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Case Report

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Case Report Using 4% Fucoidan Cream for Recurrent Oral Herpes Labialis: Patient Symptoms Markedly Improved in Terms of Time to Healing and Time to Loss of Discomfort

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ABSTRACT

Recurrent oral herpes labialis (ROHL) is a rather widespread oral ulcerative condition with an unclear etiology. The clinical characteristics of ROHL have been defined and therapies include systemic drugs and topical application of ointment to the lips. However, these approaches have not been rigorously evaluated. Persistent, painful ROHL was successfully treated with fucoidan in two patients. This study investigated the time required to complete healing and loss of discomfort. Two patients used Power Fucoidan Cream™ (PFC) (4% fucoidan cream). ROHL was markedly improved by Power Fucoidan Cream in terms of both time to healing and time to loss of discomfort. Further clinical trials are needed to confirm the value and safety of topical Power Fucoidan Cream for treating ROHL.

KEY WORDS: Recurrent oral herpes labialis; Vidarabine; Fucoidan; Cream; Clinical trial.

ABBREVIATIONS: ROHL: Recurrent Oral Herpes Labialis; HSV-1: Herpes Simplex Virus type-1; PFC: Power Fucoidan Cream; NSAIDs: Nonsteroidal Anti-Inflammatory Drugs.

INTRODUCTION

Oral herpes labialis is characterized as a recurrent condition with painful ulcerative eruptions varying from 2 mm to 2 cm in diameter on the mucous membranes of the mouth. Recurrent oral herpes labialis (ROHL), typically caused by herpes simplex virus type-1 (HSV-1), is believed to affect nearly 40% of the Japanese population.[1] As important factors in deciding treatment strategy, the diagnosis, clinical presentation, severity and medical history are considered. The goal of treatment is rapid pain management and suppression of the inflammatory response.

Antiviral drugs such as oral acyclovir (Zovirax™ 400 mg tid ×7 days), oral valacyclovir (Valtredx™ 500 mg bid ×5 days), topical acyclovir (5% Zovirax Cream™), and topical vidarabine (3% Arasena-A Cream™) have commonly been used for ROHL. Ten days was required for healing in untreated cases.[2] Fucoidan is a sulfated fucose-rich polysaccharide that was isolated from brown algae by Kylin in 1918.[3] Studies of the bioactivity and therapeutic value of fucoidan have been investigated and this compound has been confirmed to show anti-viral, anti-bacterial, anti-coagulant and anti-tumoral bioactivities.[4,5] Siddhanta and Murthy[6] demonstrated that fucoidan exerts anti-tumoral and anti-inflammatory effects. Aisa et al[7] reported that fucoidan exerted anti-cancer effects against human lymphoma HS-Sultan cells. These findings indicate that fucoidan may be useful as an antiviral medication and as therapy against various types of cancer. Furthermore, Takahashi et al[8] demonstrated that fucoidan improved quality of life in 20 patients with advanced cancer.

Power Fucoidan Cream (PFC; Daiichi Sangyo, Osaka, Japan) has been prepared as 4% fucoidan isolated from *Nemacystus decipiens*[9] in a base comprising stearic acid glyceryl, lectin, adenosine triphosphate, sodium alginate and other components that enhance permeability

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Figure 1: Power Fucoidan Cream™.

(Figure 1). Although, the medicinal uses of fucoidan have been investigated from the perspectives of cosmetics and skin-care agents, few studies have focused on oral disease. The present investigation initially examined the use of PFC for the treatment of symptomatic ROHL in two typical clinical cases involving pain upon eating and speaking and that had proven refractory to various medications. The outcomes of topical PFC application were remarkable. The results of PFC therapy from only two patients are difficult to interpret, because the observed responses might have simply reflected the natural course of the disease rather than the effects of medication. Although the mechanisms have not yet been fully elucidated, we believe that fucoidan cream exerted real therapeutic effects, because previously persistent lesions did not recur.

This is the first report of treating symptomatic ROHL with PFC.

CASE REPORTS AND STUDY DESIGN

CASE 1

A 30-year-old Japanese man presented with painful ROHL comprising multiple round, gray-based ulcers with regular margins and >1 cm in diameter on the surface of the lower lip that had persisted for 2 months (Figure 2A). His lifestyle was quite normal, he had never smoked or experienced any systemic disease, and he was unresponsive to oral or topical antivirals (Zovirax™ 400 mg tid for 7 days, and Zovirax™ 5% cream for 7 days 3 times per day) and non-steroidal anti-inflammatory drugs (NSAIDs). We prescribed PFC at 3 times per day for 1 week (Figure 2B). The patient took photographs of the affected area using his mobile phone 2 days (Figure 2C), 3 days (Figure 2D), 4 days (Figure 2E), 5 days (Figure 2F), and 6 days after starting PFC (Figure 2G). Conditions after application were also examined 1 week after starting PFC (Figure 2H). The minimum period was 1 week, and had followed-up for1 month (Figure 2I), 1 year (Figure 2J), and 3 years after this minimum period (Figure 2K).

