



# Aromatherapies using *Osmanthus fragrans* oil and grapefruit oil are effective complementary treatments for anxious patients undergoing colonoscopy: A randomized controlled study



Hideaki Hozumi\*, Sho Hasegawa, Takazumi Tsunenari, Noriko Sanpei, Yuko Arashina, Kieko Takahashi, Ayako Konno, Emi Chida, Souichi Tomimatsu

Self Defense Forces Sendai Hospital, Japan

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## ABSTRACT

**Background and aims:** Colonoscopy can be painful and uncomfortable. Aromatherapy is often used for the relief of anxiety or discomfort. Recently, it has been reported that olfactory stimulation induces various physiological effects. We investigated the effects of aromatherapy on anxiety and abdominal discomfort during colonoscopy. **Methods:** The investigation was carried out using a randomized controlled study. Aromatherapy was performed by vapor diffusion, and each patient was given one of the following treatments: no inhalation (control group), essential-oil-less vapor (vehicle group), lavender oil (lavender group), grapefruit oil (grapefruit group), or *Osmanthus fragrans* oil (*Osmanthus fragrans* group). Following total colonoscopy procedures, each patient estimated their anxiety and abdominal discomfort using the Numeric Rating Scale.

**Results:** Total colonoscopy was performed on 361 patients. No complications caused by colonoscopy or aromatherapy were experienced. In the *Osmanthus fragrans* group, anxiety was significantly attenuated. The abdominal discomfort of patients who reported strong anxiety during colonoscopy was significantly attenuated in the grapefruit group and the *Osmanthus fragrans* group.

**Conclusion:** Aromatherapies using *Osmanthus fragrans* oil and grapefruit oil are effective complementary treatments for anxious patients undergoing colonoscopy.

