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Original Article

Effect of *Baekyeum* on Intestinal Motility

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Objectives : The purpose of this study was to evaluate the effects of Baekyeum (BKE) on intestinal motility.
Methods : The effects of BKE on intestinal motility at the physiological state were evaluated by determination of intestinal motility after administration of a charcoal meal.
The effects of BKE on intestinal motility at cabachol-induced activated state and loperamide induced suppressed state were also evaluated by determination of intestinal motility after administration of charcoal meal.
Results : BKE didn't affect the intestinal motility in physiological state, and BKE didn't affect the intestinal motility at the carbachol-induced activated state. BKE activated significantly the intestinal motility at the loperamide-induced suppressed state.
Conclusions : It can be concluded that BKE is an effective herbal prescription for cancer-patients with gastrointestinal dysfunction, especially intestinal stasis.

Key Words: Baekyeum, Intestinal, motility

Introduction

Intestinal stasis or ileus is one of the frequent complications in the process of natural cancer progression or therapeutic treatment for patients suffering from cancer. It is a significant cause of mortality and morbidity in cancer patients and has been attributed to a variety of causes, including concurrent physical, psychosocial and existential problems[1-5].

So far, many studies have been done on gastrointestinal disorder in cancer patients. However, to develop more effective medicine for intestinal immobility is necessary because the condition on revelation of symptoms is not always obvious and the cause is not singular[6].

Baekyeum (BKE) is a widespread herbal formula mainly used for the treatment of gastrointestinal diseases, including constipation, bloating, abdominal distension, and the sensation of incomplete evacuation in Korea. Especially, BKE has shown significant effects on intestinal stasis or ileus of the cancer patients through the clinical application in Dunsan Oriental Hospital of Daejeon University. Although it is limited to components of BKE, several studies have been made on various bowel diseases related with anti-allergic or anti-fungal activity and anti-oxidant functions[7-10].

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Table 1. Prescription of BKE

Scientific Name	rtused	Relative Amount (g)
Citrus unshiu	Pericarpium	6
Agastache rugosa	Herba	6
Citrus aurantum	Fructus	6
Magnolia officinalis	Cortex	4
Alisma plantagoaquatica var. orientale	Rhizoma	8
indera strychnifolia	Radix	8
Cyperus rotundus	Rhizoma	8
Aucklandia lappa	Radix	4
Total amount		50

However, there has not been any works to perceive the classic effects of BKE on intestinal motility yet. Therefore, we here observed how BKE affects the passage of charcoal in mice at physiological and pathological model.

Materials and Methods

1. Preparation of BKE extracts

Medical herbs containing BKE were kindly provided from Dunsan Oriental Medical Hospital. BKE was prepared following Fig 1. BKE (50g) was mixed with 1 L of distilled water and left for 1 hr at room temperature, and then the whole mixture was boiled for 2 hrs. The extract was centrifuged for 30 min at 2000 × g and supernatant was concentrated by vacuum evaporator (BUCHI, Switzerland) and then lyophilized. The yielded BKE was 18.5% (w/w) in terms of the dried medicinal herbs.

2. Chemical preparation

Carbachol and loperamide were purchased from Sigma (USA). Carbachol was dissolved with normal saline (0.1 mg/ml) and loperamide was dissolved with normal saline (0.1mg/ml) containing 0.05% tween 80. Charcoal (Wako, Japan) meal were made by suspension

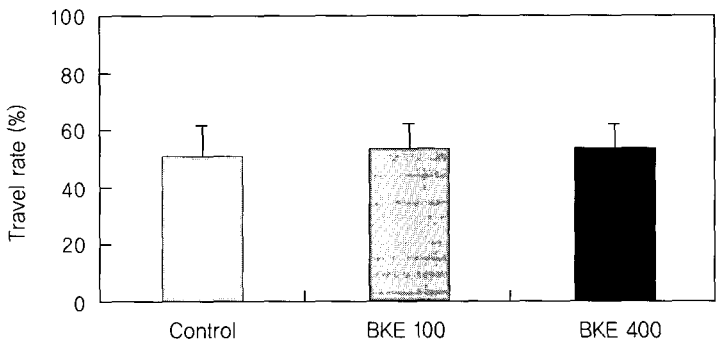

Fig. 1. Effect of BKE on intestinal motility at physiological state. Mice were administrated with BKE (100 mg/kg, 400 mg/kg) before 15 min of charcoal meal. Intestinal motility was determined at 20 min after administration of charcoal meal. The data were expressed as the mean±SD.

