Journal of Nutrition and Food Security
Shahid Sadoughi University of Medical Sciences
School of Public Health
Department of Nutrition
Nutrition & Food Security Research Center

eISSN: 2476-7425 pISSN: 2476-7417 JNFS 2024; 9(1): 45-51 Website: jnfs.ssu.ac.ir

Effect of Crataegus Extract on the Relief of Heart Palpitation and Anxiety in Teenagers: An Interventional Quasi-Experimental Study

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ARTICLE INFO

ORIGINAL ARTICLE

Article history:
Received:28 Feb 2022
Revised: 16 Jun 2022
Accepted: 6 Jul 2022

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ABSTRACT

Background: Heart palpitation is a common complaint defined as an unpleasant or abnormal heartbeat feeling. This study aimed to investigate the effectiveness of Crataegus extract on the relief of heart palpitations and anxiety in adolescents. **Methods**: This is an interventional quasi-experimental study performed from February 19, 2016 to February 19, 2017 on 120 adolescents aged 13 to 19 years with a complaint of heart palpitations, referring to heart clinic in Afshar Hospital of Yazd. The participants' demographic information, heartbeat feeling, Hamilton anxiety scaling, blood pressure, heartbeat rate, and electrocardiogram (ECG) were recorded. Patients were first treated with 20 drops every 8 hours for three days and then 25 drops every 8 hours for one month with Crataegus edible drops. They were then re-evaluated for heart palpations and anxiety. **Results**: Of 120 adolescents referring to Afshar Hospital with heart palpitations, 98 of participants (81.7%) experienced improvement. Mean differences in systolic blood pressure, heart rate, and anxiety scores before and after treatment with Crataegus extract decreased significantly by 1.71, 8.52, 6.55, respectively, but the mean difference in diastolic blood pressure increased by 1.46 (P<0.05). **Conclusion**: According to the results, Crataegus extract might be effective in reducing palpitation and anxiety in adolescents. Further studies are suggested to approve the results of the study.

Keywords: *Crataegus extract; Heart palpitation; Anxiety*

Introduction

Heart palpitation is a common complaint defined as an unpleasant and/or abnormal heartbeat feeling that can be benign or indicative of dangerous arrhythmias (Chan and Worster, 2011, Khamis and Dancy, 2009, Mayou *et al.*, 2003). Heart palpitation can be intermittent or continuous, regular or irregular, and can be expressed in terms of pounding, racing, skipping, stopping, thumping, fluttering, or irregular heartbeats. In most cases, neither physicians nor patients are able to accurately specify the case, hence they get confused in describing the problem (Barsky *et al.*, 1994, Jameson, 2018). Most patients describe it as abnormal consciousness of the heartbeat, and particularly when they feel their heartbeat is stopping or jumping, they become anxious

This paper should be cited as: Alipour MR, Asadolahi V, Sarebanhassanabadi M. ***Effect of Crataegus Extract on the Relief of Heart Palpitation and Anxiety in Teenagers: An Interventional Quasi-Experimental Study.*** *Journal of Nutrition and Food Security (JNFS)*, 2024; 9 (1): 45-51.

[DOI: 10.18502/jnfs.v9i1.14839]

