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TASTE EVALUATION OF BRANCHED-CHAIN AMINO ACIDS SUPPLEMENTATION FOR IMPROVING ADHERENCE OF CIRRHOTIC PATIENTS

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ABSTRACT

Background/Aims: Branched-chain amino acids (BCAA) are valuable in the treatment of liver cirrhosis because they increase serum albumin levels. However, poor adherence to BCAA may adversely affect prognosis. One cause of poor adherence is the problem of BCAA taste. We undertook a BCAA taste of questionnaire survey among cirrhotic patients.

Materials and Methods: The patients taking BCAA granules or unflavored jelly, and jelly with 10 different flavors for elemental diet added (total of 12 preparations), evaluated their flavor on a 5-point scale.

Results: BCAA unflavored jelly was rated lower than BCAA granules. The green apple-, pineapple-, grapefruit-, light Japanese plum-, orange-, yogurt-, and coffee-flavored jellies were rated significantly higher than the unflavored jelly. BCAA jelly added a flavor was rated higher than BCAA granules.

Conclusion: While evaluating the taste of each patient, it is necessary to improve adherence and guide it to proper internal dosing.

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INTRODUCTION

Branched-chain amino acids (BCAAs) inhibit the incidence of hepatocellular carcinoma (HCC) in patients with liver cirrhosis, indicated for improvement of hypoalbuminemia

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(Nishikawa and Osaki, 2014; Sato et al., 2005; Habu et al., 2002; Marchesini et al., 2003; Muto et al., 2005). However, they have been associated with decreased drug adherence due to unpleasant sensation when taking the drug, which is specific to BCAA. To improve the drug adherence BCAA of patients who have difficulty in taking the granules (LIVACT[®] Granules, EA Pharmaceutical, Tokyo, Japan), a newly added dosage in jelly form (LIVACT[®] Jelly, EA Pharmaceutical, Tokyo) was approved in February 2013 in Japan. The jelly was, however, still associated with a problem of flavor. Hence, it was necessary to make the jelly easier to take. In these

circumstances, we conducted a questionnaire survey among cirrhotic patients taking BCAA granules (LIVACT® Granules) or BCAA jelly (LIVACT® Jelly) to evaluate ease of taking BCAA jelly by using flavors for elemental diet as well as to compare ease of taking between BCAA granules and jelly.

MATERIALS AND METHODS

This study was conducted on 81 out-patients with liver cirrhosis in our hospital between June 2014 and January 2015. All patients with liver cirrhosis who fulfilled the Japanese National Health Insurance system criteria for receiving BCAA. The patients comprised 41 males and 40 females. The ≥65-year-old group (elderly) 40 patients and the <65-year-old group (non-elderly) 41 patients. The patients taking BCAA granules or unflavored jelly, and jelly with 10 different flavors for elemental diet added (total of 12 preparations), evaluated their flavor on a 5-point scale (Table 1).

Meanwhile, the female showed higher receptivity for the granules than the male. (Figure 2). In the elderly, the granules and unflavored jelly were rated almost equivalently and addition of green apple flavor did not produce significant difference in rating. In the non-elderly, addition of green apple flavor led to significantly higher rating than the granules and unflavored jelly. The comparison between the elderly and non-elderly showed little difference in the rating of the granules. Meanwhile, the jelly was rated significantly higher in the elderly than in the non-elderly. (Figure 3)

DISCUSSION

BCAAs are known to exert multiple pharmacological activities (Hagiwara *et al.*, 2012; Kawaguchi *et al.*, 2011). Not a few patients are reluctant to take a BCAA preparation due to its flavor. In this study, BCAA unflavored jelly was rated lower than BCAA granules.



Table 1. The questionnaire of BCAA granules or unflavored jelly, and jelly with 10 different flavors for elemental diet added (Total of 12 preparations), evaluated their flavor on a 5-point scale

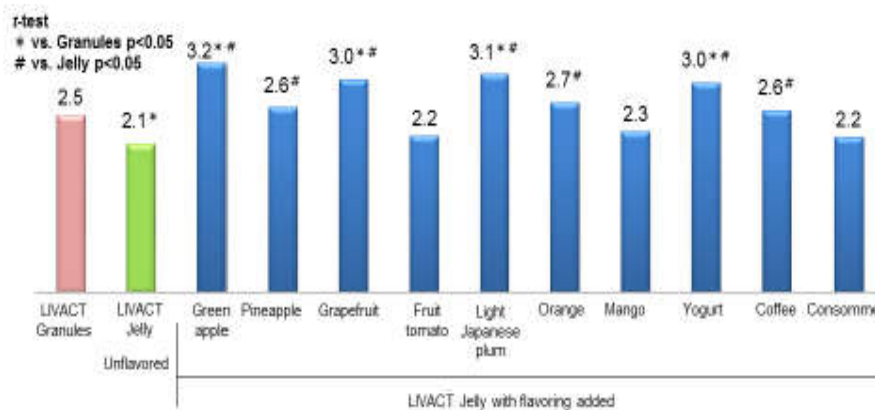


Figure 1. LIVACT Taste Evaluation of all cirrhotic patients (n=81) Comparison among LIVACT Granules, LIVACT Jelly unflavored and LIVACT Jelly with flavoring added

Written informed consent was obtained from all patients, and the Ethics Committee of Saiseikai Niigata Daini Hospital (Niigata, Japan) approved this study, which was conducted in accordance with the Declaration of Helsinki.

