Supplementation with Oligonol, Prevents Weight Gain and Improves Lipid Profile in Overweight and Obese Saudi Females

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Abstract: Background: Obesity is a global health problem, increasing susceptibility to Type 2 Diabetes (T2DM) and Cardiovascular Disease (CVD). Various of products have been proposed for treatment with varying degrees of success. Recent studies, suggested Oligonol; an optimized phenolic product mixture from Lychee Fruit Polyphenols (LFP); as such treatment in Japanese population.

Objectives: We aimed to investigate the effect of oligonol on weight, insulin resistance by (HOMA-IR), lipids profile, leptin, adiponectin, and resistin in healthy overweight and obese Saudi females.

Subjects and Methods: 60 Saudi healthy overweight and obese females were enrolled in a double blind case/control study to take either Oligonol or placebo for 12 weeks without dietary or lifestyle restrictions. Weight, height, Waist Circumference (WC), hip circumference (HC), and blood pressure were measured, and fasting blood samples of participants were taken before, and at the end of study. Total cholesterol, HDL cholesterol, triglycerides, glucose, insulin, leptin, adiponectin, and resistin were measured. LDL- cholesterol, HOMA-IR were calculated by equation.

Results: 47 subjects completed the study, 25 in placebo group, and 22 in Oligonol group. No ill effects were noted in any participant. Oligonol reduced means of serum triglycerides (P=0.008), and resistin (P=0.045) significantly. In addition, no weight gain was noted in oligonol group, unlike placebo group which exhibited significant increase in mean weight (P= 0.036), WC (P=0.027), HC (P= 0.047), and leptin (P<0.001).

Conclusion: Oligonol could be suggested as future hypolipidemic and weight controlling agent for overweight and obese Saudi females.

Keywords: Abdominal obesity, adiponectin, insulin resistance, leptin, lipid profile, oligonol, resistin.

1. INTRODUCTION

Obesity is becoming a serious health problem that is increasing globally, especially in the last four decades. Indeed, the global prevalence of obesity has doubled between 1980 and 2014 [1]. The problem is even more critical in Saudi Arabia, with 36.9%, and 35.6% of the adults aged ≥30 years reported to be overweight, and obese respectively [2]. Later in a more recent study on Saudis aged ≥15 years, 28.7% were found to be obese, with higher prevalence of obesity among female [3].

Furthermore, obesity is increasing in children, and in 2015, the WHO reported that 6% of the world’s children less than 5 years old were overweight, and at risk of obesity in adulthood. The situation in Saudi Arabia is more bleak, with a study on Saudi children aged 2-17 years old reporting that the prevalence of overweight was 21%, 13.4% and 20.1%, and that of obesity being 9.3%, 6% and 9.1% in the central, southwestern, and northern regions of the kingdom, respectively [4].

Being overweight and obesity are associated with a variety of serious medical conditions and chronic diseases including dyslipidemia, type 2 diabetes mellitus, coronary heart disease, hypertension, stroke, osteoarthritis, and cancer [5]. Furthermore, with the increase in life expectancy, obesity is causing more years of disability [6], increasing the strain on the resources of governments and individuals [7].

Therefore, efforts are made by experts in various medical fields to combat this epidemic [8-10]. Although the results of some various "lifestyle programs" are encouraging [11-14],
unfortunately, they have had limited success in dealing with rising obesity rates mainly due to difficulty in maintaining weight loss [15-17]. Furthermore, the success of dietary management and increasing physical activity depends on lifestyle and behavior modification [18, 19], which is very difficult in adults [20]. Presently the most effective method for weight loss, as well as in reducing associated morbidity and premature mortality is bariatric surgery, such as Roux-en-Y bypass or gastric banding [21, 22]. However, they are associated with various complications, some of which are serious [23, 24]. Therefore, the search for treatment is still going on, and varieties of herbal remedies have been proposed to treat obesity [25].

