REVIEW OF THE EXISTING RECOMMENDATIONS FOR ESSENTIAL MEDICINES FOR EAR, NOSE AND THROAT CONDITIONS IN ADULTS AND CHILDREN AND SUGGESTED MODIFICATIONS

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REVIEW OF THE EXISTING RECOMMENDATIONS FOR ESSENTIAL MEDICINES (Ear, Nose and Throat conditions) FOR USE IN ADULTS AND CHILDREN AND SUGGESTED MODIFICATIONS

Context: The WHO Essential Medicines List includes a section for ENT conditions in children. The current section does not make any reference to medicines and dosages recommended for adults. As most of the conditions for which the listed medicines are indicated, are common in adults, the list needs to be appropriately reviewed in that context.

Methodology:
Each of the medicines listed in the EML for children was reviewed to consider its appropriateness for inclusion in the EML for adults. The recommended dosages for adults and children were also considered.

Recommendations:
- The medicine list should include a list for adults as well as children.
- The list for adults should include Xylometazoline hydrochloride nasal spray 0.1%.
- It should be stated that the medicine (xylometazoline nasal spray) should not be used for prolonged periods of time, unless specifically advised and under medical supervision.
- The adult list should also include the other medicines mentioned in the list of children, i.e.:
  - Ciprofloxacin ear drops: 0.3%, as hydrochloride, for tropical use.
  - Aectic acid ear drops, 2% in alcohol, for topical use.
- Budesonide nasal spray listed in the EML for children needs greater, in depth review, which may be considered for the next EML update.
Xylometazoline Hydrochloride nasal spray

Indications:
Nasal congestion is obstruction of nasal passages, mainly caused by mucosal inflammation due to increased venous engorgement, nasal secretions and tissue swelling. It is a common symptom of upper respiratory disease such as rhinitis (both allergic and non-allergic), rhino-sinusitis and viral infection (common cold) as well as nasal polyps and foreign body. Nasal congestion, in turn, can also lead to sequelae such as sinusitis, otitis media, and sleeping disturbances including obstructive sleep apnea. Patients with nasal congestion have a poor quality of life related with daily activities as well as sleeping pattern. Nasal congestion is easily diagnosed by patient history, physical examination (to assess the severity) as well as measuring of nasal resistance and other methods, as needed.

Decongestants are one of the main conservative managements of nasal congestion in adults and children alike. It reduces blockage and related symptoms of mucosal hypersecretion as well as facilitates draining of blocked secretions. Easily accessible (often without prescription), they can be self-administered and have a fast action after topical application. Due of this, the need for decongestants and frequent self-medication among patients with reversible nasal congestion has increased. Most physicians are also in favour of prescribing nasal spray decongestant, especially xylometazoline, due to the quick response and long duration of effect as well as lesser myocardial and bronchiolar effects as compared to systemic decongestants.

Xylometazoline is one of topical vasoconstrictors belonging to imidazoline group of medicines, which cause local vasoconstriction by stimulating the adrenergic receptors on the lamina propria of vessels. However, studies have revealed that misuse and overuse of xylometazoline leads to rebound congestion, hyper-reactivity, tolerance, and histologic changes of nasal mucosa. The objectives of this paper are to assess the optimal dosage of xylometazoline use in adults and children; as well as to determine the duration for which the medicine can be used safely.

**Method**

Online literature search was conducted using PubMed, GIFT and Summon. Relevant articles related to the topic were identified and downloaded. Systematic review conducted on 5 exactly related articles to Xylometazoline overuse; over 11 general articles on rhinitis medicamentosa, pathophysiology and diagnosis; and medicine board report and pharmacology book one each on medicine dosage.

**Medicine preparation and dosage**

Xylometazoline hydrochloride nasal spray and drops are marketed as different brands such as Neo-Rinoleina®; Novorin®; Olynth®; Otriven®; Otrivin®; Otrivine®; Xymelin®; Sudafed® , Triofan and more. Most brands are marketed in the two strengths: 0.1% and 0.05% respectively for adults and children. Most products recommend usage of Xylometazoline nasal spray in adults and children over 12 years of age. A report of Medicines Evaluation Board in Netherlands recommends that Xylometazoline Hydrochloride Nasal Spray 1mg/ml (0.1%) be used in adults and children over 10 years of age. The prescribing information may vary with brands eg Triofan® (xylometazoline

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nasal spray) has divided the dose in three categories: as adult and children above 6 years; children until at the age of 6; and infants.

