Use of Anti-Allergic and corticosteroid drugs in upper respiratory tract infection

LEARNING OBJECTIVES

• Identify upper respiratory tract infection.
• Indication of antihistamine drugs in upper respiratory tract infection.
• Indication of corticosteroid drugs in upper respiratory tract infection.
• Mode of action, pharmacokinetic, clinical uses, side effects, adverse effects, contraindication of antihistamine and corticosteroid drugs.

RESPIRATORY INFECTION

• Infections of the respiratory tract are described according to anatomical area of involvement.
• The upper respiratory tract consist of:
  • Pharynx, larynx, and upper part of the trachea.
• The lower respiratory tract consist of:
  • Lower trachea, bronchi, bronchioles,
  • and the alveoli.

RESPIRATORY TRACT

• Upper respiratory tract includes: nares, nasal cavity, pharynx, and larynx.
• Lower respiratory tract includes: trachea, bronchi, bronchioles, alveoli, and alveolar-capillary membrane
• Air enters the upper resp. tract & travels to the lower tract
where gas exchange takes place.

**Upper Respiratory Infection (URI)**

- **Def**: Acute inflammatory process that affects mucus membrane of the upper respiratory tract
  - Includes one or more of the following problems
    - Rhinitis — also called Coryza
    - Pharyngitis
    - Laryngitis
    - Sinusitis
- Pathophysiology — see next slide
- **Sx**: low-grade fever, malaise, cephalgia, sore throat, & discharge
  - Incubation period short — 2-3 days
    - As a rule: bacterial diseases = short incubation
      - viral diseases = long incubation except URI’s
- **Etiol**: over 200 different viruses have been implicated
  - can get secondary bacterial infection
- **Tx**: symptomatic
  - As a rule: bacterial diseases = short incubation
    - viral diseases = long incubation except URI’s
- **Etiol**: over 200 different viruses have been implicated
  - can get secondary bacterial infection
  - **Tx**: symptomatic

- **Upper Respiratory Infections (URI’s)** = common cold, acute rhinitis, sinusitis, acute tonsillitis, acute laryngitis
- **Common Cold & Acute Rhinitis** -
  - Common cold caused by the rhinovirus & affects primarily the
nasopharyngeal tract.
- **Acute Rhinitis** (inflammation of mucus membranes of nose) usually accompanies the common cold
- **Allergic Rhinitis** - caused by pollen or a foreign substance

**Drugs for Upper Respiratory Infections**

- Incubation period of a cold = 1 to 4 days before onset of symptoms & first 3 days of the cold
- Home remedies = rest, chicken soup, hot toddies, Vitamins
- 4 groups of drugs used to manage symptoms = antihistamins (H-1 blocker), decongestants (sympathomimetic amines), antitussives, expectorants

**UPPER RESPIRATORY INFECTIONS**

1. **Pharyngitis**

Hemolytic streptococci infection of the upper air way (throat).

**Clinical manifestations**

- Headache
- Abdominal pain
- Anorexia
- The tonsils and pharynx may be inflamed and covered with exudates.

**PHARYNGITIS THERAPEUTIC MANAGEMENT**

Antibiotics (penicillin, oral erythromycin ....etc.
Analgesic

2. **Tonsillitis**

Tonsils are masses of lymphoid tissue located in the pharyngeal cavity.

**Etiology**
• Tonsillitis often occurs with Pharyngitis.
• Viral or bacterial

Clinical manifestations
• Difficulty swallowing and breathing.
• The child breathes through the mouth.

Therapeutic management
• Tonsillectomy
• Adenoidectomy

3. Otitis Media

An inflammation of the middle ear without reference to etiology.

Etiology
• Bacteria
• A relationship between the incidence of OM and infant feeding methods.

Clinical manifestation
• Fever
• Acute ear pain
• Pulling or rubbing in the ear.
• Bulging yellow or red tympanic membrane.
• Rhinitis, cough, diarrhea.
• Purulent discharge
• Analgesic drugs (ibuprofen).
• An ice compress placed over the affected ear may also provide comfort and reduce edema.
• If the ear drainage, the external canal cleaned with sterile cotton swabs.
PREVENTION OF RECURRENCE THROUGH:

- Education regarding antibiotic therapy.
- Sitting or holding an infant upright during bottle feeding.
- Aware of potential complications as (loss of hearing).

