Endocrine (2019) 65:286–294
https://doi.org/10.1007/s12020-019-01963-4

ORIGINAL ARTICLE

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Effect of *Nigella Sativa* oil versus metformin on glycemic control and biochemical parameters of newly diagnosed type 2 diabetes mellitus patients

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Received: 14 January 2019 / Accepted: 19 May 2019 / Published online: 31 May 2019

Abstract

Purpose Nature is a phenomenal treasure of remedies. Numerous previous studies reported that *Nigella sativa* NS improved glycemic control, reduced insulin resistance, and improved lipid profile. NS was never investigated before as a monotherapy for newly diagnosed type 2 diabetes mellitus T2DM patients. Our aim was to investigate the potential metabolic benefits of NS monotherapy in newly diagnosed T2DM patients.

Method Prospective, open-label randomized clinical trial at outpatient endocrinology clinic at Ain-Shams University hospital. Eligible patients were randomly assigned to either metformin tablets or NS oil capsules. Both groups received treatment for 3 months. Glycemic index (FBG, 2 h pp, A1C, insulin sensitivity %S, secretory function %B, insulin resistance IR), lipid profile (TC, LDL, HDL, TG), liver and kidney functions (AST, ALT, Sr cr), total antioxidant capacity TAC, weight, waist circumference WC and body mass index BMI were assessed at baseline and at the end of treatment period.

Results A concentration of 1350 mg/day NS in newly diagnosed T2DM patients was inferior to metformin in terms of lowering FBG, 2 h pp, and A1C or increasing %B. However, NS was comparable to metformin in lowering weight, WC, and BMI significantly. NS was comparable to metformin in regards of their effects on fasting insulin, %S, IR, ALT, TC, LDL, HDL, TG, and TAC. Metformin showed significant increase in AST and creatinine which was reserved in NS group.

Conclusion NS administration in newly diagnosed T2DM was tolerable with no side effects as compared to metformin; however, it was inferior to metformin in terms of diabetes management.

Keywords Newly diagnosed type 2 diabetes mellitus · Nigella sativa · Metformin

Introduction

Type 2 diabetes mellitus T2DM accounts for 90–95% of all diabetes cases. Published data showed that age [1], obesity [2], alterations to gut microbiota [3], vitamin D deficiency [4] and rapid urbanization [5] were all linked to T2DM. Diabetic Mellitus patients have high cardiovascular risk and abnormal lipid profile, characterized by high triglycerides level, low HDL-C, and elevated small dense LDL, which is known as diabetic dyslipidemia [6]. Chronic hyperglycemia, which is the primary characteristic of diabetes, also increases the formation of reactive oxygen species (ROS) and produces oxidative stress in islet cells of pancreas. It is considered as a likely risk factor in the development of insulin resistance, subsequently favoring the occurrence and progression of atherosclerotic complications, and leads to many micro- and macrovascular complications such as

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stroke, impotence, neuropathy, retinopathy and nephropathy [7, 8].

Newly diagnosed T2DM patients usually present with less prominent symptoms. Newly diagnosed diabetes patients were reported to have lower adherence rates to their prescribed medications [9]. A strict glycaemic control is advised shortly after T2DM diagnosis [10]. In newly diagnosed T2DM patients, when lifestyle is insufficient to control blood glucose level, metformin should be the initial drug of choice, unless contraindicated. Metformin is recommended as first line drug to treat T2DM because of its efficacy, safety profile, association with weight loss or neutrality, beneficial cardiovascular and metabolic effects and availability as generic formulations [11].

Natural health products (NHPs) are considered safe, cheap and accessible medicines [12]. *Nigella sativa* (NS) use is very popular in various branches of medicine [13]. Numerous previous studies reported that NS treatment improved glycemic control and reduced insulin resistance in T2DM individuals [14, 15]. Moreover, previous clinical studies reported that NS seed administration caused a significant improvement in lipid profile [16]. Of note, the main active ingredient of NS, thymoquinone, has antioxidant effects. It neutralizes free oxygen radicals and can prevent tissue damage [17, 18].

