Research Letter

Effect of a Peer-led Lifestyle Intervention on Individuals With Normal Weight Obesity: Insights From the Kerala Diabetes Prevention Program

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ABSTRACT

Purpose: Normal weight obesity (NWO) is a unique phenotype of obesity associated with high cardiovascular mortality. There is limited literature on assessing the effect of therapeutic interventions on the cardiometabolic health of these individuals. We studied the effect of a peer-led lifestyle intervention on key cardiometabolic parameters (blood glucose, blood pressure, and plasma lipids) in individuals with NWO.

Methods: This study is a secondary data analysis of the Kerala Diabetes Prevention Program, a cluster-randomized controlled study that involves a peer-led, real-life lifestyle intervention for individuals from the community between the ages of 30 and 60 years with a high diabetes risk. Participants underwent a rigorous cardiometabolic evaluation at baseline and at 2-year follow-up.

Findings: A total of 292 recruited individuals with NWO were randomized into the intervention ($n = 159$) and control ($n = 133$) arms. At 2 years of follow-up, there was minimal but statistically significant improvement in systolic blood pressure and serum HDL level in the intervention arm, but no statistical difference was seen in other lipid and glycemic parameters.

Implications: This study provides early evidence of the effect of a lifestyle intervention in a cohort of individuals with NWO. Only systolic blood pressure and serum HDL level had a mild favorable change in the intervention arm when compared with the control

Accepted for publication June 15, 2020
https://doi.org/10.1016/j.clinthera.2020.06.007
0149-2918/$ - see front matter

arm. (*Clin Ther*. 2020;42:1618−1624)

Key words: lifestyle intervention, normal weight obesity, South Asian phenotype, thin-fat phenotype.

INTRODUCTION

Normal weight obesity (NWO) is a unique phenotype of obesity seen more commonly in individuals of South Asian descent and is defined as a normal body mass index (BMI) in the presence of high body fat percentage.[1−3] We have previously reported the definition, prevalence, pathogenesis, and cardiometabolic mortality associated with this phenotype.[4] However, a key area for future research that has been identified in the literature is to study the effect of a therapeutic intervention (diet, exercise, and medications) in individuals with NWO.

The Kerala Diabetes Prevention Program (KDPP) is a real-world cluster-randomized controlled trial of a peer-led lifestyle intervention program primarily performed to study its effect on reducing type 2 diabetes incidence and cardiac mortality risk in southern India.[5] The study protocol, baseline characteristics, and 2-year outcome data have been published elsewhere.[5−7] However, this study provides high-quality data on standardized anthropometric measurements from individuals recruited from the community who have had a rigorous assessment of their cardiometabolic risk factors.[5] In addition, it provides information to study the effect of a proficient, real-life, lifestyle-based intervention in individuals who are at high risk of type 2 diabetes during a period of 2 years.[6] After this unique lifestyle intervention, it was noted that at 2 years there was a significant reduction in the predicted 10-year cardiovascular mortality risk (determined by the Framingham Risk Score) and diabetes incidence among the impaired glucose tolerance group in the intervention arm compared with controls.[6,8,9] The absolute risk reduction in the predicted 10-year cardiovascular disease risk between study groups was 0.69% (95% CI, 0.10%−1.29%; $P = 0.023$) at 2 years. The prevalence of NWO in this cohort and the associated cardiometabolic risk factors at baseline have been previously published, but now with the availability of the 2-year follow-up data, we aim to investigate the effect of this real-world, peer-led, proficient lifestyle intervention on individuals with NWO. This information is clinically relevant because individuals with NWao are often missed in clinical practice because of their apparently lean appearance despite being associated with several cardiometabolic risk factors, including but not limited to diabetes, hypertension, and dyslipidemia. Moreover, once these individuals are diagnosed to have NWO by active screening, there is a paucity of evidence about whether the conventional lifestyle intervention would effectively reduce the cardiometabolic risk factors in these individuals.[10] To address this research gap, the key objective proposed in this study was to evaluate the effect of this unique lifestyle intervention on key cardiometabolic parameters (blood glucose, blood pressure, and plasma lipids) in individuals with NWO and compare these results to a control arm with NWO.