RESULTS

The unflavored jelly was rated lower than the granules. However, after adding green apple, grapefruit, light Japanese plum, and yogurt flavors, the jelly was rated significantly higher than the granules. The green apple-, pineapple-, grapefruit-, light Japanese plum-, orange-, yogurt-, and coffee-flavored jellies were rated significantly higher than the unflavored jelly. (Figure 1). In the male, the granules and unflavored jelly were rated almost equally, while addition of green apple flavor led to significantly higher rating of the jelly than the granules. The female were significantly more receptive to the granules as compared to the jelly. Addition of green apple flavor to the jelly resulted in a rating equivalent to that for the granules. The comparison between the male and female showed equal ratings for the jelly.

Some flavored BCAA jelly, however, was rated significantly higher than BCAA granules. In gender analysis, BCAA granules and BCAA jelly were rated almost equally in the male. The females were significantly more receptive to BCAA granules as compared to BCAA jelly. The comparison between the male and female showed equal ratings for BCAA jelly. Meanwhile, the female showed higher receptivity for BCAA granules than the male. In aging analysis, BCAA granules and BCAA jelly were rated almost equivalently by the elderly and non-elderly groups. The comparison between the elderly and non-elderly showed little difference in the rating of BCAA granules. Meanwhile, BCAA jelly was rated significantly higher in the elderly groups than in the non-elderly groups. When a flavor was added, however, BCAA jelly was rated higher than BCAA granules, which suggests that drug adherence could be improved by making the drug easier to take. Meanwhile, the rating of flavors varied among subjects, indicating that a wider variety of flavors could further improve drug adherence. Currently, three dedicated flavors are available for BCAA jelly.

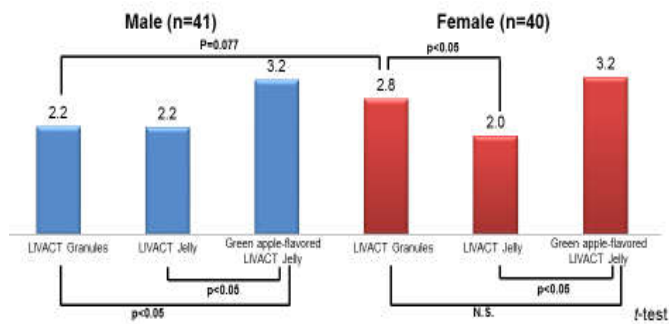


Figure 2. LIVACT Taste Evaluation in gender analysis Comparison between LIVACT Granules, Jelly, and Jelly with Green Apple Flavor for LIVACT Jelly Added

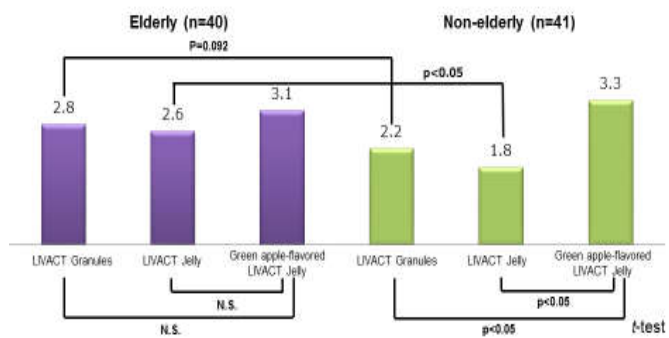


Figure 3. LIVACT Taste Evaluation between elderly and non-elderly. Comparison between LIVACT Granules, Jelly, and Jelly with Green Apple Flavor for LIVACT Jelly Added

Use of the flavors for elemental diet used in the taste evaluation to suit patient preferences will be an important means to improve drug adherence. Higher BCAA treatment adherence better raised the serum albumin level, leading to improvement of event-free survival (Takaguchi *et al.*, 2013). In the future, there is a need to improve adherence while making taste assessment, and to make full use of its usefulness. Hence, in cases of liver cirrhosis, determination of the timing of administration is also an important issue because BCAA take time to take effect. While early therapeutic intervention with BCAA can help improve the prognosis of patients with cirrhosis. More research and analysis are needed to fully explore the novel effects of BCAA including taste evaluation.

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