Clearly, the antidiabetic activity of NS oil is mediated via multiple modes of actions [19]. It improves tissue sensitivity to insulin [20], lowers intestinal absorption of glucose by inhibiting the sodium-glucose co-transporter [21], inhibits alpha-glucosidase activity [22] increase insulin secretion, induce proliferation of pancreatic β cells, protect B cells, stimulate PPAR-γ in adipocytes as do TZD, and stimulate glucose uptake in skeletal muscle and fat cells, reduces appetite and body weight [19, 23–25]. Moreover, it was reported that NS inhibits hepatic gluconeogenesis and affects lipid metabolism [26].

NS can cause a significant decrease in waist and hip circumferences [27]. The anti-obesity effect of the plant contributed to its slight anorexic effect [28]. Although *Nigella sativa* was reported to be a beneficial adjuvant to oral hypoglycemic agents in T2DM patients [29], *Nigella sativa* was never investigated before as a monotherapy for newly diagnosed T2DM patients.

Aim of the study

To investigate the effects of administration of *Nigella sativa* oil vs. metformin for 3 months in newly diagnosed type 2 diabetes mellitus T2DM patients (diabetes duration ≤6 months) on the following: (a) glycemic control, (b) oxidative stress markers, (c) biochemical parameters, (d) weight/BMI/waist circumference, (e) total antioxidant capacity TAC.

Patients and methods

Design

This is a prospective, open-label randomized clinical trial.

Setting

Outpatient endocrinology clinic at Ain-Shams University hospital.

The current study was carried out in accordance with the principles of the Declaration of Helsinki as revised in 2000. The ethics committee of Faculty of Pharmacy, Ain Shams University, Cairo, Egypt approved the study protocol and it was registered with serial number 6. All patients were informed of study protocol and only those who gave a written informed consent were enrolled.

Diabetes was diagnosed according to the criteria of the American Diabetes Association 2015 [30]. Recruitment took place between February 2016 and March 2018. All patients presenting to the Endocrinology outpatient clinic at Ain-Shams University hospital, Cairo, Egypt were screened according to the following inclusion and exclusion criteria: (a) Inclusion criteria: age: 18–60 years and newly diagnosed type 2 diabetes mellitus (diagnosed within a time duration ≤6 months). (b) Exclusion criteria: Patients were excluded if they were on other antidiabetic medications, pregnant and lactating women, patients with major organ dysfunction (hepatic failure, active hepatitis, liver cirrhosis or renal complications) patients had their standard medications changed during the 12 weeks of the study, or patients not willing to participate in the study.

Eligible patients were randomly assigned through simple random sampling using a randomizing tool [31] to either: Group I: received metformin tablets 2000 mg per day supplied by Chemical industries development CID or Group II: received *Nigella sativa* oil capsules (Baraka) 450 mgs three times daily supplied by Pharco Pharmaceuticals, Egypt.

Baseline assessment

Baseline evaluation included a full history taking and demographic data collection by a clinical pharmacist. The clinical pharmacist performed an initial patient education for patients of both groups about disease symptoms, progression, complications, lifestyle and pharmaceutical management. Both groups received treatment for 3 months. The following laboratory tests were evaluated for all patients at

baseline and at the end of the treatment period (3 months): full lipid profile (after 10–12 h fasting), glycemic control (Fasting blood glucose FBG, postprandial blood glucose (2 hPG), HbA1c, and insulin fasting levels), renal and hepatic function tests (Serum creatinine, AST, and ALT levels) and total antioxidant capacity (TAC) was assessed as an oxidative stress parameter. The output of the Insulin resistance (IR) and β-cell function were estimated using computer software HOMA2 (Homeostasis Model Assessment calculator, released by Oxford University UK in 2004 using fasting plasma glucose FPG and fasting insulin. Online HOMA calculator was used [32]. To measure the waist circumference (WC), the top of the hip bone (iliac crest) was located and the measurement was taken just above this bony landmark, just where one finger can fit between the iliac crest and the lowest rib. It was measured according to standard measuring techniques [33].

During the 3 months of the study, patients of both groups were contacted weekly by telephone, and were enquired about any new symptoms, adverse effects, hyper or hypoglycemic episodes, need for insulin administration, or hospitalization. Participants presented to the clinic every 2 weeks for follow up and received short patient education sessions. Patients were asked about their symptoms at the end of the study.