At present, there is growing evidence that Oligonol; an optimized phenolic product mixture from Lychee Fruit Polyphenols (LFP) containing catechintype monomers and lower oligomers of proanthocyanidin [26], can elicit some physiological and biochemical alterations in vitro and in vivo [27-29]. Moreover, it has also been demonstrated that oral administration of Oligonol improves the high fat diet-induced dysregulation of the genes for adipokines in mouse white adipose tissue [30]. Furthermore, dietary feeding of proanthocyanidins, which comprise Oligonol, has been reported to induce a significant attenuation of tissue fat levels, without changing the total body mass of the animals compared with non proanthocyanidins-fed animals [31]. In addition, recent studies proposed oligonol as a treatment for abdominal obesity in Japanese volunteers [32]. Safety profile of Oligonol is documented by numerous clinical and toxicological studies [26, 33]. Oligonol was certified as an NDI (New Dietary Ingredient) by the US FDA since 2007 and has attained self-determination GRAS (Generally Recognized as Safe) status in 2009.

As mentioned earlier, the prevalence of obesity is high amongst Saudi adults of both genders, with higher rates amongst females [3]. Use of safe natural products to control obesity might be a possible effective alternative to the use of chemically prepared drugs with deleterious side effects. Oligonol has been offered commercially as a new dietary ingredient, and has proved to be effective in other populations, but has not been tried on Saudi subjects. Therefore, we aimed to study its effectiveness in treating obesity in young overweight and obese Saudi females; without any change in lifestyle or dietary intake; by testing the null hypothesis that Oligonol has no effect on weight, abdominal obesity, insulin resistance, and lipid profile in overweight and obese young Saudi females, to investigate the possibility of using it in future management of obesity in Saudi population.

2. MATERIALS AND METHODS

2.1. Study Design and Subjects

A double-blind/case-control study design was employed. Oligonol, and placebo capsules were provided by the manufacturers (Amino up Chemical-Sapporo-Japan) marked A or B. Neither the researchers nor the participants knew which capsules contained the true supplement. However, after the end of the study, and completion of data analysis, the manufacturers identified B as the Oligonol supplement. The supplementation study lasted for 12 weeks, but; due to different starting points of volunteers; data collection was carried out from December 2015 to June 2016. Overweight and obese healthy Saudi females; aged 20 to 34 years; with Body mass index- BMI > 25 according to WHO classification, were recruited for the study from the student population, as well as from relatives and friends of researchers. Subjects were excluded if they were underweight or of normal weight (BMI ≤ 25), suffering from any illness, or taking any health supplements regularly. The study was approved by the Committee on the Ethics of Human Research at the “Faculty of Medicine- King Abdulaziz University”. All participants signed an informed consent form. Sample size was calculated to detect statistically significant changes in measured parameters, and a total of 60 young females were recruited.

At the first visit, height was measured without shoes to the closest 0.5 cm using a stationary stadiometer. Weight was measured to the closest 0.5 kg with participant dressed in light clothing using Omron Body Composition Monitor with Scale Device (Omron BF511). Body fat percentage was measured using the same scale after setting it according to each subject age and height. Weight and Height were used to calculate Body Mass Index (BMI= kg/m²). Waist Circumference (WC) was measured between the lowest rib and iliac crest; at the level of the umbilicus; to the closest 0.5 cm, while Hip Circumference measurement (HC) was taken at the maximal protrusion of the gluteal muscles to the closest 0.5 cm. The participants were then divided randomly into two equal groups (A and B) based on their BMI. They were given four weeks supply of labeled capsules and instructed to take “2 capsules daily before the major meal”, and to come back for more capsules and follow up at a specified date. Anthropometric measurements were taken at the beginning of the study, and at the end of the study. In addition, weight, WC was measured at each subsequent follow-up visit.

The daily physical activity, medical history, dietary and sleeping habits, as well as any noted physical or physiological changes or side effects were evaluated by a predesigned questionnaire at the beginning, and at the end of the study. Fasting Blood samples were taken twice; at the beginning and end of study, to measure glucose, lipids profile (total cholesterol, HDL- cholesterol and triglycerides), and the adipokines (leptin, adiponectin and resistin) insulin. All collected blood samples were kept frozen at -80 °C till time of analysis after completing the study.

