. Additionally, paracetamol and NSAIDs exhibited favorable effects on subsequent outcomes occurring after the first 24 hours. (58)These treatments might also work for non-infectious Pharyngitis.

Applying a combination of beclomethasone and lidocaine to the endotracheal tube proves to be a straightforward and efficient approach for diminishing the occurrence and intensity of post-operative sore throat. (60)

SYNTHETIC DRUGS

DIFFERENT DRUG COMBINATIONS

Limited research has been conducted on chronic pharyngitis, primarily consisting of small-scale studies. Flurbiprofen's effectiveness has been demonstrated (59), as it has the combination of Chinese herbs with acupuncture. (62)

Non-inferiority was confirmed, indicating that both flurbiprofen spray and lozenge delivered effective alleviation of sore throat pain as well as several other frequently reported attributes associated with Pharyngitis. (61)

Inhaled natural ether oils have also been utilized, although their composition remains largely undisclosed (63)

Montelukast belongs to a class of drugs called leukotriene receptor antagonists, it works for Bronchodilatation, reduced sputum eosinophil count, suppression of bronchial inflammation, mucus and hyperreactivity are noted in asthma patients.(74)

While the precise cause of sore throat in these individuals is not consistently well-defined, there are several treatments demonstrating potential for addressing enduring sore throat.Research focused on specific non-infectious sore throat cases remains limited. In a randomized study involving 60 patients with non-infectious acute upper respiratory tract inflammation, both nimesulide and flurbiprofen exhibited effectiveness. (64)

In experimental settings, the combination of paracetamol and caffeine has been shown to diminish the nasal tonic pain induced by dry air stimulation. Moreover, caffeine amplifies and extends the analgesic effect when compared to the control group. These findings substantiate the involvement of analgesics in managing non-infectious sore throat. (65)

Individuals experiencing sore throat due to functional dysphonia might respond well to addressing the root cause with strategies like vocal hygiene, voice training, minimizing exposure to irritants and allergens, and using co-medications such as proton pump inhibitors and anti-allergic drugs.

One of the most extensively studied groups in the non-infectious category is individuals with postoperative sore throat, which is highly prevalent, leading to numerous research endeavors. For instance, postoperative sore throat can be prevented by utilizing inhaled fluticasone propionate (66), intravenous dexamethasone (67), and lidocaine (68).

Additional remedies encompass ketamine gargle (69), topical non-steroidal anti-inflammatory drugs (NSAIDs) like benzydamine (70), perioperative use of amylmetacresol/dichlorobenzyl alcohol lozenges (Strepsils) (71), liquorice (72), and an azulene derivative extracted from chamomile (73).

The selection of the most suitable medication is influenced by its antimicrobial activity spectrum, lack of allergenicity, and absence of toxic effects. Therefore, the preferred approach often involves the local application of drugs with broad antimicrobial activity. Medications intended for the localized treatment of chronic pharyngitis can be categorized into seven groups: topical antibiotics, antiseptics, antiviral agents, immunomodulators, local anesthetics, anti-inflammatory drugs, and homeopathic remedies.

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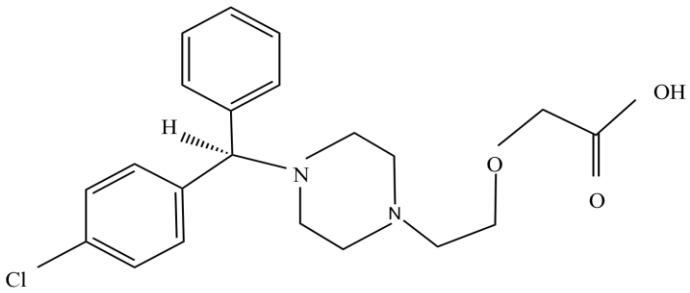

Structure: Levocetrizine

Source:ChemDraw Ultra

STRUCTURE ACTIVITY RELATIONSHIP

Levocetirizine is an antihistamine medication used primarily for treating allergies. The Structure-Activity Relationship (SAR) of levocetirizine refers to how changes in the chemical structure of the molecule affect its pharmacological activity. Here's a simplified SAR for levocetirizine:

Fundamental Structure: Levocetirizine, derived from cetirizine, belongs to the second-generation histamine H1 antagonist class, akin to loratadine and fexofenadine.(74)

Stereochemistry: Levocetirizine's efficacy is attributed to its R-enantiomer configuration, contrasting with the less active S-enantiomer of cetirizine (dextrocetirizine). (77)

Piperazine Ring: The integrity of the piperazine ring is pivotal for levocetirizine's activity. Any alterations to this ring could significantly impact its pharmacological properties.