Statistical analysis

Data management and analysis were performed using Statistical Package for Social Sciences (SPSS) vs. 23. Numerical data were summarized using means and standard deviations or medians and ranges, as appropriate. Categorical data were summarized as numbers and percentages. Numerical data were explored for normality using Kolmogrov–Smirnov test and Shapiro–Wilk test. Exploration of data revealed that the collected values were not normally distributed. Comparisons between 2 groups were done using the Mann–Whitney test. Change overtime for each group was tested using the Wilcoxon Rank Signed test. These tests were followed by the post hoc Bonferroni corrections to adjust the p-values. X^2 or Fisher's tests was used to compare between the groups with respect to categorical data, as appropriate. All p values are two-sided. P values <0.05 were considered significant.

Results

During the period from February 2016 and March 2018, out of a total of 95 patients screened, only 66 newly diagnosed type 2 diabetes mellitus patients met the inclusion criteria and were recruited to the study. Figure 1 represents the study flow chart. Out of the 66 patients recruited, 22 did not complete the study for various reasons. Of all the patients enrolled, only 44 completed the 3 months follow up duration, 23 received metformin and 21 received *Nigella sativa* oil. The high rate of drop out was due to constrains in some patients' follow up, described in the consort flow diagram (Fig. 1). From a total number of 33 patients allocated to metformin group, only 23 subjects received treatment and 10 withdrew. Twenty-three patients completed the 3-month of metformin administration. On the other hand, from a total number of 29 patients allocated to Nigella sativa oil group, only 21 received treatment and 8 withdrew. Twenty-one patients completed 3 months of Nigella sativa oil administration.

Both groups were comparable at baseline with regards to gender, age, height, disease duration, family history of diabetes, physical inactivity, active/passive smoking, presence of comorbid diseases (hypertension, dyslipidemia, coronary artery disease, peripheral artery disease, autoimmune disease, mental disease, retinopathy/altered vision, foot disease, chronic renal failure, polycystic ovary syndrome, erectile dysfunction for males, recurrent infection) or previous history (Table 1).

Both groups were comparable at baseline with regards to the occurrence of polyuria, polydipsia, polyphagia, weight loss, and nocturia. Nigella sativa group had a significantly higher number of patients reported recent weight gain vs. the metformin group 8 (27.6%) vs. 2 (5.6%) (Table 1).

At the end of the study, both groups were comparable in the occurrence of chills, sweating, tachycardia, lethargy/weakness, polydepsia, polyuria, dry skin, polyphagia, blurred vision, foot problems, or tingling/numbness. However, at the end of the study, the occurrence of foot problems was significantly lower in the NS group 1 (4.8%) vs. the metformin group 8 (33.3%) ($p = 0.025$).

Both groups were comparable at baseline in all of the followings: age, duration of disease, A1C, fasting insulin, %B, %S, IR, weight, height, BMI, waist circumference (Table 2), AST, ALT, creatinine, TC, LDL, HDL, TG, and TAC (Table 3). However, FBG values were significantly lower in *Nigella sativa* oil group 130.0 (85.0–285.0) vs. 168.0 (88.0–320.0) mg/dl in the metformin group at baseline ($P = 0.042$). Also, 2 h pp levels were significantly lower in *Nigella sativa* oil group 201.0 (104.0–329.0) mg/dl vs. metformin group at baseline 246.0 (130.0–384.0) mg/dl ($p = 0.006$) (Table 2). % B was significantly lower in the metformin group 36.9 (8.9–160.1) than in the *Nigella sativa* oil group 70.3 (12.9–209.5) at baseline ($p = 0.018$) (Table 2).

The fasting blood glucose levels, BMI and waist circumference values, significantly improved from baseline to the end of the study in both groups (Table 2). The Metformin group only, showed a significant improvement from baseline towards the end of the study in the 2h pp, A1C and