The appropriate usage of Xylometazoline in adults and children efficiently reduces congestion and related symptoms of mucosal hypersecretion as well as facilitates draining of blocked secretion. A study conducted on adults in Sweden shows that neither the increased dosage over 0.1% concentration (for example: 0.2, 0.3, 0.4%) nor the increased frequency of administration makes a difference to the decongestant effect on nasal mucosa or on rebound swelling. Therefore, the optimal adult dosage is 0.1% xylometazoline hydrochloride solution, 2-3 times spray per day; whereas it is 0.05%, 2-3 times a day for children.

**Mechanism of Action**
Facilitation of air flow in the congested nose is done by activation of α-adrenergic receptors in vessels of the nasal mucosa. The receptors that mediate this effect are α1-adrenergic and α2-adrenergic for veins and arterioles respectively. The contraction of the α2-adrenergic receptors facilitates nutritional supply of nasal mucosa, whereas α1-adrenergic receptor stimulates the erectile characteristics of blood vessels, which enhances venal fluid return. This phenomenon can be induced by spraying xylometazoline nasal decongestant and alleviates the nasal obstruction and facilitates air flow as well.

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8 Triofan product leaflet is source of the information.
Long term use:
Long term use of topical imidazoline vasoconstrictors including xylometazoline induces rebound swelling and rhinitis medicamentosa. Studies have shown that histamine sensitivity in the nasal mucosa starts after 10 days of xylometazoline use. After about 20 days use, there is a significant effect on the nasal mucosa compared to the status prior to starting the treatment. So, the most effective period of xylometazoline treatment is the first ten days; and treatment period longer than 10 days leads to rebound nasal mucosal swelling in patients.

Rhinitis medicamentosa
According to Graf, rhinitis medicamentosa is defined as “a condition of nasal hyper-reactivity, mucosal swelling, and tolerance that is induced, or aggravated, by the overuse of topical vasoconstrictors with or without a preservative”.

Patients suffering from a chronic nasal obstruction such as deviated nasal septum, nasal polyposis, and vasomotor rhinitis are more likely to overuse nasal decongestants. The frequent use of decongestant to alleviate the chronic nasal obstruction, leads them to develop an additional condition (rhinitis medicamentosa), which may aggravate the feeling of nasal obstruction.

Nasal stuffiness during pregnancy related with the state of hormonal flux is also a reason for misuse of nasal drops and for developing rhinitis medicamentosa.

Rebound congestion develops as a vicious cycle unless its onset is identified. Rebound nasal mucosal swelling usually starts after 10 days of xylometazoline spray treatment.

But most people perceive that the recurrent nasal obstruction is due to weak medicine response or re-infection, rather its rebound congestion. Hence, they seek additional, treatment, which exposes them to further expenses beside the consequent health problem.\(^{19}\) However, the obstruction is due to mis/overuse of medicine (chemical), which induces rebound nasal congestion and not because of the infection.\(^{20}\) People often do not understand the cause for this recurrent congestion. The cause of this is the decongestants such as xylometazoline, oxymetazoline and benzalkonium chloride (preservative).\(^{21,22,23}\)

\(^{21}\) Graf, P. Rhinitis medicamentosa: aspects of pathophysiology and treatment. Allergy (Copenhagen), (1997); 52, pp. 28 – 34.
Acetic Acid and Alcohol

**Class:** Otic Anti-infectives

**Preparation:** isopropyl alcohol (70%) and acid acetic (2%) and continued every 8 hours for three weeks\(^ {24}\)

**Indications:** acetic acid is used to treat Otomycosis. It is a superficial mycotic infection of the outer ear canal. The infection may be either acute or subacute and is characterized by inflammation, pruritis, scaling, feeling of fullness and severe discomfort (Sander, 2001). It also works by stopping the growth of bacteria and fungus. Treating the infection reduces pain and swelling in the ear. This condition is common in all ages, mostly in tropical and subtropical parts of the world.\(^ {25}\)

Ciprofloxacin Ear Drops

**Class:** Otic Antibiotics

**Preparation:** Ciprofloxacin 0.3% suspension

**Indications**

Ciprofloxacin Ear Drops are indicated for the treatment of infections caused by susceptible isolates of the designated microorganisms in the specific conditions listed below:

Acute Otitis Media in pediatric patients (age 6 months and older) with tympanostomy tubes due to Staphylococcus aureus, Streptococcus pneumoniae, Haemophilus influenzae, Moraxella catarrhalis, and Pseudomonas aeruginosa

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Acute Otitis Externa in pediatric (age 6 months and older), adult and elderly patients due to Staphylococcus aureus and Pseudomonas aeruginosa. Otitis media is common in all age groups and most commonly managed with use of topical antibiotics.26