

Glycemic and cardiovascular parameters improved in type 2 diabetes with the high nutrient density (HND) diet

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ABSTRACT

Objective: The purpose of this study was to provide an initial assessment of the effectiveness of the high nutrient density (HND) diet on glycemic control and cardiovascular risk factors in participants with type 2 diabetes. **Design:** This was a retrospective case series study. Participants were 13 adult type 2 diabetic U.S. women and men between the ages of 30 - 80 years old. Glycosylated hemoglobin (HbA1C), lipid profile, blood pressure, BMI, and medication requirements before and after commencement of the HND diet were compared. **Results:** After a median length on the HND diet of 7 months, the mean HbA1C dropped from 8.2% to 5.8% ($p = 0.002$), with sixty-two percent of participants reaching normoglycemic levels (HbA1C < 6.0%). There was a substantial reduction in mean blood pressure for hypertensive participants ($n=10$) from a pre-intervention level of 148/87 mmHg to 121/74 mmHg ($p = 0.0004$ for systolic blood pressure, $p = 0.01$ for diastolic blood pressure). Triglycerides significantly decreased from a mean of 171 mg/dl to a mean of 103 mg/dl ($p = 0.02$). The mean HDL increased significantly from 48.3 mg/dl to 54.6 mg/dl ($p = 0.03$). The mean number of medications dropped from 4 to 1 ($p = 0.0006$). **Conclusions:** The HND diet was very effective in controlling glycemic levels and cardiovascular risk factors in 13 participants with type 2 diabetes. Therefore, there is a well-justified need for further study with the HND diet.

Keywords: Type 2 Diabetes Mellitus; Lipids; Hypertension; Nutrition; Cardiovascular Disease; Lifestyle Medicine; HbA1C; BMI

1. INTRODUCTION

Lowering complication risk and achieving better metabolic control are the central goals of medical care for type 2 diabetes, but outcomes are inconsistent. In the 2009 consensus statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes, the organizations recommend starting a nascent type 2 diabetes patient on lifestyle changes plus metformin. According to the authors, for most individuals, lifestyle interventions fail to achieve or maintain the metabolic goals [1]. Only about 37% of type 2 diabetes patients in 1999-2000 Third National Health and Nutrition Examination Survey have achieved the ADA's recommended goal of a HbA1C < 7.0% [2].

Diets low in animal protein and saturated fat and high in complex carbohydrates, fiber and micronutrients improve glucose tolerance, postprandial glucose and overall glycemic control, as well as decrease insulin resistance [3-7]. The high nutrient density (HND) diet emphasizes micronutrients (phytochemicals and antioxidants) from greens, fruits, nuts/seeds and beans/legumes, the latter containing high amounts of viscous fiber and resistant starches. The HND diet incorporates features of other dietary interventions, but is designed to create advantages from multiple mechanisms, including the effect that high micronutrient food has in reducing cravings and overeating, and on lowering oxidative stress [8] and deposition of advanced glycation end products [9,10].

The HND diet is a plant-rich diet differing from other plant-based diets in some subtle, but significant, ways. Foods are rated based on total micronutrient content per calorie, which emphasizes consumption of greens and other non-starchy vegetables, such as onions, mushrooms, eggplant, peppers, tomatoes, and cauliflower, in unlimited quantity. High glycemic, high carbohydrate foods are reduced, while beans, peas, squash and intact grains

are permitted. Nuts and seeds are the primary source of fat, while animal products are limited to 10 percent of calories or less. Basic recommendations include:

- 1) At least one large green salad a day, with inclusion of a nut/seed derived salad dressing.
- 2) One bowl of vegetable-bean soup daily.
- 3) 1 - 2 ounces of raw seeds and nuts daily (usually in salad dressing recipe).
- 4) Approximately 3 - 4 fresh fruits per day.
- 5) One large serving of steamed or stewed greens, with mushrooms, onions and other low-starch veggies.
- 6) Only one serving a day of non-bean starch, such as squash, steel cut oats, brown/wild rice.
- 7) Exclusion of white flour, sweets, and oils, while limiting animal products to 12 ounces per week.