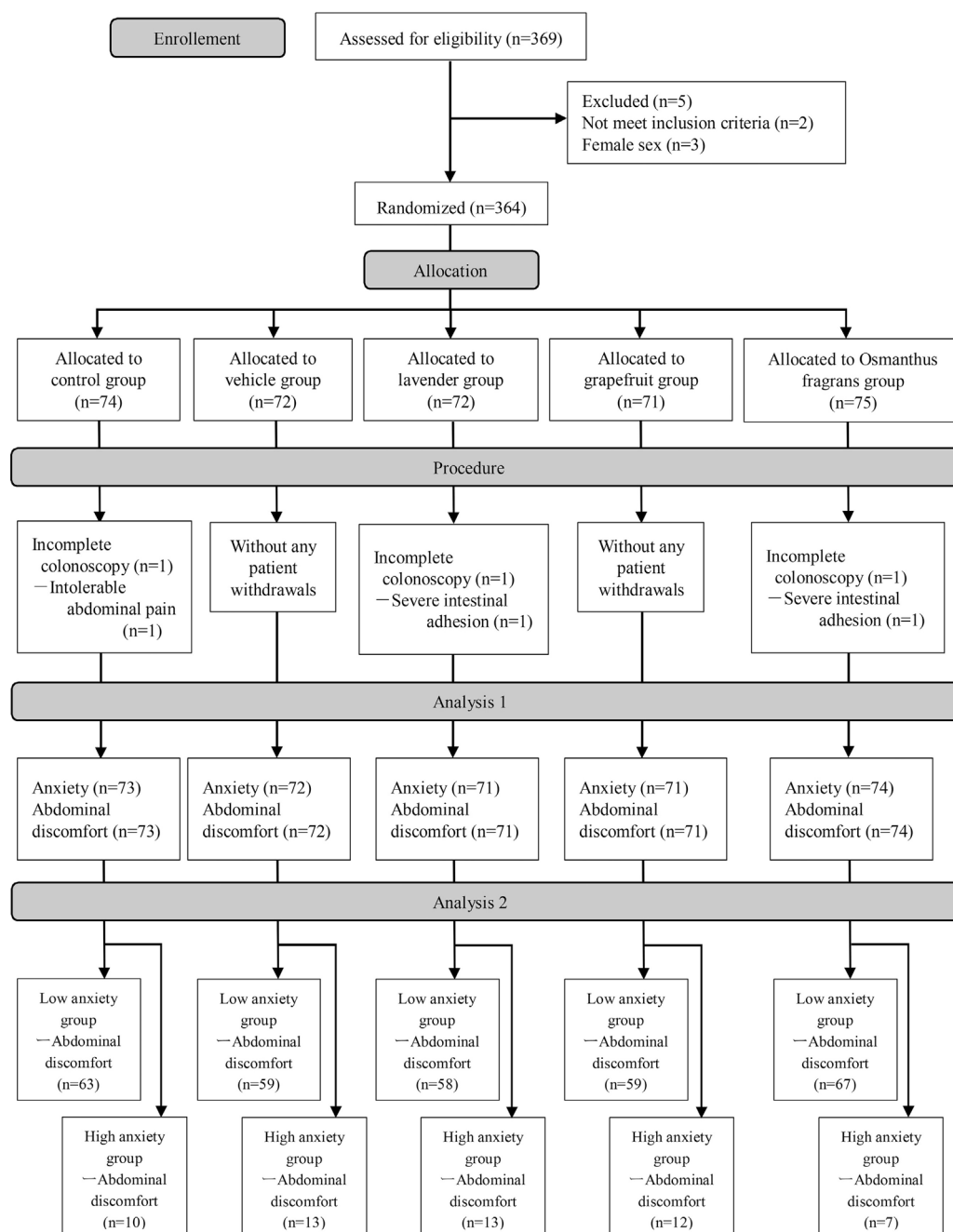
## 1. Introduction

Colonoscopy is the main procedure utilized for providing medical care to the lower digestive tract. Recently, the clinical role of colonoscopy has increased due to the progress of encephalitis as well as the continued improvement of medical equipment. However, some side effects caused by air inflation or scope operation can result from the procedure, including abdominal discomfort, full consciousness, and a sense of incongruity, which limit the comfort of patients undergoing colonoscopy. Sedatives are sometimes administered to a patient before colonoscopy to reduce anxiety and discomfort. Sedatives are effective but are accompanied by a certain amount of risk, including circulation suppression, respiratory depression, delayed awakening and anterograde amnesia.<sup>1–5</sup> After completion of the procedure, reversal agents are administered to the patient, but a certain amount of follow-up time and clinical observation is required to confirm their effectiveness. These associated risks and burdens on clinical staff sometimes limit the prescription of sedatives. Aromatherapy is a naturopathy technique for

health and cosmetic applications that uses essential oils extracted from natural plants to relieve psychosomatic distress through their odor. Recently, it has been reported that olfactory stimulation causes various physiological effects. According to these reports, lavender oil promotes appetite by stimulating parasympathetic nerves,<sup>6</sup> and grapefruit essential oil reduces appetite through sympathetic nerve stimulation.<sup>7</sup> Additionally, it has been reported that olfactory stimulation by *Osmanthus fragrans* reduces the intracerebral secretion of orexin, a hormone that alters sedation and appetite.<sup>8</sup> The autonomic nervous system, regulated through a balance between sympathetic nerves and parasympathetic nerves, is one of the important factors comprising the brain-gut axis. It regulates movement, sense, secretion and immune mechanisms in the gastrointestinal tract, and these regulations are affected by changes in feeling.<sup>9,10</sup> Orexin is a neuropeptide that was discovered by Sakurai et al. in 1998 and is produced by neurons in the lateral hypothalamic area. Reported physiological functions of orexin include up-regulation of food intake, gastrointestinal function (secretion and movement), wakefulness, mood and lipid metabolism.<sup>11–19</sup>

\* Corresponding author at: Self Defense Forces Sendai Hospital, 1-1 Minami-no-Medate Miyagino-ku, Sendai, Miyagi 983-8580, Japan.  
E-mail address: [sd37667hozu1334@yahoo.co.jp](mailto:sd37667hozu1334@yahoo.co.jp) (H. Hozumi).

Fig. 1. Flow chart of randomization.



Therefore, it was hypothesized that aromatherapy using these essential oils could reduce anxiety and abdominal discomfort during colonoscopy. Some reports have described a reduction of abdominal discomfort by aromatherapy,<sup>20–22</sup> and aromatherapy using lavender oil during colonoscopy has previously been reported.<sup>21</sup> However, there have been no reports describing the examination of grapefruit oil and *Osmanthus fragrans* oil.

In this report, we investigated the effectiveness of aromatherapy for reducing anxiety and abdominal discomfort during colonoscopy.

