

Oral Adverse Drug Reactions in Paediatric Population : A Review

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Abstract

There are so many complaints started in paediatrics patients during medications for main disease .like altered taste ,burning sensation in mouth, feeling of swelling in tongue & mouth ,ulceration, couloration ,pigmentation in teeth Some times observed either hypersalivation, or hyposalivation ,painful small lesion in mouth etc .These all symptoms started after taking drugs and observed the drug induced injury start healing, after withdrawing drugs or stopping of drug, prove its drug reactions So This paper will highlights the side effects of drugs in paediatrics in oral cavity reaction.

KEYWORDS: Xerostomia, Dysgeusia, stomatitis, ptylism, glossitis, steven johanson syndrome, angioedema,

Introduction

Now a days use of drugs has become very common. Drugs are used for variety of indications and newer drugs are being introduced into the market. Many drugs have effect on the oral tissue health. So it is better to inform the treating physician about the drug being taken. It provides better understanding of the problem and treatment needed. Oral side effects of the medicines has been reviewed in the past. The three most frequent oral side-effects encountered with these medications were xerostomia (80.5%), dysgeusia (47.5%), and stomatitis (33.9%)¹ but in paediatric population there is not much literature. Hence this review was carried to find the oral side effects of medicines which are used in the paediatric population.

Material and methods: Pubmed and google scholar were searched for the articles on oral side effects of medicines. Their references were also reviewed. Also Paediatric books was looked into for oral side effects. Medicines which are prescribed in the paediatric population were included for the review.

Results: Adverse drug reaction is defined as “An appreciable harmful or unpleasant reaction resulting from intervention related to the use of a medicinal product, which predict hazard from future administration and warrants prevention or specific treatment or alteration of the dosage regimen or withdrawal of the product.”² High turnover rate of the cell and absence of keratinization of oral micros membrane make the oral tissue a major site of occurrence of side effects. Dry mouth, ulceration, opportunistic infections like candidiasis lead to difficulty in speaking and swallowing can commonly occur because of intake of drugs.

These following main Oral drug reactions are common in Paediatrics

Stomatitis:

It is the nonspecific inflammation of oral mucosa. It can be due to irritant (contact stomatitis) or allergic reaction to topical medication (stomatitis venenata) or due to Stomatitis venenata an inflammation of the oral mucosa as the result of contact allergy. hypersensitivity to systemically administered medicines (stomatitis medicamentosa)³. Repeated contact with the causative agent results in localized reaction in the oral mucosa. It appears as erythema or ulceration with or without burning sensation. The reaction can occur as early as one day after of drug usage or may occur after years of exposure. Contact stomatitis can be caused by chewing gums, antibiotics, aspirin, chlorhexidine , sodium lauryl sulfate in tooth paste etc.

Stomatitis venenata an inflammation of the oral mucosa as the result of contact allergy. The most common causative agents are volatile oils, chewing gums, toothpastes, antibiotic lozenges, mouthwashes, and topical anesthetics. Possible manifestations include erythema, angioneurotic edema, burning sensations, ulcerations, and vesicles.⁴

Stomatitis medicamentosa: It is stomatitis due to an allergic reaction to drugs ingested, hypersensitivity to systemically administered medicines (stomatitis medicamentosa)³. absorbed through the skin or mucosa, or given by hypodermic injection. Principal symptoms include vesicles, erosion, ulcers, erythema, purpura, angioedema, burning, and itching.⁵

Hypersensitivity reactions can occur on the oral mucous membrane alone or along with generalized skin reaction. Common hypersensitivity reaction occurring on the oral tissue is mediated by sensitized T Lymphocytes and it is a delayed type of reaction⁶. Discontinuation of offending drug usually resolves the lesion. Common drugs associated with these are barbiturates chlorhexidine, indomethacin, sulphonamides, pencillamine etc.

APTHOUS STOMATITIS AND APTHOUS ULCER:

Apthous stomatitis a recurrent disease of unknown etiology, characterized by one or more small round or oval ulcer(s) on the oral mucosa, covered by a grayish fibrinous exudate and surrounded by a bright red halo as also called aphthae, apthous stomatitis, and canker sore⁵. The lesions usually persist for 7 to 14 days and then heal without scarring. Called also aphthae, apthous stomatitis, and canker sore⁵. Various drug including NSAIDS, Captopril, Losartan and Penicillamine can cause apthous ulcers. NSAIDS cause local vasoconstriction. The malnourished oral mucosa may then ulcerate spontaneously or in response to local trauma.