The Mediterranean diet, which has been shown to reduce the risk of type 2 diabetes, encourages moderate amounts of fish and dairy, including fat and non-fat varieties, and emphasizes whole grains and extra virgin olive oil [11-13]. The HND diet, in contrast, suggests only small amounts of fish, non-fat dairy [14], whole grains and minimal amounts or no oil. The HND diet encourages more calories derived from vegetables and beans, as well as the intake of a moderate amount of fats from sources, such as nuts, which contain a combination of protein, fiber, phytonutrients, antioxidants and omega 3 fatty acids [15]. Tree nuts and peanut butter reduce the risk of developing diabetes in women [16,17]. Nuts significantly reduce the risk of coronary heart disease (CHD) and the risk of death from CHD [18-22] in type 2 diabetes patients.

The combination of the plant-based micronutrients recommended in the HND diet has the potential to improve results over those obtained in other medical nutrition studies. To provide an initial evaluation of the potential efficacy of the HND diet in participants with type 2 diabetes and to provide pilot data for large randomized clinical trials of the HND diet, we report a retrospective case series examining multiple parameters in 13 participants with type 2 diabetes, both before and after initiation of the HND diet.

2. METHODS

There were multiple inclusion criteria for this retrospective case series. The cases were selected based on two main criteria. First they needed to have a diagnosis of type 2 diabetes with documented baseline HbA1C readings before starting the HND diet. Second, the participants had to participate in phone interviews tracking their ongoing diet and historical dietary recall. As a result of these phone interviews, documented compliance with the dietary intervention of $\geq 90\%$ was required for inclusion. Greater than 90% compliance was defined as

≤ 2 meals per week inconsistent with the HND diet and this minimum standard of consistency was necessary during the entire period of result tracking. The participants were not told of the compliance as an inclusion criterion until after analysis of their dietary intake was completed. Selection also required participants to fall into one of the following two categories during the pre-intervention period: they had a HbA1C $> 7.0\%$ with or without diabetes medications ($n = 9$); or they had a HbA1C $> 6.0\%$ with diabetes medications ($n = 4$). The participants were from two sources, Dr. Fuhrman's practice or Dr. Fuhrman's interactive website.

Dr. Fuhrman was not the primary care physician for these participants, but rather a specialist with expertise in medical nutrition, who contributed this dietary protocol advice to the participants. The office-based participants had an hour-long initial visit with Dr. Fuhrman, prior to starting the HND diet, and then had several 30-minute follow-up consultations. The web-based participants started the diet by reading the book *Eat to Live* and by accessing online support from the interactive website DrFuhrman.com, which provides web-based forums, recipes, and further information. Both the office-based participants and web-based participants had either visits or forum postings between 8/2007-8/2009. Data were collected and analyzed in 2009.

Ninety-seven charts and web postings from this two-year period were reviewed for eligibility. Fifty-two of these met baseline HbA1C eligibility requirements. Of these, 27 were available for phone interviews. Thirteen of these met dietary compliance eligibility criteria and were included in the study. Of these, 7 were office-based and 6 were web-based. All the participants were required to have copies of lab results sent by clinical laboratories. Participants' printed laboratory reports were collected from the charts for the office-based participants or were faxed/mailed by the participants or directly from the primary care physicians' offices for the web-based participants. For the web-based participants, biometric indices (weight, height and blood pressure) were measured at their primary care physicians' offices. For the office-based participants, the biometric parameters were measured at each visit by Dr. Fuhrman. Medication changes for the web-based participants were performed by their primary care physician. For the office-based participants, Dr. Fuhrman made the medication decisions.

This retrospective human subject analysis was reviewed and approved by the University of Pennsylvania's Institutional Review Board.