METHODS

Trial Design and Participant Recruitment

KDPP is a cluster-randomized controlled study that involves a peer-led, real-life lifestyle intervention for which individuals from the community between the ages of 30 and 60 years with a high diabetes risk were recruited. The high diabetes risk in these individuals was based on the Indian Diabetes Risk Score. This risk score assesses 4 clinical variables, including age, familial occurrence of diabetes, waist circumference, and physical activity. This score has been validated in the Indian population. A score of ≥60 was considered a strong predictor of incident diabetes in Asian Indians, and all participants in this study were recruited only if they had a high diabetes risk score. Study recruitment was performed in a random sample of 60 discrete areas segregated by electoral divisions called polling booths from the Neyyatinkara taluk of the Trivandrum district within the Indian state of Kerala. This study received institutional review board approval (Australia and New Zealand Clinical Trials Registry: ACTRN12611000262909), and all participants provided written informed consent before participation.

Randomization

Neyyatinkara taluk has 4 legislative assembly constituencies. In each legislative assembly constituency, 15 polling booths were randomly selected as the intervention and control constituencies. Randomization was performed by a qualified biostatistician who was blinded to all other population characteristics of the study population. Randomization was performed with Stata statistical software, release 12 (StataCorp, College Station, Texas).[5]

Outcome Measures

Clinical measurements, including anthropometry (BMI, waist circumference, and hip circumference), body fat assessment, and blood pressure measurements, were obtained using standardized instruments and protocols by trained staff at baseline and 2-year follow-up. Body composition was measured using a body composition analyzer (model SC330; Tanita Corp, Tokyo, Japan), which measured total body fat percentage based on bioelectrical impedance. Body composition was measured with the patient in a standing position without footwear, with each foot placed on the side in the designated area and the individual facing forward with arms by the side. This procedure is based on the World Health Organization Stepwise Approach to Surveillance (STEPS) protocol.[11] An oral glucose tolerance test with serum glycosylated hemoglobin and serum lipid measurement was performed at baseline and follow-up. NWO was defined as individuals who had a BMI (18.5–24.9 kg/m^2) with an increased body fat content (≥20.6% in men and ≥33.4% in women) based on a previously published criteria for the Asian population. The recruited participants were randomized into intervention and control arms (Figure).

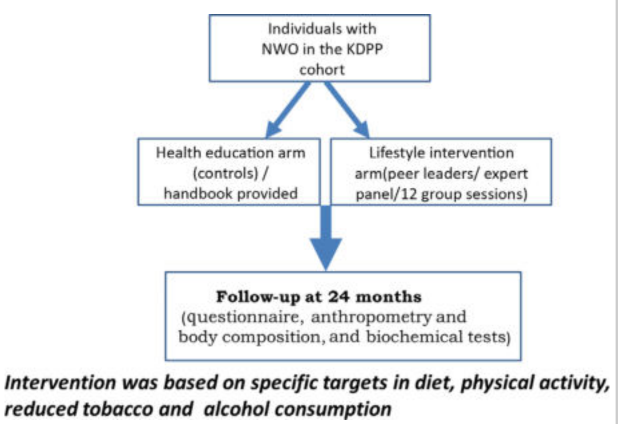

Figure. A 2-year follow-up of individuals with normal weight obesity (NWO) in the Kerala Diabetes Prevention Program (KDPP) cohort after intervention. The intervention was based on specific targets in diet, physical activity, and reduced tobacco and alcohol consumption.

Intervention

Detailed information about the intervention components have been mentioned in the protocol paper of this study.[5,6] The intervention program was designed in line with the Health Action Process Approach model with key focus on group management rather than an individualistic approach. The intervention is composed of 15 sessions, each of which was conducted in a group. The first introductory session was delivered by 1 of the members of the KDPP team; 2 education sessions were conducted by locally identified experts, and the following 12 sessions were conducted by trained peer leaders from the study group. All sessions were conducted on weekends in local community halls. The key aims of the intervention aimed to improve participants with respect to their physical activity, dietary practices, weight maintenance, tobacco cessation, minimizing alcohol consumption, and ensuring adequate sleep. Because part of the intervention involved the participants themselves in the form of peer leaders, it was not a blinded study. This made the study a real-life, more practical, and scalable intervention.

