

# Desloratadine in the Treatment of Acne Vulgaris: An Overview

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## **Abstract:**

**Background:** There are different common treatments for acne vulgaris based on the severity of lesions. In mild cases, topical drugs as topical clindamycin or erythromycin, tretinoin, benzoyl peroxide, and adapalene, and other keratolytic drugs (e.g., alpha-hydroxy acid), salicylic acid-containing medicine, and/or sulfur or azelaic acid-containing drugs are used. In more severe cases, systemic treatments, such as tetracycline, doxycycline, azithromycin, minocycline, azithromycin, and cotrimoxazole are used. Oral isotretinoin is also administered. In cases with associated hormonal abnormalities, spironolactone and dexamethasone are used. Desloratadine, the active metabolite of loratadine, is a second-generation non-sedating oral antihistamine with proven efficacy and safety in treatment of acne vulgaris. It is squalene-reducing agent, along acting tricyclic antihistamine, anti-inflammatory, mast cell degranulation inhibitor, and has antichemotactic activities against many inflammatory cells, in addition to its sebum regulatory effect

## **Acne vulgaris**

Acne vulgaris is a chronic inflammatory disease of pilosebaceous unit that can affect people of all age groups (1). It is a multifactorial disease in which several factors have been implicated, including, follicular hyperkeratinization, hormonal effects, proliferation of P. acne, environmental and genetic factors. The inflammation plays one of the major roles in the development (2).

The psychological impact of acne and body image issues is associated with the acne can result in the depression social isolation, anxiety, and low self-esteem (3).

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In acne vulgaris, gram-positive bacillus, plays a role in the inflammation and produce low-molecular weight, serum independent chemotactic factors that attract neutrophils through the epithelium wall, into the lumen of sebaceous follicles. It activates the classical and alternative complement pathways cause formation of C5a, that induces the secretion of pro-inflammatory cytokines, including (TNF  $\alpha$ ), IL-1 $\beta$ , and IL-8 by monocytes (3,4).

## **Clinical Manifestations of AV:**

Acne is generally limited to the parts of the body that have the largest and most abundant sebaceous glands. The face and upper neck are the most commonly affected but the chest, back and shoulders may have acne lesions which are comedones, inflammatory papules, pustules and nodules. Cysts and nodulocysts was described in severe cases of inflammatory acne (5).

Closed comedones are known as whiteheads because they appear as whitish to flesh coloured papules with an apparently closed overlying surface. Open comedones (black heads) appear as flat

or slightly raised brown to black plugs that distend the follicular orifices. The dark colour is due to oxidation of melanin pigment (6).

#### **Diagnosis of AV:**

Generally, patients with acne do not require further investigation apart from those required for starting treatment. The clinical suspicion of hyperandrogenism syndromes, further studies are wanted (7).

Laboratory investigations include serum luteinizing hormone: follicle stimulating hormone ratio, testosterone, dehydroepiandrosterone sulphate (DHEAS), prolactin, cortisol and 17-alpha hydroxyprogesterone. Adrenal tumors are suspected if DHEAS is greater than 8000 ng/ml. Ovarian or testicular tumors are suspected if total testosterone is greater than 200 mg/dL. There may be a place for thyroid function tests, lipids, glucose tolerance/insulin resistance tests and dexamethasone suppression. Other tests for distinguish precocious puberty. Radiological examination is required if suspecting visceral tumors or polycystic ovaries (8).

#### **Management of acne vulgaris:**

To determine the appropriate treatment, a thorough medical and family history should be obtained. Certain medications may aggravate acne and interact with the prescribed drugs, and a family history of severe acne determines a more protracted course. The duration of the disease, past and present response to therapy, and skin type are factors which guide therapeutic decisions. Grading of acne should be attempted, focusing on the severe lesions present and on the presence or psychological scarring (9).

The therapeutic goals in acne are to resolve existing lesions, prevent scarring, and suppress the development of new lesions. Successful management of acne and helping the patient to use the medications as directed (5).

#### **Desloratadine**

Desloratadine is a tricyclic H1 antagonist that is used to treat allergies. It is an active metabolite of loratadine (10).

#### **Pharmacodynamics:**

Desloratadine is a selective H1-antihistamine which functions as an inverse agonist at the histamine H1 receptor. It is an antagonist of the muscarinic acetylcholine receptors (11).

#### **Pharmacokinetics:**

Desloratadine is well absorbed from the gut and reaches highest blood plasma concentrations after about three hours. In the bloodstream, 83 to 87% of the substance are bound to plasma proteins. Desloratadine is metabolized to 3-hydroxydesloratadine in a three-step sequence in normal metabolizers. 3-hydroxylation of desloratadine N-glucuronide by CYP2C8; and a non-enzymatic deconjugation of 3-hydroxydesloratadine N-glucuronide occurred. Desloratadine and 3-hydroxydesloratadine are eliminated via urine and feces with a half-life of 27 hours in normal metabolizers (12).

