Original Article

Nigella sativa: A potential natural protective agent against cardiac dysfunction in patients with type 2 diabetes mellitus

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ABSTRACT

Objectives: To study the effect of *Nigella sativa* supplementation on cardiac functions in Type 2 diabetic patients treated with oral hypoglycemic agents. **Background:** Diabetes mellitus is associated with a high risk of cardiovascular morbidity and mortality. A number of reported beneficial effects of *N. sativa* on cardiovascular function were the inspiration for this study. **Materials and Methods:** Sixty patients with uncontrolled diabetes (hemoglobin A_{1c} [HbA_{1c}] >7%) and with no known cardiovascular complications were recruited from the outpatient diabetes clinic. They were assigned, by convenience, to two groups; the control group received activated charcoal as placebo while the test group received 2 g/day of powdered *N. sativa* for 1-year. All patients continued with their standard oral hypoglycemic agents. Echocardiography was used to evaluate the diastolic function, systolic function, and left ventricular mass (LVM) before the intervention and after 6 and 12 months of the treatment. **Results:** HbA_{1c} decreased significantly in the *N. sativa* group but did not change in the control group. Echocardiographic assessment in the control group showed impairment in diastolic function after 12 months, but there were no significant changes in fractional shortening (FS) or ejection fraction (EF). Furthermore, left ventricular (LV) dimensions at diastole and systole, LVM, and LVM index were significantly increased. In *N. sativa* group, no significant changes were found in diastolic function or LVM. LV dimension at systole was decreased while FS and EF were significantly increased after 6 and 12 months. **Conclusion:** *N. sativa* supplementation may protect the hearts of type 2 diabetic patients from diastolic dysfunction while improving LV systolic function.

Key words: Diabetes mellitus, diastolic function, echocardiography, left ventricular mass, Nigella sativa, systolic function

INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disorder caused by a defect in insulin secretion, insulin action, or both. The prevalence of DM is growing rapidly. According to the latest International Diabetes Federation (IDF) data, the worldwide prevalence of DM in 2012 was 371 million, and it is projected to reach 552 million by the year 2030.

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Studies have also indicated that the current prevalence of diabetes in the Arab world is among the 10 highest in the world.[1,2] Patients with diabetes are at an increased risk of cardiovascular disease, and DM adds to the impact of other atherosclerosis risk factors such as dyslipidemia and hypertension for the prediction of cardiovascular manifestations.[3] It was estimated that 4.8 million people died as a result of diabetes in 2012, and cardiovascular complications were the most common cause of the death of those patients.[1,4,5] Cardiomyopathy characterized by an early diastolic and late systolic dysfunction is another manifestation of cardiac complications in patients with diabetes.[6,7]

Nigella sativa (*N. sativa*) has been reported to possess hypoglycemic,[8,9] hypolipidemic,[10] and antioxidant properties.[11] Hypotensive and diuretic effects of *N. sativa*

have been reported in spontaneously hypertensive rats.[12] It was also reported to induce homogenous physiologic cardiac hypertrophy with increased inotropic effect in rats.[13,14] Despite several published studies, there is still a gap in the information on the effect of *N. sativa* on human hearts and specifically the hearts of diabetics. With this background, the objective of this study was to explore the effects of a 1-year supplementation with *N. sativa* on cardiac function, evaluated by echocardiography, in uncontrolled type 2 diabetic patients treated with oral hypoglycemic agents.

MATERIALS AND METHODS

This was a phase 2 participant blinded placebo-controlled clinical trial, carried out at the College of Medicine, University of Dammam, Kingdom of Saudi Arabia, from May 2009 to December 2011. The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki. The study was approved by the local ethical research committee of the University of Dammam and registered in the clinical trial registry– India, under the reference no. CTRI/2013/06/003781.

We calculated a sample size of 24 for each group assuming the probability of Type I error (α) to be 0.05, Power (1-β) to be 0.8, paired difference to be detected as 0.6 and expected standard deviation (SD) of difference to be 1.00. However, assuming from previous experience that there would be about 15% dropout or failure to follow-up, we increased the sample size to 30 for each group.