Descriptive analysis was performed for the participant characteristics using mean and standard deviation (SD) for continuous variables and proportion for categorical variables. The change of parameters over time after the start of the HND diet was plotted for each individual

participant. For statistical comparison, the mean parameters measured before and at the last time point after starting the HND diet were calculated and compared using both the absolute change and percentage change. *p*-Values for testing whether absolute change and percentage change statistically differs from zero were determined using one-sample *t*-test. The correction for multiple statistical testing of many parameters was not considered as this study is a small pilot investigation. *p*-Value ≤ 0.05 was considered to be significant. For a participant with missing data in a parameter, the participant was excluded from the statistical comparison of this parameter, but was still included in the analysis of other parameters with complete data. The data analyses were performed using SAS v9.1 (SAS Institute Inc., Cary, NC).

3. RESULTS

Multiple baseline characteristics of each participant are illustrated (**Table 1**). The majority (69%) of participants was female. The demographics include 11 Cauca-

sians and 2 African-Americans. The mean age was 57 years old, ranging from 30 to 80 years old. BMI at baseline ranged from 25 to 45.6 kg/m². The mean HbA1C at baseline was 8.2%. Seventy-seven percent of the participants had hypertension ($\geq 130/80$ mmHg; based on ADA [23] and JNC7 [24] guidelines) and 92% had hyperlipidemia (based on the NCEP III guidelines [25]) before the HND diet. Sixty-two percent of participants had a family history of heart disease. The median length of follow-up with complete laboratory result time-points was 7 months (range: 5 to 42 months). During baseline and follow-up, a median of 3 laboratory result time-points (range: 2 to 8) per participant were obtained, with 92% having ≥ 3 laboratory result time-points. Most of the participants are/were on the diet for much longer than the median follow-up period, though they did not have laboratory result time-points during this extended period.

After participants were on the HND diet for a median length of 7 months, most of the parameters showed significant improvements relative to pre-intervention levels (**Table 2**). The mean HbA1C dropped from 8.2% to

Table 1. Characteristics of participants at pre-intervention.

Pts	Sex	Age	Mo since Dx DM	HbA1C (%)	BMI (kg/m ²)	# meds	# DM meds	SBP (mm Hg) for pts with HTN	DBP (mm Hg) for pts with HTN	HDL (mg/dL)	Chol/HDL	Trig (mg/dL)
1	F	56	1	9.6	42.4	8	2	158	77	35	6.3	174
2	F	47	84	12.2	32.3	NA	NA	150	110	36	7.8	260
3	F	66	120	7.3	28.9	2	1	NA	NA	46	5.9	368
4	F	60	24	7.5	45.6	NA	NA	150	90	49	4.1	76
5	F	80	252	7.3	28.7	4	4	172	82	60	4	136
6	F	54	240	6.5	42.3	7	3	NA	NA	38	4	232
7	F	57	84	6.3	41.2	5	4	110	80	35	3.2	147
8	F	49	24	6.3	27.8	8	1	NA	NA	62	2.7	90
9	F	68	18	7.6	31.6	3	NA	160	90	59	4.9	190
10	M	30	12	10.7	32.0	1	1	150	90	48	6.1	102
11	M	74	84	7.6	25.5	3	1	158	75	63	2.4	102
12	M	39	84	10.4	43.3	2	2	145	90	NA	NA	NA
13	M	56	84	6.7	25.0	4	2	125	85	NA	NA	NA
Mean		57	85.0	8.15	34.3	4.3	2.1	148	87	48	4.7	171
SD		13.7	80.3	1.92	7.47	2.5	1.2	18	10	11	1.7	88
Mdn		56	84.0	7.50	32.0	4.0	2.0	150	88	48	4.1	147

^apts = patients; Mo since Dx DM = months since diagnosed with type 2 diabetes; # meds = number of overall medications; # DM meds = number of diabetes medications; SBP for pts with HTN = systolic blood pressure for participants with hypertension; DBP for pts with HTN = diastolic blood pressure for participants with hypertension; chol/HDL = cholesterol to HDL ratio; Trig = triglycerides; Total Chol = total cholesterol; Mdn = median; ^bNA = not applicable; NA = not available for lipids.

Table 2. A comparison of pre- and post-HND diet intervention parameters.