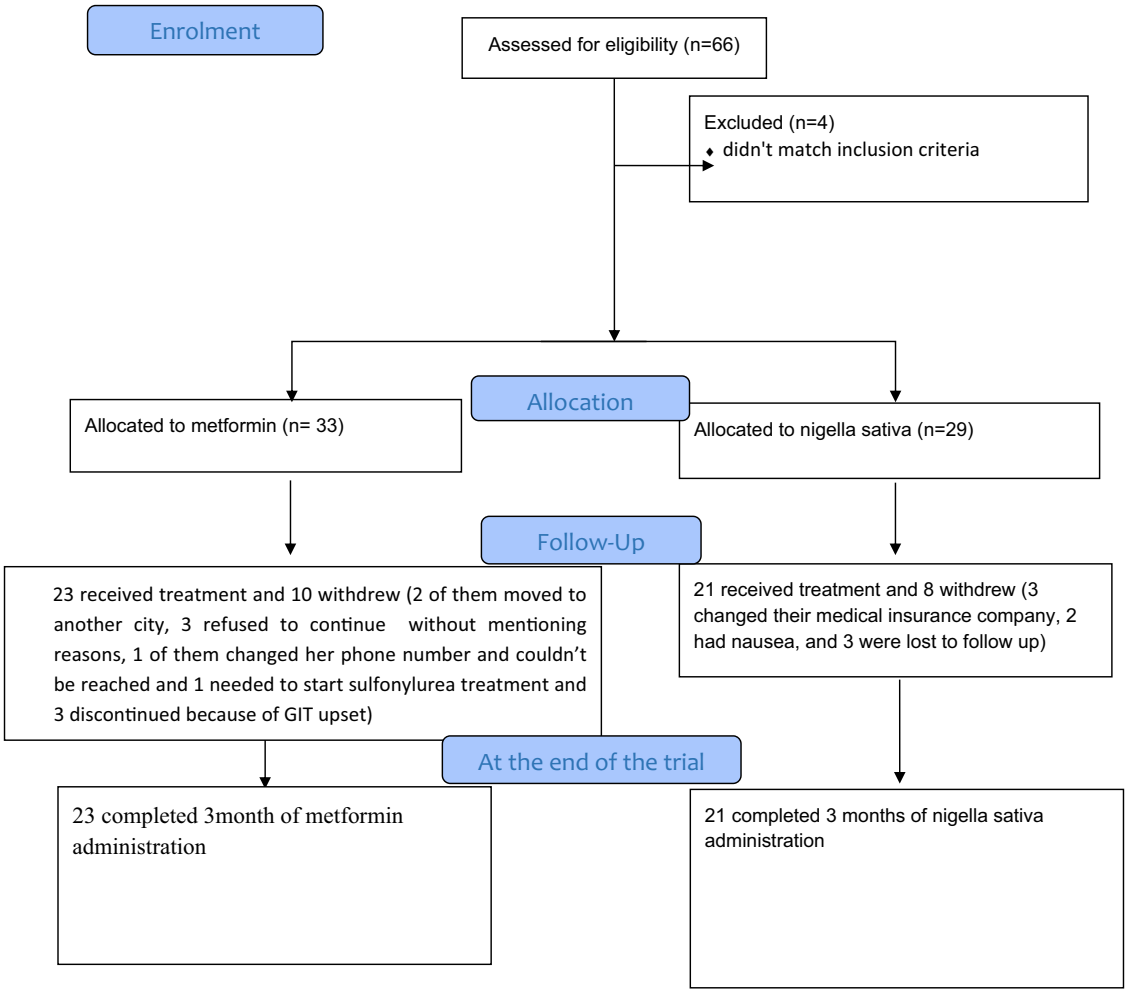

Fig. 1 Trial flow chart (consort diagram)

%B (Table 2). All of the other parameters did not significantly change from baseline towards the end of the study in both groups. Comparing the difference between the two groups at end of the study, the metformin group showed a significant improvement vs. the NS group in the percentage change of; FBG, 168 (88–320) at baseline to 119 (74–164) at the end with $p < 0.001$, 2hpp 246 (130–384) at baseline vs. 168 (90–272) at the end with $p < 0.001$, and A1C 7.6 (5.4–11.9) at baseline vs. 6.5 (5.1–8.6) at the end with $p = 0.003$ (Table 2). On the other hand, the metformin group showed a significant increase in AST 19.0 (11–44) and S. creatinine 0.9 (0.6–1.5) vs. the NS group whose levels were not altered significantly, 17 (11–59) and 0.8 (0.6–1), respectively, (Table 3).