Sixty patients with type 2 diabetes of both genders were recruited from the outpatient diabetes clinic of King Fahd Hospital of the University-Al Khobar and its affiliated primary health care center. The inclusion criteria were uncontrolled type 2 DM (based on two consecutive readings 3 months apart of hemoglobin A_{1c} [HbA_{1c}] of >7%), aged between 18 and 60 years, using standard oral hypoglycemic drugs regularly and consenting for intervention and regular follow-up. Patients with HbA_{1c} >9%, treated with insulin therapy, with a body mass index (BMI) of ≥40 kg/m^2 or with known cardiovascular diseases (coronary artery disease, valvular heart diseases, and heart failure), uncontrolled hypertension or nephropathy were excluded from the study.

For convenience, based on patients with lower HbA_{1c} assigned to the placebo group, the patients were divided into two equal groups (n = 30 each), the control group (received placebo) and the test group (received *N. sativa*).The rationale for this division was to minimize the number of patients in the placebo group exceeding HbA_{1c} of 9, in the 1-year treatment period, which would increase the dropout from the study.

Two visits at the 6th and 12th months were scheduled for a general follow-up after the initial visit. Patients were also contacted by phone every month in between the scheduled visits to check for compliance to their medications and any untoward effects.

a. *N. sativa* seed powder in the form of 500 mg capsules (BioExtract [Pvt.] Ltd., Srilanka) was used in a dose of 2 g/day in two divided doses. Dose selection was based on a previous study by our group[8]
b. Activated charcoal capsules (260 mg) similar in size and color to the capsules of *N. sativa* (Arkopharma Pharmaceutical Laboratories Carros, France) were used as placebo and given 2 h before the standard oral hypoglycemic drugs, in two divided doses/day. In addition, the patients in both groups continued to use their regular standard oral hypoglycemic drugs.

Baseline data including age, gender, and duration of diabetes were recorded during the initial visit. Blood pressure, radial pulse rate, BMI, and HbA_{1c} were measured prior to treatment and in each follow-up visit.

Echocardiogram was done at baseline and repeated at 6th and 12th months of follow-up. These measurements were performed in the same cardiac laboratory and interpreted by the same cardiologist. All patients underwent routine echocardiography using commercially available cardiac ultrasound diagnostic equipment (Toshiba Xario) with a 3 MHz transducer. Echocardiograms were obtained in the left lateral position at the end of expiration.[15] The following measurements were obtained in two-dimensional guided M-mode, and at the end of both diastole and systole: End-diastolic left ventricular internal dimension (LVIDd), end-systolic left ventricular internal dimensions (LVIDs), end-diastolic interventricular septal wall thickness (IVSd), end-diastolic left ventricular posterior wall thickness (LVPWd).

Left ventricular mass (LVM) and corrected LVM (LVMc) were calculated according to the following:[16]

$$LVM = 1.04\ \{(LVIDd + IVSd + LVPWd)^3 - (LVIDd)^3\}\ (g).$$

$$LVMc = 0.8\ (LVM) + 0.6\ (g)$$

This was indexed to body surface area (BSA) as follows: Left ventricle mass index (LVMI) = Corrected ventricle mass/BSA (g/m^2).[17]

For LV diastolic function, pulse wave Doppler was used to measure E/A ratio (the ratio of left ventricle early filling phase velocity, E, to late filling phase velocity, A, at the

tip of mitral valve leaflets). Left atrial volume indexed to BSA (LAVI) was used to confirm the changes in E/A ratio and to differentiate between type 2 diastolic dysfunction and the pseudo normalization pattern of E/A ratio.