## 2. Materials and methods

### 2.1. Patients

In total, 364 male patients who did not have any contraindicated diseases for antispasmodic agents (such as glaucoma, severe heart disease

and prostatomegaly), asthma, or allergies to foods or plants were enrolled in this study (average age:  $45.6 \pm 5.4$  years old) (Fig. 1). The number of female patients who underwent colonoscopy was very small ( $n = 3$ ), due to the special characteristics of our hospital and the observation that being of the female sex has been reported to be one of the factors that worsen abdominal discomfort during colonoscopy.<sup>23</sup> For these reasons, female patients were excluded from this study. The survey was conducted as a randomized controlled study. Eligible patients who agreed to participate in our study were randomized to the following five groups using a computer-generated simple randomization based on the content of aromatherapy: no aromatherapy (control group), essential-oil-less vapor (vehicle group), lavender oil (lavender group), grapefruit oil (grapefruit group), and *Osmanthus fragrans* oil (*Osmanthus fragrans* group). Allocation was concealed using serially numbered, sealed opaque envelopes. A study coordinator managed the informed consent and randomization process. Outcome adjudication

was blinded. This study was approved by the ethics committees at the Self Defense Forces Sendai Hospital, where the study was conducted. The study was also registered in the UMIN Clinical Trials Registry with the following registration number: UMIN000024123.

## 2.2. Sample size

We hypothesized that 1% of patients who are randomized to each group would find the procedure unacceptable after the procedure was explained to them. The estimated sample size to detect differences with a power of 0.8 at a significance level of 0.05 was 300 patients undergoing total colonoscopy.

## 2.3. Aromatherapy

We utilized the vapor diffusion method using lavender oil, grapefruit oil, and *Osmanthus fragrans* oil (supplied by Seikatsu-no-ki, Tokyo, Japan) to perform aromatherapy during colonoscopy. We used a commercial aroma diffuser (Middle colors, Dousisya, Tokyo, Japan). It was placed at the side of patient's head on an examining table. In total, 70 mL of tap water was put in the diffuser, and 0.05 mL of lavender oil, 0.30 mL of grapefruit oil or 0.05 mL of *Osmanthus fragrans* oil was dropped into the water. The quantities of each essential oil were determined according to their specific blending factor, which reflects the strength of the odor of aroma oils.

## 2.4. Colonoscopy

All patients underwent non-sedative colonoscopy after receiving an intramuscular injection of 10 mg of scopolamine butylbromide as an antispasmodic agent. All colonoscopies were performed by the same endoscopist. After the colonoscopy, each patient was asked to grade their anxiety and abdominal discomfort during colonoscopy on the Numeric Rating Scale (NRS) from 0 to 10.

## 2.5. Statistics

All results were expressed as the mean  $\pm$  standard error of the mean. Differences between control group and other groups were evaluated by Bonferroni's method. The statistical significance of all analyses was set at  $P < 0.05$ .

## 3. Results

The study was conducted from October 1st, 2016, to December 31st, 2016. In total, 364 patients were enrolled in this study, and total colonoscopy was performed on 361 patients (99.1%) (Table 1). In 3 cases, total colonoscopy was not completed due to intolerable abdominal pain or severe intestinal adhesions. No complications resulting from colonoscopy or aromatherapy were experienced.

We investigated the effects of aromatherapy on anxiety and abdominal discomfort during colonoscopy. Comparing the mean value of each factor, a significant reduction in anxiety was observed in the *Osmanthus fragrans* group compared to the control group (Fig. 2).

No significant difference was observed in abdominal discomfort between each group.

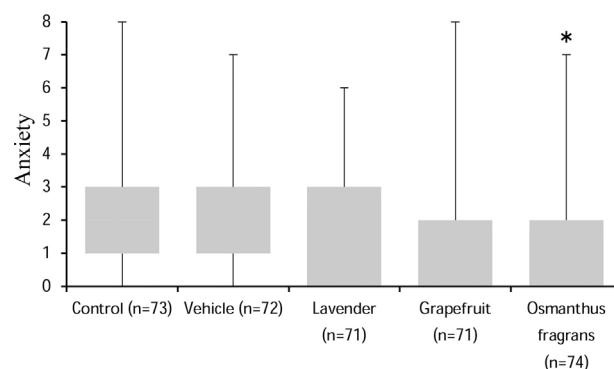


Fig. 2. Comparison of anxiety.

Abdominal discomfort during total colonoscopy was significantly attenuated in the *Osmanthus fragrans* group.

\* $P < 0.05$  as compared with control group.

Next, we divided the patients into a low anxiety group (NRS score  $< 4$ ) and a high anxiety group (NRS score  $\geq 4$ ), and compared the abdominal discomfort between each group. In the high anxiety group, a significant amelioration of abdominal discomfort in the grapefruit group and the *Osmanthus fragrans* group was observed (Fig. 3). In the lavender group, no significant change was observed in either anxiety or abdominal discomfort. These results suggest the likelihood that aromatherapy using grapefruit oil and *Osmanthus fragrans* oil could serve as a complementary treatment for anxious patients undergoing colonoscopy.

