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CASE STUDY

Usefulness of oral administration of the specialized amino acid supplement consisting of β-hydroxy-β-methylbutyrate, L-arginine and L-glutamine (Abound™) for chronic soft tissue diseases in the mouth.

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CONFLICTS OF INTEREST
THERE ARE NO CONFLICTS OF INTEREST FOR ANY OF THE AUTHORS.

ABSTRACT:
Background: Abound™ is a nutritional supplement containing β-hydroxy-β-methylbutyrate, L-glutamine, and L-arginine (HMB/Gln/Arg). In recent years, the effects of these nutrients in promoting wound healing have been reported. Here we report our experience of using this supplement for the treatment of chronic oral mucosal diseases.
Methods *:* We clinically investigated the effects of HMB/Gln/Arg on 9 cases of chronic oral mucosal diseases such as oral lichen planus and recurrent aphthous stomatitis.
Results*:* Improvement in subjective symptoms was observed in 7 out of 9 cases of oral mucosal diseases.
Conclusion*:* We found that the use of this supplement was effective in the treatment of 7 out of 9 cases of chronic oral mucosal diseases. Thus, we believe that HMB/Gln/Arg use should be considered as a treatment option.

KEYWORDS:
a nutritional supplement, β-hydroxy-β-methylbutyrate, L-glutamine, L-arginine, oral lichen planus, recurrent aphthous stomatitis.

INTRODUCTION

Abound™ is a nutritional supplement containing three nutrients that are effective in muscle and skin tissue regeneration: β-hydroxy-β-methylbutyrate (HMB), L-glutamine, and L-arginine (HMB/Gln/Arg). Recently, reports have suggested that these nutrients promote wound healing, and HMB/Gln/Arg is a product developed with an aim to promote the effect from the nutritional viewpoint [1]. Moreover, in clinical settings, this supplement is reported to be effective in treating decubital ulcers accompanying infection and diabetic foot ulcers [2, 3] and in the alleviation of skin disorders caused by chemotherapy [4]. Although, it have reported that the intraoral administration of HMB/Gln/Arg has markedly improved mouth ulcers caused by chemoradiotherapy [1], limited reports are available regarding its effectiveness in treating oral mucosal diseases.

Here we report our experience of using HMB/Gln/Arg in the treatment of chronic oral mucosal diseases.

MATERIALS AND METHODS

The subjects included were 9 patients diagnosed with chronic oral mucosal diseases such as oral lichen planus (OLP) or recurrent aphthous stomatitis (RAS) who selected HMB/Gln/Arg treatment when suggested. The OLPs included 5 females aged 51–82 years, whereas the RAS patients included 1 male and 3 females aged 54–83 years (Table 1). The subjects were instructed to consume 1 packet of Abound™ per day for at least 2 weeks and to continue if they experienced any positive effects.

RESULTS

With regard to the subjective and objective symptoms of OLP, subjective symptoms such as oral pain and roughness of the mucosal surface improved in 3 out of 5 OLP cases at the time of four to eight weeks after treatment, but no effects were observed in the remaining 2 cases (case No4 and 5, Table 1). Subjective symptoms improved in 4 out of 4 RAS cases at the time of three to six weeks after treatment. Thus, improvement was observed in 7 out of the overall 9 subjects.

Case	Age/gender	Clinical diagnosis	Complications
1	51, F	Tongue, OLP	Rheumatism
2	70, F	Tongue, OLP	Purpura
3	82, F	Gingiva, cheeks,O LP	Hypertension
4*	57, F	Tongue, OLP	Anemia
5*	64, F	Gingiva, OLP	-
6	63, F	RAS	-
7	76, F	RAS	-
8	83, M	RAS	-
9	54, F	RAS	-

OLP: Oral lichen planus, RAS: Recurrent aphthous stomatitis.
*: Case of no change by treatment.

Some typical examples of OLP and RAS are provided below.

CASE 1

A 51-year-old female was referred to our clinic with chief complain of tongue pain. She experienced tongue pain on the left border of the tongue at eating approximately from 1 month ago. She was being treated for rheumatoid arthritis and dermatomyositis at the departments of connective tissue disorders and dermatology, respectively, at our hospital. She had a history of steroid therapy for approximately 10 years prior to presentation, and was receiving 17 other types of medication including bisphosphonate and antifungal agents. Clinical investigation revealed ulceration on the left border of the tongue, surrounded by white lesions. Palpation revealed no induration (Fig 1). Clinical diagnose of OLP was made. Then, she was prescribed with dexamethasone oral ointment. However, no changes in symptoms were observed after 4 weeks of applying the ointment; therefore, the patient was proposed Abound™ administration 1 packet per day. Symptoms gradually began to improve 2 weeks after the initiation of treatment with this supplement and had almost completely disappeared after 8 weeks. The white lesions of the tongue gradually improved and the ulceration disappeared (Fig 2). The patient continued to receive 1 packet every 2 days for 16 weeks after the initiation of the treatment.

CASE 6

A 63-year-old female was referred to our clinic with chief complain of RAS since approximately 5 years ago. The involved sites were every soft tissue in the mouth such as tongue, upper and lower lips, buccal mucosa, palate and gingiva. Although an ulcer healed within 1–2 weeks, new ulcers immediately appeared, resulting in constant presentation. She was examined at multiple medical institutions and received treatment in the form of orally-administered steroids and ointments; however, radical cure proved to be impossible. In the oral examination, A 2 × 3 mm oval-shaped aphtha was noted on the right side of the tongue (Fig3). Then, she was requested to select either

kampo medicine or HMB/Gln/Arg therapy. She selected the latter, and treatment with 1 packet of Abound™ per day was initiated. No aphthae, including the one noted initially, were observed in the oral cavity upon re-examination after 3 weeks (Fig 4). As she did not develop any new aphthae for >2 weeks, this supplement was considered to be effective, and she was instructed to continue receiving it. There has been no sign of recurrence for six months.