LAVI was calculated as based on cube method[18] as follows:

Left atrial volume = π (constant) × (atrial dimension in cm) $^{3}/6$

LAV = 3.14159265 × $D^{3}/6$

LAVI = LAV/BSA= (cm^{3}/m^{2})

LV systolic function was assessed by end-systolic LV internal dimension and by both fractional shorting (FS) and ejection fraction (EF) of the left ventricle.

Statistical analysis was performed using the Statistical Package of Social Science (SPSS) version 16 (SPSS Inc. Released 2007. SPSS for Windows, Version 16.0. Chicago, SPSS Inc). Data are presented as means ± SD. In each group, readings were compared to their corresponding baseline values using Student's *t*-test for paired data. Results in the two groups were compared using Student's *t*-test for unpaired data. $P < 0.05$ was considered as significant.

RESULTS

Table 1 shows the comparison of baseline data between the placebo (control) and *N. sativa* Groups. The demographic and pretreatment baseline data of all patients in the two groups did not differ significantly, except for HbA_{1c}, which was higher in the *N. sativa* group than the controls. All patients in the *N. sativa* group tolerated the treatment and showed no adverse effects throughout the study period.

Table 2 shows changes in echocardiographic measurements of diastolic and systolic functions. E/A ratio was decreased in the placebo group in both readings. This decrease was only significant at 12th month reading ($P < 0.05$). However, the *N. sativa* group did not show any decrease in E/A ratio. On the contrary, the ratio insignificantly increased. There was no significant change in LAVI in both the groups. As regards the parameters of systolic function, LVIDs at 6th month was significantly increased in the placebo group ($P < 0.05$), while it was significantly decreased in *N. sativa* group at both 6th ($P < 0.05$) and 12th ($P < 0.01$) months. Interestingly, there was a significant improvement in both FS% and EF% in *N. sativa* group, unlike the placebo group.

Table 3 illustrates changes in echocardiographic measurements of left ventricular (LV) internal dimensions and mass at different treatment durations in both the groups. LVIDd increased significantly ($P < 0.05$) in the control group both at 6th and 12th months. This increase was, however, not seen in the *N. sativa* group. There was no significant change in LVPWd or IVSd in any reading in both groups. However, the reading at 6 months for both LVMc and LVMI were significantly ($P < 0.05$) increased in the Control group, but not in the *N. sativa* group.

Table 1: Comparison of baseline data between the placebo group (control) and *N. sativa* groups

Parameter (mean±SD)	Placebo group (*n*=30)	*N. sativa* group (*n*=30)	*P* value
Age (years)	47.97±6.03	46.00±8.73	0.318
Duration of diabetes (years)	5.24±4.51	7.20±4.19	0.086
BMI (kg/m^2)	30.70±3.59	30.14±3.71	0.556
HbA_{1c} (%)	8.17±0.83	8.78±0.95	0.010*
Mean arterial pressure (mmHg)	96.55±8.06	100.55±9.32	0.082
M mode/2D measurements and calculations			
End-diastolic (cm)	4.63±0.42	4.72±0.37	0.414
End-systolic LVIDd (cm)	2.95±0.32	2.93±0.32	0.855
End-diastolic LVPWd (cm)	0.96±0.12	0.98±0.14	0.557
End-diastolic IVSd (cm)	1.00±0.16	1.01±0.18	0.858
Corrected LVM (g)	160.92±41.43	169.75±51.18	0.468
LVMI (g/m^2)	80.29±15.16	86.31±22.06	0.227
Doppler measurement			
LAVI (ml/m^2)	11.09±4.46	10.61±3.36	0.640
LVEF (%)	67.27±4.30	66.77±3.58	0.631
LVFS (%)	36.36±4.30	37.81±4.89	0.231
E/A ratio	1.31±0.45	1.17±0.46	0.236

Values are given as mean±SD. *n*=number of patients. Variables were compared using independent samples *t*-test. *Difference is significant at $P < 0.05$. SD: Standard deviation; HbA_{1c}: Hemoglobin A_{1c}; LV: Left ventricular; *N. sativa: Nigella sativa*; BMI: Body mass index; LVIDd: Left ventricular internal dimension; LVPWd: Left ventricular posterior wall thickness; IVSd: Interventricular septal wall thickness; LVM: Left ventricular mass; LVMI: Left ventricle mass index; LAVI: Left atrial volume indexed; EF: Ejection fraction; FS: Fractional shortening