Discussion

The alarming rising trend of diabetes prevalence in the Arabic countries offers a great challenge for heath decision makers. Although the number of people with diabetes is increasing in every country, about 80% are in low- and middle-income countries [34]. Standard treatment is failing to achieve required glycemic goals in many patients. Because nature is an extraordinary source of medicines, there is a need for investigating potential hypoglycemic drugs or herbs to improve glycemic control in diabetic individuals [35]. Based on current evidence, metformin should be if tolerated and unless contraindicated the initial drug of choice when lifestyle modification is insufficient to control glucose levels because of its efficacy, relatively good safety profile, association with weight loss or weight neutrality, beneficial cardiovascular and metabolic effects, and availability as a generic formulation [11]. Because of *Nigella sativa's* favorable clinical and biochemical effects on glycemic control, lipid profile, weight, and oxidative stress [16, 29], it was investigated as an adjuvant to oral hypoglycemic agents in T2DM patients [24]. This current study is the first published work investigating the efficacy of *Nigella sativa* oil

Table 1 Baseline comparison between both groups in demographics and history

Parameter	Groups		*P* value
	C; *n* (%)	NS; *n* (%)	
Gender			
F	25 (69.4%)	22 (75.9%)	0.565
M	11(30.6%)	7 (24.1%)	
Family history			
N	9 (25.0%)	5 (17.2%)	0.449
Y	27 (75.0%)	24 (82.8%)	
Physical activity			
N	22 (61.1%)	22 (75.9%)	0.206
Y	14 (38.9%)	7 (24.1%)	
Recent weight gain			
N	34 (94.4%)	21 (72.4%)	0.014*
Y	2 (5.6%)	8 (27.6%)	
HTN			
N	26 (72.2%)	23 (79.3%)	0.510
Y	10 (27.8%)	6 (20.7%)	
Dyslipidemia			
N	19 (52.8%)	18 (62.1%)	0.452
Y	17 (47.2%)	11 (37.9%)	
CAD			
N	30 (83.3%)	28 (96.6%)	0.120
Y	6 (16.7%)	1 (3.4%)	
PAD			
N	31 (86.1%)	25 (86.2%)	1.000
Y	5 (13.9%)	4 (13.8%)	
Autoimmune disease			
N	33 (91.7%)	24 (82.8%)	0.450
Y	3 (8.3%)	5 (17.2%)	
Mental disease			
N	36 (100.0)%	26 (89.7%)	
Y	0 (0.0%)	3 (10.3%)	
Retinopathy/altered vision			
N	18 50.0%	13 (44.8%)	0.678
Y	18 (50.0%)	16 (55.2%)	
Foot disease			
N	32 (88.9%)	24 (82.8%)	0.477
Y	4 (11.1%)	5 (17.2%)	
CRF			
N	36 (100.0%)	29 (100.0%)	
PCOS			
N	35 (97.2%)	28 (96.6%)	
Y	1 (2.8%)	1 (3.4%)	
Obstetric History of large babies			
N	30 (83.3%)	22 (75.9%)	0.454
Y	6 (16.7%)	7 (24.1%)	
Gestational diabetes			
N	31 (86.1%)	28 (96.6%)	0.213
Y	5 (13.9%)	1 (3.4%)	
Erectile dysfunction			
N	33 (91.7%)	26 (89.7%)	1.000
Y	3 (8.3%)	3 (10.3%)	
Recurrent infection			
N	25 (69.4%)	20 (69.0%)	1.000
Y	11 (30.6%)	9 (31.0%)	
Smoking-active			
N	34 (94.4%)	24 (82.8%)	
N/Stopped	1 (2.8%)	0 (0.0%)	
Y	1 (2.8%)	5 (17.2%)	
Smoking-passive			
N	34 (94.4%)	23 (82.1%)	0.225
Y	2 (5.6%)	5 (17.9%)	

Data are expressed as number and percent, $*P < 0.05$ is significant

F female, *M* male, *N* no, *Y* yes, *HTN* hypertension, *CAD* coronary artery disease, *PAD* peripheral artery disease, *CRF* chronic renal failure, *PCOS* polycystic ovarian syndrome

as a monotherapy in newly diagnosed type 2 patients, compared to metformin.

Significant reduction in body weight and BMI were demonstrated in the *Nigella sativa* oil group at the end of the study, compared to baseline. Similarly, previous studies reported weight and BMI reduction after administration of nigella sativa [13, 36]. On the contrary, a previous study conducted Saudi Arabia reported no significant weight loss with NS administration [24]. The discrepancy between this study and our study may be due to different study populations and difference in the lifestyle of the study participants.

Moreover, a significant reduction in waist circumference was observed in the *Nigella sativa* oil group from their baseline values. Similarly, a reduction in waist circumference after administration of *Nigella sativa* was previously reported [27, 37].

