RISK MANAGEMENT STRATEGIES FOR REDUCING ORAL ADVERSE DRUG EVENTS

Ann Eshenaur Spolarich, RDH, PhD[a,b]

SORT SCORE			
A	**B**	C	NA

SORT, Strength of Recommendation Taxonomy

LEVEL OF EVIDENCE		
1	**2**	3

See page A8 for complete details regarding SORT and LEVEL OF EVIDENCE grading system

ABSTRACT

Oral adverse drug effects negatively impact oral health, comfort and function.

Background

Patients treated in the oral health care environment take multiple medications, many of which cause oral complications. Dental professionals are challenged with making recommendations to prevent or minimize drug-induced oral disease risks, while reducing symptoms to improve oral health quality of life.

Methods

This paper presents a critical analysis of current evidence regarding common oral adverse drug events, and reviews existing clinical practice guidelines based upon findings from published systematic reviews.

Results

There is a lack of sufficient, high quality evidence to support most recommendations for interventions to relieve signs and symptoms of drug-induced oral adverse events. Existing recommendations are largely based on data obtained from observational studies and case reports, and from randomized controlled clinical trials with significant design flaws and potential reporting bias. Outcome measures, especially those related to symptom relief and long-range benefits, are either insufficient or lacking.

Conclusions

Oral adverse drug effects are a common problem, and additional data is needed to support best practices for product recommendations to improve oral health in medicated patients.

Key word: Oral adverse drug events, xerostomia, drug-induced ulceration, mucositis, lichenoid drug reaction

[a]Division of Dental Public Health and Pediatric Dentistry, Ostrow School of Dentistry of USC, Los Angeles, CA 90089-0641, USA.

[b]National Center for Dental Hygiene Research & Practice, Ostrow School of Dentistry of USC, Los Angeles, CA 90089-0641, USA

Corresponding author. Tel.: +1 480 575 6630; fax: +1 480 629 5859. E-mail: spolaric@usc.edu

J Evid Base Dent Pract 2014;14S: [87-94]

1532-3382/$36.00

http://dx.doi.org/10.1016/j.jebdp.2014.04.009

INTRODUCTION

Patients seen in the oral health care environment often take multiple medications, which cause side effects that impact oral health, comfort and function. Dental professionals are expected to make recommendations for product interventions to prevent and/or reduce symptoms and to improve oral health quality of life. This paper examines current scientific evidence and existing clinical practice guidelines to support best practices to minimize risks associated with oral adverse drug events.

Alterations in Saliva

Hyposalivation and perception of dry mouth (xerostomia) are well-documented adverse drug effects. Decreased salivation is frequently observed with anticholinergic medications, as well as with sympathomimetics, sedative hypnotics, opiates,

Table 1. Drugs that cause dry mouth by decreasing salivary flow

Alpha receptor antagonists
Amphetamines
Anticancer drugs (cytotoxic drugs)
Anticholinergics
Antidepressants (selective serotonin reuptake inhibitors; norepinephrine/serotonin reuptake inhibitors; tricyclics)
Antihistamines
Anti-HIV drugs
Antihypertensives
Antimigraine drugs
Antipsychotics
Appetite suppressants
Benzodiazepines
Bronchodilators
Cytokines (interferons)
Decongestants
Diuretics
Drugs of abuse (cannabis, Ecstasy)
H_2 receptor blockers
Muscarinic receptor antagonists
Opioids
Proton pump inhibitors
Retinoids
Sedatives
Skeletal muscle relaxants
Sympathomimetics

Data from: Scully C. Drug effects on salivary glands: dry mouth. Oral Dis 2003;9:165–76; Abdollahi M, Radfar M. A review of drug-induced oral reactions. J Contemp Dent Pract 2003;4:10–31; Scully C, Bagan JV. Adverse drug reactions in the orofacial region. Crit Rev Oral Biol Med 2004;15:221–39.

antihistamines and muscle relaxants.[1] Drugs that cause dry mouth by decreasing salivary flow are listed in Table 1. Xerostomia also occurs without changes in salivary flow rate, notably with psychological conditions such as anxiety and depression, and following use of inhaled medications. More than 500 medications are associated with adverse effects on the salivary glands, and these mechanisms have been described elsewhere.[1]

Drug-induced salivary changes alter normal oral homeostasis, resulting in increased risk for bacterial, fungal and viral infections. Decreased production of salivary mucins decreases mucosal protection, contributing to risk for abrasion and trauma from foods, dental restorations and prosthetics, and oral hygiene devices. Loss of lubrication and mucosal integrity contributes to pain and discomfort from ulceration and inflammation. Patients may experience difficulty with normal oral function, especially eating, swallowing and speaking.

Interventions for Xerostomia

A wide range of commercial products are marketed for the relief of dry mouth. Clinicians can choose from both pharmacologic and non-pharmacologic interventions to help patients manage their symptoms. Dental professionals frequently recommend use of over-the-counter (OTC) salivary replacement therapies that contain carboxymethylcellulose to simulate the viscosity of natural saliva. These products provide only temporary relief from xerostomia. Many products also contain glycerin as a humectant and coating agent for lubrication, and some contain sugar alcohols for caries protection. All are alcohol-free and sugar-free. These products are affordable, but compliance may be problematic due to the limited duration of improvement of symptoms, taste, viscosity and inconvenience of frequent dosing.

Parasympathomimetic drugs (e.g. pilocarpine, cevimeline) stimulate salivary flow, and are approved for use in patients who have undergone radiation therapy and for those with Sjögren's syndrome. Because these drugs are taken systemically, there are risks for side effects, drug interactions and contraindications which limits their widespread applicability. A small systematic review of 3 randomized controlled clinical trials (RCTs) found that pilocarpine was more effective than placebo, and was at least as effective as salivary substitute for subjects with radiation-induced xerostomia. However, only half of participants responded positively to the intervention, and dose-dependent side effects and the delayed time to onset of relief limited compliance and utility of this intervention. There is a lack of evidence to support using pilocarpine and other parasympathomimetics for this population.[2]

Acupuncture and electrostimulation have also been studied as non-pharmacologic interventions in subjects with a history of radiation therapy or Sjögren's syndrome. Most studies utilized small sample sizes, and outcome measures on relief of dry mouth symptoms were either missing or limited. Long-range effects on salivary production and symptom relief have not been studied.[3] One small RCT with 61 subjects with medication-induced xerostomia demonstrated that use of a sonic toothbrush improved salivary flow as compared to a manual toothbrush, and after 3 years, follow-up survey results showed that 98.2% of subjects reported enhanced salivary flow, and 92.7% indicated that they would continue to use the brush to increase salivary flow. Despite the small sample size and high bias potential, these findings add to the growing evidence base that supports the benefits of and compliance with sonic toothbrushing.[4]

There are numerous RCTs that have examined efficacy of salivary stimulants and salivary substitutes against one another and against a placebo. However, many studies are at high risk for bias due to their commercial nature, and measures and outcomes vary considerably across trials.[5]

A systematic review examining the efficacy of topical interventions for treatment of dry mouth symptoms found that there is a lack of strong evidence to support any particular topical therapy for this indication.[5] For salivary substitutes, oxygenated glycerol triester spray appears to be more