Parameters (# participants available for analysis)	Pre-intervention	Post-intervention	Change from baseline	<i>p</i> -Value***	Percent change from baseline	<i>p</i> -Value***
	Mean (SE)	Mean (SE)	Mean (SE)		Mean (SE)	
HbA1C (n = 13)	8.15 (0.53)	5.80 (0.15)	-2.35 (0.58)	0.002	25.4 (4.84)	0.0002
BMI (n = 13)	34.4 (2.07)	26.8 (1.72)	-7.79 (1.28)	<0.0001	-21.8 (2.56)	<0.0001
SBP (n = 10)	148 (5.70)	121 (4.72)	-25.8 (4.37)	0.0004	-17.2 (2.61)	0.0002
DBP (n = 10)	87 (3.14)	73.7 (1.53)	-12.9 (3.92)	0.01	-13.9 (3.57)	0.005
Chol/HDL ratio (n = 11)	4.67 (0.51)	3.62 (0.27)	-1.03 (0.50)	0.07	-13.9 (9.98)	0.19
Triglycerides (n = 11)	171 (26.6)	103 (11.2)	-69.2 (24.7)	0.02	-30.8 (11.0)	0.02
Total cholesterol (n = 11)	217 (19.0)	188 (11.8)	-21.2 (18.2)	0.27	-4.19 (8.86)	0.65
Weight (n = 13)	217 (15.4)	173 (13.8)	-47.0 (7.69)	<0.0001	-21.0 (2.66)	<0.0001
HDL (n = 11)	48.3 (3.40)	54.6 (4.80)	7.40 (2.93)	0.03	15.9 (6.16)	0.03
LDL (n = 11)	135 (17.7)	113 (8.64)	-15.7 (15.1)	0.33	2.8 (14.7)	0.85
Overall Meds (n = 11*)	4.27 (0.74)	1.36 (0.36)	-2.91 (0.59)	0.0006	-67.1 (7.72)	<0.0001
Diabetes Meds (n = 10*)	2.10 (0.38)	0.30 (0.15)	-1.80 (0.44)	0.003	-80 (11.1)	<0.0001
Hypertension Meds (n = 5*)	1.80 (0.37)	0.60 (0.25)	-1.20 (0.37)	0.03	-63.3 (18.6)	0.03
Lipid Meds (n = 4*)	1.25 (0.25)	0.50 (0.50)	-0.75 (0.25)	0.06	-75 (25.0)	0.06

*Restricted to those who were on study medications in pre-intervention; **Based on the last follow-up visit with data available; ***From one-sample t-test whether the change from pre-intervention is statistically significant from 0.

5.8%, a 30% relative reduction that reached statistical significance ($p = 0.002$). The mean systolic blood pressure (SBP) decreased from 148 mmHg to 121 mmHg, with an 18% reduction from the pre-intervention period ($p = 0.0004$). Triglycerides decreased significantly from the pre-intervention period, with an absolute reduction of 67.2 mg/dl ($p = 0.02$) from a mean of 170.6 mg/dl to 103.4 mg/dl. Cholesterol/HDL ratio changed from 4.67 to 3.62 ($p = 0.07$). Of the 11 participants on medications, the mean number of drugs dropped from 4.3 to 1.4 ($p = 0.0006$) and 90% of participants on diabetes medications ($n = 10$) were able to completely discontinue or reduce their diabetes drug therapy. The one participant (ID = 11) who did not change diabetes medication was on the lowest starting dose of Glucophage XR 500 mg, once daily.

All of the participants ($n = 13$) had a decrease in HbA1C (**Figure 1(a)**). Sixty-two percent reached non-diabetic HbA1C levels of <6.0% at the last data point for the HND diet. There was a substantial and rapid reduction in mean HbA1C at 1 - 4 months ($n = 11$) on the HND diet (8.15% at baseline, 6.52% at 1 - 4 months, $p = 0.02$), and it declined further, reaching normoglycemic levels, to a mean HbA1C 5.95% ($p = 0.006$ as compared to baseline) at 5 - 9 months ($n = 11$). Three participants (ID = 1, 4, 12) had HbA1C data substantially beyond this

time period. One of the participants (ID = 1) started with glycosylated hemoglobin of 9.6%, reached a non-diabetic HbA1C of 5.4% at 15 months, and declined even further at 42 months to 4.8%, the participant's last lab results. The second participant (ID = 4) initially had a HbA1C of 7.5%, which approached near normoglycemic levels of 6.2% at the last time point of 18 months. The HbA1C of the third participant (ID = 12) dropped substantially from 7.6% to a non-diabetic level of 5.9% at the last data point of 34 months.