In two previous studies, nigella sativa demonstrated a mild reduction in triglycerides and low-density lipoprotein levels [38, 39]. On the contrary, no significant reduction in triglycerides and low-density lipoprotein was reported in this work, similar to two previous studies [19, 40].

Nigella sativa was previously reported to elevate HDL-C level [41]. On the contrary, the current study didn't show any significant effect on HDL-C after administration of *Nigella sativa*, similar to one previous study [39].

Table 2 Comparison of glycemic control and anthropometric parameters between both groups over the study period

Parameter	Groups				*P* value
	C ($n = 23$)		N ($n = 21$)		
	Mean ± SD	Median (IQR)	Mean ± SD	Median (IQR)	
FBG-0	166.2 ± 52.8	168.0 (88.0–320.0)	142.5 ± 50.4	130.0 (85.0–285.0)	0.042*
FBG -End	120.7 ± 25.4	119.0 (74.0–164.0)	119.8 ± 23.7	116.0 (87.0–192.0)	0.796
P value		<0.001*		0.001*	
FBG_change	21.9 ± 22.7	19.2 (−37.5–69.1)	11.7 ± 15.3	9.6 (−7.9–61.1)	0.028*
2hpp-0	245.9 ± 60.0	246.0 (130.0–384.0)	201.4 ± 48.1	201.0 (104.0–329.0)	0.006*
2hpp -End	171.7 ± 57.9	168.0 (90.0–272.0)	184.1 ± 47.5	181.0 (94.0–296.0)	0.549
P value		<0.001*		0.06	
2hpp_change	26.2 ± 30.2	30.4 (−56.9–70.8)	6.5 ± 22.2	9.0 (−46.0–46.7)	0.013*
A1C-0	7.58 ± 1.63	7.60 (5.40–11.90)	7.44 ± 1.16	7.30 (5.80–10.00)	0.823
A1C -End	6.55 ± 0.72	6.50 (5.10–8.60)	7.01 ± 0.83	7.00 (5.50–8.80)	0.040*
P value		0.003*		0.177	
A1C_change	10.7 ± 16.4	13.2 (−16.1–42.9)	4.2 ± 14.9	1.4 (−27.9–37.8)	0.217
f. insu.-0	12.7 ± 5.9	11.3 (5.2–24.0)	18.2 ± 12.9	13.4 (5.0–56.4)	0.226
f.insul -End	11.5 ± 5.3	11.8 (3.2–23.8)	16.5 ± 13.1	10.4 (3.6–54.5)	0.589
P value		0.361		0.715	
F.insu_change	−1.8 ± 54.0	5.6 (−173.1–75.6)	−1.9 ± 50.9	3.4 (−114.462.6)	0.972
%B-0	53.2 ± 38.1	36.9 (8.9–160.1)	83.3 ± 52.5	70.3 (12.9–209.5)	0.018*
%B -End	78.6 ± 47.5	68.2 (22.8–242.4)	97.1 ± 63.7	71.0 (19.0–273.2)	0.307
P value		0.004*		0.23	
B_change	−113.5 ± 245.9	−38.6 (−1085.4–41.7)	−32.5 ± 72.3	−27.8 (−288.6–45.2)	0.162
%S- 0	66.4 ± 32.0	61.7 (27.4–134.8)	59.7 ± 39.0	50.3 (10.6–143.0)	0.285
%S -End	83.1 ± 51.4	67.0 (31.5–224.8)	67.3 ± 40.8	70.4 (14.8–204.7)	0.655
P value		0.153		0.375	
S_change	−38.2 ± 85.3	−16.0 (−351.4–62.0)	−33.3 ± 71.7	−24.2 (−165.3–51.1)	0.823
IR-0	1.87 ± 0.87	1.62 (0.74–3.65)	2.59 ± 2.00	1.99 (0.70–9.43)	0.285
IR -End	1.58 ± 0.72	1.49 (0.44–3.17)	2.20 ± 1.65	1.42 (0.49–6.76)	0.647
P value		0.089		0.266	
IR_change	5.5 ± 51.8	13.9 (−163.5–78.1)	1.8 ± 50.2	19.3 (−104.3–62.2)	0.823
wt-0	87.7 ± 17.0	83.0 (66.0–134.0)	86.9 ± 17.9	82.0 (63.5–131.0)	0.681
wt -End	83.3 ± 15.4	79.0 (62.0–130.0)	84.4 ± 17.1	79.0 (61.0–125.0)	0.944
P value		0.002*		0.002*	
wt_change	4.8 ± 5.7	5.0 (−4.0–16.7)	2.9 ± 3.2	2.9 (−3.5–8.5)	0.264
BMI-0	34.4 ± 5.5	34.2(27.0–54.5)	33.3 ± 6.8	30.1 (24.8–48.9)	0.177
BMI -End	32.6 ± 4.3	32.5 (27.2–46.2)	32.3 ± 6.4	30.6 (23.8–46.1)	0.312
P value		0.001*		0.002*	
BMI_change	4.8 ± 5.7	5.1 (−3.9–16.8)	2.9 ± 3.1	2.9 (−3.4–8.7)	0.245
waist-0	109.2 ± 11.7	107.0 (94.0–144.0)	106.1 ± 13.3	102.0 (86.0–133.0)	0.318
Waist -End	105.8 ± 11.4	104.0 (92.0–137.0)	103.0 ± 11.7	100.0 (79.0–124.0)	0.410
P value		0.004*		0.004*	
Waist_change	3.0 ± 4.4	3.2 (−8.5–13.9)	2.8 ± 4.4	2.0 (−7.9–12.1)	0.573

