



ELSEVIER

International Journal of Cardiology xx (2007) xxx–xxx

International Journal of
Cardiology

www.elsevier.com/locate/ijcard

Relaxation effects of lavender aromatherapy improve coronary flow velocity reserve in healthy men evaluated by transthoracic Doppler echocardiography

Yumi Shiina^a, Nobusada Funabashi^{a,*}, Kwangho Lee^a, Tomohiko Toyoda^a, Tai Sekine^a, Sachiko Honjo^a, Rei Hasegawa^a, Takayuki Kawata^a, Yu Wakatsuki^a, Shinichiro Hayashi^b, Shio Murakami^b, Kazuo Koike^c, Masao Daimon^a, Issei Komuro^a

^a Department of Cardiovascular Science and Medicine, Chiba University Graduate School of Medicine, 1-8-1 Inohana, Chuo-ku, Chiba City, Chiba 260-8670, Japan

^b Green Flask Laboratory, Green Flask Co., Ltd. 1-25-1 Jiyugaoka, Meguro-ku, Tokyo 152-0035, Japan

^c Faculty of Pharmaceutical Sciences, Toho University, 2-2-1 Miyama, Funabashi City, Chiba 274-8510, Japan

Received 4 May 2007; accepted 30 June 2007

Abstract

Purpose: It has been reported that mental stress is an independent risk factor for cardiovascular events and impairs coronary circulation. Lavender aromatherapy, one of the most popular complementary treatments, is recognized as a beneficial mental relaxation therapy. However, no study has examined the effect of this therapy on coronary circulation. We aimed to assess the effect of lavender aromatherapy on coronary circulation by measuring coronary flow velocity reserve (CFVR) with noninvasive transthoracic Doppler echocardiography (TTDE).

Material and methods: We enrolled 30 young healthy men (mean age 34±4.7 years, range 24–40 years). Coronary flow velocities in the left anterior descending coronary artery were recorded by TTDE at rest and during hyperemia induced with an intravenous infusion of adenosine triphosphate (ATP). CFVR was calculated as the ratio of hyperemic to basal mean diastolic flow velocity. CFVR was assessed at baseline and immediately after lavender aromatherapy (four drops of essential oil diluted with 20 ml of hot water and inhaled for 30 min). Simultaneously, serum cortisol was measured as a marker of stress hormones. To exclude the relaxation effects of rest, the same measurements were repeated in the same volunteers without aromatherapy as a control study.

Results: CFVR measurements were obtained in all volunteers (100%). Blood pressure and heart rate responses to ATP infusion were not affected by lavender aromatherapy. Serum cortisol significantly decreased after lavender aromatherapy (8.4±3.6 to 6.3±3.3, $p<0.05$), but remained unchanged in controls (9.1±3.5 to 8.1±3.9, $p=ns$). In addition, CFVR significantly increased after lavender aromatherapy (3.8±0.87 to 4.7±0.90, $p<0.001$), but not in controls (3.9±0.8 to 3.9±0.8, $p=ns$).

Conclusions: Lavender aromatherapy reduced serum cortisol and improved CFVR in healthy men. These findings suggest that lavender aromatherapy has relaxation effects and may have beneficial acute effects on coronary circulation.

© 2007 Elsevier Ireland Ltd. All rights reserved.

Keywords: Relaxation effects; Lavender aromatherapy; Coronary flow velocity reserve; Healthy men; Transthoracic Doppler echocardiography

1. Introduction

Lavender aromatherapy is becoming increasingly popular and is recognized as a complementary therapy that is be-

neficial for mental relaxation. Additional effects, such as antioxidant and acetylcholinesterase inhibitory activities, have been also reported [1,2], and these moderate effects have been assessed in individuals with various chronic and degenerative diseases, including atherosclerosis. By contrast, there have been few clinical reports about the relationship between lavender aromatherapy and coronary circulation.

* Corresponding author.

E-mail address: nobusada@w8.dion.ne.jp (N. Funabashi).

