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Effect of lemongrass (*Cymbopogon citratus*) essential oil on cardiac autonomic function in female Generalized Anxiety Disorder: A poincaré analysis of heart rate variability

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Abstract

Background: Generalized anxiety disorder (GAD) is a worldwide, one of most prevalent mental disorder and associated with autonomic dysfunction. Poincaré plot of heart rate variability (HRV) is a nonlinear method to assess cardiac autonomic nerve function (CANF). Lemongrass (*Cymbopogon citratus*) essential oil (LEO) has been reported with anxiolytic effect and autonomic improvement in human. **Objective:** To assess the effect of LEO inhalation on CANF in female patients with GAD by analysis of poincaré plot of HRV. **Method:** This Quasi experimental study was conducted on 60 newly diagnosed female GAD patients with 20-40 years of age. Among them, 30 patients were treated with LEO inhalation for 15 min for once a week for one month (30 days) along conventional treatment and 30 patients were without LEO inhalation and continued only conventional treatment for 30 days. Thirty (30) apparently healthy subjects were control group. HRV data of all patients and control were recorded at baseline and after 30 days of intervention or follow up respectively. HRV was recorded by a data acquisition device,

Power Lab 8/35 and Poincaré plot analysis was done by lab chart software. For statistical analysis ANOVA followed by post-hoc test and paired sample 't' test were done. **Results:** In this study, at baseline, the standard deviation of the short-term RR interval variability (minor axis of the cloud, SD1), the standard deviation of the long-term RR interval variability (major axis of the cloud, SD2) and SD1/SD2 were found significantly lower ($p < 0.001$) in all GAD patients compared to control group. After 30 days of intervention with LOE, significant increase of SD1 ($p < 0.001$) and SD2, SD1/SD2 ($p < 0.01$) were found in GAD patients whereas no significant difference was found in patients without LEO after 30 days. Moreover, significantly higher values of SD1 and SD2 were observed in GAD patients after aroma therapy with LEO compared to GAD patients not under aroma therapy. Furthermore, LEO could restore the BP of the GAD to the control level. **Conclusion:** This study concluded that, aromatherapy with LEO inhalation may be effective to improve cardiac autonomic dysfunction in female GAD patients.

Key words: GAD, SD1, SD2, aromatherapy, lemongrass essential oil (LEO).

Introduction

Generalized Anxiety Disorder (GAD) is a worldwide, common psychological disorder which can appear at any age.¹ In every year, GAD affects 6.8 million adults in general population and women are found to be twice in number.²⁻³ According to Diagnostic and Statistical Manual 5th edition (DSM-V), GAD is associated with anxiety and uncontrolled worry with duration of six months accompanied by various symptoms like restlessness, lack of concentration, fatigue, muscle tension, irritability, and sleep disturbance.^{2,4} GAD and cardiovascular diseases (CVD) often coexist.^{5,6} Impaired vagal regulation is associated with anxiety disorders along with hyperactive of sympathetic activity.^{7,8} HRV reflects the impact of central autonomic network on autonomic nervous system. Among the methods for HRV analysis, Poincaré plot is a common nonlinear method which is a two dimensional graphical and quantitative technique with three indices: SD1, SD2 and SD1/SD2. Here, SD1 represents

parasympathetic tone; SD2 represents both sympathetic and parasympathetic tone and SD1/SD2 measures sympathovagal balance.⁹⁻¹¹ Previous studies reported reduced HRV in GAD patients. Their results suggested parasympathetic withdrawal and sympathetic predominance in autonomic tonic discharge based on frequency and time domain methods.^{8,11-13} Earlier studies showed anxiolytic drugs such as selective serotonin reuptake inhibitor, mirtazapine in GAD patients had no significant effect on HRV. Moreover, tricyclic antidepressants and clozapine were found associated with reduced HRV in GAD patients.¹⁴⁻¹⁵

Research evidence indicated that aromatherapy; acupuncture and massage are in addition to conventional treatment often effective to relieve stress and anxiety.² Role of aromatherapy has been highlighted to quell anxiety and restore autonomic balance by analyzing HRV.¹⁶⁻¹⁹ Both animal and human studies reported, LEO has anxiolytic effect with significant autonomic

improvement.²⁰⁻²² But the potentials of LEO for improvement of autonomic dysfunction in GAD patients has not properly explored. So this study has been designed to investigate the effect of LEO inhalation on CANF by analyzing Poincaré plot of HRV in female GAD patients.

