

## Case report

# Facial Itching With Missed Doses of Vilazodone

### ABSTRACT

**Aims:** Our aim is to describe a case of moderate to severe facial itching associated with missed doses of vilazodone.

**Presentation of Case:** This report concerns a 53-year old woman with systemic lupus erythematosus and major depressive disorder who experienced sporadic episodes of moderate to severe facial itching around her eyes, cheeks, and forehead after she was prescribed vilazodone.

**Discussion:** Investigation into the potential causes of the reaction determined that it was not consistent with a SLE malar rash, photosensitivity, hydroxychloroquine-induced lichenoid eruption, or menopausal-related dry skin. The facial pruritus did not respond to antihistamine pharmacotherapy. Symptoms always recurred following missed doses and resolved immediately within 90 minutes after taking the vilazodone. Full compliance with vilazodone has eliminated any further facial itching symptoms.

**Conclusion:** The authors conclude that vilazodone is the most likely source of the intense pruritus. The reaction occurred consistently after missed doses of the medication and other potential causes were ruled out. This case provides important evidence for health care practitioners to utilize when monitoring and educating of their patients about vilazodone.

*Keywords: vilazodone, facial itching, withdrawal symptom, nonadherence, treatment emergent adverse effect*

### 1. INTRODUCTION

It is estimated that 340 million people internationally, including 18 million US adults, suffer from major depressive disorder (MDD) [1]. MDD often recurs and may require lifelong therapy. MDD is most prevalent in those with chronic illness causing significant disability and health care expenditures [2-3]. The World Health Organization reports that unipolar depressive disorders are the third leading cause of global disease burden [4].

Systemic lupus erythematosus (SLE) is a chronic autoimmune disorder affecting women that targets several organs including the central nervous system. SLE often causes neuropsychiatric illness including depression and anxiety [5]. The prevalence of comorbid depression in SLE patients is high and ranges from 12 to 47% [6-8]. Therefore, antidepressant pharmacotherapy is a vital component for successful treatment of comorbid mental illness (e.g. depression, anxiety) experienced by SLE patients [9].

Many patients with MDD do not achieve an adequate response to pharmacotherapy even after several changes in their medication regimen. Additionally, treatment emergent adverse events (TEAEs) associated with antidepressants such as sexual dysfunction, weight gain, sleep disturbances, and fatigue are common causes for nonadherence and poor response [10]. In 2011, vilazodone was introduced in the United States for the treatment of MDD. It is considered a novel antidepressant and the first member of the serotonin partial agonist-reuptake inhibitor (SPARI) class that combines serotonin reuptake inhibition with 5-HT<sub>1A</sub> partial antagonism [11]. Vilazodone provides an alternative for those patients who do not respond or experience intolerable TEAEs to traditional first line pharmacotherapy such as selective serotonin reuptake inhibitors (SSRIs) and serotonin norepinephrine reuptake inhibitors (SNRIs). Based on its mechanism of action, vilazodone may also be beneficial in those with comorbid anxiety disorders and has less frequent sexual side effects than those reported with SSRIs and SNRIs. [11].

Vilazodone is generally well tolerated and the most common side effects are diarrhea, nausea, vomiting, headache, dizziness, dry mouth, and insomnia [12-15]. The manufacturer reports that abrupt discontinuation of vilazodone can lead to a myriad of symptoms including nausea, dysphoric mood, irritability, sweating, agitation, anxiety, tremor, headache, lethargy, hypomania, tinnitus,

42 sensory disturbances (e.g. paresthesia, electric shock sensations), seizures, and confusion [15]. As a  
43 result, gradual dosage reduction is recommended by the manufacturer when discontinuing vilazodone  
44 and abrupt cessation should be avoided whenever possible [15].  
45