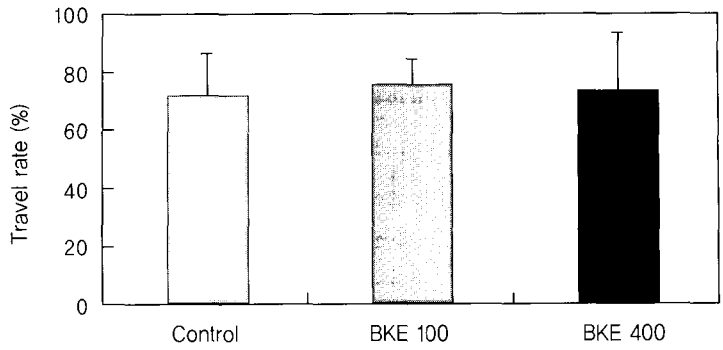

Fig. 2. Effect of BKE on intestinal motility at physiological state. Mice were administrated with BKE (100 mg/kg, 400 mg/kg) before 15 min of charcoal meal. Intestinal motility was determined at 20 min after administration of charcoal meal. The data were expressed as the mean±SD.

of 5% charcoal in 10% gum arabic solution.

3. Animals and treatment

Seven-week old male ICR mice were purchased from Daehan-Biolink (Yeumsung, Korea) and were housed in an environmentally controlled room at 22±2℃ relative humidity at 55±10% and 12 hrs light/dark and fed with commercial pellets (Samtako, Korea) and tap water ad libitum. The mice were divided into 9 groups of 7 animals. After five-day acclimation, these mice were used in this experiment in a state of 24-hour fasting as follows.

Mice were pre-treated with loperamide (0.5mg/kg, sc) or carbachol (0.5mg/kg, po), and were administrated with BKE at 15 min and charcoal meal at 30 min respectively. Control groups were treated in the same manner with normal saline as the carrier of BKE.

The travel rates of charcoal were recorded by calculating the percentage of passage distance to the total small intestine after sacrifice by cervical dislocation at 20 minute after charcoal meal administration.

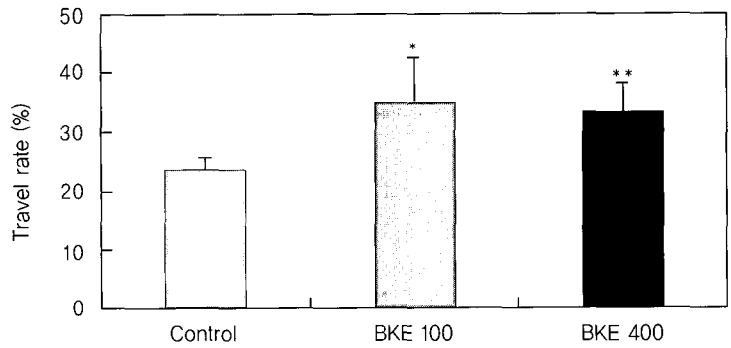

Fig. 3. Effect of BKE on intestinal motility at physiological state. Mice were administrated with BKE (100 mg/kg, 400 mg/kg) before 15 min of charcoal meal. Intestinal motility was determined at 20 min after administration of charcoal meal. The data were expressed as the mean±SD.

4. Statistical analysis

Results were expressed as the mean±SD. Statistical analysis of the data was carried out by Student's *t*-test. A difference from the respective control data at the levels of $p<0.05$, $p<0.01$ were regarded as statistically significant.

RESULTS

1. Effect of BKE on intestinal motility at physiological state

Mice were administered with distilled water as a control group or BKE group to investigate if BKE affects the intestinal motility in normal condition or not. Even intestinal motility was increased slightly, there were no significant differences between groups of control and BKE such around 50%.

