

# RESPOSTAS HORMONAIS DE MULHERES INSERIDAS EM PROGRAMA PARA PERDA DE PESO DE 12 SEMANAS BASEADO EM TREINAMENTO FÍSICO REGULAR E DIETA COM BAIXO TEOR DE CARBOIDRATOS Hormonal responses of women insert in a 12 week weight loss program based on regular physical training and a low carbohydrate diet

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# RESUMO

**Objetivo:** O presente estudo teve como objetivo analisar o efeito da perda de peso baseado na redução de carboidratos na dieta, sobre respostas hormonais após seguimento dietético e prática regular de treinamento intermitente em doze semanas. **Resultados**: Ambos os grupos apresentaram semelhanças na redução de peso e melhoria na composição corporal após as 12 semanas de realização do programa com treinamento físico e dietas hipocaloricas, independente do tipo de dieta. Porém os marcadores de T4, T4 livre e testosterona apenas demonstraram diminuição ao longo do tempo para o grupo R-CHO. **Conclusão:** A redução de peso atraves de dietas hipocaloricas em combimnação com exercicio físico resulta em alterações favoraveis para insulina e controle do catabolismo . Por outro lado a dieta restrita em carboidratos promoveu alterações indesejáveis na homeostase de hormônios tireoidianos e anabólicos.

Palavras-Chave: Obesidade; Redução de peso; Carboidratos; Dieta; Hormônios; Treinamento.

# ABSTRACT

**Aim:** The present study aimed to analyze the effect of a 12-week low-carbohydrate diet and regular intermittent training on weight loss and hormone levels. **Results:** Participants of both groups exhibited weight loss and improvements in body composition with training and hypocaloric diets, regardless of the diet's CHO content. However, reduced levels of the hormones T4, free T4, and testosterone were found in the L-CHO but not the A-CHO group. **Conclusion:** Weight loss through hypocaloric diets in combination with training resulted in hormonal changes favorable to insulin and catabolic control. The low-carbohydrate diet, in contrast, resulted in undesirable changes in the homeostasis of thyroid and anabolic hormones.

Keywords: Obesity, Weight Loss, Diet; Carbohydrate, Hormones, Training

#### **1. INTRODUCTION**

Lifestyle changes, such as increased physical activity and better eating habits, are essential for the prevention and treatment of excessive weight gain of the population (Kaila & Raman, 2008; Poobalan, Aucott, Precious, Crombie, & Smith, 2010; Makris & Foster, 2011; Machado, Silveira, & Silveira, 2012). Recently, altering the nutrient content in weight loss diet plans has been receiving increased attention (Sacks et al., 2009; Abete, Astrup, Martinez, Thorsdottir & Zulet, 2010) in this context, low-carbohydrate (L-CHO) diets have been widely adopted as a strategy to promote weight loss (Foster et al., 2010; Kirk, Penney, McHugh & Sharma, 2012; Gu et al., 2013). In a metaanalysis, Hu *et al.* (2011) analyzed studies that included diets with CHO levels ranging from 4% to 40% of the total energy intake (TEI) and those using a CHO intake restricted to 20g/day; they found that these diets were associated with improvements in the lipid and insulin profiles of the participants. These findings are similar to those of other studies that proposed weight loss based on caloric restriction; these studies reported reduce in the metabolic stress and increase in the levels of appetite-regulating hormones, thyroid hormones, and sex hormones (Sumithran et al., 2011; Van Gemert et al., 2013; Agnihothri et al., 2014).

However, when CHO restriction is too severe (<20g/day or <4% of the TEI), a lowered enthusiasm for physical activity, decreased lean mass, subsequent weight gain, and lower adherence to dietary follow-up have been reported (Gremeaux et al., 2012; Hovanloo, Arefirad, & Ahmadizad, 2013)

Regular high-intensity intermittent training (HIIT) can also contribute to weight loss and favorably affect the resting metabolic rate and anabolic hormonal responses in individuals participating in weight reduction programs (Thomson et al., 2012; Mancilla et al., 2014; Peake et al., 2014; Marquis Gravel et al., 2015).