Statistical Analysis

Data analysis was performed using the Stata statistical software program, version 14 (StataCorp). For the analysis of continuous metabolic parameters, mixed-effects linear regression models were fitted for included outcomes at onset and at 2 years. Study arms (intervention versus control), time of assessment (baseline versus 2-year follow-up), and a study arm × assessment time interaction were specified as fixed effects. Random effects were specified for the clustered study design and for the study participants

Table. Effect of a lifestyle intervention in individuals with normal weight obesity at 2 years.

Parameter	Control Arm		Intervention Arm		*P*
	Baseline (n = 133)	2-Year Follow-up (n = 133)	Baseline (n = 159)	2-Year — Follow-up (n = 159)	
Fasting blood glucose, mean (SD), mg/dL	104.80 (9.15)	107.82 (17.61)	103.84 (8.80)	107.25 (12.30)	0.16
2-Hour blood glucose, mean (SD), mg/dL	103.91 (26.94)	108.55 (34.12)	104.21 (28.86)	110.44 (35.22)	0.23
HDL-C, mean (SD) [mean difference], mg/dL	51.40 (15.78)	48.03 (12.83) [−3.37]	48.53 (14.69)	45.79 (14.79) [−2.74]	0.016
Total cholesterol, mean (SD), mg/dL	226.97 (47.67)	220.70 (34.29)	226.24 (37.80)	219.52 (39.19)	0.29
LDL-C, mean (SD), mg/dL	160.45 (37.80)	151.57 (29.16)	156.86 (36.49)	150.99 (35.03)	0.083
Triglycerides, mean (SD), mg/dL	133.31 (102.20)	149.15 (97.39)	123.42 (63.86)	130.50 (66.80)	0.080
Systolic BP, mean (SD), mm Hg	125.53 (17.56)	126.76 (18.53)	126.91 (19.65)	125.45 (19.16)	0.02
Diastolic BP, mean (SD), mm Hg	75.54 (11.74)	75.09 (11.70)	77.58 (12.47)	74.44 (11.91)	0.11
HbA_{1c}, mean (SD)	5.63 (0.50)	5.60 (0.47)	5.58 (0.46)	5.59 (0.53)	0.84

BP = blood pressure; HbA_{1c} = glycosylated hemoglobin.

to account for the correlation between the repeated measurements on the same individual. The *P* value of the study arm × assessment time interaction was used to test the significant change between study groups.

RESULTS

Among the total 364 individuals with NWO in the baseline survey, 292 were randomized into the intervention (n = 159) and control (n = 133) arms. The baseline characteristics, including the mean (SD) age (intervention versus control: 47.8 [7.6] vs 47.1 [7.5]), sex distribution (intervention vs control: 97 vs 102 women), and anthropometric parameters (intervention vs control: mean [SD] BMI: 23.6 [2.43] vs 23.5 [2.1] kg/m^2; body fat percentage: 26.9% [6.02%] vs 27.9% [6.1%]) were similar in both study groups ($P > 0.05$).

At 2 years of follow-up, there was a statistically significant reduction in systolic blood pressure and a smaller decrease in the serum HDL level in the intervention arm, but no statistical difference was found in other lipid and glucose-related parameters (Table). No statistical difference was found in the mean body fat percentage in the intervention and control arms (intervention arm: baseline: 27.9% [6.02%]; follow-up: 28.3% [5.9%]; control arm: baseline: 26.9% [6.02%]; follow-up: 27.1 [5.9%]).

DISCUSSION

In this study, we examined the effect of a proficient lifestyle intervention on individuals with NWO at 2 years of follow-up. A total of 292 recruited individuals with NWO were randomized into the intervention (n = 159) and control (n = 133) arms. At 2 years of follow-up, there was minimal but statistically significant improvement in systolic blood pressure and serum HDL level in the intervention arm, but no statistical difference was found in other lipid and glycemic parameters. However, these improvements were minimal and overall may not be clinically significant.