Methods

Study design and setting

This Quasi-Experimental study was conducted at the Department of Physiology of Bangabandhu Sheikh Mujib Medical University (BSMMU) from September, 2022 to August, 2023 to observe the effect of LEO inhalation on CANF in female GAD patients by Poincaré analyzing.

Study participants

For this study, 60 female GAD patients with age of 20-40 years were enrolled from the Out Patient Department of the Department of Psychiatry, BSMMU and they were diagnosed by psychiatrist following the DSM-V.⁴ All the patients were newly diagnosed and they were not under any kind of medicine. Thirty apparently healthy subjects with similar age, sex and BMI were selected as control. All participants had normal sense of smell and they were non-smoker.^{1-4,13,23}

Sampling

Purposive sampling was adopted to select both patients and control.

Exclusion criteria

Patients were excluded if they had other psychiatric comorbidity, substance abuse, neurological, cardiovascular, endocrine diseases. Pregnancies, lactation, menstrual phase, use of hormonal contraceptive were also excluded.^{11,17-19}

Collection of essential oil

The LEO (in liquid form in an aluminum bottle) was purchased from Aarnov Global Exports. (Ghaziabad, U.P, India) The major ingredients of LEO are citral 38.82%, neral 38.52%, linalool 7.73%, geraniol 2.19% and some other minor

components according to the Gas Chromatography- Mass Spectrometry (GC/MS) analysis which are similar to the usual LEO as per literature review. The aroma of LEO was dispersed through room air by placing oil drops in a diffuser.

Experimental Procedure

Sixty GAD patients were divided into two groups. Thirty patients were assigned to lemongrass essential oil inhalation (LEO) and 30 patients were not given lemongrass essential oil inhalation (NLEO). The healthy subjects were not exposed to LEO and referred as control. The LEO group received LEO 15 minutes once for a week for one month at Noorzahan Begum Neurophysiology lab, Department of Physiology, BSMMU along conventional treatment and the schedule was carefully maintained. The NLEO group continued only conventional treatment. Control group did not receive any aroma inhalation. HRV measures were recorded at baseline before aroma inhalation or follow-up and after 1 month in GAD patients of both group and in control subjects.

Data collection procedure

After explaining the whole procedure of the study, N- butanol odor threshold test was also done to identify any abnormality in sense of smell. After final selection, informed written consent was taken from all subjects after explaining the detail procedure of the study. They were advised to take preparation for HRV test beginning from the previous night. They were instructed to finish their meal by 9:00 pm, to have a sound sleep and to avoid physical or mental stress, sedatives at night before measurement of HRV. For the recording day, they were also advised to take light breakfast without tea or coffee and should not use any perfume or spray. After they reported at Noorzahan Begum Neurophysiology lab, a thorough physical examinations were done which included pulse, BP and anthropometric measurements. Subjects were kept in complete bed rest in supine position for 15-20 minutes in a cool and calm sound proof room. The temperature

of the laboratory was set to 25°C-28°C and lights were kept dim. HRV was recorded in lead II for 5 min as baseline data by 8 active channels device, power lab 8/35 (AD instrument, Australia). Auto data report generated by Labchart software was used for Poincaré analysis of HRV. Then for intervention with LEO, the subjects of LEO group were asked to sit on the chair with arm support. 4 drops LEO was added in 400ml of water in a diffuser and switch turned on to subjects for fifteen minutes. The diffuser was kept at a distance 10-15 cm away from the subjects. Thus, LEO group carried out the session every once a week for one month. After one month of intervention another HRV data was taken. The baseline data and follow up data after one month were also recorded by HRV in both NLEO and control group.

Statistical analysis

Data were expressed as mean±SD. Statistical analysis was done by One way analysis of variance (ANOVA) followed by Bonferroni's post hoc test and paired sample 't' test were done using SPSS version 25. The P value <0.05 was considered as statistically significant.