Table 2: Comparison of echocardiographic parameters of cardiac diastolic and systolic function at 6 months and 12 months after treatment with their corresponding baseline values in the control and *Nigella sativa* groups

Variable	Placebo group				Nigella group			
	Baseline	6 months	Baseline	12 months	Baseline	6 months	Baseline	12 months
Diastolic function								
E/a ratio	1.32±0.46	1.22±0.39	1.28±0.42	1.12±0.303	1.21±0.46	1.26±0.38	1.20±0.45	1.25±0.42
n	26		25		24		25	
P	0.084		0.031*		0.432		0.386	
Lavi (ml/m^2)	10.58±3.19	10.89±3.32	10.94±4.71	11.56±4.22	10.90±3.49	11.17±3.92	10.80±3.45	10.95±4.08
n	26		25		24		25	
P	0.50		0.43		0.667		0.771	
Systolic function								
Lvids (cm)	2.94±0.34	3.02±0.32	2.90±0.34	2.97±0.33	2.91±0.34	2.82±0.35	2.93±0.34	2.79±0.37
n	26		25		24		25	
P	0.011*		0.135		0.039*		0.001*	
Fs (%)	36.07±4.03	35.28±3.48	36.80±4.67	36.17±4.53	38.28±5.19	39.61±4.58	37.93±5.26	39.07±4.91
n	25		24		24		25	
P	0.32		0.35		0.036*		0.048*	
Ef (%)	66.57±3.83	65.21±5.93	67.80±4.56	67.12±6.79	67.27±3.60	69.81±4.63	66.71±3.79	70.23±4.97
n	25		24		24		25	
P	0.32		0.61		0.029*		0.003*	

All the values are given as Mean±SD. *n*=Number of patients. Means were compared by paired sample *t*-test. *Difference is significant at $P < 0.05$. The baseline values and number of patients varies for 6 months and 12 months as for paired sample tests only the data of the patients attended that particular follow-up was used. SD: Standard deviation; LAVI: Left atrial volume indexed; LVIDs: Left ventricular internal dimensions; FS: Fractional shorting; EF: Ejection fraction; LV: Left ventricular

Table 3: Changes in echocardiographic measurements of LV internal dimensions at different treatment durations in the control group and *N. sativa* group compared to their corresponding baseline values

Parameter	Duration of treatment							
	Control group				*N. sativa* group			
	Baseline	6 months	Baseline	12 months	Baseline	6 months	Baseline	12 months
LVIDd (cm)	4.59±0.42	4.74±0.43	4.59±0.44	4.80±0.41	4.72±0.41	4.70±0.43	4.73±0.39	4.69±0.43
n	26		25		24		25	
P	0.038*		0.015*		0.626		0.436	
LVPWd (cm)	0.95±0.11	0.97±0.11	0.97±0.12	0.98±0.12	0.99±0.15	0.97±0.16	0.99±0.14	0.99±0.19
n	26		25		24		25	
P	0.30		0.46		0.681		0.881	
IVSd (cm)	0.99±0.16	0.98±0.14	1.01±0.18	0.98±0.12	1.02±0.19	1.02±0.21	1.01±0.20	1.00±0.25
n	26		25		24		25	
P	0.54		0.25		0.663		0.681	
LVMc (g)	155.77±39.22	164.63±38.59	159.88±44.84	171.72±43.79	171.70±55.03	163.72±60.05	170.57±54.26	163.43±69.21
n	26		25		24		25	
P	0.045*		0.06		0.269		0.357	
LVMI (g/m^2)	78.21±14.49	82.99±14.38	79.91±16.34	86.02±15.35	86.68±24.03	82.31±26.27	86.68±23.67	81.99±29.47
n	26		25		24		25	
P	0.024*		0.051		0.210		0.248	