Table 1
Clinical characteristics

Characteristics	Aromatherapy (n=30)	Control (n=30)	P value
Age (years)	32±4.7	32±4.7	ns
Men	30 (100%)	30 (100%)	ns
BMI	23±3.1	23±3.1	ns
Smoking	10 (33%)	10 (33%)	ns
Total cholesterol (mg/dl)	181±28.7	181±28.0	ns
High-density lipoprotein cholesterol (mg/dl)	53.5±12.7	53.9±12.0	ns
Low-density lipoprotein cholesterol (mg/dl)	110±27.6	110±27.8	ns
Triglyceride (mg/dl)	117±69.2	112±65	ns
Fasting blood sugar (mg/dl)	94.8±11.7	93.9±11.5	ns

Data are presented as mean±SD.
ns indicates not significant.

Mental stress has been reported to impair coronary circulation [3], to induce vasospastic angina [4], and to cause endothelial dysfunction. Some studies have shown that stress management improves coronary ischemia and its clinical outcome [5]. Coronary flow velocity reserve (CFVR), which is partly endothelium dependent, is considered as a useful physiologic index for coronary microcirculation [6]. Transthoracic Doppler echocardiography (TTDE) is a useful technique for measuring coronary flow velocity and for assessing CFVR non-invasively [7–9]. The aim of this study was to evaluate the beneficial effects of aromatherapy on CFVR in healthy men using TTDE.

2. Materials and methods

2.1. Subjects

We studied 30 healthy men (mean age 34±4.7 s, range 24–40 years) (Table 1), and excluded female subjects because CFVR is affected by the menstrual cycle [10]. None of subjects had hyperlipidemia, hypertension, diabetes mellitus, left ventricular hypertrophy, atrial fibrillation or abnormal wall motion of left ventricle. Ten subjects were smokers. All volunteers had to refrain from smoking, tea, caffeine, wine, other known sources of rich flavonoids, and antioxidant supplements for 3 h preceding assessment. Each subject gave written informed consent before enrollment.

2.2. Study protocol

In this single-blind (operator) study, the subjects were studied on two separate days: one day with lavender aromatherapy, and another day without aromatherapy (control study). All studies were performed in the evening after a regular work. In a quiet, air-conditioned room (14 m², 22–25 °C), the room lights were dimmed, background noise was maximally reduced, and the subjects were encouraged to relax. After 30 min of rest in a supine position, a blood sample was taken immediately and an initial measurement of

Table 2
Hemodynamics

		Before baseline	Before hyperemia	After baseline	After hyperemia
Lavender	BPs	112±13	107±12	109±14	106±12
	BPd	63±9.4	59±10	62±12	59±9.1
	HR	67±6.8	74±8.4‡	65±6.6	73±9.8‡
	RPP	7502±1252	7966±1298	7072±1150	7722±1420*
Control	BPs	110±14	106±12	108±14	105±13
	BPd	65±10	59±9.7*	62±12	57±9.8
	HR	66±5.5	74±8.1‡	64±6.5	71±7.9‡
	RPP	7284±1105	7760±1104	6833±1065	7463±1190*

Data are presented at the mean±SD.

**p*<0.05 vs. baseline; †*p*<0.01 vs. baseline; ‡*p*<0.001 vs. baseline.

BP_d indicates diastolic blood pressure (mm Hg), BP_s indicates systolic blood pressure (mm Hg), HR indicates heart rate (/min), RPP indicates rate pressure product (beats per minute×mm Hg).

coronary flow velocity reserve was performed. Aromatherapy was then carried out by inhalation of lavender essential oil (linalyl acetate 43.73%, linalool 29.26%, terpinen-4-ol 3.46%, cineol 0.61%) for 30 min using four oil drops diluted with 20 ml of hot water. After lavender aromatherapy, a second blood sample was taken and coronary flow velocity reserve was assessed again. On a later day, control studies without aromatherapy were performed as above in the same 30 volunteers to exclude the relaxation effects of rest. The blood samples taken immediately before and after aromatherapy were used to determine serum concentrations of blood sugar and lipid profiles (total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, triglyceride levels). Serum cortisol was measured as a marker of stress hormones.