Phenyl Ring Substituents: Levocetirizine's phenyl ring, adorned with various substituents, plays a crucial role in determining its potency, selectivity, and pharmacokinetic attributes. Modifying these substituents can lead to nuanced changes in the molecule's behavior. (75)

Chiral Center: Levocetirizine's chiral center is essential for its stereochemistry, influencing its interactions with biological targets. (75)

Aromaticity: The aromatic character, especially in the phenyl ring, is pivotal for levocetirizine's affinity towards histamine receptors. (75)

Functional Groups: Different functional groups within the molecule, such as the carboxyl group, contribute to receptor binding and other molecular interactions critical for its pharmacological activity.

Understanding levocetirizine's SAR is instrumental in designing novel antihistamine drugs with enhanced efficacy and safety profiles.

Mechanism of Action in Chronic Pharyngitis

Binding to Histamine Receptors:Levocetirizine is a selective antagonist of the histamine H1 receptor.It binds to these receptors on the surface of cells in the respiratory tract, blood vessels, and gastrointestinal tract.(78)

Blocking Histamine Action:By binding to the H1 receptors, Levocetirizine prevents histamine, a chemical released during allergic reactions, from attaching to these receptors. This action blocks the effects of histamine, which include inflammation, swelling, and increased mucus production.(78)

Reducing Inflammatory Response:Histamine is a key mediator in allergic reactions and inflammation. By blocking histamine, Levocetirizine reduces the inflammatory response, which helps alleviate symptoms such as swelling, redness, and irritation in the pharynx (throat).

Symptom Relief:The reduction in histamine activity leads to a decrease in symptoms associated with chronic pharyngitis, such as sore throat, itching, and discomfort. This makes breathing easier and reduces the urge to cough.

Additional Effects:Levocetirizine also has a mild sedative effect, which can help in reducing the discomfort and irritation caused by chronic pharyngitis. However, it is less sedative compared to first-generation antihistamines.

Internal Mechanism

Absorption:Levocetirizine is rapidly absorbed from the gastrointestinal tract after oral administration . It reaches peak plasma concentrations within 0.9 to 1 hour.

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Distribution:Once absorbed, it is distributed throughout the body, including the respiratory tract where it exerts its effects.

Metabolism and Excretion:Levocetirizine undergoes minimal metabolism in the liver and is primarily excreted unchanged in the urine. This means it has a relatively long duration of action, providing symptom relief for up to 24 hours. (as per drug bank online data of Levocetrizine)

By blocking the action of histamine and reducing inflammation, Levocetirizine effectively manages the symptoms of chronic pharyngitis, providing relief from discomfort and improving quality of life.

II. DISCUSSION

Chronic pharyngitis, characterized by persistent inflammation of the throat, requires a multifaceted approach that focuses on boosting immunity and promoting respiratory health.Treating Chronic Pharyngitis by Enhancing Immunity. Here are key discussion points:

1. Immune Support through Nutrition: A diet rich in vitamins (especially A, C, and E), minerals like zinc, and antioxidants supports immune function. Incorporating fruits, vegetables, whole grains, and lean proteins helps in combating inflammation and strengthening the body's defense against chronic pharyngitis.
2. Role of Aerobic Exercise in Respiratory Health: Regular aerobic exercise improves cardiovascular fitness and enhances respiratory efficiency. It facilitates the exchange of oxygen and carbon dioxide, promoting healthier lung function and reducing the likelihood of respiratory infections, including chronic pharyngitis.
3. Gargling with Warm Water: Gargling with warm saltwater or herbal solutions soothes the throat, reduces inflammation, and helps in clearing mucus and pathogens. This practice is beneficial in alleviating symptoms associated with chronic pharyngitis.
4. Nutritional Strategies for Immunity Boosting: Beyond specific nutrients, maintaining a balanced diet and staying adequately hydrated are essential for supporting immune function. Hydration helps in maintaining mucosal integrity in the throat, reducing irritation and discomfort associated with chronic pharyngitis.
5. Lifestyle Factors and Immune Function: Adequate sleep, stress management, and avoidance of tobacco and excessive alcohol consumption play pivotal roles in maintaining overall health and supporting immune response. These lifestyle factors contribute significantly to managing chronic pharyngitis and preventing its recurrence.
6.Pharmacological Intervations:In cases where the chronic pharyngitis is non-infectious or viral, antibiotics would not be appropriate.In case of infectious treatment the Antibiotics like Amoxicillin, Azithromycin and Cephalexin is effective for the infectious cause.
And the Anti-Allergic drugs like Levocetrizine and Montelukast intake usually works for the chronic condition of Pharyngitis.
7. Consultation with Healthcare Professionals: While self-care practices are beneficial, individuals with chronic pharyngitis should seek guidance from healthcare professionals for comprehensive diagnosis and treatment. Medical intervention may include medications to manage symptoms and address underlying causes, ensuring effective management and relief.

By discussing these points, individuals can gain insights into holistic approaches to managing chronic pharyngitis. Emphasizing immune-boosting strategies and lifestyle modifications not only aids in symptom relief but also promotes long-term throat health and overall well-being.

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