4. CROUP
(Acute Spasmodic laryngitis)

Definition
A severe inflammation and obstruction of the upper airway (larynx).

Causes
- Viral (RSV, Influenza virus,
- Bacteria (pertussis, diphtheria, mycoplasma).
- Signs and symptoms
- Barking cough or hoarseness.
- Worse at night and can last 5 to 6 days.
- Decrease breath sounds.
- Dyspnea
- Fever

Complications
Respiratory insufficiency

Diagnostic test
- Throat cultures
- Laryngoscopy
- Neck Xray
HISTAMINE RECEPTORS

- H1
  - Bronchial constriction
  - Musous secretion
  - Intestinal smooth muscle contraction
  - Itching and pain at sensory nerve endings
- **H1** and **H2**
  - Reduces BP
  - Increase permeability in skin

<table>
<thead>
<tr>
<th>Location</th>
<th>Type of receptor</th>
<th>Effect</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>H1</strong></td>
<td>Throughout the body, specifically in smooth muscles, vascular endothelial cells, heart &amp; CNS</td>
<td>G-protein coupled, linked to intercellular Gq, which activates phospholipase C</td>
<td>Mediate an increase in vascular permeability at sites of inflammation induced by histamine</td>
</tr>
<tr>
<td><strong>H2</strong></td>
<td>Mainly in gastric parietal cells, low level can be found in vascular smooth muscle, mast cells, neutrophils, CNS, heart, &amp; uterus</td>
<td>G-protein coupled, linked to intercellular Gs</td>
<td>Increases the release of gastric acid</td>
</tr>
<tr>
<td><strong>H3</strong></td>
<td>Found mostly presynaptically in the CNS, with a high level in the thalamus, caudate nucleus &amp; cortex, also a low level in small intestine, testis &amp; prostate.</td>
<td>G-protein coupled, possibly linked to intercellular Gi</td>
<td>Neural presynaptic receptor, may function to release histamine</td>
</tr>
<tr>
<td><strong>H4</strong></td>
<td>They were discovered in 2000. They are widely expressed in components of the immune system such as the spleen, thymus &amp; leukocytes.</td>
<td>Unknown, most likely also G-protein coupled</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

- **H2**
  - Gastric secretio
Clinical Uses of Antihistamines

- Allergic rhinitis (common cold)
- Allergic conjunctivitis (pink eye)
- Allergic dermatological conditions
- Urticaria (hives)
- Angioedema (Swelling of the skin)
- Puritus (Atopic Dermatitis, insect bites)
- Anaphylactic reactions (severe allergies)
- Nausea and vomiting (first generation H₁-antihistamines)
- Sedation (first generation H₁-antihistamines)

Antihistamines compete with histamine for specific receptor sites

- **Two histamine receptors**
  - H₁ (histamine₁)
    - H₁ antagonists commonly referred to as **antihistamines**
    - Antihistamines have several properties
      - Antihistaminic
      - Anticholinergic
      - Sedative
  - H₂ (histamine₂)
    - H₂ blockers or H₂ antagonists
Used to reduce gastric acid in peptic ulcer disease

**RESPIRATORY SYSTEM DRUGS**

**ANTIHISTAMINES**

- 10% to 20% of the general population is sensitive to various environmental allergies

- **Histamine-mediated disorders**
  - Allergic rhinitis (hay fever, mold, and dust allergies)
  - Anaphylaxis
  - Angioneurotic edema
  - Drug fevers
  - Insect bite reactions
  - Urticaria (itching)

**RESPIRATORY SYSTEM DRUGS**

**ANTIHISTAMINES**

- **Mechanism of Action:**
  - Block action of histamine at the $H_1$ receptor sites
  - Compete with histamine for binding at unoccupied receptors
  - The binding of $H_1$ blockers to the histamine receptors prevents the adverse consequences of histamine stimulation
    - Vasodilation
    - Increased GI and respiratory secretions
    - Increased capillary permeability
Antihistamines

**Mechanism of Action**

Cannot push histamine off the receptor if already bound

- More effective in preventing the actions of histamine rather than reversing them
- Should be given early in treatment, before all the histamine binds to the receptors