2.3. Measurements of CFVR with TTDE

The method of measuring CFVR with TTDE has been described previously [7–9]. Coronary flow velocities in the left anterior descending coronary artery (LAD) were recorded with an Acuson Sequoia 512 instrument (Siemens Medical Solutions USA, Inc., Mountainview, California) using a frequency of 5–7 MHz (Doppler frequency,

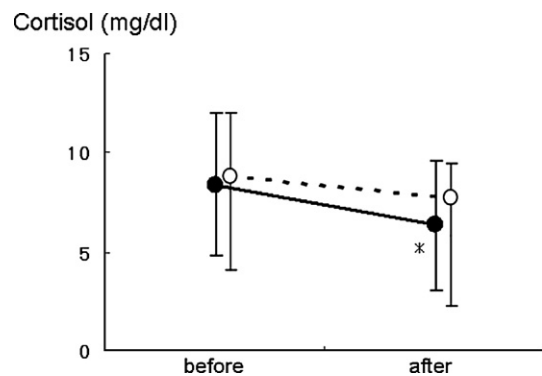


Fig. 1. Serum cortisol in aromatherapy group (closed circles) and control group (open circles). In the lavender aromatherapy subjects, cortisol was significantly reduced after aromatherapy. **p*<0.05 vs. before aromatherapy.

Table 3
Mean diastolic velocity measurements

		Before aromatherapy (mm/s)	After aromatherapy (mm/s)
Lavender	Baseline	16.6±5.4	15.1±4.9
	Hyperemia	60.7±17.2	71.3±21 ^a
Control	Baseline	15.3±4.9	16.2±5.5
	Hyperemia	57.0±16	60.4±18.7

Data are presented at the mean±SD.

^a $p < 0.01$ vs. baseline before aromatherapy hyperemia.

3.5 MHz) with color flow mapping guidance. We tried to align the ultrasound beam parallel to the direction of flow in the distal LAD, and angle correction was needed in each examination because of incidental Doppler angle (mean angle $25 \pm 21^\circ$, range 0 – 56°). Intravenous adenosine triphosphate (ATP) was administered (0.14 mg/kg/min) to induce hyperemia. Mean diastolic velocities (MDV) were measured at baseline and at peak hyperemic conditions and were averaged over three cardiac cycles. CFVR was defined as the ratio of hyperemic MDV to basal MDV.

2.4. Statistical analysis

All data were expressed as mean±SD. We used Student's *t*-test to compare clinical characteristics between the lavender aromatherapy subjects and controls. To compare the effects of ATP administration and aromatherapy, we used repeated-measure ANOVA for serum cortisol, hemodynamic parameters (blood pressure, heart rate and rate pressure product), mean diastolic velocities and coronary flow velocity reserve. The Fisher protected least-significant difference test was used for the post hoc test. For all analyses, $p < 0.05$ was considered significant.

3. Results

Adequate spectral Doppler recordings of diastolic coronary flow in the LAD were obtained in all volunteers (100%). None

of the subjects experienced any symptoms or showed any electrocardiogram changes during ATP administration.

3.1. Hemodynamics

As shown in Table 2, there was no difference in systolic blood pressure, diastolic blood pressure, heart rate and rate-pressure product at baseline between the lavender aromatherapy subjects and controls. Heart rate and rate-pressure product at hyperemia significantly increased in both groups of subjects in response to ATP infusion.

3.2. Serum cortisol

Serum cortisol was measured as a marker of stress hormones. There was no difference in serum cortisol levels between the lavender aromatherapy subjects and controls before aromatherapy (8.4 ± 3.6 vs. 9.1 ± 3.5), but serum cortisol levels were significantly lower after lavender aromatherapy than before aromatherapy (8.4 ± 3.6 to 6.3 ± 3.3 , $p < 0.05$) (Fig. 1). By contrast, serum cortisol levels in controls did not change significantly.

3.3. CFVR

Mean diastolic velocities in both groups of subjects are shown in Table 3. MDV values at baseline were quite similar between the lavender aromatherapy subjects and controls. Repeated-measures ANOVA showed a significant interaction for MDV and ATP administration between the before and after aromatherapy groups ($p < 0.001$), and MDV in hyperemia after aromatherapy significantly increased in comparison to that before aromatherapy (60.7 ± 17.2 to 71.3 ± 21 , $p < 0.01$). In addition, CFVR after aromatherapy also significantly increased as compared with that before aromatherapy (3.8 ± 0.87 to 4.7 ± 0.90 , $p < 0.001$) (Fig. 2). By contrast, MDV and CFVR in controls did not change significantly.