2.2. Biochemical Assays

All serum biochemical parameters were assayed in the fully accredited clinical chemistry laboratory at King Abdulaziz Medical City-Jeddah. Serum glucose, cholesterol, triglycerides, and high-density lipoprotein (HDL-C) were assayed on ABBOTT, Architect c8000 auto-analyzer using spectrophotometric method. The Low-Density Lipoprotein Cholesterol (LDL-C) level was calculated using the Friedwald equation [34]. Fasting serum insulin was measured by using Chemiluminescent Microparticle Immunoassay (CMIA) on ABBOTT, Architect i1000 auto-analyzer. The obtained results from both fasting insulin and glucose were used to estimate insulin resistance by using the equation of homeostasis model assessment (HOMA-IR) [35].

The adipokines, adiponectin, leptin, and resistin were assayed in collected serum samples at the “Food, Nutrition and
Table 1. Changes in weight, BMI, and WC throughout the study period presented as Mean ± SD.

|                      | Group A (Mean ± SD) | Group B (Mean ± SD) | P-value |
|----------------------|---------------------|---------------------|---------|
|                      | 1st Visit (Baseline)  | 1st Follow up Visit | 2nd Follow up Visit | Last Visit (Endpoint) |
| Weight (kg)          | 72.66 ± 10.8        | 73.56 ± 11.15       | 73.68 ± 10.99      | 73.52 ± 10.62         | 0.009 | 81.91 ± 13.2 | 82.15 ± 13.1 | 81.72 ± 13.6 | 81.29 ± 13.5 | 0.229 |
| BMI (kg/m²)          | 29.3 ± 3.97         | 29.66 ± 4.11        | 29.72 ± 4.09       | 29.65 ± 3.88          | 0.007 | 31.63 ± 4.16 | 31.81 ± 3.97 | 31.64 ± 4.13 | 31.4 ± 4.23  | 0.225 |
| WC (cm)              | 82.3 ± 7.13         | 84.32 ± 6.6         | 84.22 ± 7.28       | 85.54 ± 6.76          | 0.000 | 91.06 ± 9.2  | 90.15 ± 7.63 | 90.88 ± 7.87 | 89.38 ± 8.3  | 0.058 |

During the supplementation period of three months, eight participants dropped out; or were excluded; from group B, and five from group A. The main causes of withdrawal as stated in writing were: lack of noticeable effect noted after the first month (4 in group B, and 1 subject in group A), and transportation difficulty (4 in group B, and 1 subject in group A). On the other hand, three subjects were excluded from group A due to pregnancy in one case, and lack of compliance in the other two. The recalculated mean age for the remaining subjects in groups A and B was 21.6 ± 4.1, and 22.8 ± 4.3 respectively, without a significant difference between them (P= 0.329).

During supplementation, there were no statistically significant differences between the two groups in lifestyle habits at the start of the study (P= 0.442 for sleep duration, 0.613 for usual sleeping time, 0.649 for time spent sitting down, 0.282 for physical activity, and 0.659 for smoking), and no changes were reported during the study. At the end of the study, there were no statistically significant differences between the two groups with respect to reported changes in appetite (P=0.495), gastrointestinal habits (P=0.595), or skin (P=0.797).

Results of effect of supplementation on measured anthropometric parameters in Table 1 and Fig. (1). Due to drop out during the study, the recalculated mean BMI of the remaining participants was significantly higher in group B at the start of the study (P= 0.007). However, this difference disappeared following supplementation at the end of the study (P= 0.17), due to the significant increase in mean weight in group A at the end of the study (P= 0.009). Similar pattern was noted for means of BMI, and WC which showed significant increase following supplementation in group A (P=0.007, and 0.000 respectively), but not in group B, which showed a slight insignificant decrease (P=0.225, and 0.058 respectively), resulting in disappearance of significant differences between the corresponding means of the two groups at the end of the study (P= 0.065, 0.202 respectively).

Mean hip circumference was significantly higher in group B compared to group A at the start (P= 0.001), but not at the end of the study, and the mean of group A increased significantly at the end compared to starting mean (P= 0.047). Similarly mean percentage fat was significantly
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Results of effect of supplementation on measured biochemical and endocrine parameters are presented in Table 2. The most important changes in measured biochemical parameters noted after supplementation were the significantly decreased mean of serum triglycerides in group B, compared to a significant increase in group A, resulting in disappearance of significant difference between the means of the two groups at the end of the study. In addition, at the end of the study a significant increase was noted in the mean of leptin in group A, compared to a significant decrease in the mean of resistin in group B (Table 2).