Every participant ($n = 13$) showed a reduction in BMI (**Figure 1(b)**). Forty-six percent of participants reached a normal BMI (<25 kg/m²) [26] at their last data point. Five of the participants experienced an almost 10 kg/m² or greater drop in BMI.

Each hypertensive type 2 diabetes participant ($n = 10$) in the study experienced a reduction in their SBP (**Figure 1(c)**) and 80% had a decrease of ≥ 20 mmHg. Of these participants, 7 experienced the considerable reduction within six months of starting the HND diet. Three hypertensive type 2 diabetes participants (ID = 1, 4, 13) had a sustained decline in their SBP with data out to 42, 18 and 34 months, respectively. Overall, participants who were on anti-hypertensive medications ($n = 5$) had a mean reduction in hypertensive medications of 67%.

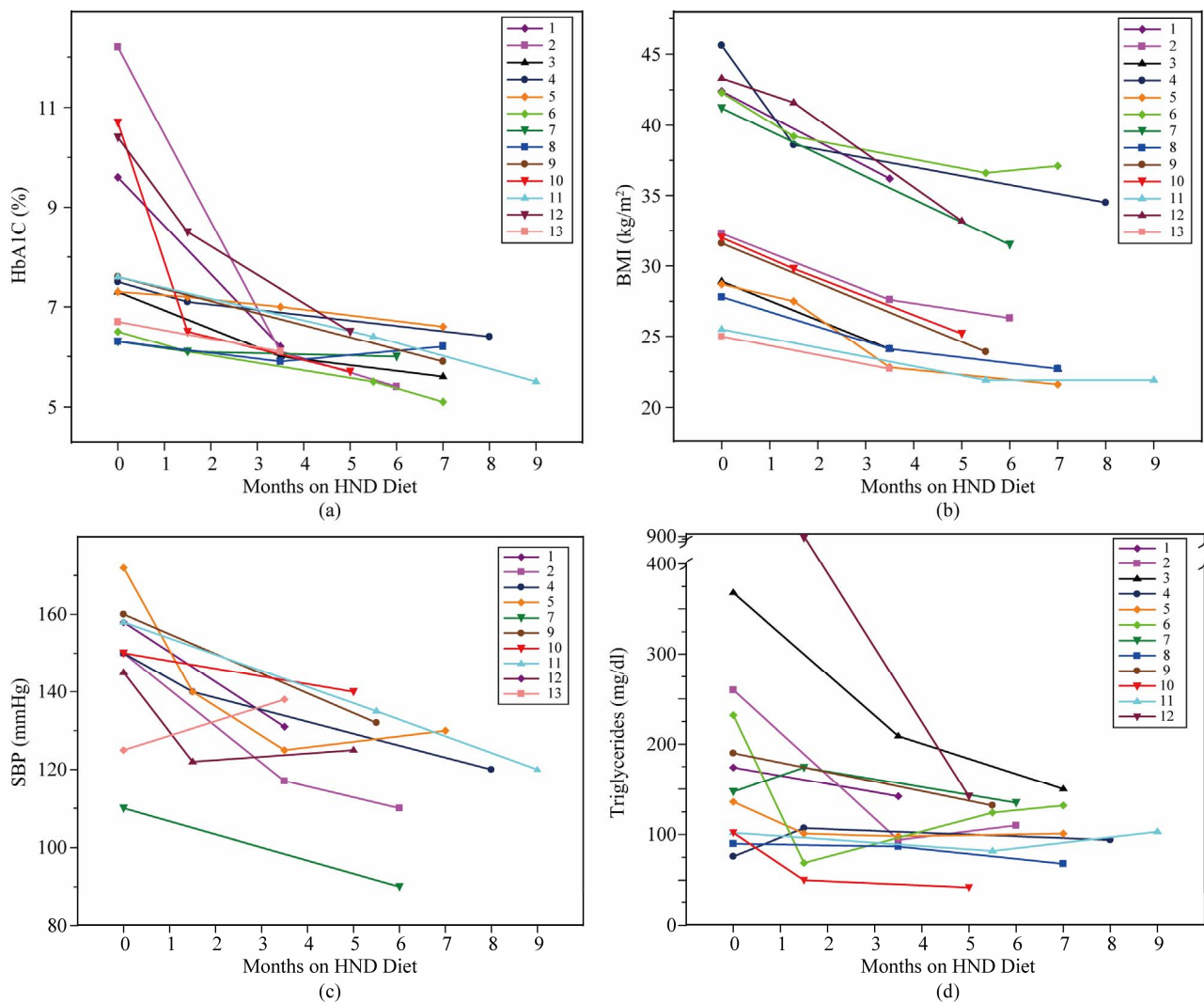


Figure 1. Graphs showing biometric data for each of the 13 study participants over time. Hemoglobin A1C (HbA1C; (a)), body mass index (BMI; (b)), systolic blood pressure (SBP; (c)) and triglycerides (d) are illustrated.

Most of the participants ($n = 12$) had a substantial drop in triglycerides within 6 months of starting the HND diet (**Figure 1(d)**). There were 11 participants who started the HND diet with dyslipidemia. Three participants (ID = 2, 3, 6) had triglycerides at pre-intervention that were >200 mg/dl. Their mean at baseline was 286 mg/dl with a precipitous mean reduction of 161 points. Another participant (ID = 12), whose pre-intervention levels were not obtained, had triglycerides of 885 mg/dl at 2 months which dropped to 142 mg/dl in 3 months, while still severely obese.

4. DISCUSSION

This case series of 13 type 2 diabetes participants demonstrated the mean reduction of 2.35% in the HbA1C, achieving statistical significance, with 62% reaching non-diabetic levels (HbA1C $< 6.0\%$). Those with hyper-

tension reached a mean normotensive level.