Therefore, it is important to clarify the effect of L-CHO diets in combination with regular HIIT training on hormone levels, taking the metabolic consequences resulting from this type of intervention into account. In the present study, we analyzed the effects of dietary CHO reduction associated with HIIT on weight loss and hormonal responses.

## 2. METHODS

## **Population**

The present study was a randomized controlled clinical trial designed to assess changes in weight, body composition, and hormone levels of women participating in a 12-week weight loss program. Women aged 18–59 years with a body mass index (BMI) between 25 kg/m<sup>2</sup> and 34.9 kg/m<sup>2</sup>who were linked to an academic institution and who were defined as being sedentary or

having a low activity level based on their International Physical Activity Questionnaire (IPAQ) scores were included in this study. Participants who self-reported the continuous use of anorectic drugs or undergoing hormone therapy and those who were under medical/nutritional monitoring for weight loss were ineligible.

The study followed the recommendations of the Declaration of Helsinki and was approved by the research ethics committee of the university at which the study was conducted. We obtained registration in the Brazilian Clinical Trials Registry, n. RBR-5n9g5f.

## Study design

All participants followed a weight loss program that involved semi-supervised HIIT sessions three times/week and a monthly nutrition consultation. Study participants were randomly allocated into two groups. The first group received a dietary plan containing reduced CHO levels (L-CHO group), while the dietary plan given to the second group included adequate CHO levels (A-CHO group) (Figure 1). Both diets were low-calorie diets.

During the monthly individualized nutrition consultation, dietary (24-hour dietary recall) and anthropometric (body weight and abdominal circumference) assessments were performed. The subjects answered a questionnaire asking questions on their adherence to the diet and a 24-hour dietary recall. The participants were also asked to complete at least three food records/month.

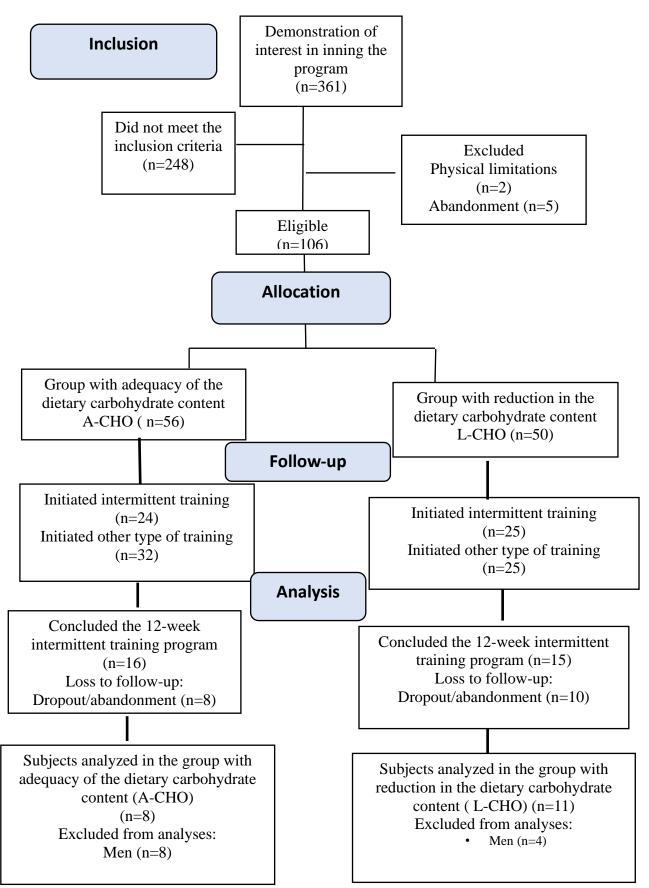


Figure 1. Flowchart of the experimental design.