**Histamine vs. Antihistamine**

**Cardiovascular (small blood vessels)**
- **Histamine effects**
  - Dilation and increased permeability (allowing substances to leak into tissues)
- **Antihistamine effects**
  - Reduce dilation of blood vessels
  - Reduce increased permeability of blood vessels

**Smooth muscle (on exocrine glands)**
- **Histamine effects**
  - Stimulate salivary, gastric, lacrimal, & bronchial secretions
- **Antihistamine effects**
  - Reduce salivary, gastric, lacrimal, and bronchial secretions
Immune system (release of substances commonly associated with allergic reactions)

• Histamine effects
  — Mast cells release histamine and other substances, resulting in allergic reactions

• Antihistamine effect
  — Binds to histamine receptors, thus preventing histamine from causing a response

Skin

• Reduce capillary permeability, wheal-and-flare formation, itching

• Anticholinergic
  — Drying effect that reduces nasal, salivary, and lacrimal gland secretions (runny nose, tearing, and itching eyes)

• Sedative
  — Some antihistamines cause drowsiness

Respiratory System Drugs
Antihistamines: Adverse Effects

• Anticholinergic (drying) effects, most common
  — Dry mouth
  — Difficulty urinating
  — Constipation
  — Changes in vision

• Drowsiness
  — Mild drowsiness to deep sleep
Drugs Used for Upper Respiratory Tract Infection

Adverse Effects
1. sedation
2. dry mouth
3. blurred vision

DRUGS FOR UPPER RESPIRATORY INFECTIONS - ANTIHISTAMINES

- Antihistamines or H-1 blockers - compete w/ histamine for receptor sites → prevents a histamine response.
- 2 types of histamine receptors - H-1 & H-2
- H-1 stimulation = extravascular smooth muscles (including those lining nasal cavity) are constricted
- H-2 stimulation = an increase in gastric secretions = peptic ulcer disease.
- Do not confuse the 2 receptors - antihistamines decrease nasopharyngeal secretions by blocking the H-1 receptor

DRUGS FOR UPPER RESPIRATORY INFECTIONS - ANTIHISTAMINES

- Histamines - A compound derived from an amino acid histadine.
- Released in response to an allergic rxn (antigen-antibody rxn) - such as inhaled pollen
  - When released it reacts w/ H-1 receptors = arterioles & capillaries dilate = inc. in bld flow to the area = capillaries become more permeable = outward passage of fluids into extracellular spaces= edema (congestion) = release of secretions (runny nose & watery eyes)

DRUGS FOR UPPER RESPIRATORY INFECTIONS - ANTIHISTAMINES

- Large amounts. of released histamine in an allergic infection= extensive arteriolar dilation = dec. BP, skin flushed & edematous = itching, constriction & spasm of bronchioles = increase secretion of pulmonary & gastric secretions

DRUGS FOR UPPER RESPIRATORY INFECTIONS - ANTIHISTAMINES

- Astemizole (Hismanal), Cetirizine (Zertec), Loratadine (Claritin), Chlorpheniramine (Chlortrimeton), Diphenhydramine (Benadryl)
• Actions = competitive antagonist at the histamine receptor; some also have anticholinergic properties
• Uses = Treat colds; perennial/seasonal allergic rhinitis (sneezing, runny nose); allergic activity (drying & sedation); some are also antiemetic
• SE = Drowsiness, dizziness, sedation, drying effects
• CI = glaucoma, acute asthma

Drugs Used for Upper Respiratory Tract Infection

ANTIHISTAMINES
> H1 receptor antagonist are chemical agents that act by competing with the allergy-liberated histamine for H1 receptor sites in the arterioles capillaries and secretory glands

> pt may develop tolerance and changing to another antihistamine may be effective

> more effective if taken before exposure to allergen

Examples
1. Brompheniramine Maleate (Dimetapp)
2. Diphenhydramine HCL (Benadryl)

Histamine H1 - Antagonists
First Generation: Sedating
Second Generation: Nonsedating

First Generation Agents

Examples

Ethanolamines: DIPHENHYDRAMINE (Benadryl)
CLEMASTINE (Tavist)

Ethylenediamine: TRIPELENAMINE

Alkylamine: CHLORPHENIRAMINE (Chlortrimeton)