Triglycerides were reduced while HDL was increased, both significantly. There was a substantial drop in the total number of drugs, and 90% of participants discontinued or decreased diabetes medications. None of these effects was due to hypoglycemic, hypertensive or lipid lowering medications, since there was no added or increased dose of medication in the study participants.

In addition to the substantial decrease in diabetes medications ($n = 10$) seen in this HND diet case series, 85% of participants ($n = 11$) were able to discontinue or reduce the dose of overall medications, including diabetes, hypertensive and lipid therapies. These participants were not nascent to diabetes, but had a mean disease duration of 7.1 years prior to the HND diet. The overall number of medications was reduced by 67%.

Although there are no head-to-head comparisons with other plant-based diets in type 2 diabetes patients, this

study provides an initial assessment of the HND diet's effectiveness for diabetes. In several studies, it has been demonstrated that with a low fat vegan diet, type 2 diabetes could be better controlled than with the ADA diet [27,28]. In a randomized clinical trial contrasting a low fat vegan diet with the ADA diet, 43% of patients in the low fat vegan arm and 26% of patients in the ADA arm had a reduction in diabetes medications. Also, the HbA1C was reduced by a mean of 0.96% in 49 patients in the low fat vegan arm, and in the ADA arm, HbA1C was reduced by a mean of 0.56% in 50 patients [27].

Since there was a selection bias introduced into our study based on participant choice to participate on Dr. Fuhrman's website and/or office visits with Dr. Fuhrman, an accurate comparison of diet programs would best be accomplished by head-to-head analysis in a randomized prospective trial. However, the magnitude of effect of the HND diet in this case series indicates that the HND diet can be very effective in some participants.