2. Effect of BKE on intestinal motility at carbachol-induced activated state

Mice were pre-treated with carbachol (0.5 mg/kg, po) to activate intestinal motility. The mice were administrated with distilled water as a control group or BKE group to investigate if BKE affects the intestinal motility in activated condition. Even BKE slightly increased intestinal motility, there was no statistical significance.

3. Effect of BKE on intestinal motility at loperamide-induced suppressed state

Mice were pre-treated with loperamide (0.5mg/kg, sc) to suppress intestinal motility. Mice were administrated with distilled water as a control group or BKE group to investigate if BKE affects the intestinal motility in suppressed condition. Loperamide treatment decreased intestinal motility by 24%. BKE treatment improved intestinal motility suppressed by loperamide by 34%. This difference presented statistical significance as smaller than 0.01, compared BKE (400 mg/kg) with control.

Discussion

Gastrointestinal dysfunction in cancerous disease results from various factors such as abdominal surgery, chemotherapy, radiation or medication of mainly morphine and other opioids. These complications cause that therapeutic dosage of the drugs should be lower than effective dosage and the following treatment would be delayed or stopped. It can also lower the quality of life and duration of survival[1-5]. Therefore, it is necessary to develop more effective remedies for gastrointestinal dysfunction in cancer patients.

On the other hand, it has been well known that BKE is one of clinically important herbal formulas for cancer patients with intestinal stasis or ileus. However, we have far less knowledge about the role of BKE on the function of digestive system. To achieve this basic answer, we measured the passage rate of charcoal after BKE treatment based on the fact that intestinal motility directly or indirectly represents the healthy or ill feature of alimentary canal. Here, we simply adapted three different mice models, normal and Carbachol or Loperamide-induced pathologic situations.

As shown in Fig.1, BKE didn't affect the passage rate of the charcoal meal compared with the control group. Both groups presented the same rate of around 50% at twenty minutes after administration of charcoal. This result might come from the general feature that BKE don't show its effect as pathogenic manner in healthy animals.

We also applied BKE to pathological models, drug-induced activated or suppressed motility. A synthetic parasympathetic drug, Carbachol treatment (0.5 mg/kg, po) increased intestinal motility more than 70% at 17 min after administration of the charcoal meal. In this

model, BKE didn't affect any valuable change compared with the control in charcoal travel rate as shown in Fig.2. Though BKE slightly increased intestinal motility, there was no statistical significance.

On the other hand, a synthetic anti-diarrheal agent, loperamide treatment (0.5 mg/kg, sc) induced significantly the decreased travel rate of charcoal by around 24% compared with 50% normally. But in this model, BKE stimuli ameliorated the suppressed intestinal motility by improving till 34% as shown in Fig.3. This result meant that BKE might function to reform the pathologically suppressed intestinal peristalsis.

From what has been discussed above, we can conclude that BKE can improve intestinal stasis or ileus through restoring the suppressed motility.

In terms of Oriental medicine, gastrointestinal diseases generally result from the reversed flow and stagnation of qi, retention of food, and hyperactive liver-qi attacking the stomach. In order to cure these diseases, a medical treatment should have the effects such as invigorating the spleen for eliminating dampness, strengthening the stomach to promote digestion, promoting circulation of qi to alleviate stagnation in the middle-jiao, and regulating the liver-qi.

BKE has the effects which strengthen the function of the stomach, resolve phlegm, check upward adverse flow qi, air which leads to relive such symptom as nausea, vomiting, fullness and pain in the epigastrium.

BKE is generally used for the treatment of patients with dyspepsia, constipation, bloating, abdominal distension, and the sensation of incomplete evacuation due to hypo-function of the spleen and stomach with obstruction in the channels.

In the clinical application, BKE is used for the diseases due to qi stagnation and the adverse rising of qi.

Accordingly, our study might explain an underlying mechanism through the fact that BKE can be applied scientifically for many similar disorders with this model in clinical fields.

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