All the values are given as Mean±SD. *n*=number of patients. Means were compared by paired sample *t*-test. *Difference is significant at $P < 0.05$. The baseline values and number of patients varies for 6 months and 12 months as for paired sample tests only the data of the patients attended that particular follow-up was used. LVIDd: Left ventricular internal dimension; LVPWd: Left ventricular posterior wall thickness; IVSd: Interventricular septal wall thickness; LVMc: Corrected left ventricular mass; LVMI: Left ventricle mass index; SD: Standard deviation; LV: Left ventricular; *N. sativa: Nigella sativa*

Table 4 demonstrates a comparison of all the echocardiographic parameters between the control group and *N. sativa* group at the baseline, 6 months and 12 months after initiation of treatment. There was no significant difference in any baseline reading for all echocardiographic parameters evaluated. LVIDs at 6th month were significantly ($P < 0.05$) less in the *N. sativa* group. FS(%) was significantly more in the *N. sativa* group both at 6th ($P < 0.01$) and 12th ($P < 0.05$) months while EF(%) was significantly ($P < 0.01$) higher in the *N. sativa* group at the 6th month reading only.

Table 4: Comparison of echocardiographic measurements of diastolic function, systolic function, and LV internal dimensions

Variable	Treatment duration	Control group	*N. sativa* group	*P* value
Diastolic function				
E/A ratio	Baseline	1.31±0.45 (30)	1.17±0.46 (30)	0.236
	6 months	1.22±0.39 (26)	1.26±0.38 (24)	0.685
	12 months	1.12±0.30 (25)	1.25±0.42 (25)	0.20
LAVI (ml/m^2)	Baseline			
	6 months	10.89±3.32 (26)	11.17±3.92 (24)	0.788
	12 months	11.56±4.22 (25)	10.95±4.08 (25)	0.607
Systolic function				
LVIDs (cm)	Baseline	2.95±0.32 (30)	2.93±0.32 (30)	0.855
	6 months	3.02±0.32 (25)	2.82±0.35 (24)	0.048*
	12 months	2.97±0.33 (24)	2.79±0.37 (25)	0.072
FS (%)	Baseline	36.36±4.30 (30)	37.81±4.89 (30)	0.231
	6 months	35.28±3.48 (25)	39.61±4.58 (24)	0.001*
	12 months	36.17±4.53 (24)	39.07±4.91 (25)	0.037*
EF (%)	Baseline	67.27±4.30 (30)	66.77±3.58 (30)	0.631
	6 months	65.21±5.93 (25)	69.81±4.63 (24)	0.004*
	12 months	67.12±6.79 (24)	70.23±4.97 (25)	0.75
LVM calculation				
LVIDd (cm)	Baseline	4.63±0.42 (30)	4.72±0.37 (30)	0.414
	6 months	4.74±0.43 (26)	4.70±0.43 (24)	0.734
	12 months	4.80±0.41 (25)	4.69±0.43 (25)	0.372
LVPWd (cm)	Baseline	0.96±0.12 (30)	0.98±0.14 (30)	0.557
	6 months	0.97±0.11 (26)	0.97±0.16 (24)	0.940
	12 months	0.98±0.12 (25)	0.99±0.19 (25)	0.884
IVSd (cm)	Baseline	1.00±0.16 (30)	1.01±0.18 (30)	0.858
	6 months	0.98±0.14 (26)	1.02±0.21 (24)	0.555
	12 months	0.98±0.12 (25)	1.00±0.25 (25)	0.807
LVMc (g)	Baseline	160.92±41.43 (30)	169.75±51.18 (30)	0.468
	6 months	164.63±38.59 (26)	163.72±60.05 (24)	0.73
	12 months	171.72±43.79 (25)	163.43±69.21 (25)	0.616
LVMI (g/m^2)	Baseline	80.29±15.16 (30)	86.31±22.06 (30)	0.227
	6 months	82.99±14.38 (26)	82.31±26.27 (24)	0.911
	12 months	86.02±15.35 (25)	81.99±29.47 (25)	0.547