## 4. Discussion

Colonoscopy is necessary for early detection or periodic follow-up of lower digestive tract diseases. However, anxiety and abdominal discomfort during colonoscopy procedures prevent patients from undergoing examination. Previous reports have shown that abdominal discomfort during colonoscopy is associated with the female sex, a history of gynaeco-pelvic surgery and anxiety.<sup>20,23–26</sup> Several trials focused on the reduction of abdominal discomfort during colonoscopy have been reported and have suggested that clinical education before testing, calm music and sufficient communication are effective interventions.<sup>27–33</sup> Aromatherapy has been used as a complementary treatment or supportive care for the reduction of anxiety and pain in several clinical settings; however, there are few references that demonstrate any significant curative effect.<sup>34–44</sup> In this study, we investigated whether aromatherapy attenuates anxiety and abdominal discomfort during colonoscopy.

Initially, we investigated the effect of aromatherapy on anxiety and abdominal discomfort. In the *Osmanthus fragrans* group, anxiety was significantly attenuated. However, no significant change was observed in abdominal discomfort. According to previous reports, abdominal discomfort during colonoscopy is exacerbated by anxiety,<sup>20,24–26</sup> and a significant relationship was also observed in our study (data not shown). Therefore, we hypothesized that aromatherapy may reduce abdominal discomfort only in anxious patients. Analysis of patients with high anxiety revealed that the mean abdominal discomfort was significantly attenuated in the grapefruit group and the *Osmanthus*

Table 1  
Characteristics of patients who underwent total colonoscopy.

Characteristic	Control group (N = 73)	Vehicle group (N = 72)	Lavender group (N = 71)	Grapefruit group (N = 71)	<i>Osmanthus fragrans</i> group (N = 74)
Age	46.2 $\pm$ 5.5	45.8 $\pm$ 5.6	44.2 $\pm$ 5.2	46.1 $\pm$ 5.0	45.6 $\pm$ 5.1
Body Mass Index	24.6 $\pm$ 2.7	24.3 $\pm$ 3.3	24.7 $\pm$ 2.4	24.8 $\pm$ 2.8	23.8 $\pm$ 2.7
Intubation time (min)	8.5 $\pm$ 3.9	7.4 $\pm$ 3.2	7.3 $\pm$ 3.6	6.5 $\pm$ 2.5	7.5 $\pm$ 3.4
Total testing time (min)	15.3 $\pm$ 4.3	14.4 $\pm$ 3.3	14.1 $\pm$ 3.7	13.7 $\pm$ 2.8	14.1 $\pm$ 3.7

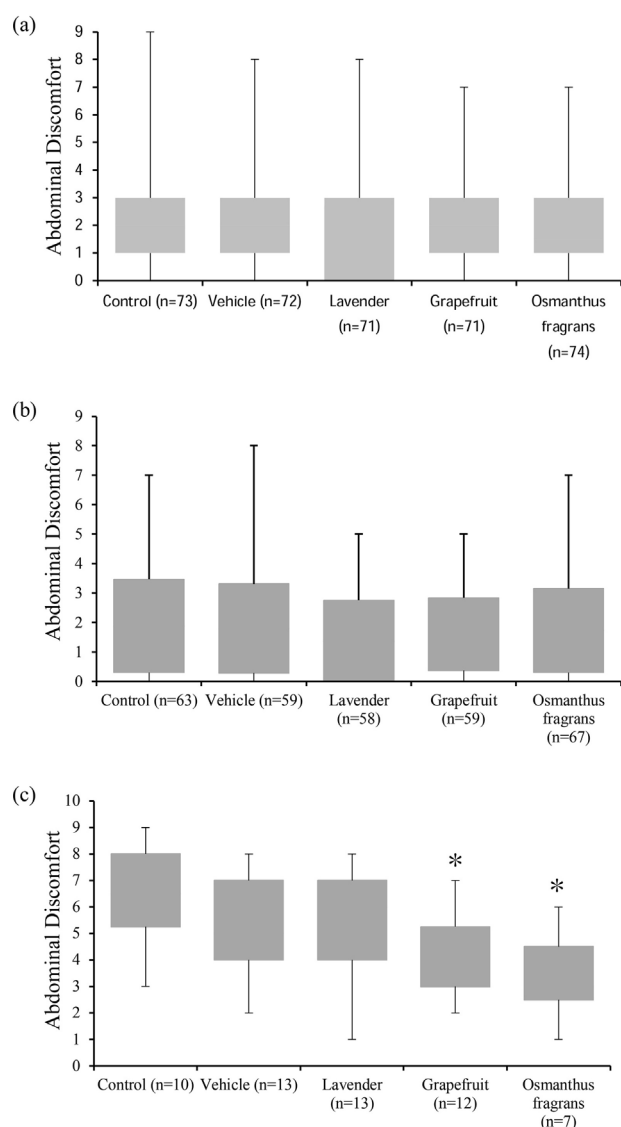


Fig. 3. Comparison of abdominal discomfort during colonoscopy.