DRY MOUTH (XEROSTOMIA)

Reduced salivary flow is known as xerostomia. The drugs which cause xerostomia not only cause reduced salivary flow but also decrease calcium & phosphate concentration which alter the buffer capacity of the saliva⁷. Salivation is controlled by autonomic nervous system. Dryness of mouth results from parasympatholytic activity or

sympathomimetic activity of drugs. Common problems encountered are altered taste, burning sensation, constant sore throat, hoarseness, speech and swallowing difficulty³ and dental caries. Anticholinergic drugs including, dimenhydrinate, diphenhydramine, imipramine, loratidine, chlorpromazine, promethazine. Sympathomimetics including isoproterenol, labetalol and methyldopa and miscellaneous drugs including metronidazole, omeprazole, amantadine, calcitriol, calcium supplements, metoclopramide, cisapride, ondansetron, carbamezipine, hydrochlorothiazide and frusemide also cause xerostomia.

PTYALISM

Increased salivation can be due to either impaired swallowing or increased formation of saliva. Increased rate of formation of saliva is known as ptyalism.⁸ It can occur because of altered function of salivary glands. Their saliva is watery and without its buffering capacity leading to decay of hard and soft tissues of the oral cavity. These drugs are causing Xerostomia Examples includes physostigmine, pilocarpine, dimercaprol, bethanecol.

TEETH DISCOLORATION

Teeth Discoloration may be intrinsic or extrinsic. Intrinsic stains are caused by drugs taken during development of tooth that is during the formation of enamel and dentin eg. Tetracycline which accumulates in enamel and dentin during development of teeth and appear yellow, brown discoloration of the tooth after development. Therefore Tetracyclines are not recommended below the age of eight. Extrinsic stains are taken up by tooth after development including tea & coffee stains, chlorhexidine and iron salts taken by mouth.

ORAL PIGMENTATION

Pigmentation may occur either due to local use or systemic absorption of drug in oral cavity. Heavy metals in dental amalgam result in pigmentation especially around the gingival margin of the teeth. Systemic medications causing mucosa pigmentation include antimalarials, zidovudine, ketoconazole, phenothiazines, phenytoin and minocycline⁹. It becomes more prominent in presence of plaque and inflammation the pigmentation may be temporary or permanent but usually discontinuation of drug resolve the pigmentation.

BLACK HAIRY TONGUE

Elongation of filiform papillae of the tongue result in formation of long hair like overgrowth which is black or brown in colour. It can occur over the time due to tea, coffee, food products, poor oral hygiene, due to chromogenic microorganisms which can occur because of excessive antibiotics such as methicillin, metronidazole, ampicillin-sulbactam and penicillin V potassium¹⁰. Drugs causing black tongue include methyldopa and bismuth subsalicylate¹⁰.

GLOSSITIS :

Inflammation of the tongue is known as glossitis and is characterized by intense pain and swelling that may referred to the ear. It usually results in difficulty in speaking and swallowing along with systemic signs such as fever and enlarged lymph nodes. Glossitis

though not a common side effect is seen with penicillin, tetracycline, lansoprazole etc. Atrophic glossitis is caused by Pyrimethamine¹⁰ due to folate deficiency.

LICHENOID REACTIONS

It is a drug induced reaction which has characteristic appearance as a white lace pattern on the buccal mucosa and may have erythematous erosive and ulcerative lesions. Usually these are unilateral and occur in close contact with restorative materials¹¹. They disappear after the discontinuation of the offending drug but may take several months. NSAIDS, angiotensin converting Enzyme inhibitors, chloroquine, pyrimethamine and sulfonamides have potential to cause oral lichenoid reactions¹².

