Study Effects of Nigella Sativa Seeds Oilin Some Physiological Parameters in Experimental Heart Failure Induced by Ivabradine in Male Rats

Heba A. Abd-Alsalam Alsalame

Assist. Prof., College of Education for Pure Science, Kerbala University, Iraq

Abstract

Aim of this study was to investigate the effects of Nigella Sativa Seeds oil In some physiological parameters against heart failure Induced By Ivabradine in rats .A total of 60 male rats were used in this experiment, the rats were divided into three groups: control rats (n = 20); IBD (n = 20); IBD+ N. sativa oil (n = 20). The first group (G1) was a control group. The second group (G2) was given 10 mg/kg of IBD, while the third group (G3) was injected with 10 mg/kgIBD + oral dosage of 2.5 mg/kg N. sativa oil for three months., after three months, the blood was withdrawn from the heart. to measure the concentration of ANP, BNP, NE, A-II, ALDO, ACE, MDA, SOD, TNF-α and IL-6 the Results revels that Levels of BNP, NE, MDA, IL-6 and TNF-α. were significantly increasead in G2 rats, with no significant difference was observed in ANP in rats in G2 compared to G1 rats . The level of ACE, A-II, SOD and ALDO in G2 rats had significantly decreased compared to that observed in G1 rats, oral administration of Nigella Sativa seeds oil (G3) showed no significant difference inANP, BNP, NE, A-II, ALDO, ACE, MDA, SOD, TNF-α and IL-6 compared with G1 group.

Keywords: *Nigella Sativa, heart failure, Ivabradine, male, rats.*

Introduction

Ivabradine (IBD) It is a commonly used medication Lately used to alleviate the pain and treatment patients with chronic angina pectoris, chiefly applied to the Patients who suffer from sinus rhythm who cannot treated with beta blockers [1]. Many of studies have proved that treatment with ivabradine can enhance the function of global left ventricular and decrease accumulation of cardiac collagen in congestive heart failure in rats[2]. Other studies has been reported that IBD can acts under the control of autonomic nervous system, thus it can reduce unsuitable sinus tachycardia[3]. Moreover, IBD has been found used as cardioprotective drug that used in regulating myocardial ischemic injury. IBD has been utilized for lowering risk of hospitalization and cardiovascular death rate in chronic heart failure patients[4,5]. In spite of there are little data about the mechanisms that make IBD used as benefit drug for chronic heart failure there wasmany studies demonstrated that many drugslike IBD, ranolazine candecrease the sodium influx in heart muscle [6], decrease thesize of myocardial muscle, increases thefunction of left ventricular, decreases arrhythmias and thereby improves myocardial ischemic injury[7,8]. Nigella sativa (N. sativa) belong to Ranunculaceae Family,This plant is vastly used over the world as herbal medicines . N. sativa is considerd as one of the most widlyused plants for treatment or preventing of many diseases [9]. The seeds and oils of this plant are also used in diverse of traditional systems of herbal medicine [10]. The seeds and oils of N. sativa are also used as a good food components in many of systems such as food preservative and spice. Many studies reviled that, both seeds and oils have several biological effects such asanti-inflammatory, anticancer, antioxidant, antimicrobial, diuretics, antihypertensive, analgesics, anti-diarrheal and appetite stimulant, thus the N. sativa seeds can be used as effective food components[11]. Therefore, in this study, our first focus was to investigate the effects of IBD on cardiac system and study the effects of N. sativa seeds oil against heart failure that induced by IBD .

MATERIALS AND METHOD

Experiment Design: A total of 60 male rats were used in this research, the rats were equally divided into three groups: control (n = 20); IBD (n = 20); IBD+N. sativa seeds oil (n = 20). The first group (G1) was given normal saline and considered as a control group. The second group (G2) was given intraperitonealy with 10 mg/kg of IBD as described by [1] . while the third group (G3) was injected inerperitonially with 10 mg/kgIBD+ oral dosage of 2.5 mg/kg N. sativa seeds oil for three months. After three months, 5 ml of blood was withdrawn from the heart. to measure the following parameters: concentration of atrial natriuretic peptide (ANP), brain natriuretic peptide (BNP), Noradrenaline (NE), angiotensin- II (A-II), aldosterone (ALDO), angiotensin converting enzyme (ACE), malondialdehyde (MDA), Superoxide dismutases (SOD), tumour necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6) Plasma concentration of ANP, BNP, NE, A-II, ALDO, ACE, SOD, TNF-α and IL-6were measured by ELISA using commercially available kits. The concentration of MDA was measured according to thiobarbituric acid (TBA) reaction by Muslih et al (2001) [12]

Plant material and extractions: The Nigella sativa seeds utilized in this study were obtained from the local market of kerbala, Iraq. The seeds were manually checked up to eliminate bad ones. The oil from N sativa seeds was extracted by Soxhlet apparatus for 12 h and petroleum ether (60-80°C boiling range) was used as a solvent according to the method described by AOCS[13]. Later that the solvent was evaporated and finally the oil was obtained and stored -4oC .

Statistical Analysis: SPSS program was used to analysis the results and we tested the correlation coefficient by means of the analysis of variance by complete randomized design (CRD). We used the least significant difference (L.S.D.) to show the significance of the results[14].