Table 2. Biochemical and endocrine parameters in the placebo group (Group A), and the oligonol group (Group B) before and after supplement, presented as mean ±SD.

| Variable                  | Group A (N= 25) | Group B (N= 22) | P-value A/B PRE | P-value A/B POST |
|---------------------------|-----------------|-----------------|-----------------|-----------------|
| Total Cholesterol (mmol/L)| 4.35±0.62       | 4.48±0.72       | 0.227           | 0.142           |
| HDL-C (mmol/L)            | 1.27±0.19       | 1.33±0.26       | 0.157           | 0.030           |
| LDL-C (mmol/L)            | 2.73±0.55       | 2.76±0.60       | 0.803           | 0.685           |
| Triglycerides (mmol/L)    | 0.74±0.18       | 0.88±0.3        | 0.011           | 0.008           |
| FBG (mmol/L)              | 4.80±0.37       | 4.86±0.35       | 0.390           | 0.055           |
| Insulin (µU/mL)           | 9.7±4.8         | 8.3±3.4         | 0.225           | 0.862           |
| HOMA-IR                   | 2.1±1.2         | 2.0±0.9         | 0.453           | 0.822           |
| Leptin (ng/mL)            | 34.0±12.1       | 43.1±13.5       | <0.001          | 0.067           |
| Adiponectin (ng/mL)       | 10457±2990      | 10817±3890      | 0.436           | 0.218           |
| Resistin (ng/mL)          | 6.40±2.26       | 6.31±1.52       | 0.535           | 0.045           |

4. DISCUSSION

The increasing prevalence in overweight and obesity in Saudi Arabia [2] and the expected deleterious effects on health, and productivity [4, 36] warrants serious investigations to find suitable and practical ways to combat this epidemic. Lifestyle modifications can be successful, but is difficult to adhere to, requiring professional support and guidance [9, 10], which is not widely available in Saudi Arabia, and when available is quite costly. In this double blind, case/control study we investigated the effect of supplementing the usual diet of overweight, and obese young and healthy Saudi females with Oligonol on their weight, BMI, WC, HC, and percentage fat, as well as serum lipid profile, lower in group B compared to A at the beginning (P=0.023), but not at the end of the study (P=0.157) (Fig. 1).

Results of effect of supplementation on measured biochemical and endocrine parameters are presented in Table 2.
and various biochemical, and endocrine parameters reflecting adiposity and insulin resistance, without attempting to change their dietary or lifestyle practices. The recruited volunteers were divided into two equal and similar groups with respect to their BMI. However, due to dropout during the study for reasons other than feeling of adverse effects as stated in the results section, the recalculated means of BMI, and all measured anthropometrics of the remaining group taking oligonol were significantly higher at the start of the study. Even though oligonol supplement was not able to decrease weight, or any of the anthropometric measurements, it was successful in preventing further weight gain, and the accompanied increase in WC, HC and BMI, in contrast to the significantly increased means in the group taking placebo. As a result, the difference in means between the two groups disappeared at the end of the study.

This is in partial agreement with the only study in literature investigating the effect of Oligonol supplement on weight, and visceral fat obesity in healthy Japanese subjects with Abdominal Circumferences (AC) over 85 cm [32], which reported that body weight, abdominal circumference and visceral fat volume were all significantly decreased in the Oligonol group by the end of the study, while no significant changes in the means were found in the control group. In a similar manner to our study, the same Japanese study investigated the effects of supplement on lipid profile, insulin resistance, and the levels of adipokines: leptin, adiponectin and resistin. Our results differed from their findings with respect to effects on serum lipid profile. We found that Oligonol supplement caused a significant decrease in the mean of triglycerides, in contrast to no effect reported by Nishihira et al. The duration of the study could be the cause for difference in results. Our study lasted for 12 weeks; allowing adequate time for changes in lipid profile to become apparent; unlike the 10 weeks period taken by the Japanese study.