CASE 2

A 38-year-old Japanese woman presented with painful ROHL comprising a single round, brown-based ulcer with regular margins, >1 cm in diameter, that had persisted for 1 month on the commissura labiorum (Figure 3A). ROHL had appeared intermittently over the past 5 years and had caused pain in the lips, as well as on the buccal and alveolar mucosa. Symptoms had been largely unresponsive to topical vidarabine (3% Arasena-A Cream™), anesthetic gel (lidocaine 2% viscous solution), vitamin B12 supplements, and NSAIDs. However, symptoms improved significantly after applying PFC 3 times per day (Figure 3B) for 1 week after starting PFC (Figure 3C). The patient remained free of side effects or recurrence after the minimum period for over 3 months of follow-up (Figure 3D).

Figure 2A: Before PFC Therapy.

Figure 2B: During PFC Therapy.

Figure 2C: Two Days After Starting PFC.

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Figure 2D: Three Days After Starting PFC.

Figure 2E: Four Days After Starting PFC.

Figure 2F: Five Days After Starting PFC.

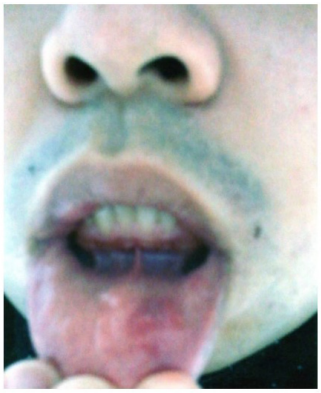

Figure 2G: Six Days After Starting PFC.

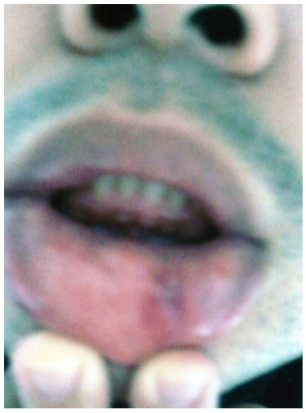

Figure 2H: One Week After Starting PFC.

Figure 2I: One Month After Completing the Minimum Period [is this what you mean?]

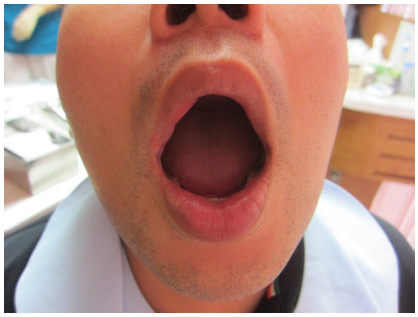

Figure 2J: one Year After Completing the Minimum Period.

Figure 2K: Three Years After Completing the Minimum Period.

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Figure 3A: Before PFC Therapy.

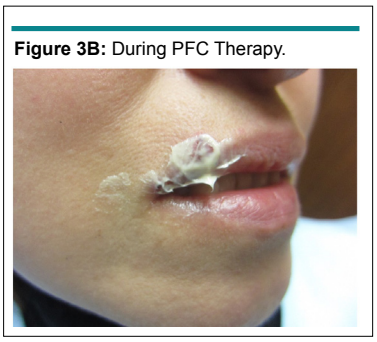
Figure 3B: During PFC Therapy.


Figure 3C: One Week After Starting PFC.


Figure 3D: Three Months After Completing the Minimum Period.


Figure 3E: One Year After Completing the Minimum Period.

Patient Criteria

All patients met the following criteria: 1) underwent an initial interview to elicit a medical history of general diseases, include any seafood allergy; 2) received an investigation of ulcers, such as size, sites, type, symptoms and medication history; 3) received consultation on how to use PFC; 4) applied PFC for a minimum period of one week; 5) follow-up after a minimum period of 1 month; 6) continue follow-up of three months each; and 7) received taking photographed on all days of follow-up.

Application of Topical PFC™

Areas of ROHL were blotted dry, then the patient applied a small amount of PFC with their own finger, and left the PFC for 5 min without removing. Patients used PFC twice daily, and were required to refrain from eating or drinking for 30 minutes after application.

DISCUSSION

ROHL is one of the most widespread oral mucous inflammatory diseases, with a reported prevalence in 20-40% of the Japanese population. However, little is known about the status of ROHL in Japan. Pica and Volpi[10] developed a practical guide for the management of oral herpes labialis, including local and systemic therapies, and suggested that immune mechanisms might play important roles in the etiology of oral herpes labialis. Furthermore, they identified several non-immunological factors associated with ROHL. However, evidence supporting the causative roles of these factors is scarce. Although both cases experienced severe pain, treatments were not rigorously evaluated. Various therapies have been attempted, including oral and topical antivirals, oral NSAIDs, topical anesthetic gels and vitamin B12 supplements, but few effects on ROHL were seen.

Under consideration of the histological characterization of ROHL and the most recent relevant therapies, we decided to apply fucoidan cream. After 1 week, ulcers improved without side effects and no exacerbation was found during follow-up. Thus, PFC was more effective than any other commercial medications.

Our patients did not develop any side effects after using PFC. Topical application caused no stinging at application sites and healing in under 1 week. Conventional medicines require an average of at least 1 week to elicit effects, so PFC has the advantage of being fast-acting, requiring an average of 5 days for symptomatic relief. Fucoidan results in early tissue remodeling and repair processes that might depend on anti-inflammatory properties together with enzyme-like activities.[11] Such activity inhibits various enzymes, including matrix metalloproteinases, hyaluronidases and elastases.[12] A clinical study has also indicated that PFC helps ameliorate skin aging.[13]

The clinical activity, value and safety of topical fucoidan cream as a treatment for ROHL remains to be determined in clinical trials.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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CONSENT

We obtained the written consent statements by each patients.

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