

The Effect of Combined Respiratory Muscle Training and Ketogenic Diet on Obese Patients Risky to Obesity Hypoventilation Syndrome

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ABSTRACT

Back ground: Obesity is reaching epidemic proportions and is a strong risk factor for a number of cardiovascular and metabolic disorders .Despite the constant recommendations of health care organizations regarding the importance of weight control, this goal often fails. **Aim of the study** : to investigate the effect of combined Respiratory muscle training and Ketogenic diet on patients risky to obesity hypoventilation syndrome. **Methods:** Forty five obese patients from both sexes (15 males &30 females)at risk to develop obesity hypoventilation syndrome aged from 30-40 years old andrecruited from Oman rehabilitation center , Sultanate Oman. They were assigned into threegrups: **Group A** : included15 patients who practiced respiratory muscle training by using threshold inspiratory muscle training(IMT) combined with ketogenic diet for 12 weeks. **Group B:** included15 patients who followed ketogenic diet only for 12 weeks. **Group C:** included 15 patients whofollowed low caloric diet for 12 weeks. **Results:** Group (A) , showed a statistical significant improvement in ABG parameters (PH, , Paco2 and Pao2) that were (0.82%, 14.52%, 36.6.%) respectively and showed improvement in (WHR and BMI)(17.2%,14.12%)respectively , more than the improvement in group (B)and group (C),for group B that were(0.41%, 5.22%, 21.2%) respectively, and(14.8%,11.52%)respectively, and for group Cthat were (0.54%,3.37%15.7%)respectively,and (8.13%,5.8%) respectively. **Conclusions** :it is concluded that,combination of Respiratory muscle training and Ketogenic diet have an effect on patients at risk to develop obesity hypoventilation syndrome.

Key words: Respiratory muscle trainer ,ketogenic diet,Obesity hypoventilation syndrome.

INTRODUCTION

Obesity-related physiological changes are heightened during supine sleep. The frequent occurrence of OSA, with prevalence close to 90% in the morbidly obese, is explained by a combination of co-existing factors. Excessive fat depositions surrounding the upper airway and reduced lung volume are key features by which obesity synergistically decreases pharyngeal size and increases collapsibility, predisposing the upper airway to closure or significant narrowing during sleep.(1)

Although obesity, defined by a body mass index (BMI) 30 kg/m², is associated with an increased rate of death from cardiovascular diseases and certain cancers, the mechanisms involved in these relationships are incompletely understood. Obstructive sleep apnoea syndrome is commonly associated with obesity² and is a risk factor for cardiovascular morbidity.³ Beyond obstructive sleep apnoea syndrome, a particular subgroup of obese patients is affected by chronic respiratory failure, the so-called obesity hypoventilation syndrome (OHS). These patients are characterized by a greater morbidity than obese apnoeic patients, although this condition is often underdiagnosed. The present work reports definition, epidemiology, physiopathology and treatment modalities of OHS.(2)

Obesity hypoventilation syndrome (OHS) is defined as a combination of obesity (body mass index 30 kg/m²), daytime hypercapnia (partial arterial carbon dioxide concentration 45 mm Hg) and sleepdisordered breathing after ruling out other disorders that may cause alveolar hypoventilation.(3)

Obesity Hypoventilation Syndrome is a modern name for an past syndrome, the term “pickwickian syndrome” that is as a respiratory outcome with higher morbidity and lower quality of life.(4)

Patients with OHS are at greater risk of hospitalization and death, supposedly as a result of cardiovascular morbidity.(5)

For patients who are unsatisfied by medicinal intervention, the ketogenic diet continues to be a promising solution to a growing problem.(6)

The ketogenic diet is a high-fat, adequate-protein, and low carbohydrate diet designed to mimic many of the biochemical changes associated with prolonged starvation.(7)

Most ketogenic diets start with carbohydrate restriction of less than 20 to 50 g/d (10% of energy intake) for about 2 months before slow reintroduction.(8).