Results

Total seventy two newly diagnosed female GAD patients and 31 healthy controls were participated for this study. Among 72 GAD patients, 37

patients were assigned for LEO group and rest 35 patients were as NLEO group. Data of 7 LEO and 5 NLEO group and 1 control were discarded due to incomplete task and technical error. In this study, age, BMI and Smell Test Score (STS) were found similar in all GAD patients compared to control (Table I). At baseline, before intervention, resting pulse rate ($p<0.001$), SBP, DBP ($p<0.05$) were found significantly higher whereas SD1, SD2 and SD1/SD2 were found ($p<0.001$) significantly lower in patient groups compared to control group. Moreover, these parameters were not significantly different in two patient groups at baseline before intervention (Table II). After one month of LEO inhalation, pulse rate ($p<0.001$), SBP and DBP significantly ($p<0.01$) decreased and SD1 ($p<0.001$), SD2 and SD1/SD2 significantly ($p<0.01$) increased compared to baseline values (Table III), though there were no significant changes found in these parameters compared to the baseline values of NLEO patients. Again, post intervention values after one month showed, significantly lower of resting pulse rate ($p<0.01$), SBP ($p<0.05$), DBP ($p<0.01$) and significantly higher SD1, SD2 ($p<0.01$) in LEO group compared to NLEO group. When compared to control, SBP and DBP after LEO inhalation was similar to control though LEO inhalation could not restore rest of the parameters (Table IV).

Table I : Age, BMI, STS in different groups (N=90)

Variables	LEO (n=30)	NLEO (n=30)	Control (n=30)
Age (Years)	28.20±4.94	27.47±4.99	28.87±3.82
BMI (Kg/m ²)	23.01±2.1	22.4±2.14	22.4±1.8
STS	9.73±1.01	9.83±0.98	9.80±0.92

Data were expressed as Mean ± SD. Statistical analysis was done by One-way ANOVA; BMI- Body Mass Index; STS- Smell Test Score; LEO- Patients as lemongrass essential oil group; NLEO- Patients as non-lemongrass essential oil group; Control- Healthy control; N- Total number of subjects; n- Number of subjects in each group.

Table II : SD1, SD2, SD1/SD2, resting pulse rate and BP in different groups at baseline(N=90)

Variables	LEO(n=30)	NLEO(n=30)	Control (n=30)
SD1	14.53±4.93***	15.36±7.36***	41.77±8.23
SD2	40.84±10.87***	34.99±9.70***	73.34±15.79
SD1/SD2	0.361±0.102***	0.443±0.167***	0.585±0.126
Pulse rate(beats/min)	86.51±8.80***	85.13±9.12***	72.33±5.38
SBP(mmHg)	116.67±7.11*	116.00±8.55*	110.33±8.40
DBP(mmHg)	78.83±8.37*	79.17±9.92*	72.83±7.73

*This depicts comparison with control group, ***p<0.001 and *p<0.05. Data were expressed as Mean ± SD. Statistical analysis was done by One-way ANOVA followed by post-hoc Bonferroni test;SD1-Standard deviation of short term RR interval variability;SD2-Standard deviation of long term RR interval variability; SD1/SD2- Ratio of short term RR interval and long term RR interval variability; SBP- Systolic Blood Pressure; DBP- Diastolic Blood Pressure; LEO- Patients as lemongrass essential oil group; NLEO- Patients as non-lemongrass essential oil group; Control- Healthy control;N- Total number of subjects; n- Number of subjects in each group.

Table III : Pre and post intervention/follow up values ofSD1,SD2, SD1/SD2, resting pulse and BP in female GAD patients(N=60)

Variables	LEO		NLEO	
	Pre (n=30)	Post(n=30)	Pre (n=30)	Post(n=30)
SD1	14.53±4.93	22.17±5.58 ^{ooo}	15.36±7.36	15.34±6.76
SD2	40.84±10.87	49.89±11.91 ^{oo}	34.99±9.70	37.62±10.12
SD1/SD2	0.361±0.102	0.468±0.172 ^{oo}	0.443±0.167	0.415±0.152
Pulse rate(beats/min)	86.51±8.80	78.37±6.49 ^{ooo}	85.13±9.12	83.83±7.95
SBP(mmHg)	116.67±7.11	110.83±7.08 ^{oo}	116.00±8.55	116.17±6.90
DBP(mmHg)	78.83±8.37	73.16±6.75 ^{oo}	79.17±9.92	79.50±9.03

^oThis depicts comparison between LEO₀ and LEO₃₀ group,^{ooo}p<0.001 and^{oo}p<0.01. Data were expressed as Mean ± SD. Statistical analysis was done by Paired sample t-test; SD1-Standard deviation of short term RR interval variability; SD2-Standard deviation of long term RR interval variability; SD1/SD2- Ratio of short term RR interval and long term RR interval variability;SBP- Systolic Blood Pressure; DBP- Diastolic Blood Pressure; LEO- Patients as lemongrass essential oil group; NLEO- Patients as non-lemongrass essential oil group ;Control- Healthy control; N- Total number of subjects; n- Number of subjects in each group.