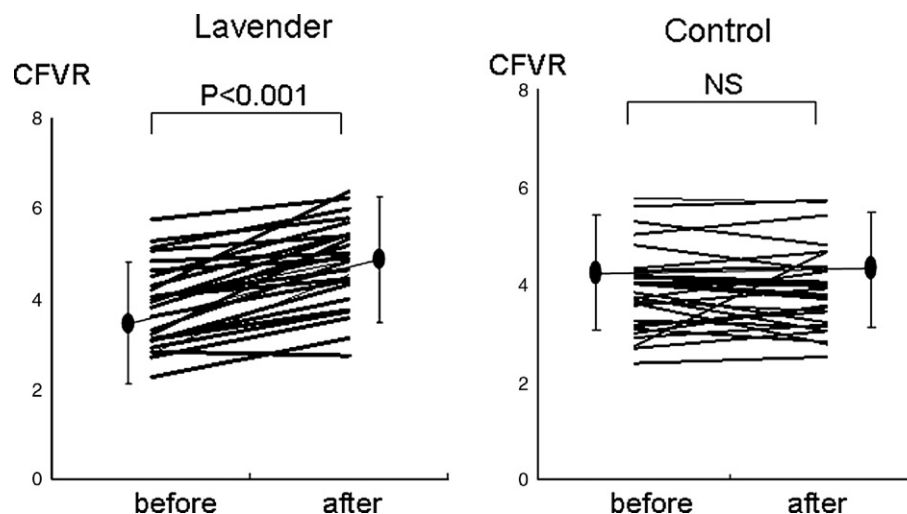


Fig. 2. Individual changes in CFVR in subjects before and after aromatherapy with lavender oil (left) and in controls (right). CFVR improved in lavender aromatherapy subjects.

The inter- and intraobserver variabilities (error) for measurement of the Doppler velocity recording were 5.0% and 3.9%, respectively.

4. Discussion

Many effects of lavender aromatherapy have been documented, including mood and emotion control (sedative, anxiolytic, antidepressant, hypnotic, alert), control of autonomic nervous system, and endocrine effects [11–15]. In addition, lavender aromatherapy has been reported to have antioxidant activities and to inhibit acetylcholinesterase [1,2]. Oxidative damage, caused by the action of free radicals, may initiate and promote the progression of a number of chronic diseases, such as neurodegenerative disorders, cancer, atherosclerosis, cataract formation, and inflammation [16,17]. As a result, antioxidant effects of lavender aromatherapy have been studied in relation to the prevention of degenerative brain disorders, such as Alzheimer's and Parkinson's diseases, and cancer [18,19]. By contrast, there have been few reports about the relationship between lavender aromatherapy and coronary circulation. In an animal study, linalyl acetate, as the major ingredient of lavender essential oil, has been shown to relax the vascular smooth muscle in rabbit carotid arteries, and to be partially associated with activation of the nitric oxide/cyclic guanosine monophosphate pathway [20]. To our knowledge, our study is the first to show that lavender aromatherapy improves coronary circulation in healthy men.

Negative mental stress has been shown to increase serum cortisol levels in many reports [22]. On the other hand, a pleasant mental situation, such as watching a good video and smelling a favorite scent, have been found to decrease cortisol levels and to increase free radical scavenging activities [21–23]. The 5-year incidence of cardiovascular events has been reported to be significantly higher in men with abnormal cortisol secretion as compared with those with a normal pattern [24]. This suggests that stressful situations leading to elevated cortisol impair coronary circulation. Epidemiological studies indicate that psychosocial factors contribute to the development of both coronary artery disease and endothelial dysfunction, and coronary atherosclerosis worsens in response to social disruption [25,26]. Our recent study has also shown that mental stress decreases CFVR within 30 min [3]. However, the underlying mechanisms are complex and elusive. Among many possible factors, endothelial dysfunction, hypercoagulability, impaired autonomic function, exaggerated hemodynamic responses, and reactive oxygen species responses to stress have been related to cardiovascular outcomes and enhanced atherosclerosis [27,28].