Phenothiazine: PROMETHAZINE (Phenergan)
Piperazines: HYDROXYZINE (Vistaril) CYCLIZINE (Antivert)

**FIRST GENERATION AGENTS**

- Adjunctive in anaphylaxis and other cases where histamine release can occur (H₂ antagonist, and epinephrine must also be used in anaphylaxis)
- Antiallergy (allergic rhinitis, allergic dermatoses, contact dermatitis)
- Sedative/sleep aid
- To prevent motion sickness (meclizine, cyclizine)

**FIRST GENERATION AGENTS**

- Antiemetic: prophylactic for motion sickness (promethazine)
- Antivertigo (meclizine)
- Local anesthetic: (diphenhydramine)
- Antitussive (diphenhydramine)

**FIRST GENERATION AGENTS**

- Sedation (Paradoxical Excitation in children)
- Dizziness
- Fatigue
- Tachydyrsrhythmias in overdose - rare
- Allergic reactions with topical use
- Peripheral antimuscarinic effects
  - dry Mouth
  - blurred Vision
• constipation
• urinary Retention

FIRST GENERATION AGENTS

• Additive with classical antimuscarinics

• Potentiate CNS depressants
  • opioids
  • sedatives
  • general and narcotic analgesics
  • alcohol

Pharmacokinetics:
• Well absorbed from the GI-tract
• Widely distributed
  • Cross BBB
  • Placental transfer
• Hepatic transformation, renal elimination of the metabolites (induce hepatic microsomal enzymes)

SECOND GENERATION AGENTS

• Antiallergy
  • CETIRIZINE (Zyrtec)
  • FEXOFENADINE (Allegra)
  • LORATADINE (Claritin)
  • DESLORATADINE (Clarinex - FDA Approved In 2002)
• LORATADINE (Claritin Hives Relief - FDA Approved In 2004)
• AZELASTIN (Intranasal Spray)

SECOND GENERATION AGENTS

Adverse effects

• in general, these agents have a much lower incidence of adverse effects than the first generation agents.

• terfenadine (seldane) and astemizole (hismanal) were removed from the market due to effects on cardiac K+ channels - prolong QT interval (potentially fatal arrhythmia “torsades de pointes”)

• fexofenadine is active metabolite of terfenadine

Second Generation Agents

Adverse effects:

• Cetirizine appears to have more CNS actions (sedative) than fexofenadine or loratadine. recommended that cetirizine not be used by pilots.

• Erythromycin and ketoconazole inhibit the metabolism of fexofenadine and loratadine in healthy subjects, this caused no adverse effects.

Second Generation Agents

Pharmacokinetics:
Cetirizine (C), loratadine (L), fexofenadine (F)
• well absorbed and are excreted mainly unmetabolized form.
• C and L are primarily excreted in the urine
• F is primarily excreted in the feces
• They induce Cyt P450 liver enzymes

CORTICOSTEROIDS
Used to treat allergic nasal obstruction & chronic rhinitis (reduce: sneezing, itching, rhinorrhea & congestion).

**TOPICAL STEROID SPRAYS**
e.g., beclomethasone, budesonide, & fluticasone.

Corticosteroids have **anti-inflammatory action** by inhibiting leukotrienes & prostaglandins formation.

Histamine, platelet-activating-factor, kinins, & substance P are affected indirectly by the inhibitory effects of the corticosteroids on inflammatory cells.

Corticosteroids **Cont’**

Local corticosteroids are more effective compared to systemic antihistamines for allergic & non allergic rhinitis.

**Side effects:**
Localized to intranasal (nasal irritation, nose bleed, sore throat, candidiasis) Due to the anti-inflammatory & immunosuppressive effect of steroids.

**DRUGS FOR UPPER RESPIRATORY INFECTIONS - INTRANASAL GLUCOCORTICOIDS**

- Beclomethasone (Beconase, Vancenase, Vanceril), Budesonide (Rhinocort), Dexamethasone (Decadron) fluticasone (Flonase)
- Action - steroids used to dec. inflammation locally in the nose
- Use - Perennial/seasonal allergic rhinitis (sneezing, runny nose) - May be used alone or with/ antihistamines
- SE - rare, but w/ continuous use dryness of the nasal mucosa may occur

THANK YOU