## Weight loss program

The calorie restriction protocol of the diets was based on the target of a reduction of 5% to 10% of the study participants' body weight within 12 weeks. After analyzing the Estimated Energy Requirement (EER) of the individuals (IOM, 2005), the calorie restriction required for each participant was individually calculated based on a 500-kcal deficit for individuals classified as overweight (BMI 25–29.99 kg/m<sup>2</sup>), and a 1,000-kcal deficit for those classified as obese (BMI>30.0 kg/m<sup>2</sup>). Two types of hypocaloric diets that differed by their CHO content were administered. The diet adopted by the L-CHO group contained a CHO restriction that allowed a daily intake of around 100 g/day, which represents the minimum content of this nutrient according to the Dietary Reference Intake (DRI) (IOM, 2005). In contrast, individuals in the A-CHO group were given a diet with a CHO content of around 250 g/day.

HIIT was performed 3 times/week in sessions lasting approximately 60 minutes. Two of the three sessions were supervised by coach and guidance was offered on the third day of training that was otherwise performed by the participants without direct supervision. Each training session was conducted in three stages. The first stage was a standardized dynamic warm-up routine. The second stage included neuromuscular stimuli and was subdivided into neuromuscular sessions I and II. The neuromuscular I session was characterized by pushing, pulling, and, squatting exercises in a circuit training routine that was designed for achieving greater power, speed, agility, and coordination. The neuromuscular II session comprised strength exercises. For the neuromuscular sessions, five-minute circuits comprising five different exercises lasting one minute each were performed twice. The rest intervals between the exercises decreased along the 12-week duration of the program, with increased training intensity. The third stage included cardiorespiratory exercises using cognitive stimuli and lasted for five minutes.

## Body composition and hormone markers

During the initial evaluation and at the end of the 12-week period, the participants' weight was measured with a 100g-capacity precision digital scale (LIDER®, P150C, Ribeirão Preto, São Paulo, Brazil). Waist and hip circumferences were evaluated with a non-elastic tape measure (SANNY<sup>®</sup>, American Medical do Brazil Ltda., São Bernardo do Campo, São Paulo, Brazil), and body composition was measured through electrical bioimpedance (Biodynamics®, 310, Corporation, EUA 310).

The participants underwent blood tests both, pre- and post-intervention. A 12-mL aliquot of blood was extracted by venipuncture of an antecubital vein after a 12-hour fast. Hormone analyses

of insulin, cortisol, T3, T4, thyroid-stimulating hormone (TSH), and testosterone were performed using the Immunoassay Analyzer (Abbott Architect i1000SR Analyzer, USA).

## **Statistical analysis**

Descriptive statistics, Delta Variation, and standard errors were used for data comparison between groups and as a function of time. The Shapiro-Wilk test was performed to determine the normality of the data. Two-way analysis of variance (ANOVA) and when F-ratio was significant, Bonferroni's post hoc test was applied to identify the differences between the groups (G: L- CHO *vs* A-CHO), time (T: Pre - *vs* Post intervention), and time *vs* group interaction (G x T).

Data were analyzed with the statistical software Statistical Package for the Social Sciences SPSS, version 20 for Windows, Chicago, USA. For all statistical analyses, p<0.01 was considered significant. The effect size (ES) was calculated by the post-intervention mean minus the pre-intervention mean, divided by the mean pre- and post-intervention standard deviations. To classify the magnitude of the differences, the clinical effect was considered small when the ES ranged from 0.20 to 0.49, medium when the ES ranged from 0.50 to 0.79, and large when the ES was >0.80 (Cohen, 1988).

## **3. RESULTS**

A total of 19 adult women with overweight and obesity (11 and 8 in the L-CHO and A-CHO groups, respectively) were included in the study. Both group shad similar characteristics (L-CHO *vs.* A-CHO: age, $32 \pm 7.7$  years *vs.*28.5  $\pm$  9.3 years; body weight, 79.4  $\pm$  9.1 kg *vs.*76.7  $\pm$  10.5 kg; and BMI, 30.4  $\pm$  2.3*vs.* 28.8 $\pm$  2.3 kg/m<sup>2</sup>).