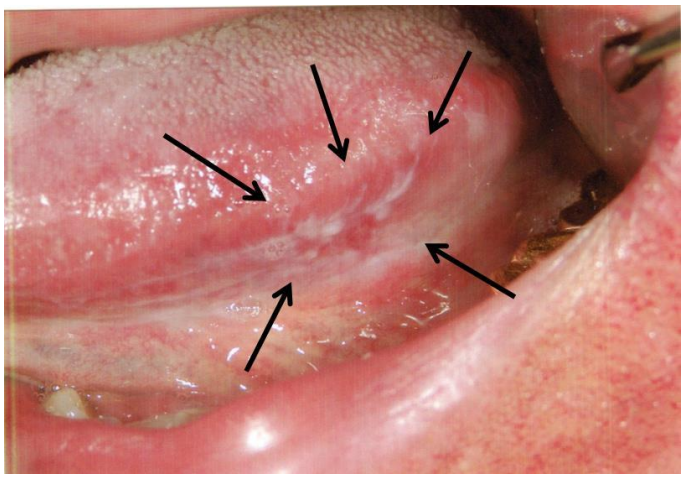

Figure 1 : White lesions were observed on both edges of the tongue, surrounded by relatively extensive ulceration and strong haphalgesia. This photograph was obtained at initial examination, and it shows the left side of the tongue where symptoms were strongly observed.

Figure 2: White lesions on both edges of the tongue were beginning to improve and the ulcers had disappeared. Similarly, the left side has been shown.

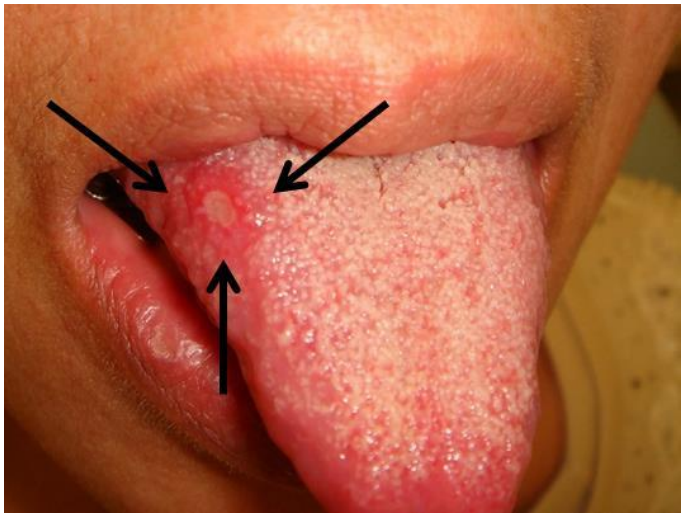

Figure 3: At initial examination, a 2 × 3 mm oval-shaped aphtha was noted on the right side of the tongue.

Figure 4: No aphthae were observed in the oral cavity 3 weeks later, including those observed during initial examination.

DISCUSSION

Abound™ is composed of the three components HMB, glutamine, and arginine, which complement each other when administered together, thereby increasing the effectiveness compared with that when administered alone.

HMB is a metabolite of leucine, which is considered to be most effective in promoting musculoskeletal protein synthesis. However, the amount of HMB metabolized from leucine is only 5% of the overall quantity, causing difficulty in ingesting HMB through food [5]. It has been reported that the actions of HMB

inhibit inflammatory reaction by suppressing invasive proteolysis within the body, promoting protein synthesis [6, 7], and blocking the action of NF-κB [8]. Reports have shown that it also activates hepatic triacylglycerol lipase and promotes tissue repair through involvement in lipoprotein and energy metabolism.

Glutamine is a source of energy for fibroblasts, immunocompetent cells, and intestinal epithelial cells involved in collagen production [9]. It promotes protein and collagen synthesis, imparts immunity, and maintains the alimentary canal mucosa structure.

Arginine acts on the pituitary gland to promote the secretion of growth hormones. It promotes synthesis of proteins and proline, which is a component of collagen; therefore, it promotes collagen synthesis. Moreover, it imparts immunity because it is involved in T cell activation and has sterilizing effects on macrophages [10].

The wound healing process can mainly be classified into three stages: the inflammation, growth, and maturation periods. In the inflammation period, the leachate appear as an inflammatory response, triggered by tissue destruction, necrosis, or bleeding at the wound site. Polynuclear leucocytes, mononuclear cells, and proteolytic enzymes contained in this leachate remove bacteria and foreign objects from the wound [11, 12]. In the growth period, new granulates are formed, and fibroblasts and macrophages appear in the wound and synthesize collagen to produce new capillaries. These vessels then supply enzymes and nutrients to the wound site, enabling the formation of new granulation tissue. In the maturation period, there is further increase in collagen and cicatrization is performed. This cicatrized tissue gradually returns to a normal state [11, 12].

We found that the use of HMB/Gln/Arg was effective in the treatment of 7 out of 9 cases of chronic oral mucosal diseases. It suggested that healing was promoted by a similar mechanism, although it is not identical to the wound healing process of the oral mucosal diseases targeted in this study. We believe that, in addition to the protein synthesis-promoting actions of HMB, glutamine, and arginine, the anti-inflammatory properties and tissue repair-promoting actions of HMB play an important role. Although we understand that this supplement is not the first-line of treatment for oral mucosal diseases, we recommend that the use of HMB/Gln/Arg for the treatment of such cases should be considered as a treatment option. However, because this mechanism of action has not been completely clarified, further basic research requires to be conducted with a larger sample size.

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