Data are expressed as number, mean, SD, median, IRQ, $*P < 0.05$ is significant

-0 baseline, FBP fasting blood glucose, *2h pp* 2 h post prandial, *A1C* glycated hemoglobin, *%B* secretory function, *%S* insulin sensitivity, *IR* insulin resistance, *Wt* weight, *Ht* height, *BMI* body mass index, *WC* waist circumference

Table 3 Comparison of biochemical parameters between both groups over the study period

Parameter	Groups				*P* value
	C ($n = 23$)		N ($n = 21$)		
	Mean ± SD	Median (IQR)	Mean ± SD	Median (IQR)	
AST-0	27.2 ± 17.2	21.0 (6.0–90.0)	24.1 ± 13.4	19.0 (11.0–69.0)	0.540
AST -End	20.5 ± 7.5	19.0 (11.0–44.0)	21.6 ± 11.6	17.0 (11.0–59.0)	0.680
P value		0.046*		0.139	
AST_change	9.0 ± 39.8	11.8 (−100.0–74.4)	1.0 ± 50.8	10.5 (−181.0–54.5)	0.769
ALT-0	26.6 ± 16.4	26.0 (3.0–74.0)	29.6 ± 16.4	22.0 (9.0–65.0)	0.672
ALT -End	20.3 ± 8.9	20 (10–41)	24.8 ± 11.9	24.0 (11–45)	0.269
P value		0.095		0.082	
ALT_change	2.3 ± 61.1	6.3 (−233.3–80.9)	6.2 ± 40.1	25.0 (−72.7–52.9)	0.991
Sr cr-0	0.78 ± 0.18	0.80 (0.40–1.20)	0.82 ± 0.15	0.80 (0.60–1.10)	0.482
Sr Cr -End	0.89 ± 0.20	0.90 (0.60–1.50)	0.82 ± 0.12	0.80 (0.60–1.00)	0.247
P value		0.039*		0.992	
SrCr_change	−19.0 ± 36.2	−11.1 (−125.0–22.2)	−1.1 ± 15.6	0.0 (−33.3–22.2)	0.092
TC-0	205.9 ± 54.4	207.0 (93.0–324.0)	206.8 ± 51.5	211.0 (109.0–286.0)	0.778
TC -End	190.0 ± 40.5	185.0 (106.0–283.0)	198.2 ± 35.9	198.0 (127.0–280.0)	0.438
P value		0.057		0.543	
TC_change	3.8 ± 25.0	7.8 (−81.7–39.5)	−0.3 ± 25.0	8.0 (−66.7–32.4)	0.565
LDL-0	124.2 ± 47.6	111.7 (39.0–212.0)	127.0 ± 52.5	129.0 (38.3–205.5)	0.796
LDL -End	115.6 ± 37.2	111.0 (51.0–202.0)	116.4 ± 33.9	114.0 (51.8–202.0)	0.981
P value		0.287		0.289	
LDL_change	−3.2 ± 47.8	13.2 (−170.8–47.6)	−7.8 ± 54.8	6.1 (−159.0–46.4)	0.698
HDL-0	52.4 ± 13.0	49.0 (29.0–75.0)	48.0 ± 10.1	47.5 (28.0–79.4)	0.318
HDL -End	50.7 ± 12.3	51.0 (22.3–74.0)	49.9 ± 11.3	51.0 (27.0–77.0)	0.769
P value		0.626		0.14	
HDL_change	0.7 ± 22.9	1.5 (−44.1–53.7)	−4.9 ± 18.2	−10.3 (−40.0–34.5)	0.488
TG-0	150.4 ± 66.6	129.0 (46.0–325.0)	159.4 ± 78.3	161.0 (38.0–359.0)	0.605
TG -End	127.8 ± 59.1	112.0 (44.0–285.0)	159.4 ± 94.4	138.0 (46.0–455.0)	0.254
P value		0.066		0.917	
TG_change	11.1 ± 29.7	13.4 (−52.1–51.2)	−2.9 ± 36.9	5.5 (−85.4–46.1)	0.162
TAC-0	0.79 ± 0.24	0.88 (0.10–1.08)	0.77 ± 0.27	0.77 (0.10–1.15)	0.922
TAC -End	0.79 ± 0.29	0.89 (0.14–1.14)	0.67 ± 0.33	0.72 (0.04–1.18)	0.195
P value		0.751		0.332	
TAC_change	−4.1 ± 35.7	−1.1 (−75.0–75.7)	−18.3 ± 151.9	−2.5 (−630.0–94.7)	0.575