Furthermore, we did not find a significant effect on HOMA-IR unlike to the improvement reported by Nishihira et al. Instead, we found a significant increase in mean leptin by the end of the study in the placebo group, and a significant decrease in the mean resistin in the oligonol group, compared to the no change reported in the Japanese study.

Leptin is an adipokine secreted by the adipocytes, and was originally thought to signal to the brain to inhibit food intake and decrease weight [37, 38]. However, older and more recent studies on different populations found that obesity was associated with high leptin levels [39-42]. Indeed leptin levels were reported to correlate positively with BMI and the percentage of body fat [39, 42]. Hence, the noted increase in mean leptin found in the placebo group at the end of the study is as expected due to their increased mean weight.

The difference in our results from that of Nishihira et al. could be due to the difference in genders of the studied population. In our study, the subjects were all females, while there were 4 females and 14 males in the Japanese study. Earlier studies reported difference in leptin levels between males and females [43, 44]. Hence, changes in levels could have been undetectable at a statistically significant level in the Japanese study. The duration of the study could be another cause for difference in results. Similar explanation could be given for differences in our resistin results to that reported by Nishihira et al. Resistin levels were reported to be higher in females [45], and their correlation with cardiometabolic risk indicators were also reported to be mainly in women [46-48], hence differences were detected in our study, but not in the Japanese study carried on mixed population, with a predominance of males. Moreover, resistin was reported to be highly correlated with serum triglycerides [47], which is noted in our decreased mean triglycerides parallel to the decreased resistin mean following supplement in the Oligonol group.

Our results also differed to that by Nishihira et al. with respect to effects on adiponectin level. They reported that Oligonol up regulated the expression of this adipokine, while we found no change after the supplement. Genetic differences between our populations could explain this, since Nishihira et al. also reported that effect of oligonol on the expression of adiponectin is genetically determined.

Our study has limitations, which could not be avoided. First of all; and due to withdrawal from the study; the two groups became dissimilar at the start of the study, with the group taking Oligonol having higher mean BMI. The main reason for withdrawal was overexpectations of participants, who were eager to lose weight quickly, expecting a loss of 3-4 kg/month, and losing interest in continuing the study when this was not found during their first follow up visit. To overcome this we compared before, and after means within the same group by paired t-test, then compared respective means between the two groups using unpaired t-tests. The second limitation was the inability to completely randomize the subjects with respect to all characteristics, including their biochemical profile. This was because all biochemical measurements were conducted at the end of the study in one batch to avoid day to day variations in measurements. However, since the aim of the study was to investigate the effectiveness of “Oligonol” in treating obesity in young overweight and obese Saudi females, it was considered more important, and appropriate to divide the participants randomly according to their BMI. Furthermore, finding the difference in the mean of triglycerides was an unexpected results since it was not reported in the earlier Japanese study, and possible reasons for the different findings were discussed fully. The third limitation was our inability to follow dietary intake accurately. The subjects were free living; hence, we had to depend on their judgment concerning changes in dietary intake and appetite. However, the ones completing the study were mainly from the student population in health sciences, hence were aware of the importance of accuracy in reporting.

CONCLUSION

In conclusion, our study indicated that Oligonol supplement can be useful in controlling weight gain, and decreasing serum triglycerides in free living Saudi overweight and obese females, without any change in dietary or lifestyle practices. Thus, Oligonol has potential in combating the obesity epidemic in Saudi Arabia. Dietary restriction and/or increased physical activity in addition to Oligonol might lead to more weight loss than is achieved without the supplement. Future studies should focus on this latter point, along with characteristics of best responders.
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ETHICAL APPROVAL

All studies were approved by the Committee on the Ethics of Human Research at the “Faculty of Medicine-King Abdulaziz University”.

HUMAN AND ANIMAL RIGHTS

No animals were used in this study. All research procedures followed on human were in accordance with the ethical standards of the committee responsible for human experimentation (institutional and national), and with the Helsinki Declaration of 1975, as revised in 2008 (http://www.wma.net/en/20activities/10ethics/10helsinki/)

CONSENT FOR PUBLICATION

Informed consent use taken from patient to participate in the study.

CONFLICT OF INTEREST

The authors confirm that there is no conflict of interest.

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