Except for our study, there has been no report that directly indicates that lavender aromatherapy improves coronary circulation in men, although some recent investigations have evaluated the complex mechanisms that may link stress reduction to improved cardiovascular outcomes. Daily

relaxation and stress reduction have been associated with reduced carotid atherosclerosis [29]. In patients with mental stress-induced coronary ischemia, Blumenthal et al. have shown improved coronary ischemia and improved clinical outcome with a CBT-based stress management program [5].

Stress-induced myocardial ischemia often occurs at lower levels of oxygen demand than exercise-induced ischemia, and its incidence has no correlation with the angiographic severity of coronary artery disease [30]; thus, it is very difficult to predict. Furthermore, mental stress sometimes causes vasospastic angina [4]. Both prevention of mental stress and promotion of mental relaxation may be important factors for cardiovascular morbidity and mortality. Lavender aromatherapy may be one of the inexpensive but beneficial complementary therapies for coronary circulation.

5. Limitation

There are several limitations in this study. First, we measured not coronary flow volume, but coronary flow velocity, and coronary diameter changes were not assessed because of the limitation of this method. However, it has been reported that changes in coronary flow velocities during drug-induced hyperemia closely reflect changes in coronary blood flow. Moreover, there is a good agreement between CFVR, as assessed from the flow velocity, and the results of positron emission tomography. Next, we assessed CFVR after only 30 min of lavender aromatherapy; thus, the long-term effects of lavender aromatherapy remain unknown. In addition, we studied only young healthy men; therefore, further investigations are needed for lavender aromatherapy effects on patients with ischemic heart disease. Despite these limitations, our results suggest that lavender aromatherapy has acute positive effects on coronary circulation.

6. Conclusion

This study has demonstrated for the first time that the acute effects of lavender aromatherapy improve CFVR and reduce serum cortisol in healthy men. Lavender aromatherapy has mild relaxation effects and may have beneficial effects on coronary circulation.

References

- [1] Parejo I, Viladomat F, Bastida J, et al. Comparison between the radical scavenging activity and antioxidant activity of six distilled and nondistilled Mediterranean herbs and aromatic plants. *J Agric Food Chem* 2002;50:6882–90.
- [2] Ferreira A, Proenca C, Serralheiro ML, Araujo ME. The in vitro screening for acetylcholinesterase inhibition and antioxidant activity of medical plants from Portugal. *J Ethnopharmacol* 2006;108:31–7.
- [3] Hasegawa R, Daimon M, Toyoda T, Teramoto K, Sekine T, Komuro I. Effect of mental stress on coronary flow velocity reserve in healthy men. *Am J Cardiol* 2005;96:137–40.
- [4] Yoshida K, Utsunomiya T, Morooka T, et al. Mental stress test is an effective inducer of vasospastic angina pectoris: comparison with cold pressor, hyperventilation and master two-step exercise test. *Int J Cardiol* 1999;70:155–63.