## 46 2. CASE REPORT

47  
48 A 53-year old woman with SLE, fibromyalgia, chronic neck and low back pain, MDD, and post-  
49 traumatic stress disorder was taking escitalopram 30mg daily for several years. She experienced  
50 significant sexual side effects with the escitalopram and reported moderately severe morning fatigue.  
51 In late April, 2014, her psychiatrist tapered her off the escitalopram and prescribed vilazodone. The  
52 starting dose for vilazodone was 10mg a day followed by gradual increases of 10mg per week over a  
53 30-day period to a final dose of 40mg daily. Two months later, her rheumatologist prescribed  
54 hydroxychloroquine 400mg at bedtime for joint pain and swelling. Previously reported TEAEs for this  
55 woman include a rash with amoxicillin, severe nausea and vomiting with meperidine, and exacerbated  
56 SLE symptoms from ibuprofen. Menopausal symptoms experienced by the patient include occasional  
57 hot flashes, fluid retention, weight gain, and vaginal dryness. The patient reports that she has no  
58 difficulties with dry skin or hair loss.  
59

60 In addition to the vilazodone, she was taking bupropion XL 300mg daily, loratadine 10mg daily and  
61 fluticasone nasal 1 spray each nostril daily. Her "as needed" (prn) medications included: alprazolam  
62 0.5 to 1mg (3 to 4 doses/month), hydrocodone and acetaminophen 10/325 (3 to 4 doses/month),  
63 zaleplon 5mg (2 doses/month), acetaminophen 500mg (2-4 doses/week), and naproxen sodium  
64 220mg (2-3 doses/month). Of important note is that she has been maintained on these medications  
65 for several years without any significant TEAEs.  
66

67 In late September, 2014, the patient began having sporadic episodes of moderate to severe facial  
68 itching around her eyes, cheeks, and forehead. The patient states that she experienced a SLE  
69 butterfly or "malar" rash when she was first diagnosed in 1981 but it has not recurred. She  
70 consistently wears sunscreen when spending time outdoors. She reports taking diphenhydramine  
71 50mg as needed for the facial itching but do not receive any relief. Her rheumatologist determined  
72 that the reaction was not consistent with SLE-induced malar rash, photosensitivity, or a  
73 hydroxychloroquine-related lichenoid eruption.  
74

75 Upon further investigation, the patient reported missing one or more doses of vilazodone on occasion  
76 and noticed that the symptoms always reappeared during these instances. When she forgot to take  
77 her morning dose, the reaction began to manifest later in the evening and grew in intensity over time.  
78 She discovered that after taking the missed vilazodone dose all of her symptoms resolved within 90  
79 minutes. This finding was confirmed with repeated challenges and observation.  
80

81 The patient's SLE is currently in remission with normal findings on inflammatory and immunity  
82 markers (ESR 6 mm/HR; CRP < 0.20 mg/dl; C3 116 mg/dl, C4 20.4 gm/dl). She continues to have  
83 episodes of itching whenever she forgets to take her vilazodone.  
84

## 85 3. DISCUSSION

86  
87 There are several potential causes for the facial itching in this patient including SLE-related,  
88 medication-induced (vilazodone, hydroxychloroquine, hydrocodone), menopause, and  
89 photosensitivity. Her pain is well controlled, requires very little hydrocodone, and the itching does not  
90 coincide with hydrocodone dosing. The patient regularly wears sunscreen making a photosensitivity-  
91 like reaction highly unlikely. Additionally, it was determined that the dermatological characteristics  
92 associated with SLE, hydroxychloroquine, and menopause facial outbreaks are not consistent with  
93 the patient's presenting symptoms (See Table 1).  
94

95 SLE causes several cutaneous manifestations including malar or "butterfly" rash, photosensitivity,  
96 calcinosis, cutaneous vasculitis, nonscarring hair loss, petechiae, livedo reticularis, palmar erythema,  
97 Raynaud's syndrome, and mucosal ulcerations [9]. Most SLE-related cutaneous reactions occur on  
98 the torso or extremities. The malar rash is the primary facial manifestation, has a distinctive  
99 appearance, and is characterized by an erythema over the cheeks and nasal bridge that forms the  
100 shape of a butterfly [9]. The SLE malar rash is persistent and may appear scaly but is not pruritic or  
101 involve the eyes and forehead region [9].