Prior to starting the HND diet, 9 participants experienced diabetes-related complications and/or symptoms, including peripheral neuropathy in five participants, hypoglycemic episodes, cerebrovascular attack (CVA) or transient ischemic attack (TIA), and lethargy. All of the participants reported a reduction or complete dissipation of these symptoms. Further, none of the participants during the study period had any heart attacks, strokes, limb amputations, nephropathy or visual complaints.

Atherogenic dyslipidemia is a risk factor for heart disease [29]. Four of the participants in the HND diet case series (ID = 2, 3, 6, 12) had atherogenic dyslipidemia, which are triglycerides > 200 mg/dl and HDL < 50 mg/dl for a female or < 40 mg/dl for a male. After commencing the HND diet, all four of the participants' triglyceride levels were substantially reduced by over 100 points to 150 mg/dl or lower. The mean HDL rose 6.3 points to 54.6 mg/dl (n = 11), a statistically significant result compared to pre-HND diet levels ($p = 0.03$).

The CDC reports that 75% of type 2 diabetes patients also have hypertension, [30] of which only 36% are controlled [2]. The risk for cardiovascular disease begins to increase when blood pressure is > 115/75 mmHg. For every 20 mmHg increase in SBP and/or 10 mmHg increase in diastolic blood pressure, the risk for heart disease doubles [24]. Hypertensive type 2 diabetes participants (n = 10) in this HND diet case series showed a significant reduction in mean blood pressure from 148/87 mmHg to a normotensive level of 121/74 mmHg.

One potential mechanism for the decreases in glyce-mic levels, hypertension and hyperlipidemia in this HND diet case series is weight loss. However, the mean BMI at the last intervention point was 26.6 kg/m², which is considered overweight, yet the mean HbA1C reached a normoglycemic level of 5.8%. Six of the participants

whose BMIs decreased were still overweight or obese, yet 3 out of 6 reached normoglycemic levels (ID = 2, 6, 10). The remaining three (ID = 4, 7, 12) reached near normoglycemic levels. In fact, two of the participants (ID = 4 and 6) had BMIs at their last data points that are considered severely obese. Even participants (ID = 4, 6, 11, 13) who experienced either an increase or no change in BMIs (mean = +1.3%) between two data points demonstrated a decrease in HbA1C (mean = -6.8%) between these data points. Thus, the HND diet's beneficial effects on HbA1C appear to extend beyond weight loss.

In this case series, the HND diet has shown substantial sustainability and feasibility. The mean duration of the study with the 13 participants was 12.3 months. Of these participants, 62% were still on the diet at the study end point. Though five participants' HND diet compliance eventually lapsed, they all expressed interest in resuming, and four have been back on the diet for at least a few months. In terms of feasibility, 46% of the participants were able to garner knowledge about the HND diet for type 2 diabetes from the book *Eat to Live* and/or the supplemental interactive website. These six participants did not have a phone consult or office visit before initiating the diet or during the study period, though they could ask questions on the "ask the doctor" portion of the website. This is an indicator of the accessibility and clarity of the HND diet.

However, there are limitations to this study. It was a small retrospective case series with no control group. The study had selection bias, primarily because participants who reported their results on the website or chose to see Dr. Fuhrman in person may not represent the "typical" type 2 diabetes patient. In the study, 9 of 13 participants were female; its effectiveness in males needs further study. The HND diet may not work as effectively for everyone. For some, the HND diet may fail for numerous reasons, especially compliance. In this case series, participants were required to be at least 90% compliant with the diet. Of course, many patients also are not compliant with medications. To be successful, patients must have the proper knowledge and willpower. For the highly motivated individual, the HND diet appears to be an important weapon in the arsenal against type 2 diabetes.

5. CONCLUSION

This HND diet case series suggests benefits for patients with type 2 diabetes, its complications, and with some co-morbidities, such as heart disease risk, hypertension and hyperlipidemia. The HND diet may work well for some type 2 diabetes patients, but compliance with the HND diet may be an issue. This small case series has selection bias. However, the results of this study

demonstrate that the HND diet can be a very effective intervention for some with type 2 diabetes. Therefore, further study is needed

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