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Abstract A controlled study demonstrated the efficacy of lafutidine for BMS. This study examined the efficacy of lafutidine for FM. Lafutidine 20 mg/day was administered to patients with FM. During the administration of lafutidine, there were no new medicines added to the regimen and there were no changes in the dose of any other medication being co-administered. Subjective pain before administration of lafutidine was regarded as 10, and patients were then asked to estimate subjective pain after the administration of lafutidine. Twenty-six patients with FM consisted of 23 females and 3 males ranging from 14 to 83 years of age (average: 43.0). The mean duration of lafutidine administration was 29.7 days (range 14-70 days). Lafutidine reduced pain in 8 patients (30.8%), did not reduce pain in 17 patients (65.4%), and increased pain in 1 patient (3.8%). Of the 17 patients who did not respond to lafutidine, 2 discontinued administration because of gastric distress. Of the 17 patients who did not respond to lafutidine, stomach heaviness was relieved in 1 patient, and abdominal discomfort was relieved in 1 patient. When the patient with aggravation was excluded, the average subjective pain after administration of lafutidine was 8.6. Lafutidine activates the mucosal defensive mechanisms in the gastrointestinal tract by sensitizing capsaicin-sensitive afferent neurons (CSAN). Capsaicin, one component of hot pepper, has an analgesic effect and capsaicin sensitizes CSAN. Although the analgesic mechanism of lafutidine is unclear, it may be an analgesic effect.

Keywords Fibromyalgia · Lafutidine · H₂ blocker · Central Sensitivity Syndromes · Chronic Widespread Pain

Introduction

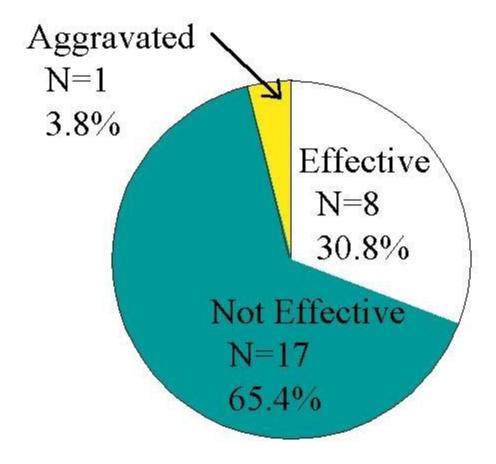
Fibromyalgia (FM) is a disorder that causes a widespread pain [1]. The etiology is unknown, but a dysfunction theory of the brain, the central sensitization theory, is a leading hypothesis[2].

Burning mouth syndrome (BMS) and vulvodynia exist independently, but are often comorbid with FM. A controlled study demonstrated the efficacy of lafutidine for BMS[3, 4]. This study examined the efficacy of lafutidine for FM.

Materials and method

Lafutidine 20 mg/day was administered orally to patients with FM treated at Hatsukaichi Memorial Hospital between April 2007 and March 2010. Patients were eligible for study participation if they met the criteria for fibromyalgia as defined by the American College of Rheumatology[5]. During the administration of lafutidine, there were no new medicines added to the regimen and there were no changes in the dose of any other medication being co-administered. Subjective pain before administration of lafutidine was regarded as 10, and patients were then asked to estimate subjective pain after the administration of lafutidine.

Efficacy of lafutidine (H₂ blocker) for fibromyalgia



Results

Twenty-six patients with FM consisted of 23 females and 3 males ranging from 14 to 83 years of age (average: 43.0). The mean duration of lafutidine administration was 29.7 days (range 14-70 days). One patient became aggravated and one patient discontinued treatment due to adverse effects and both were excluded from analysis of the mean duration. Lafutidine reduced pain in 8 patients (30.8%), did not reduce pain in 17 patients (65.4%), and increased pain in 1 patient (3.8%) (Fig 1). Of the 17 patients who did not respond to lafutidine, 2 discontinued administration because of gastric distress. Of the 17

patients who did not respond to lafutidine, stomach heaviness was relieved in 1 patient, and abdominal discomfort was relieved in 1 patient. In the patient with aggravation, symptoms such as pain became aggravated after administration of all medicines and after discontinuation of all medicines. Subjective pain after administration of lafutidine was rated as more than 100 in this patient. When the patient with aggravation was excluded, the average subjective pain after administration of lafutidine was 8.6. The subjective pain of the responded eight patients after administration of lafutidine was 2 in one patient, 3 in one, 5 in one, 6 in one, 7 in three, and 8 in one. Wilcoxon signed rank test yielded a P value less than 5%.

Discussion

Lafutidine is an H₂ blocker. Lafutidine activates the mucosal defensive mechanisms in the gastrointestinal tract by sensitizing capsaicin-sensitive afferent neurons (CSAN)[6, 7]. Capsaicin, one component of hot pepper, has an analgesic effect and capsaicin sensitizes CSAN. Although the analgesic mechanism of lafutidine is unclear, it may be an analgesic effect.

BMS, orofacial pain, vulvodynia, tension-type headache, FM, and chronic widespread pain (CWP) are included in central sensitivity syndromes (CSS). Therefore, a treatment that is effective for one disorder is expected to be effective for other CSS disorders. In my experience, symptomatic relief of FM or CWP usually results in symptomatic relief of BMS, orofacial pain vulvodynia, tension-type headache in patients with FM or CWP who also demonstrate these disorders. For example, amitriptyline, tricyclic antidepressant, is effective for BMS[8], orofacial pain[9], vulvodynia[10], and tension-type headache[11] as well as FM[12]. Efficacious treatments for each disorder of CSS show strong similarities.

Noting that efficacious treatments for each CSS disorder show strong similarities is beneficial in the treatment of CSS overall. First, a treatment that is effective for one disorder can be applied to other disorders. Second, one physician can treat various disorders involved in CSS. Specific disorders other than FM or CWP should be excluded.

Patients with FM or CWP are more likely to demonstrate functional gastrointestinal disorder[13]. Because lafutidine is an H₂ blocker, it may be effective in patients with a combination of FM (or CWP) and functional gastrointestinal disorder.

Tricyclic antidepressants, one of the most efficacious medicines for FM, show an efficacy rate between 25% and 37%[14]. The efficacy rate of lafutidine in this study was 30.8%. This efficacy rate is equal to the efficacy rate of tricyclic antidepressants. The definition of efficacy in articles documenting the efficacy of tricyclic antidepressants differed from that used in this study. In my experience, the analgesic effect of lafutidine is weaker than that of tricyclic antidepressants. However, lafutidine is a useful medicine, considering its mild and rare adverse effects.

I have prescribed various medicines for FM. In my experience, lafutidine provides a weaker analysesic effect than amitriptyline, gabapentine, milnacipran, but it causes milder and fewer adverse effects than these medicines. The greatest benefit of lafutidine is its mild and rare adverse effects. The analysesic mechanism of lafutidine differs from the

mechanism of other medicines effective for FM. Therefore, it is desirable to prescribe lafutidine with other powerful analgesic medicines. However, this is a short-term study without a control group. A long-term double-blind study is needed.

In conclusion, lafutidine reduced pain in 8 patients with FM (30.8%), it did not reduce pain in 17 patients (65.4%), and it increased pain in 1 patient (3.8%). Lafutidine 20 mg/day appears to be a useful medicine for FM.

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