- [5] Blumenthal JA, Jang W, Morris JJ. Stress management and exercise training in cardiac patients with myocardial ischemia. *Arch Intern Med* 1997;157:2213–23.
- [6] Hirata K, Amudha K, Elina R, Hozumi T, Yoshikawa J, Homma S, et al. Measurement of coronary vasomotor function: getting to the heart of the matter in cardiovascular research. *Clin Sci (London)* 2004;107:449–60.
- [7] Fusejima K. Noninvasive measurement of coronary artery blood flow using combined two-dimensional and Doppler echocardiography. *J Am Coll Cardiol* 1987;10:1024–31.
- [8] Kenny A, Wisbey CR, Shapiro LM. Measurement of left anterior descending coronary artery flow velocities by transthoracic Doppler ultrasound. *Am J Cardiol* 1994;73:1021–2.
- [9] Daimon M, Watanabe H, Yamagishi H, et al. Physiologic assessment of coronary artery stenosis by coronary flow reserve measurements with transthoracic Doppler echocardiography: comparison with exercise thallium-201 single-photon emission computed tomography. *J Am Coll Cardiol* 2001;37:1310–5.
- [10] Hirata K, Shimada K, Watanabe H, et al. Modulation of coronary flow velocity reserve by gender, menstrual cycle and hormone replacement therapy. *J Am Coll Cardiol* 2001;38:1879–84.
- [11] Lehtner J, Eckersberger C, Walla P, Postsch G, Deecke L. Ambient odor of orange in a dental office reduces anxiety and improves mood in female patients. *Physiol Behav* 2000;71:83–6.
- [12] Komori T, Fujisawa R, Tanida M, Nomura J, Yokoyama MM. Effects of citrus fragrance on immune function and depressive states. *Neuropsychopharmacol* 1995;5:477–80.
- [13] Cooke B, Ernst E. Aromatherapy: a systemic review. *Br J Gen Pract* 2000;50:493–6.
- [14] Vickers A, Zollman C. ABC of complementary medicine: massage therapies. *BMJ* 1999;319:1254–7.
- [15] Buchbauer G, Jirovetz L, Jager W, Dietrich H, Plank C. Aromatherapy: evidence for sedative effects of the essential oil of lavender after inhalation. *J Biosci* 1991;46:1067–72.
- [16] Desmarchelier C, Ciccio G, Coussio J. Recent advances in the search for antioxidant activity in South American plants. *Stud Nat Prod Chem* 2000;22:343–67.
- [17] Cos P, Calomme M, Pieters L, Vlietinck J, Vanden D. Structure–activity relationship of flavonoids as antioxidant and pro-oxidant compounds. *Stud Nat Prod Chem* 2000;22:307–41.
- [18] Gilani AH, Aziz N, Khan MA, et al. Ethnopharmacological evaluation of anticonvulsant, sedative and antispasmodic activities of *Lavandula stoechas* L. *J Ethnopharmacol* 2001;49:161–7.
- [19] Kähkönen MP, Hopia AI, Heinonen M. Berry phenolics and their antioxidant activity. *J Agric Food Chem* 2001;49:4076–82.
- [20] Koto R, Imamura M, Watanabe C, et al. Linalyl acetate as a major ingredient of lavender essential oil relaxes the rabbit vascular smooth muscle through dephosphorylation of myosin light chain. *J Cardiovasc Pharmacol* 2006;48:850–6.
- [21] Hwang JH. The effects of the inhalation methods using essential oils on blood pressure and stress responses of clients with essential hypertension. *Taehan Kanho Hakhoe Chi* 2006;36:1123–34.
- [22] Takai N, Yamaguchi M, Aragaki T, Eto K, Uchihashi K, Nishikawa Y. Effect of psychological stress on the salivary cortisol and amylase levels in healthy young adults. *Arch Oral Biol* 2004;49:963–8.
- [23] Atsumi T, Tonosaki K. Smelling lavender and rosemary increases free radical scavenging activity and decreases cortisol level in saliva. *Psych Res* 2007;150:89–96.
- [24] Rosmond R, Wallerius S, Bjorntorp P. A 5-year follow-up study of disease incidence in men with an abnormal hormone pattern. *J Intern Med* 2003;254:386–90.
- [25] Kaplan JR, Pettersson K, Manuck SB, Olsson G. Role of sympathoadrenal medullary activation in the initiation and progression of atherosclerosis. *Circulation* 1991;84:23–32.
- [26] Strawn WB, Bondjers G, Kaplan JR. Endothelial dysfunction in response to psychosocial stress in monkeys. *Circ Res* 1991;68:1270–9.
- [27] Rozanski A, Blumenthal JA, Kaplan J. Impact of psychological factors on the pathogenesis of cardiovascular disease and implications for therapy. *Circulation* 1999;99:2192–217.
- [28] Von Kanel R, Kudielka BM, Fischer JE. Hypercoagulability in working men and women with high levels of panic-like anxiety. *Psychother Psychosom* 2004;73:353–60.
- [29] Castillo-Richmond A, Schneider RH, Salerno J. Effects of stress reduction on carotid atherosclerosis in hypertensive African Americans. *Stroke* 2000;31:568–73.
- [30] Strike PC, Steptoe A. Systematic review of mental stress-induced myocardial ischemia. *Eur Heart J* 2003;24:690–703.