(Jameson, 2018). Crataegus is one of the oldest known herbal medicines in Europe, first modified by Dioscorides in the first century as having an effect on the heart (Weihmayr and Ernst, 1996). The properties of bioflavonoid-like compounds in the leaves, flowers, and fruits of Crataegus (including oligometric procyanides (OPC), vitexin, quercetin, and hyperoside) on the cardiovascular system are well known (Rastogi *et al.*, 2016). Therefore, the extract prepared from Crataegus flower triggers relaxing-dilating peripheral blood vessels, increases myocardial metabolism, dilates coronary arteries, and improves blood flow to the heart, thus assisting in curing heart disease and relieving symptoms in the early stages of heart failure (Verma *et al.*, 2007). Daniele conducted a systematic review on the side effects and safety of Crataegus and found that the extract is well tolerated despite some reports of its severe side effects (Daniele *et al.*, 2006). Crataegus extract is used in the treatment of chronic congestive heart failure stage I and II, high blood pressure, high blood fat, angina pectoris, arrhythmias, and peripheral vascular disorders and is also regarded as an antispasmodic agent in the treatment of asthma, diarrhea, gallbladder diseases, uterine contractions, and has been applied as a sedative to treat insomnia (Wang *et al.*, 2013, World Health Organization, 1999). The extract is also used for digestive diseases, shortness of breath, kidney stones, mild changes in heart rhythm, stress, nervousness, sleep disorders, and pain control (Can *et al.*, 2010, Orhan, 2018, Rigelsky and Sweet, 2002). Recommended dosage for this drug includes 250 mg of standardized extract three times a day or 300 mg of Crataegus fruit three times a day or 1 ml of Crataegus tincture three times a day or 200 mg of raw Crataegus daily or 160 mg of Crataegus leaf and flower extract equivalent to 3.5 mg of flavonoids daily (Verma *et al.*, 2007). Contraindications include allergy to active ingredients of the drug, during pregnancy and lactation, worsening of symptoms while taking the drug with symptoms such as swelling of the legs, chest pain with spread to hands, upper abdomen or areas around the neck, or asthma requiring to refer to a doctor immediately (European Medicines Agency, 2008). The aim of this study was to evaluate the effectiveness of Crataegus extract on the relief of heart palpitations in adolescents aged 13-19 years with a complaint of heart palpitations referred to Afshar Heart Clinic in Yazd.

Materials and Methods

Study design and participants: This interventional quasi-experimental study was conducted from February 19, 2016 to February 19, 2017. A total of 120 adolescents aged 13 to 19 years with a complaint of heart palpitations referred to Afshar Heart Clinic in Yazd were involved in the study. The patients with mental retardation, psychosis and serious mental illnesses, ischemic heart disease, valvular heart disease, malignant complement arrhythmias, cardiomyopathies, overt heart failure, uncontrolled hypertension, serious chronic diseases, thyroid disease, anemia, pregnancy, and those taking antidepressants, anti-anxiety drugs and beta-blockers were excluded from the study. Moreover, information regarding those who had no desire to continue participating in the study and did not return was not analyzed.

Herbal medicine: Crataegus oxyacanta (hawthorn) plant consists of flavin polymers including heptahydroxy flavin glycoside. Flavonoid compounds and oligometric procainides as key elements of Crataegus oxyacanta are responsible for the healing properties of this plant. Crataegus leaves, flowers, and fruits contain a variety of bioflavonoid-like compounds that are primarily responsible for heart-affecting properties of this plant. The bioflavonoids in the Crataegus plant include oligometric ocular procyanides (OPCs), vitexin, quercetin, and hyperoside. The properties of these compounds and their effect on the cardiovascular system have led to the extraction of Crataegus leaf and flower compounds that are widely used in Europe (Rastogi *et al.*, 2016).

Procedure: First, written consent form was obtained from all participants and a history was

[DOI: 10.18502/jnfs.v9i1.14839]

taken from the patients. Blood pressure and heart rate were then measured and recorded. Electrocardiogram (ECG) was also taken from the patients and a checklist including sex, age, heart rate, Hamilton score of anxiety questionnaire, blood pressure, and heart rate were completed by a physician. Patients were first treated with 20 drops every 8 hours for three days and then 25 drops every 8 hours for one month (according to the recommended dosage of the drug manufacturer, Iran Daruk Company). After administrating the drug for one month, the patients referred for follow-up. During this visit, the necessary examinations were performed and blood pressure and HR were taken from the patients and recorded, and the same form and anxiety questionnaire were completed once more. Furthermore, patients were asked about the side effects of the drug during this visit and they were recorded as well. This study was conducted according to the Declaration of Helsinki.