Moreover, both groups showed significant reductions in anthropometric measures and body composition after the 12-week intervention; no differences were seen between the two groups (Table 1). A large clinical effect was observed for most variables except lean mass and Estimated Energy Requirement (EER), which showed small effects.

Table 2 depicts the variations in hormone levels after 12 weeks of HIIT and dietary follow-up. We found a significant reduction in plasma T3, insulin, and cortisol levels in both groups; these changes were classified as large clinical effects (ES>0.8).

The plasma levels of T4, free T4, and testosterone showed significant reductions over time in the L-CHO but not the A-CHO group; however, these effects were not significant in the  $G \times T$  interaction analysis (p>0.05).TSH levels did not show any changes in the G, T, and G×T analyses.

Table 1. Variations in anthropometric measures and body composition in overweight and obese women according to

#### dietary plan

	Variation, mean (SE)			ANOVA	
	L-CHO	A-CHO	ANOVA	F	р
	(n = 11)	( <b>n</b> = 8)	effect		
Weight (kg)	<b>50.05 (0.00</b> )		G	50.41	0.001
Pre-intervention Post-intervention	79.35 (2.92)	76.67 (3.42)	G T	50.41	<0.001
	73.35 (2.78)* -6.04 (-7.51)	71.73 (3.26)* -4.94 (-6.42)	$G \times T$	0.25 0.142	0.621 0.712
$\Delta (\Delta\%)$ ES	-0.54	-4.94 (-0.42) -0.66	0 × 1	0.142	0.712
BMI (kg/m <sup>2</sup> )	-0.54	-0.00			
Pre-intervention	30.38 (0.70)	28.80 (0.82)	G	1.644	0.214
Post-intervention	28.07 (0.69)*	26.97 (0.81)*	T	56.30	<0.001
$\Delta$ ( $\Delta$ %)	-2.32 (-7.51)	-1.83 (-6.42)	$\mathbf{G}  imes \mathbf{T}$	1.037	0.323
ËS	-0.94	-0.73			
Abdominal					
circumference					
(cm)	07.02(1.00)	07.25 (2.20)	C	0.004	0.051
Pre-intervention Post-intervention	97.03 (1.96) 90.16 (2.10)*	97.35 (2.30) 89.47 (2.47)*	G T	0.004 90.12	0.951 <0.001
$\Delta (\Delta\%)$	-6.87 (-7.13)	-7.87 (-8.04)	$G \times T$	0.12	0.835
ES	-0.95	-1.0	0 ~ 1	0.45	0.055
Fat (%)	0.95	1.0			
Pre-intervention	36.97 (0.95)	34.31 (1.11)	G	1.99	0.172
Post-intervention	33.03 (0.87)*	31.83 (1.02)*	Т	87.75	<0.001
$\Delta$ ( $\Delta$ %)	-3.94 (-10.57)	-2.47 (-7.18)	$\mathbf{G} \times \mathbf{T}$	0.796	0.385
ES	-0.9	-1.02	01	01770	01000
Fat (kg)					
Pre-intervention	29.46 (1.56)	26.55 (1.83)	G	0.90	0.356
Post-intervention	24.34 (1.38) <sup>*</sup>	$23.05(1.62)^*$	T	69.57	<0.001
$\Delta$ ( $\Delta$ %)	-5.12 (-17.21)	-3.5 (-13.04)	$G \times T$	0.369	0.552
ES	-0.78	-0.91	U × I	0.507	0.552
Lo Lean mass (kg)	0.70	0.71			
(g)					
Pre-intervention	50.78 (1.66)	49.01 (1.89)	G	0.67	0.423
Post-intervention	49.37 (1.55)*	47.15 (1.76)*	Т	35.45	<0.001
$\Delta$ ( $\Delta$ %)	-1.41 (-2.75)	-1.86 (-3.71)	$\mathbf{G}  imes \mathbf{T}$	0.888	0.365
ES	0.31	-0.39			
EER (kcal)					
Pre-intervention	1544.77 (50.7)	1490.14 (57.5)	G	0.67	0.422
Post-intervention	1501.00 (47.4)*	1434.0(53.8)*	Т	37.68	<0.001
$\Delta$ ( $\Delta$ %)	-28.36(-1.76)	-43.62 (-2.91)	$\mathbf{G}\times\mathbf{T}$	0.869	0.362
ES	0.31	-0.39			

