Advances in Dentistry & Oral Health
ISSN: 2472-6389

Juniper Publishers
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Review Article
Volume 5 Issue 2 – June 2017
DOI: 10.19080/ADOH.2017.05.555656

Adv Dent & Oral Health

Challenge Management of Oral Lichenoid Drug Reaction

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Submission: May 18, 2017; **Published:** June 20, 2017

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Review

Table 1: Drug-induced Oral Lichenoid Reactions (OLDR).

ACE inhibitors, Abatacept, Adalimumab, Allopurinol, Aminosalicylate sodium, Amiphenazole, Amphotericin B, Antimalarials, Arsenic, Atenolol
Barbiturates, BCG vaccine, Benzodiazepines, Beta-adrenoceptor blockers, Bismuth
Captopril, Carbamazepine, Carbimazole, Chloral hydrate, Choroquine, Chlorpropamide, Chorothiazide, Cholera vaccine, Cemetidine, Cinnarizine, Clofibrate, Clopidrogel, Colchicine, Cyamide (calcium carbamide), Cyanamide, Cycloserine
Dactinomycin, Dapsone, Demeclocycline, Dipyridamole
Enalapril, Escitalopram, Etanercept, Ethambutol, Ethionamide
Fenclofenac, Flunarizine, Furosemide
Glipizide, Gold salts, Griseofulvin
Hepatitis B vaccine, Hydrochlorothiazide, Hydroxychloroquine
Imatinib, Indomethacin, Infiximab, Insulin, Interferon-alpha, Isoniazid
Ketoconazole
Lebetalol, Levamisole, Levopromazine, Lincomycin, Lithium, Lorazepam
Mepacrine, Mercury (amalgam), Metformin, Methyldopa, Metoprolol, Metronidazole, Methopromazine
Naproxen, Niridazole, NSAIDs
Oral contraceptives, Oxcarbazepine, Oxprenolol (AQ)
Palladium, Para-aminosalicylate, Penicillamine, Penicillins, Phenindione, Phenothiazines, Phenylbutazone, Phenytoin, Piroxicam, Practolol, Prazosin, Procainamide, Propranolol, Propylthiouracil, Protease inhibitors, Prothionamide, Pyrazinamide, Pyrimethamine, Pyritinol
Quinacrine, Quinidine, Quinine
Rifampicin, Rifampin, Rituximab, Rofecoxib
Simvastatin, Spironolactone, Streptomycin, Sulfametoxazole, Sulfasalazine, Sulfonylureas, Sulphonamides
Tetracycline, Thiazides, Thyroxine, Tocainide, Tolbutamide, Tricyclic antidepressants, Triprolidine
Valproate sodium
Zidovudine

Medications have been extensively used for the treatment of patients with systemic diseases; however, some of those drugs may have side-effects to the oral cavity or other organs [1]. Clinicians and oral medicine specialists should thoroughly assess the patients' systemic diseases, current medications and previous medication use when lesions first appeared in the oral cavities. Red and white oral lesions in the patients could be diagnosed as oral lichen planus (OLP), oral lichenoid drug reaction (OLDR), OLP/Lupus erythematosus (LE), immune complex mediated disease, chronic ulcerative stomatitis-like diseases (CUS-like diseases) and etc. [2,3]. Previous reviews have demonstrated that many drugs can induce OLDR [4-7] (Table 1). Nevertheless, management of such oral lesions is challenging, particularly because the patients could not remember the exact onset of oral lesions before or after taking their medications. Therefore, definitive diagnosis of OLDR is difficult because the confirmation of drug-induced lesion is when discontinuation of the suspected drug leads to the improvement or resolution of lesion and when the same drug is re

challenged, the lesion recurs. However, in reality, it is impossible to perform the diagnosis of OLDR by this method as the ethics is strongly concerned during treatment and management of the patients. Naranjo algorithm is found to be useful for oral medicine specialists to analyze the possibility of drug induced oral lesions (Table 2). Treatment of OLDR in patients who had systemic diseases and taking multiple medications is very difficult and requires alternative treatment methods because those medications are essential for the patient's life [8]. Our challenging OLDR case with a long-term course of observation, although the patient had been taking several medications, she reported that her oral symptoms and lesions appeared after taking hypolipidemic drug (Simvastatin). By Naranjo algorithm, her score indicated of +3 (1-4 = possible ADR). We suggested that this hypolipidemic drug may be the cause of her OLDR. Nonetheless, due to the fact that this drug was not withdrawn in this case, the relationship between OLDR and this drug cannot be directly established. Finally, the patient later developed oral epithelial dysplasia and carcinoma in-situ within areas of OLDR approximately 7 - 8 years respectively after its initial presentation [9]. We recommend oral medicine specialists to inquire and investigate the list of OLDR-induced drugs in patients who with suspected drug-induced oral lesions. If those drugs possibly relate to oral lesions, then refer the patients to the physicians for consideration of changing the suspected drug to the others as appropriate. For examples, some medications such as anti hypertensives have different drug groups and one could be possibly replaced by the others. Understanding genetic risk factors for adverse drug reaction (ADR) requires well-organized patient genetics information and analysis by pharmacogenomic approaches. Clinicians can be assisted with the integrated knowledgebase to minimize the risk of ADR [10]. In summary, medications used in the patients with systemic diseases are required to investigate carefully by the oral medicine specialists through medical history taking. It is very important to know the exact causative drug that can induce oral lesion. In addition, the eruption of oral lesion after taking medication is also key information for the diagnosis of OLDR. Cooperation between physician and oral medicine specialist have been found to be useful in the successful management of OLDR.

Table 2: Naranjo algorithm and scoring guide.

Questionnaire	Naranjo Score
1. Are there previous conclusive reports on this reaction?	Yes (+1) No (0) Do not know or not done (0)
2. Did the adverse events appear after the suspected drug was given?	Yes (+2) No (-1) Do not know or not done (0)
3. Did the adverse reaction improve when the drug was discontinued or a specific antagonist was given?	Yes (+1) No (0) Do not know or not done (0)
4. Did the adverse reaction appear when the drug was readministered?	Yes (+2) No (-1) Do not know or not done (0)
5. Are there alternative causes that could have caused the reaction?	Yes (-1) No (+2) Do not know or not done (0)
6. Did the reaction reappear when a placebo was given?	Yes (-1) No (+1) Do not know or not done (0)
7. Was the drug detected in any body fluid in toxic concentrations?	Yes (+1) No (0) Do not know or not done (0)
8. Was the reaction more severe when the dose was increased, or less severe when the dose was decreased?	Yes (+1) No (0) Do not know or not done (0)
9. Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	Yes (+1) No (0) Do not know or not done (0)
10. Was the adverse event confirmed by any objective evidence?	Yes (+1) No (0) Do not know or not done (0)

Scoring

a. ≥9 = definite ADR

b. 5-8 = probable ADR

c. 1-4 = possible ADR

d. 0 = doubtful ADR

Acknowledgement

We would like to thank Research Unit in Oral Diseases Oral Medicine staff for their kind assistance.

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How to cite this article: Paswach W, Patamaporn N, Kobkan T. Challenge Management of Oral Lichenoid Drug Reaction. Adv Dent & Oral Health. 2017; 5(2): 555656. DOI:10.19080/ADOH.2017.05.555656.

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