Ethical considerations: Written consent was obtained from all the participants. This study was approved in Ethics Committee, Shahid Sadoughi University of Medical Sciences (ethics code: IR.SSU.MEDICINE.1397.184).

Data analysis: Paired samples t-test was used to compare the mean scores of variables before and after drug administration. Chi-square test was employed to examine the relationship between age, age groups, and gender with heart rate. Data analysis was performed using SPSS software, version 16. Significance level was set at 5%.

Results

Out of 120 adolescents who had complained of palpitation at the heart clinic of Afshar Hospital in Yazd, 98 of participants (81.7%) experienced improvement. The mean age of the participants was 16.3±2.0 year. 59 of participants were boys (49.2%) and 61 were girls (50.8%), and 28, 46, and 46 individuals lied in the age groups of 13-14 years (23.3%), 17-15 years (38.3%), and 18-19 years (38.3%), respectively (**Table 1**).

Based on the results of Chi-square test, there was no significant relationship between age groups and gender with heart rate improvement (P> 0.05). Heart rate improvement in the age groups of 13-14, 15-17, 18-19, were 86% (24 people), 85% (39 people), and 76% (35 people), respectively, and 85% (n=50) of boys and 78% (n=48) of girls recovered after treatment with Crataegus (**Table 1**).

Table 1. Frequency distribution of demographic characteristics based on improved heart rate after Crataegus intervention.

Variables	Improved	Non-Improved	P-value[a]
Age category (y)			0.45
13-14	24(86)[b]	4(14)	
15-17	39(85)	7(15)	
18-19	35(76)	11(24)	
Gender			0.39
Boys	50(85)	9(15)	
Girls	48(78)	13(22)	
Total	98(81.7)	22(18.3)	

[a]: Chi-square test; [b]: N(%).

The results of paired samples t-test indicated that the mean systolic blood pressure before and after intervention with Crataegus extract was 112.46±7.08 and 110.75±7.70 mmHg, respectively; it had a significant decrease of 1.71 mmHg (P<0.05). The mean diastolic blood pressure before and after intervention was 72.55±5.62 and 74.02±4.96 mmHg, which showed an increase of 1.46 mmHg (P=0.03). The mean heart rate of the patients before and after intervention with Crataegus extract reached 113.1±9.39 and 104.58±13.74 beats per minute, which significantly reduced by 8.52 beats per minute (P<0.001). Moreover, the mean score of anxiety before and after intervention with Crataegus extract was 26.39±8.12 and 20.33±5.99, which had a statistically significant decrease of 6.05 (P<0.001, **Table 2**).

[DOI: 10.18502/jnfs.v9i1.14839]

Figure 1 represents the frequency distribution of anxiety rate before and after intervention with Crataegus extract. Before intervention, 22 patients (18.3%) had mild, 29 patients (24.2%) moderate, 27 patients (22.5%) severe, and 42 others (35%) intolerable anxiety. After intervention, however, 47 patients (38.3%) had mild, 47 (39.2%) moderate, 16 (13.3%) severe, and 11 patients (9.2%) had intolerable anxiety. As can be seen, the frequency of patients decreased after drug administration in terms of the severity of anxiety.

Side effects: No clinical complaints on the side effects were reported during and after drug administration.

Table 2. Comparison of mean ±SD of variables before and after intervention with Crataegus variable.

Variables	Before	After	P-value[a]
SBP (mmHg)	112.46±7.08	110.50±7.70	0.05
DPB (mmHg)	72.55±5.62	74.02±4.96	0.03
Heart rate	113.10±9.39	104.58±13.47	< 0.001
Anxiety score	26.39±8.12	20.33±5.99	< 0.001