In a study by Wiklund et al,[12] longitudinal follow-up of school children with NWO revealed increased cardiometabolic risk in early adulthood, 7 years after diagnosis. Compared with our results in relatively older individuals, we found a mild improvement in only some cardiovascular risk factors. In another large Swedish cohort of 3010 adults, NWO was associated with higher serum triglyceride levels, LDL-C levels, C-reactive protein levels, apolipoprotein B levels, higher blood pressure, and lower HDL-C levels. Among these parameters in our study, at least 2, the HDL-C level and systolic blood pressure, were improved significantly with lifestyle intervention.[13] These findings are pertinent because NWO increases the risk of developing atherosclerosis and macrovascular disease.[14] However, at this point, it is unclear whether individuals with NWO would respond better after a longer duration of lifestyle change or if they are inherently more resistant to improvement after such intervention. Another area that is yet to be explored is the effect of different drugs, such as metformin and pioglitazone (insulin sensitizers), on improving the cardiometabolic profile of this unique phenotype.

Individuals with NWO have a worse cardiometabolic profile when compared with people with normal BMI and body fat content. A study by Marques-Vidal et al[15] found a significant association between NWO and the components of the metabolic syndrome. Marques-Vidal et al[15] found that women with NWO had a higher blood pressure, serum cholesterol level, and fasting blood glucose level when compared with their low body fat counterparts. In the same study, they found that women with NWO have elevated leptin, interleukin 1a, interleukin 1b, and interleukin 8 levels. In another study, the authors analyzed 6171 individuals >20 years of age from the Third National Health and Nutrition Examination Survey (NHANES III) and the NHANES III mortality study. They selected individuals with normal BMI (18.5–24.9 kg/m^2) and those who had data that included body composition assessment, blood parameters, and a comprehensive assessment of their cardiovascular risk factors. Survival information was available for >99% of the individuals after a median follow-up of 8.8 years. They found that women with NWO had an independent association with cardiovascular mortality.[16] Moreover, the association was maintained after adjusting for known clinical risk factors, such as hypertension, dyslipidemia, and waist circumference. Although several studies have been mentioned in this article, currently no literature is available to compare the effect of a lifestyle intervention on this phenotype.

The major strength of this analysis is that these are the first data to support the effect of any therapeutic intervention in individuals with NWO. In addition, standardized measurements, a practical peer-led intervention, real-world setting, and no loss to follow-up add to the robustness of this analysis. The key limitations of this secondary data analysis are that currently only 2-year follow-up data are available. However, funding has now been provided to follow up these individuals at 5 years after the last follow-up. In addition, because only individuals with high diabetes risk were included in this study, these findings may only be applicable to a similar study population.

CONCLUSION

NWO is common in individuals of South Asian descent and is associated with a high cardiometabolic risk. This study provides early evidence of the effect of a lifestyle intervention in a cohort of individuals with NWO. This study found that at 2 years only systolic blood pressure and serum HDL level had a favorable change in the intervention arm when compared with the control arm. Additional studies are needed to determine whether individuals with NWO need more time to improve their cardiometabolic parameters or are inherently more resistant to lifestyle change.

ACKNOWLEDGMENTS

We acknowledge the Excellence in Noncommunicable Disease Research Between Australian and India (ENCORE) program for facilitating this joint publication. Nitin Kapoor conceived of the presented idea and wrote the manuscript. Mojtaba Lotfaliany and John Furler approved the main conceptual ideas and proof outline. Mojtaba Lotfaliany and Thirunavukkarasu Sathish helped with statistical analysis. Nihal Thomas, Kavumpurathu R. Thankappan, Robyn J. Tapp, John Furler, and Brian Oldenburg provided critical feedback to the final manuscript. All authors provided final edits and approved the manuscript.

FUNDING SOURCES

The KDPP was funded by the National Health and Medical Research Council, Australia (project grant 1005324). Nitin Kapoor was supported by the ENCORE (Excellence in Noncommunicable Disease Research Between Australian and India) programme for his PhD, funded by the University of Melbourne. Thirunavukkarasu Sathish was supported by the ASian Collaboration for Excellence in Non-Communicable Disease (ASCEND) program, funded by the Fogarty International Centre of the National Institutes of Health under award D43TW008332.

DISCLOSURES

The contents of this article are solely the responsibility of the authors and do not reflect the views of National Health and Medical Research Council, National Institutes of Health, University of Melbourne, or the ASCEND Program. The authors declare no conflict of interest including grants, honoraria, consultancies, speakers' bureau, advisory-board positions, significant stock holdings, or role of any study sponsors in this work.

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