It exhibits peripheral activity since it does not cross the blood-brain barrier; therefore not cause drowsiness and not enter the central nervous system. Desloratadine not have a strong effect on tested enzymes in the cytochrome P450 system. It was found to weakly inhibit CYP2B6, CYP2D6, and CYP3A4/CYP3A5, and not to inhibit CYP1A2, CYP2C8, CYP2C9, or CYP2C19. Desloratadine was found to be a potent and relatively selective inhibitor of UGT2B10, a weak to moderate inhibitor of UGT2B17 and UGT2B4, and not inhibit UGT1A1, UGT1A3, UGT1A9, UGT2B7, UGT2B15, UGT1A7, and UGT1A8 (13).

**Medical uses:**

Desloratadine is used to treat allergic rhinitis, nasal congestion and chronic idiopathic urticaria and major metabolite of loratadine and both are similar in safety and effectiveness. Desloratadine is available in dosage forms and under many trade names worldwide. An emerging indication for desloratadine is in the treatment of acne, as an inexpensive adjuvant to isotretinoin and possibly as maintenance therapy or monotherapy (14).

Desloratadine inhibits inflammatory mediators as IL-4, IL-6, IL-13, prostaglandins, leukotriene and histamine. Thus, desloratadine acts as an anti-inflammatory role and reduces the formation of squalene of the sebum (15).

In general, antihistamines had a sebum regulating effect; notably, they reduce squalene release, a biomarker of sebum by blocking the overexpressed histamine receptors in sebocytes, and this phenomenal effect and influenced by concomitant isotretinoin therapy due to retinoids (15).

A low release of sebum minimize microcomedone formation and subsequent inflammation antihistamines had a remarkable anti-inflammatory and antipruritic effects, minimizing the inflammation and scar formation (16).

The effect of adding antihistamine on the outcome of acne treatment. They pointed out that patients with a moderate type of acne were treated with isotretinoin with oral desloratadine achieved 77.1% reduction in the inflammatory lesions at the end of the trial (10).

Different types of inflammatory lesions responded variably to treatment; the pustules in those who received additional desloratadine demonstrated earlier reduction (within first 4 weeks of treatment) compared to the control group; this finding is difficult to explain, however, it may be related to the synergistic effect of desloratadine in ameliorating the inflammatory acne lesions and antichemotactic effect by reducing the release of leukotrienes and chemotactic substances from mast cells (17).

An evidence for the involvement of inflammatory events in the very earliest stages of acne lesion development was shown by the favorable effect of desloratadine may not only involve the already formed lesions but also in prevent new lesion development (18).

Acne patients may experience better efficacy and clinical cure from the adjuvant use of H1-antagonists in combination with systemic isotretinoin, although the occurrence of cutaneous side effects of isotretinoin is not affected by such combination (18).

Therefore, antihistamines used as an 'adjuvant' in the treatment of all types of acne and the efficacy and tolerability of using H1-antagonist, as adjuvant therapy to oral retinoids in treating acne vulgaris in the clinical setting (19).

**Side effects:**

The most common side-effects are fatigue, dry mouth, and headache(20). Research indicates a correlation between intake of antihistamines by adults, adolescents and children, and weight gain, development of obesity and signs of metabolic syndrome by affecting dietary lipid absorption or lipid metabolism (21). Thus, desloratadine, a common second-generation antihistamine, and development of obesity-like phenotype and metabolic syndrome (22).

**Drug-drug interaction:**

- **Azithromycin:**

The risk or severity of QTc prolongation can be increased when azithromycin is combined with desloratadine (23).

- **Statins:**

There is a synergistic myotoxicity of simvastatin and desloratadine, suggesting a role in loratadine–simvastatin interaction (24). However, no interactions were found between desloratadine and Rosuvastatin (25).

- **Azelastine:**

Desloratadine may increase the central nervous system depressant (CNS depressant) activities of Azelastine (26).

- **Hydrochlorothiazide:**

Hydrochlorothiazide is a thiazide diuretic used to treat edema associated with a number of conditions, and hypertension. The risk or severity of QTc prolongation can be increased when hydrochlorothiazide is combined with desloratadine (27).

- **Hyaluronidase:**

Some studies suggested using of oral antihistamines (5 mg desloratadine following injection with hyaluronic acid for decreasing the inflammatory reactions (28). the use of desloratadine is recommended for facial angioedema following hyaluronic acid injection(29). While administration of oral desloratadine may interfere with the action of hyaluronidase(30,31).

Histamine has a possible role in acne pathogenesis by working as an inflammatory mediator in the process of immune reaction of inflammatory acne (32,33). Also, *Propionibacterium acnes* changes the pH of the microenvironment of the acne follicle which is an optimal environment for the production of histamine or histamine-like products leading to itching in patients with acne (34,35). In addition, in vitro study identifying histamine receptors and reduction of squalene levels by an antihistamine in sebocytes proved the role of histamine in sebum production (33). Putting together, antihistamine not only acts as an effective anti-inflammatory drug but also has shown to decrease the lipogenesis in sebocytes. However, evidence is lacking regarding the clinically relevant action of antihistamine in the treatment of acne, and its potential efficacy also needs to be clarified.

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