\* Intragroup difference over time (pre-  $\times$  post-intervention)A-CHO, adequate carbohydrate diet; ANOVA, analysis of variance; BMI, body mass index; EER, Estimated Energy Requirement, G, group; G  $\times$  T, group  $\times$  time interaction; ES, effect size; L-CHO, low-carbohydrate diet; SE, standard error; T, time

Variables	Variation 1	nean (SE)	ANOVA		
	L-CHO	A-CHO	ANOV	F	р
	( <b>n</b> = 11)	( <b>n</b> = <b>8</b> )	A effect		
Т3					
Pre-intervention	1.25 (0.086)	1.30 (0.10)	G	0.551	0.468
Post-intervention	0.95 (0.07)*	1.08 (0.08)*	T	48.38	< 0.00
$\Delta$ ( $\Delta$ %)	-0.30 (-22.3)	-0.23 (-17.7)	$\mathbf{G}\times\mathbf{T}$	1.215	0.286
ES	-0.75	-1.08			
<b>T4</b>					
Pre-intervention	6.81 (0.66)	7.09 (0.70)	G	0.29	0.596
Post-intervention	6.16 (0.65)*	6.91 (0.69)	Т	5.45	< 0.05
$\Delta$ ( $\Delta$ %)	-1.4 (-14.19)	-0.19 (-2.95)	$\mathbf{G}  imes \mathbf{T}$	0.61	0.444
ES	-0.12	-0.37			
Free T4					
Pre-intervention	1.01 (0.04)	0.96 (0.04)	G	0.03	0.862
Post-intervention	0.92 (0.03)*	0.96 (0.03)	Т	4.72	<0.05
$\Delta$ ( $\Delta$ %)	-0.08 (-7.79)	-0.005 (-0.3)	$\mathbf{G}  imes \mathbf{T}$	0.46	0.501
ES	-0.37	-0.52			
TSH					
Pre-intervention	2.24 (0.40)	1.63 (0.46)	G	0.13	0.722
Post-intervention	1.62 (0.29)	1.88 (0.34)	Т	0.54	0.475
$\Delta$ ( $\Delta$ %)	-0.62 (-11.3)	0.25 (9.3)	$\mathbf{G}  imes \mathbf{T}$	0.33	0.574
ES	-0.19	-0.27			
Insulin					
Pre-intervention	8.23 (0.84)	9.21 (1.03)	G	0.085	0.772
Post-intervention	6.35 (0.74)	5.96 (0.91)*	Т	11.49	< 0.00
$\Delta$ ( $\Delta$ %)	-3.91 (-27.9)	-5.57 (-32.9)	$G \times T$	0.10	0.743
ES	-0.87	-0.97			-
Cortisol					
Pre-intervention	12.53 (1.20)	10.32 (1.61)	G	1.34	0.272
Post-intervention	9.15 (0.94)*	7.54 (1.26)*	Т	17.58	<0.00
$\Delta$ ( $\Delta$ %)	-5.3 (-31.17)	-4.65 (-25.7)	$\mathbf{G}  imes \mathbf{T}$	1.04	0.322
ES	-0.92	-0.93			
Testosterone					
Pre-intervention	0.48 (0.06)	0.37 (0.06)	G	0.61	0.445
Post-intervention	0.41 (0.05)*	0.38 (0.06)	Т	2.68	0.124
$\Delta$ ( $\Delta$ %)	-0.06 (-12.48)	0.01 (3.36)	$G \times T$	0.12	0.733
ES	-0.04	-0.29		•·- <b>=</b>	000

Table 2. Variation in hormone levels in overweight and obese women according to the type of diet.