SBP: Systolic blood pressure; DBP: Diastolic blood pressure; [a]: Paired t-test

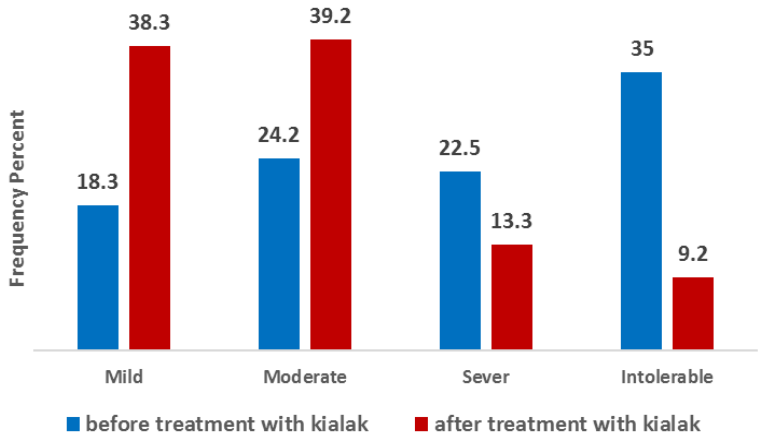

Figure 1. Frequency distribution of anxiety in the studied adolescents based on the score of anxiety questionnaire.

Discussion

The present study investigated the effectiveness of Crataegus extract on the relief of heart palpitations in adolescents aged 13-19 years with a complaint of heart palpitations at Afshar Heart Clinic in Yazd. The results demonstrated 81.7% reduction in heart rate after intervention with Crataegus. The mean score of heart rate, systolic blood pressure, and anxiety of the patients before and after treatment had a significant decrease, whereas diastolic blood pressure showed a significant increase.

Heart palpitation occurs for a variety of reasons and studies have shown that 43%, 31%, 10%, and 16% of palpitations are due to cardiac, psychiatric, miscellaneous, and unknown reasons (Alijaniha *et al.*, 2015). Herbal medicines are used as an alternative to conventional medicines for different diseases (Alijaniha *et al.*, 2015).

In the current study, the girls complaining of heart palpitations were more than the boys. Moreover, heart rate complaints were higher in women than in men; this is the case when heart palpitations are particularly associated with mental disorders, including anxiety. In a double-blind randomized trial conducted by Alijaniha, it was found that the reduction in heart rate using Melissa officinal leaf extract was greater in women than in men (Alijaniha *et al.*, 2015). In studies by Bobbo (Bobbo *et al.*, 2019), Johnsbu (Jonsbu *et al.*, 2011), Weber (Weber and Kapoor, 1996), and Summerton (Summerton *et al.*, 2001), 52%, 72%,

[DOI: 10.18502/jnfs.v9i1.14839]

61%, and 67% of women complained more of heart palpitations than men, respectively.

O'Connolly reported that Crataegus extract significantly reduced mean heart rate, as well as systolic and diastolic blood pressure in the drug group compared to the placebo (O'Conolly *et al.*, 1986, O'Connolly *et al.*, 1987). In the study by Eichstädt, after 4 weeks with Crataegus extract treatment, the mean heart rate of patients at rest before and after using Crataegus had a significant decrease (68.6 vs 66.2 mg). Moreover, systolic blood pressure at rest and activity phases decreased significantly from 136.5 to 134 mmHg and from 188.42 to 176.84 mmHg (Eichstädt *et al.*, 1989), respectively. In Tauchert's study, the patients consumed Crataegus extract for 24 weeks, and the mean systolic and diastolic blood pressures was 5.9 mmHg (from 142.9 to 137) and 2.2 mmHg (from 84.5 to 82.3), respectively. Also, the mean heart rate decreased to 3.4 beats per minute (from 76.7 to 73.3), and the heart rate significantly decreased from 1.22 before taking the drug to 0.35 after using (Tauchert *et al.*, 1999).

A significant decrease was also observed in the anxiety score of the Hamilton questionnaire (**Table 2**). Similar results have been reported in laboratory studies which confirm significant effects of this plant in reducing stress in mice (Can *et al.*, 2010). In studies by O'Connolly *et al*. regarding the psychological evaluation of patients after consuming Crataegus extract, there was a 93% improvement in participants' mental health, including a reduction in anxiety in the drug group (O'Conolly *et al.*, 1986, O'Connolly *et al.*, 1987). In addition, in Walker's study, the level of anxiety in patients consuming Crataegus group decreased in comparison with the placebo and other groups (Walker *et al.*, 2002). A study evaluated the effect of a short-term program of cognitive behavioral therapy on mild heartbeat, which found it only effective in improving some aspects of patients' quality of life but not useful to change the frequency of heartbeat (Jonsbu *et al.*, 2011).