Data are presented as means±SD. Variables were compared using independent samples *t*-test. *Difference is significant at $P < 0.05$. Number of patients is given in parenthesis (*n*). SD: Standard deviation; EF: Ejection fraction; LAVI: Left atrial volume indexed; LVIDs: Left ventricular internal dimensions; LVIDd: Left ventricular internal dimension; FS: Fractional shorting; EF: Ejection fraction; LVPWd: Left ventricular posterior wall thickness; IVSd: Interventricular septal wall thickness; LVMc: Corrected Left ventricular mass; LVMI: Left ventricle mass index; LV: Left ventricular; LVM: Left ventricular mass

Table 5 shows a comparison of BMI, HbA_{1c}, pulse rate and mean arterial pressure (MAP) between baseline, 6 months and 12 months for both the groups. HbA_{1c} was reduced in the *N. sativa* group at both follow-ups; but, this reduction was only significant at 12 months ($P < 0.05$). Pulse rate was significantly ($P < 0.05$) reduced at 12 months follow-up in the *N. sativa* group. MAP was significantly ($P < 0.05$) reduced at both the 6th month and 12th month follow-up in the *N. sativa* group.

DISCUSSION

A review of the literature shows that the current study is the first to examine the effects of *N. sativa* on cardiac functions in patients with type 2 DM. The results indicated potential protective effects of *N. sativa* on cardiac diastolic and systolic functions and LVM in diabetic patients. *N. sativa* supplementation tended to prevent diastolic dysfunction as well as improve systolic function. In addition, it showed a trend of preventing an increase in the LVM.

Cardiac dysfunction in patients with DM manifests as diabetic cardiomyopathy that is characterized by an early diastolic and late systolic dysfunction.[6,7] Diastolic dysfunction has been reported in diabetic animals[19] as well as diabetic patients.[20,21] Transmitral flow (E/A) ratio as a marker of diastolic dysfunction has been found to be impaired in diabetic patients without overt cardiovascular disease.[22,23] In this study, the placebo group showed a trend towards diastolic dysfunction, as E/A ratio was significantly

Table 5: Changes in baseline measurements at different treatment durations in the placebo and *N. sativa* group compared to their corresponding baseline values

Parameter	Duration of treatment							
	Control group				*N. sativa* group			
	Baseline	6 months	Baseline	12 months	Baseline	6 months	Baseline	12 months
BMI (kg/m^2)	31.10±3.48	31.04±3.43	30.77±3.89	30.79±3.68	30.33±3.87	30.27±3.31	30.41±3.70	30.61±3.36
n	27		26		24		26	
P	0.589		0.945		0.769		0.459	
HbA1c (%)	8.14±0.79	8.28±0.80	8.18±0.77	8.26±0.90	8.78±0.95	8.14±1.69	8.84±0.96	8.40±1.07
n	27		26		25		27	
P	0.273		0.676		0.073		0.022*	
PR (beats/min)	87.93±9.58	87.85±9.38	87.62±10.18	87.31±9.87	86.46±7.91	85.08±8.88	86.42±6.22	83.12±8.05
n	27		26		24		26	
P	0.927		0.706		0.248		0.043*	
MAP	96.41±8.12	97.08±7.95	97.17±8.37	98.13±10.30	99.86±9.28	94.07±11.47	101.64±8.62	94.29±10.63
n	27		26		24		26	
P	0.529		0.439		0.001*		0.00*	

The baseline values and number of patients varies for 6 months and 12 months as for paired sample tests only the data of the patients attended that particular follow-up was used. The values are given as mean±SD. *n*=Number of patients. Means were compared using student's t-test for paired data *Difference is significant at $P < 0.05$. BMI: Body mass index; HbA_{1c}: Hemoglobin A_{1c}; MAP: Mean arterial pressure; SD: Standard deviation; *N. sativa: Nigella sativa*

decreased at the end of the study, while in *N. sativa* group, the diastolic function was preserved. This may imply a protective role of *N. sativa* against diastolic dysfunction in diabetic patients.