Data are expressed as number, mean, SD, median, IQR, $^*P < 0.05$ is significant

-0 baseline, AST aspartate aminotransferase, *ALT* alanine aminotransferase, *Sr cr* serum creatinine, *TC* total cholesterol, *LDL* low-density lipoprotein, *HDL* high density lipoprotein, *TG* triglycerides, and *TAC* total antioxidant capacity

In the current study, administration of *Nigella sativa* oil at a dose of 1350 mg per day demonstrated a significant reduction in fasting blood glucose, similar to previous studies [14, 24]. Yet, it had no significant effect on reduction of either 2 h pp or A1C. On the other hand, a previous clinical trial demonstrated that HbA1c was lowered significantly at the end of the 12 weeks of treatment using either 2 or 3 grams daily supplementation of *Nigella sativa*, but was not affected significantly by the one gram dose [24]. This may indicate that a dose of 2 g/day or higher may be essential to significantly affect glycemic improvements measured in terms of 2 h pp and HbA1C levels.

Insulin resistance and B-cell secretory functions were previously estimated by the homeostasis model assessment (HOMA) in several studies [24, 42]. In the current study, 1350 mg per day of NS did not affect %B. On the contrary, two grams of NS per day for 3 months resulted in enhancement in the secretory function of pancreatic β cells

in a previous study [43]. The discrepancy between the current study and this study may be attributed to the difference in the daily doses used in both studies.

Both groups demonstrated reduction in weight, BMI, and waist circumferance. However, there was no significant difference in the % change between NS oil and metformin in terms of weight, BMI, or waist circumference reduction.

Both *Nigella sativa* oil and metformin resulted in a significant reduction in FBG. The % change in the metformin group was significantly higher.

Recommendations

The main strength of this study lies in being the first attempt to evaluate the effect of NS on the glycemic control, weight loss, and lipid profile in patients with type 2 DM as monotherapy vs. metformin.

Further blinded, randomized placebo-controlled clinical trials are needed to be performed on larger scale using 2 g or more of NS to support current promising results and to explain the exact underlying mechanism(s) of NS effects on insulin secretion, sensitivity and resistance. We recommend more research about the use of NS as an add on therapy in treating T2DM patients.

Conclusion

NS oil administration at a dose of 1350 mg per day in newly diagnosed patients with type 2 diabetes mellitus was inferior to metformin in terms of lowering FBG, 2 h pp, A1C, %B. NS oil was comparable to metformin in lowering weight, waist circumference, and BMI significantly. NS was comparable to metformin in regards of their effects on fasting insulin, %S, IR, ALT, TC, LDL, HDL, TG, and TAC. *Nigella sativa* oil administration in newly diagnosed T2DM was tolerable with no side effects as compared to metformin administration. Metformin showed significant increase in AST and creatinine which was reserved in NS oil group.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors.

Informed consent Informed consent was obtained from all individual participants included in the study.

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