\* Intragroup difference over time (pre-  $\times$  post-intervention)

A-CHO, adequate carbohydrate diet; ANOVA, analysis of variance, G, group;  $G \times T$ , group  $\times$  time interaction; ES, effect size; L-CHO, low-carbohydrate diet; SE, standard error; T, time; TSH, thyroid-stimulating hormone

## 4. DISCUSSION

The results of this study showed that participants of both groups exhibited weight loss and improvements in body composition with HIIT and hypocaloric diets, regardless of the diet's CHO content. However, reduced levels of the hormones T4, free T4, and testosterone were found in the L-CHO but not the A-CHO group.

Agnihothri et al. (2014) observed that moderate weight reduction was sufficient to affect the homeostasis of thyroid hormones. Similarly, in the present study, overweight and obese individuals who underwent individualized diets planned to create a deficit of 500–1000 kcal/day with the goal of achieving a 5–10% weight loss, exhibited decreased T3 levels. On the other hand, only the L-CHO group showed decreased T4 and free T4 levels after the 12-week intervention. Hashimoto et al. (2016) reported a negative correlation between free T4 levels and weight reduction in 29 obese female premenopausal patients; higher free T4 levels were associated with successful weight loss after a six-month intervention. Therefore, a decrease in free T4 might reflect a reduction in the basal metabolic rate, which in the long run might impair the weight loss process (Kim, 2008; Traish, 2014; Cunningham, 2015; Sanyal, & Raychaudhuri, 2016;) and might result in subsequent weight gain.

The total weight and fat mass loss seen in both groups in this study might have caused the reduction in cortisol and insulin levels (Toscani, Mario, Radavelli-Bagatini & Spritze, 2011). However, dietary CHO reduction was sufficient to compromise testosterone homeostasis, despite that other studies relate the benefits of HIIT routine in anabolic profile (Hainer et al., 2008; Araújo, 2008; Tibana et al., 2014). The main strengths of this study include: 1) the use of a CHO reduction diet that complied with the minimum limits proposed by standard nutritional guidelines, 2) individualized dietary planning, and 3) follow-up performed by health professionals to improve program adherence. However, this study also has a limitation, where we could not include an experimental group with very low CHO (<20g/d) diet in this study. This would have required greater monitoring of patients which was not possible in our study design.

#### 5. CONCLUSION

This study suggests that weight loss through hypocaloric diets in combination with HIIT promotes hormonal changes favorable to insulin and catabolic control. CHO reduction resulted in undesirable changes in the homeostasis of thyroid and anabolic hormones. The diet and exercise strategies adopted in this study are easily reproducible and low-cost. This facilitates the development of weight loss programs, for example in primary healthcare settings.

## 6. REFERENCES

Abete, I., Astrup, A., Martinez, J.A., Thorsdottir, I. & Zulet, M.A. (2010). Obesity and the metabolic syndrome: role of different dietary macronutrient distribution patterns and specific nutritional components on weight loss and maintenance. *Nutrition Reviews*, 68 (1): 214–231.

Agnihothri, R.V., Courville, A.B., Linderman, J.D., Smith, S., Brychta R., Remaley A., Chen K.Y., Simchowitz, L. & Celi F.S. (2014). Moderate weight loss is sufficient to affect thyroid hormone homeostasis and inhibit its peripheral conversion. *Thyroid*, 24(1):19-26.

Araújo, M.R. (2008). A influência do treinamento de força e do treinamento aeróbio sobre as concentrações hormonais de testosterona e cortisol. *Motri*. 4(2): 67-75.

Cohen, J. (1988). *Statistical power analysis for the behavioral sciences*. (pp.8-14). EUA:Ed. Lawrence Erlbaum Associate.