Considering that few studies have been carried out on the effect of Crataegus extract on heart rate and there is no other similar study to compare the results, its effect was compared with other drugs. Due to the frequency distribution of patients in terms of heart rate improvement after drug administration, 98 (81.7%) out of 120 patients showed improvement or partial improvement, while in 22 patients (18.3%), no improvement was achieved after taking the drug. The results of the study by Alijanis *et al*. regarding the effect of Lemongrass (Melissa officinalis) on mild heartbeat indicated that Lemongrass (36.8%) significantly reduced patients' heart rate compared to the placebo group. Also, anxiety disorders decreased by 32.2% after drug administration (Alijaniha *et al.*, 2015). In Ptaszynski's study on patients with heart palpitations due to sinus tachycardia, 70% of symptoms improved after taking ivabradine and 45% with metoprolol (Ptaszynski *et al.*, 2013). McDonald studied the effect of ivabradine in patients with tachycardia syndrome and complaining of palpitations. An improvement or a relative improvement was identified in 55% of patients after using the drug (McDonald *et al.*, 2011). According to Tauchert's study, 76.6% of physicians have referred to good or very good effect of Crataegus extract, while 98.7% have reported good or very good tolerance after consumption of the drug (Tauchert *et al.*, 1999).

The findings of the present study showed the rate of recovery of patients with mild heart palpitations using Crataegus extract. Therefore, this drug can be regarded for the treatment of mild heart palpitations in adolescents.

This is the first study evaluating the effectiveness of alkaline extract on relieving heart palpitations in adolescents aged 13-19 years in Iran. The current study was limited by the number of adolescents who had referred to the heart clinic for heart palpitations or had been referred to the center by other colleagues with a diagnosis of mild heart palpitations. Moreover, non-referral of patients for follow-up and short duration of treatment can be regarded as other limitations of the study. Subsequent studies are recommended to be conducted with longer duration. It is also recommended that further research be conducted on different age groups and more investigations

[DOI: 10.18502/jnfs.v9i1.14839]

around the effectiveness of Crataegus extract in comparison with other standard and aromatic treatments for heart palpitations and also in combination with other drugs. Moreover, research is also needed to determine the therapeutic effect of the drug on other diseases associated with heart palpitations such as inappropriate sinus tachycardia or postural orthostatic tachycardia syndrome.

Conclusion

The results of this study regarding the effect of Crataegus extract on reducing heart palpitations as well as its effect on heartbeat and anxiety are consistent with past laboratory and clinical studies as well as the traditional use of the drug. In the light of this finding, it can be hypothesized that Crataegus may exert its heart rate-lowering properties not only through its effect on the heart, but also through some psychological effects. Based on the results, the use of Crataegus extract is effective in reducing heart rate in adolescents and it can be relied on as a useful, more effective, and safer treatment to improve heart rate in adolescents and consequently to reduce patients' anxiety compared to other treatments.

Acknowledgment

The authors express their gratitude to all participants who assisted in this study.

Authors' contribution

The study concept and design were created by Alipour MR and Asadolahi V. Data collection was carried out by Alipour MR and Asadolahi V. The manuscript was written with the participation of Alipour MR, Asadolahi V, and Sarebanhassanabadi M. The critical revision was carried out by Alipour MR and Sarebanhassanabadi M. The final version of the manuscript was read and approved by all authors.

Funding

No specific grants were received from funding agencies in the public or commercial sectors for this research.

Conflict of interest

There was no conflict of interest in the present study.

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[DOI: 10.18502/jnfs.v9i1.14839]