102

103 Hydroxychloroquine can cause lichenoid skin reactions which are described as scaly, annular  
 104 eruptions that are centrally clear, very pruritic, persistent, and erythematous [15-17]. The lesions  
 105 produced by hydroxychloroquine are found on both sun-protected and exposed areas involving the  
 106 face, trunk, and extremities [16-18].

107

108 Menopause is commonly associated with several skin changes such as dryness and changes in  
 109 texture and tone [19-20]. Dry skin can occur just about anywhere on the body (e.g. face, back, chest,  
 110 elbows, genitals, fingernails) and is often associated with pruritus. Menopausal-induced pruritus is  
 111 manifested by small bumps on the skin surface, red or irritated skin, rash, and abnormal touch  
 112 sensations such as numbness, prickling, tingling, and crawling [20].

113

114 **Table 1. Symptom characteristics of patient presentation compared to SLE malar rash,  
 115 hydroxychloroquine lichenoid eruptions, and menopausal dry skin.**

116

Characteristic	Patient	SLE	Hydroxychloroquine	Menopause
Annular appearance	No	No	Yes	No
Centrally clear lesions	No	No	Yes	No
Dry skin	No	No	No	Yes
Eye area involvement	Yes	No	No	No
Persistent	No	Yes	Yes	Yes
Photosensitivity-related	No	Yes	No	No
Pruritic	Yes	No	Yes	Yes
Scaly	No	Yes	Yes	No
Torso and extremities involvement	No	No	Yes	Yes

117

118 Pruritus is not listed amongst vilazodone's adverse effects or withdrawal symptoms reported by the  
 119 manufacturer [15]. There is however anecdotal evidence available on internet blogs and online forums  
 120 discussing severe facial itching from vilazodone missed doses or during abrupt withdrawal of the  
 121 medication. Unfortunately, no published cases or FDA Medwatch reports are currently available to  
 122 inform the medical community of this significant TEAE.

123

124 Based on the evidence presented, vilazodone is the most likely source of the facial pruritus. The  
 125 patient's MDD and PTSD are well controlled, she no longer experiences morning fatigue or sexual  
 126 dysfunction and has decided to remain on vilazodone pharmacotherapy. She has not experienced  
 127 any further facial itching as long as she is 100% compliant with her vilazodone.

128

#### 129 4. CONCLUSION

130

131 Those suffering from chronic illnesses such as SLE frequently struggle with depression and anxiety.  
 132 Antidepressant pharmacotherapy is associated with several TEAEs (e.g. fatigue, sexual dysfunction,  
 133 sleep disturbance, weight gain, and gastrointestinal complaints) that often result in poor adherence  
 134 and discontinuance of pharmacotherapy [10]. Recognition and management of TEAEs can be vital to  
 135 successful treatment and improvement in health related quality-of-life. Many patients with MDD do not  
 136 achieve an adequate response to pharmacotherapy even after several changes in their treatment  
 137 regimen. The new SPARI class antidepressant vilazodone may offer a valuable alternative, be of  
 138 great benefit in those with comorbid anxiety disorders, and have less frequent sexual side effects than  
 139 those reported with other antidepressants [11].

140

141 This is the first case report documenting vilazodone-induced moderate to severe facial itching  
 142 associated with missed or delayed doses. There is anecdotal evidence available online, but  
 143 vilazodone-induced facial pruritus has yet to be reported to FDA Medwatch or by the manufacturer.  
 144 Thus, the information presented here offers valuable evidence for health care providers to consider as  
 145 part of educating and monitoring their patients taking vilazodone.

146

147 **CONSENT**

148

149 All authors declare that 'written informed consent' was obtained from the patient (or other approved  
150 parties) for publication of this case report."

151

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