Cunningham G.R. Testosterone and metabolic syndrome. (2015). Asian J Androl. 17(2):192-6.

Foster, G.D., Holly, R.W., Hill, J.O., Makris, A.P., Rosenbaum, D.L., Brill, C., Stein, R.I., Mohammed, B.S., Miller, B. & Rader, D.J. (2010). Weight and Metabolic Outcomes After 2 Years on a Low-Carbohydrate Versus Low-Fat Diet: A Randomized Trial. *Ann Inter Med.*, 153(3): 147-57 Ghoch, M.E., Calugi, S. & Grave, R.D. (2016). The Effects of Low-Carbohydrate Diets on Psychosocial Outcomes in Obesity/Overweight: A Systematic Review of Randomized Controlled Studies. *Nutrients*, 8(1): 402-41

Gremeaux, V., Drigny, J., Nigam, A., Juneau M, Guilbeault V., Latour E. & Gayda M. (2012) Long-term lifestyle intervention with optimized high-intensity interval training improves body composition, cardiometabolic risk, and exercise parameters in patients with abdominal obesity. *Am J Phys Med Rehabil*, 91(11):941-50.

Gu. Y., Yu. H., Li, Y., Ma, X., Lu, J., Yu, W., Xiao, Y., Bao, Y. & Jia, W. (2013). Beneficial effects of an 8-week, very low carbohydrate diet intervention on obese subjects. *Evid Based Complement Alternat Med*, 1(1): 1-8.

Hainer, V., Hlavatá, K., Gojová, M., Kunešová, M., Wagenknecht, M., Kopský, V., Pařízková, J., Hill, M. & Nedvídková, J. (2008). Hormonal and Psychobehavioral Predictors of Weight Loss in Response to a Short-Term Weight Reduction Program in Obese Women. *Physiol. Res.* 57(1): 17-27. Hashimoto, K., Tagami, T., Yamakage, H., Muranaka, K., Tanaka, M., Odori, S., Kono, S., Shimatsu, A., Ogawa, Y. & Satoh-Asahara, N. (2016). Serum free thyroxine levels are associated with the efficacy of weight reduction therapy in obese female patients. *Endocrine Journal.* 63 (3): 221-229 Hovanloo, F., Arefirad, T. & Ahmadizad, S. (2013) .Effects of sprint interval and continuous endurance training on serum levels of inflammatory biomarkers. *J Diabetes Metab Disord*, 12 (22):1-5.

Hu, T., Mills, K.T., Yao, L., Demanelis, K., Eloustaz, M., Yancy Jr, W.S., Kelly, T.N., He, J. & Bazzano, L.A. (2012). Effects of Low-Carbohydrate Diets Versus Low-Fat Diets on Metabolic Risk Factors: A Meta-Analysis of Randomized Controlled Clinical Trials. *Am J Epidemiol*.176 (7): 44-54.

Institute of medicine (IOM) (2005). *Dietary Reference Intakes for energy, carbohydrate, fiber, fat, fatty acids, cholesterol, protein and amino acids (macronutrients)*. Washington (DC): National Academy Press.

Kaila, B. & Raman, M. (2008). Obesity: A review of pathogenesis and management strategies. *Can J Gastroenterol*, 22(1): 61-68.

Kim, B. (2008). Thyroid hormone as a determinant of energy expenditure and the basal metabolic rate. *Thyroid*, 18(1): 141-144

Kirk, S.F., Penney, T.L., McHugh, T.L. & Sharma, A.M. (2012). Effective weight management practice: a review of the lifestyle intervention evidence. *Int J Obes*. 36(2): 178-85

Machado, E.C., Silveira, M.F. & Silveira, V.M. (2012). Prevalence of weight-loss strategies and use of substances for weight-loss among adults: a population study. *Cad Saúde Pública*. 28 (8):1439-49. Makris, A. & Foster, G.D. (2011). Dietary approaches to the treatment of obesity. *Psychiatr Clin North Am.*, 34(4):813-27.