Table IV : Post intervention/follow up values ofSD1, SD2, SD1/SD2, resting pulse rate and BP in different groups(N=90)

Variables	LEO (n=30)	NLEO (n=30)	Control (n=30)
SD1	22.17±5.58 ^{***££}	15.34±6.76 ^{***}	41.29±11.13
SD2	49.89±11.91 ^{***££}	37.62±10.12 ^{***}	70.85±14.94
SD1/SD2	0.468±0.172 ^{**}	0.415±0.152 ^{***}	0.599±0.164
Pulse rate(beats/min)	78.37±6.49 ^{*££}	83.83±7.95 ^{***}	73.53±7.95
SBP(mmHg)	110.83±7.08 [£]	116.17±6.90 [*]	110.50±7.69
DBP(mmHg)	73.16±6.75 ^{££}	79.50±9.03 [*]	73.83±6.78

*This depicts comparison with control₃₀ group, *p<0.05, **p<0.01, ***p<0.001. £This depicts comparison between LEO and NLEO group, £p<0.05 and ££p<0.01. Data were expressed as Mean ± SD. Statistical analysis was done by One-way ANOVA followed by post-hoc Bonferroni test; SD1-Standard deviation of short term RR interval variability; SD2-Standard deviation of long term RR interval variability; SD1/SD2- Ratio of short term RR interval and long term RR interval variability; SBP- Systolic Blood Pressure; DBP- Diastolic Blood Pressure; LEO- Patients as lemongrass essential oil group; NLEO- Patients as non- lemongrass essential oil group; Control- Healthy control; N- Total number of subjects; n- Number of subjects in each group.

Discussion

The results of resting pulse rate, SBP, DBP, SD1, SD2 and SD1/SD2 indicate cardiac autonomic dysfunction with poor parasympathetic discharge was associated with all drug naïve female GAD patients. These findings agreed with other investigators who observed relationship between hypertension, cardiovascular risk with anxiety and GAD by analyzing poincaré plot and physiologic measures (BP, HR).²⁴⁻²⁶ These results also indicate the higher risk of cardiovascular diseases in these GAD patients due to imbalance autonomic function.

In this study, aromatherapy with LEO inhalation for one month showed significant decrement of pulse rate, SBP, DBP and significant increment of SD1, SD2 andSD1/SD2 in patients from their baseline suggest improvement of CANF. These findings agreed to the results of others.^{21,22,27-30} In contrast, in this study, non- significant change in these parameters of NLEO group suggests autonomic dysfunction retained in these GAD patients. Although aromatherapy with LEO inhalation could not restore poincaré

parameters to control levels but it provides evidence for effective improvement of autonomic function in GAD patients. How aromatherapy works on autonomic nerve function is not clearly understood. It has been suggested that, after inhalation, the aromatic particles trigger the olfactory receptors and signals are conveyed to primary olfactory cortex and limbic system. Thus, the aromatic stimulation can change mood, emotions and autonomic function.³¹ Studies also revealed that due to various chemical compositions, aromatic agents exert anxiolytic effects, specially citral, linalool, myrcene, limolene, neral, are the chemical components found various EO are believed to reduce anxiety level both in animal and human models. Researches also showed, citral possibly acts as an agonist to both GABA and 5-HT1A receptor.³²⁻³³ So the observed effects of lemongrass EO inhalation on autonomic nerve function in this study might be through stabilizing both GABA and serotonergic system in brain as LEO contains citral, neral, geranial, linalool components.

Conclusion

From the outcome of the present study, it can be concluded that, inhalation of lemongrass essential oil was effective to improve the autonomic dysfunction in the female GAD patients due to its quality, compositions and pharmacological effect. As it is a safe, convenient and comfortable technique, it can be recommended as a complement to medication and thereby reduce the cardiovascular risk.

Ethical Issue

The ethical clearance was approved by the Institutional Review Board (IRB) of the BSMMU

Conflict of interest

Authors of this study have no conflict of interest.

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