(a) All patients.

(b) Low anxiety group (NRS score < 4).

(c) High anxiety group (NRS score ≥ 4). In the high anxiety group, abdominal discomfort was significantly attenuated in the grapefruit group and the *Osmanthus fragrans* group, suggesting that exacerbation of abdominal discomfort caused by severe anxiety was significantly attenuated in these two groups compared to the control group.

\*P < 0.05 as compared with control group.

*fragrans* group but not in patients with low anxiety.

This result suggests that aromatherapy using these two aromatic oils does not have an antinociceptive action in and of itself, but attenuates the exacerbation of visceral hypersensitivity caused by severe anxiety, potentially by acting on the brain-gut axis. Many physiological studies concerning the brain-gut axis have been performed, and the insular cortex and anterior cingulate gyrus have been identified as parts of the visceral sensory pathway activated by psychological stress.<sup>45–47</sup> It has been reported that the insular cortex participates in pain perception, and its activation is regulated by emotional experiences.<sup>45</sup> In addition, the anterior cingulate gyrus is strongly activated not only by noxious stimuli themselves but also by the expectation of noxious stimulation and the presentation of a noxious stimulus.<sup>46,47</sup> These observations suggest that anxiety during colonoscopy activates these regions and exacerbates abdominal discomfort. In the *Osmanthus fragrans* group, mean anxiety was significantly attenuated, which suggests that it may have a sedative effect by reducing orexin signaling. In the lavender

group, no significant change was observed in either anxiety or abdominal discomfort compared with the control group, which is consistent with previous reports.<sup>21</sup> Grapefruit oil has been reported to induce sympathetic nerve stimulation,<sup>6</sup> which exacerbates visceral hypersensitivity.<sup>48,49</sup> Interestingly, grapefruit oil attenuated abdominal discomfort only in the high anxiety group, but it did not attenuate anxiety. These observations suggest the possibility that olfactory stimulation by grapefruit oil has additional effects, perhaps by suppressing the activation of either the insular cortex or the anterior cingulate gyrus, which can be induced by severe anxiety.

Taken together with prior reports,<sup>6,10</sup> it is hypothesized that olfactory stimulation by grapefruit oil and *Osmanthus fragrans* oil suppresses this activation through the transmission of olfactory neural information from peripheral olfactory receptor cells to the brain, and not through a humoral effect of the odor molecules absorbed from the respiratory mucosa.

In our study, we had no complications resulting from aromatherapy treatment. However, one case report described an airborne contact dermatitis in the context of inhaled aromatherapy,<sup>50</sup> so detailed questioning about allergies must be performed before colonoscopy.

Our study showed for the first time that aromatherapy using grapefruit oil and *Osmanthus fragrans* oil could serve as an effective complementary treatment for colonoscopy. However, our study did have a few limitations. First, the patients in our investigation were restricted to males in their 40s–50s. We cannot exclude the possibility that the effect received from aromatherapy could be altered by differences in age, race, and other demographic factors. Additionally, it has not been elucidated how aromatherapy physiologically acts in a human body to bring about these results. Further studies are needed to address these considerations.

## 5. Conclusion

The odor of *Osmanthus fragrans* significantly attenuated anxiety during colonoscopy. Additionally, the odor of *Osmanthus fragrans* and grapefruit significantly attenuated abdominal discomfort for anxious patients. These results suggest that aromatherapy can serve as an effective complementary treatment for making colonoscopy procedures more tolerable.

## Author's contributions

Hideaki H has made substantial contributions to conception and design, acquisition of data, and interpretation of data; has been involved in drafting the manuscript; and has given final approval of the version to be submitted. Souichi T has been involved in drafting the manuscript; has been involved in revising the manuscript critically for important intellectual content; and has given final approval of the version to be submitted. Sho H and Takazumi T have made contributed to statistical analysis, have been involved in revising the manuscript critically for important intellectual content; and have given final approval of the version to be submitted. Noriko S, Yuko A, Kieko T, Ayako K and Emi C have made substantial contributions to acquisition of data and have given final approval of the version to be submitted. All authors have read and approved the final manuscript.

## Conflict of interest disclosure

The authors have nothing to disclose.

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