STEVEN JOHNSON SYNDROME: This is a drug allergy caused by the following drugs Demeclocycline, lamotrigine, mephobarbital, minoxidil, Nevirapine, Nystatin, acetazolamide, azithromycin, carbamazepine, clindamycin, cotrimoxazole, phenytoin and sulfa drugs

DRUG INDUCED GINGIVAL HYPERPLASIA

It is the painless overgrowth of the gingival tissue, usually the interdental papillae are affected, later may extend to the other areas of gingivae¹³. This condition is aggravated in the presence of poor dental hygiene. Common drugs are cyclosporine, phenytoin, calcium channel blockers like nifedipine and oral contraceptives. Phenytoin causes deficiency of folic acid and folic acid supplementation may decrease gingival hyperplasia in some patients¹³. Sore gums are caused by potassium iodide and probenecid.¹⁰

TASTE DISTURBANCE(DYSGEUSIA)

Saliva plays an important role in taste perception. If the function of salivary glands is affected it also affects than it also affects the taste perception. It can also occur because of drugs which can cause total loss of taste or disturbance in correct identification of taste. Drugs causing dysguesia are Aspirin, cetirizine, antibiotic like pencillamine, ofloxacin, metronidazole, terbutaline, diltiazem, niclosamide, clarithromycin, cyclophosphamide.¹⁰

ANGULAR CHEILITIS

Oral Inflammation and cracking of corners of the lips this conditions is known as angular cheilitis. It is usually associated with fungal infections or due to drugs such as isotretinoin and drugs causing xerostomia.

ORAL CANDIDIASIS

At times the systemic drug therapy altering the oral microflora predispose the month to various bacterial and fungal infectious. Drugs suppressing the immunity of the individual also make the person more prone to opportunistic infections such as candidiasis. Examples include corticosteroids, antimicrobials (ampicillin alone and sulbactam combination, tetracycline , meropenem, griseofulvin), immunosuppressive agents, anticancer drugs etc.

ANGIOEDEMA

It is a drug induced hypersensitivity reaction occur either due to direct histamine release or as a consequence of alteration in bradykinin metabolism³. It manifests as swelling of

lips and tongue¹⁴ and there is risk of airway obstruction³. Drugs such as captopril, enalapril, lisinopril, itraconazole, lamotrigine, azithromycin, brompheniramine, penicillamine, quinidine, promethazine are important causes. Discontinuation of the offending drug helps to reduce or treat the oedema.

ABNORMAL BLEEDING

Drugs such as aspirin, NSAIDS, anticoagulants which thin the blood and drug induced thrombocytopenia as caused by chloramphenicol, penicillins, streptomycin and sulfonamides may lead to oral bleeding. Aspirin use in children younger than 19 years is limited to diseases such as Kawasaki disease and the juvenile arthritis. Broad spectrum antibiotics such as cephalosporins decrease Vitamin K level by altering gastrointestinal flora and may lead to bleeding disorder.

CARIOGENIC POTENTIAL OF PAEDIATRIC SYRUPS:

Many paediatric medicines showed high sugar concentration, pH values below the critical value and high titratable acidity values, all of which increase the medicines' cariogenic and erosive potentials¹⁵.

VESICO – BULLOUS LESIONS

Drug induced pemphigoid can occur with penicillamine, sulfonamides, NSAIDS, beta lactam antibiotics.¹⁶ They present with flaccid or tense bullae on an erythematous base and may affect other areas of the body as well. It is difficult to distinguish from lichen planus therefore careful history is important and responds to discontinuation of drug^{3,17}.

FIXED DRUG ERUPTIONS

An idiopathic skin eruption, which often recurs at the same place, every time a particular drug or a related congener is administered; FDRs may also occur with chemically unrelated drugs or disappear with repeated administration of the same drug. Clinical Sharply circumscribed edematous red-brown or purplish plaque that may be surmounted by a bulla¹⁸, Agents causing FDR phenazone, barbiturates, sulfonamides, quinine, tetracycline, food dyes, toothpaste.

TAKING CARE OF YOUR ORAL HEALTH DURING DRUG USE

Some easy ways to prevent or reduce the adverse effect of various drug therapies are as follows:

- Use of soft bristle tooth brush.
- Brush or rinse after every meal.
- Use mild tooth paste.
- Regular use of floss without injury in gums.
- Eat dry nuts & alters food that stimulate salivary flow.
- Have regular dental check up.
- Use of ice chips to decrease pain and dryness of mouth(3).

Whenever a patient comes with oral lesions ask about history of medications and if significant then either reduce to the minimum dose required or switch to alternative regimen depending upon the severity of symptoms. Sometimes active treatment of the concerned effect may also be required.

CONCLUSION: Although side effects of drugs which are used in Paediatric population have been reviewed further studies are required to look into the paediatric population actually using these drugs.

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