Results and Discussion

Effects of Ivabradine and N. sativa seeds oil on level of ANP, BNP, NE, ACE, A-II and ALDO: Levels of BNP and NE were significantly higher among rats in G2, While no significant difference was observed in ANP in G2 compared to that observed in G1 rats (table 1) . The level of ACE, A-II, and ALDO in G2 rats had significantly reduced compared to that observed in G1 rats, the rats in G3 showed no significant difference in all above parameters (table 1).

Table (1): Effect of Ivabradine and N. sativa seeds oil at the level of ANP, BNP, NE, ACE, A-II and ALDO in serum of male rats .

Groups Parameters	(G1)	(G2)	(G3)
ANP	1.68±0.48	1.92±0.51	1.71 ± 0.56
BNP	1.39±0.14	*2.46±0.22	1.43 ±0.17
NE	6.45±0.11	*6.73±0.23	6.48±0.16
ACE	1.68±0.17	1.39*0.26	1.66±0.22
A-II	5.46±0.32	*4.56±0.38	5.41±0.28
ALDO	11.31±.714	*8.93±3.15	11.27±3.92

Mean ± standard error, * = significant difference

Our data prove IB causedchronic heart failure(CHF) and amplifies the concentration of BNP and NE in plasma. This results suggest the Malfunction in left ventricle may stimulate elevation of plasma concentration of BNP and NE .

The plasma concentration of BNP and NE have been investigate as a marker for diagnosis, prognosis,screening, and monitoring treatment of CHF patients the secretion of both of these parameters(NE and BNP) which under the control of sympathetic nerves was elevated with the development of CHF [15]. Many of studies demonstrated that BNP level in patients with HF are associted with alters of its plasma level[16]. Thus, in this study, we measured the plasma level of BNP and NE in rats that administrated with IBD.

In this study we also observed that the ivabradine therapy caused a reduction in sympathetic overdrive in rats showed by reduction inplasma levels of renin–angiotensin–aldosterone system (RAAS) components, proved by reduction inplasma levels of ACE, A-II, and ALDO. The continuation of sympathetic overdrive and long activation of RAAShave been accounted amain mediators of developing HF by developingnecrotic, fluid retention, apoptotic cell death and vasoconstriction. This may be proved by increased uptake of $Ca2^{+}$ with ivabradine administration could have also participated to improve the diastolic function of ivabradine [17].

N. Sativa have many effects on cardiac system including cardiac depressant effect, diuretic effect and calcium channels blocking effects [18]. As well as,N. Sativa was improving the inflammatory effects in many organs and protect many organs from any lesion, and we have been found that the daily use of NS with

diet can protect the body from exposure to the sepsis [19]. Thymoquinone(TQ), the active components of Nigella sativa found in its seeds, is the active quinone used in pharmacology, which play a vital role chiefly asanti-inflammatory and analgesic factor[20]. Many studies has been reported that thymoquinonealso act as apowerful antioxidant which protects many of body organs fromoxidative injury in various studies in rats [21]. and protects cell membranefrom lipid peroxidation in many tissues [22]. in addition, N. Sativa seed has a many of actions such as antioxidant [23], calcium channel blocker effects[24], anti-eicosanoid [25] and a regulate the level of intracellular calcium in mast cells [26]. NS have also myocardial protective effect which could be due to its protective activity of its components such as thymoquinone, thymohydro-quinone, thymol, dithymoquinone, 4-terpineol,carvacroland tanethole [27].

Effects of Ivabradine and N. sativa seeds oil on Myocardial Cytokines and Oxidative Stress: The results of Table 2 showed a significant increase ($P < 0.05$) in the level of serum MDA and significant decrease in SOD in the rats injected with ivabradine (G2) the level of IL-6 and TNF-α. Were significally increased in G2 compared with control group (G1), oral administration of 2.5 mg/kg of Nigella Sativa seeds oil lead to enhance the level of SOD, with no significant difference was observed in level of MDA, IL-6 and TNF-α in G3 compared with G1 group.

Several studies have indicated that there was many effects of ivabradine on cardicsystem especially inflammation[28,29]. Lately, some of studiesproved that IBDcan reduce the level of inflammatory cytokines in mice[28]. And canmodify the gene expression of inflammatory cytokine while elevate the activity of endothelial nitricoxide synthase (eNOS) in rats[29]. Other studies suggested that, treatment with ivabradine can promote the function of left ventricle, with modifying in cytokines expression mainly TNF-α and IL-6 . This cytokines are responsible for any defect in cardiac system[30]. Especially TNF-α and IL-6 which stimulate cardiac dysfunction. In this resrearch, we found that ivabradine causedcardiac inflammationby increased levels of IL-6 and TNF- α.

Table (2): Effect of Ivabradine and N. sativa seeds oil at the level of MDA, SOD, TNF-α, and IL-6 in serum of male rats

Groups Parameters	(G1)	(G2)	(G3)
MDA	0.0492 ±0.022	0.055 * ± 0.310	0.0488 ± 0.019
SOD	58.46 ±11.05	42.62 * ±6.05	58.97 ±6.35
TNF-α	2.19 1.59 ±	* 3.85 1.77±	2.11 ±1.35
IL-6	35.24 ±8.17	39.92 * ±3.14	34.97 ±6.14

Mean ± standard error, * = significant difference

Conclusion

The results suggest that injection with Ivabradine can induce heart failure and oral administration of Nigella Sativa Seeds oil has protective effects against heart failure Induced By Ivabradine.

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Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under the College of Education for Pure Science and all experiments were carried out in accordance with approved guidelines.

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