Mancilla, R., Torres, P., Álvarez, C., Schifferli, I., Sapunar, J. & Díaz, E. (2014). Ejercicio físico interválico de alta intensidad mejora el control glicémico y la capacidad aeróbica en pacientes con intolerancia a la glucosa. *Rev. Méd. Chile*, 142(1):34-39.

Mansoor, N., Vinknes, K.J., Veierød, M.B. & Retterstøl, K. (2016). Effects of low-carbohydrate diets vs. low-fat diets on body weight and cardiovascular risk factors: a meta-analysis of randomised controlled trials. *Br J Nutr*. 115(1): 466–479.

Marquis-Gravel, G., Hayami, D., Juneau, M., Nigam, A., Guilbeault, V., Latour, E. & Gayda, M. (2015). Intensive lifestyle intervention including high-intensity interval training program improves insulin resistance and fasting plasma glucose in obese patients. *Prev Med Reports*. 2(1):314–318

Peake, J.M., Tan, S.J., Markworth, J.F., Broadbent, J.A., Skinner, T.L. & Cameron-Smith, D. (2014). Moderate-intensity exercise high-intensity interval exercise and continuous: Metabolic and hormonal responses to isoenergetic. *Am. J. Physiol. Endocrinol. Metab*, 307(1):539-552.

Poobalan, A.S., Aucott, L.S, Precious, E., Crombie, I.K. & Smith, W.C. (2010). Weight loss interventions in young people (18 to 25 year olds): a systematic review. *Obes Rev.*11 (8): 580-92.

Sacks, F.M., Bray, G.A, Carey, J.C, Smith, S.R., Ryan, D.H., Anton, S.D., McManus, K., Champagne, C.M., Bishop, L.M. & Laranjo, N. (2009). Comparison of Weight-Loss Diets with Different Compositions of Fat, Protein, and Carbohydrates. *N Engl J Med*, 360 (9):859-873.

Sanyal, D. & Raychaudhuri. M. (2016). Hipothyroidism and obesity: An intriguing link. *Indian J Endocr Metab.* 20(1):554-557.

Sumithran, P., Prendergast, L.A., Delbridge, E., Purcell, K., Shulkes, A., Kriketos, A. & Proietto, J. (2011). Long-Term Persistence of Hormonal Adaptations to Weight Loss. *N Engl J Med.* 365(1): 1597-1604.

Thomson, R.L., Brinkworth, G.D., Noakes, M., Clifton, P.M., Norman, R.J. & Buckley, J.D. (2012). The effect of diet and exercise on markers of endothelial function in overweight and obese women with polycystic ovary syndrome. *Hum Reprod*. 27(7):2169-76.

Tibana, R.A., Nascimento, D.C., Sousa, N.M., Souza, V.C., Durigan, J., Vieira, A., Bottaro, M., Nóbrega, E.T., Almeida, J.A. & Navalta, J.W. (2014). Enhancing of women functional status with metabolic syndrome by cardioprotective and anti-inflammatory effects of combined aerobic and resistance training. *PLoSOne*. 9 (11):1-8.

Toscani, M.K., Mario, F.M., Radavelli-Bagatini, S. & Spritzer, P.M.(2011). Insulin resistance is not strictly associated with energy intake or dietary macronutrient composition in women with polycystic ovary syndrome. *Nutrition Research* 31(1): 97–103

Traish, A.M. (2014). Testosterone and weight loss: the evidence. *Curr Opin Endocrinol Diabetes Obes*. 21(5):313-22.

Van Gemert, W.A., Schuit, A.J., Van der Palen, J., May, A.M., Iestra, J.A., Wittink, H., Peeters, P.H. & Monninkhof, E.M.(2015). Effect of weight loss, with or without exercise, on body composition and sex hormones in postmenopausal women: the SHAPE-2 trial. *Breast Cancer Res.* 17(120): 1-12.