Left ventricular systolic dysfunction has been linked to DM as a late manifestation of diabetic cardiomyopathy.[24,25] Interestingly, in the current study, *N. sativa* supplementation for 1-year improved systolic function manifested by a significant decrease in LVIDs, and a significant increase in both FS% and EF% compared to their baseline readings and to the corresponding control group values. Studies on cardiac contractility in experimental rat models fed with *N. sativa* for 2 months resulted in a positive inotropic effect manifested as better contractility,[13,14] which supports our findings in the *N. sativa* treated group. In contrast to our results, Boskabady *et al*.[26] reported a potent inhibitory effect on the muscle contractility of guinea pig isolated heart produced by perfusing the myocardium with *N. sativa* extract. However, since we have investigated the effect of *N. sativa* supplementation on cardiac parameters, our study is closer to that of the first group of researchers[13,14] who reported enhanced cardiac performance than the Boskabady group. Therefore, it is likely that the direct effect of *N. sativa* on cardiac muscle fibers is inhibitory, while long-term ingestion of *N. sativa* may lead to structural and/or functional myocardial modifications that enhance cardiac performance.

Previous studies have demonstrated that LV hypertrophy occurs in patients with type 2 DM independent of hypertension or coronary artery disease.[27] In diabetic rats, LV hypertrophy was found to be associated with increased left ventricle internal dimensions in both diastole and systole.[28] Likewise, in the current study, both LVID in systole and diastole were increased significantly in the placebo group compared to their baseline values. LVMc was also increased in this group. However, this increment in LVMc was not associated with a parallel increment in the posterior wall thickness (LVPWd) or interventricular septum thickness (IVSd), which indicates that this increase may be due to the increase in LV internal dimensions. In contrast, a previous study on elderly individuals (≥65 years) reported that increased LVM in diabetics was associated with a greater interventricular septum and left posterior wall thicknesses rather than in dimensions when compared to nondiabetic patients.[29] However, the age of the patients in that study was much higher (≥65 years) than our patients age (mean age 46.9), which might explain this difference. Indeed, it has been reported that LVM age coefficient in diabetic women was significantly higher than the estimate for nondiabetics.[30] Interestingly, in the test group, *N. sativa* supplementation tended to prevent such an increase in ventricular mass and ventricular dimensions.

Felicio *et al*.[31] reported reductions in LVM index associated with a fall in blood glucose while the mass index increased in those who did not achieve glycemic control. In addition, a close relationship was found between glycemic control and improvement in LV diastolic[32] and systolic[33] functions. Therefore, the beneficial effects of *N. sativa* on cardiac parameters, encountered in our study, might be partly due to the improvement in glycemic

control in these diabetic patients. Indeed, a study on newly diagnosed diabetic patients showed a significant improvement in cardiac functions after 15 months of better glycemic control in these patients.[34]

The improvement in blood pressure observed in the *N. sativa* group, compared to their baseline values, is consistent with our recent report on the short-term effect of *N. sativa* in diabetic patients.[35] Other human studies have also demonstrated the hypotensive effect of *N. sativa* in patients with mild hypertension[36] and those with central obesity.[37]

Limitations of this study include small sample size, aggravated by the loss of some patients who did not turn up for follow-up, and the relatively short duration of the intervention. Further studies on a larger sample size in a longer duration utilizing advanced echocardiography techniques such as tissue Doppler, might confirm these promising effects of *N. sativa* on the heart and explore possible mechanisms.

CONCLUSION

The present study indicates the potential beneficial effects of a 1-year supplementation of *N. sativa* in protecting the hearts of type 2 diabetic patients against diastolic dysfunction and left ventricle mass increment, and improving systolic function.

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