Ketogenic Diet plays a main role on fat loss. It exerts positive effects

on adipose tissue through: a decrease of liposynthesis, an increase of lipid oxidation and an increase in adiponectin..(9)

Very Low Calorie Ketogenic Diet induced weight loss is faster than the weight loss induced by a balanced low-caloric diet, while the subsequent weight gain is not faster than the weight gain following a low-caloric diet.(10)

Inspiratory muscle training is a targeted strengthening of the inspiratory muscles through the application of resistance during inspiration.(11)

Inspiratory muscle training was performed using an electronic tapered flow resistive loading device.(13)

Inspiratory muscle training can be performed in both ventilator-dependent and independently breathing ICU patients and ideally is conducted with the patient in an upright sitting position.(12)

MATERIALS AND METHODS

Subjects:

Forty five obese patients from both sexes at risk to develop obesity hypoventilation syndrome aged from 30-40 years old and recruited from Oman rehabilitation center , Sultanate Oman. All patients were examined and referred by chest specialist enrolled in that study. They were

assigned into three groups: Group A : included 15 patients practiced respiratory muscle training by using threshold inspiratory muscle training(IMT) combined with ketogenic diet for 12 weeks.

Group B: included 15 patients who will follow ketogenic diet only for 12 weeks.

Group C: included 15 patients who will follow low caloric diet for 12 weeks.

Inclusion criteria:

Adult obese patients risky to develop symptomatic hypoventilation syndrome as $Paco_2(40-45\text{mmHg})$ and $Pao_2 >70\text{ mmHg}$,Their age ranges from 30 to 40 years old of both sexes and Body mass index range (30-35) kg/m^2

Exclusion criteria:

Unstable cardio/respiratory condition, such as uncontrolled hypertension ,cardiovascular accident or myocardial infarction within the last 2 months,patients who done Surgery within 6 weeks of enrolment.and patients that suffer from Blood glucose level $>13\text{ mmol/dl}$ (i.e. uncontrolled)

Instrumentation:

Threshold Inspiratory muscle trainer:(Respironics, Cedar Grove, NJ 07009- 1201 USA)is an inspiratory muscle trainer, which has been widely used with various health

conditions. This device contains, at its end, a valve closed by the positive pressure of a spring, which can be graded from 9 to 41 cm H₂O and allows resistance changes by 2 cm H₂O increments. It has a one-way spring-loaded valve, that closes during inspiration and requires that participants inhale hard enough, to open the valve and let the air enter. This device provides constant pressure for inspiratory muscle training, regardless of how quickly or slowly the participants breathe, and the optimal loading pressure can be adjusted, based upon the individual characteristics of the participants.(18)

For safety criteria, all patients were evaluated for hemodynamic (blood pressure, heart rate and double product) and lung function (respiratory rate and oxygen saturation), before, during and after the session. If there was an increased heart rate and higher blood pressure above baseline value, session will stopped. , performing 3 sets 40 % of MIP, with 10 repetitions.

Evaluating Procedures:

1-Weight and Height scale to assess BMI (Kg/m²).

2-Tape measurement to assess Waist to Hip ratio.

3-Bioelectrical Impedance Analysis device(BIA) : Bioscan.MedeiaInc –USA.

Used for estimating body composition, to get a quick overview of the water and fat percentage in a body.

4- Acid-base analyzer: ABL 30 700 NB by radiometer A/S COPENHAGEN. For measuring partial pressure of oxygen in arterial blood (PaO₂), partial pressure of carbon dioxide (PaCO₂) and pH Arterial blood gases (ABGS) to assess oxygenation level and adequacy of ventilation.

Treatment Procedures:

Patients in Group (A) used threshold inspiratory trainer (IMT) for 30minutes (one minute training followed by 2 minutes rest), twice per day, 5 days per week,(3days attending in the center& the other 2 days as ahome program) for 12 weeks. During training, subjects were instructed to maintain diaphragmatic breathing exercise (12-15 breath/min) while patients in comfortable half lying and knee slightly flexed and supported by pillow. Inspiratory load was set at 30% of maximal static inspiratory pressure (P_Imax), and the training loads were increased weekly 5% of P_Imax during all study period

2-Ketogenic diet:

Ketogenic diets are characterized by a marked reduction in carbohydrates (usually to <50 g/day) and a relative increase in the proportions of protein and fat -

usually extremely high percentages of fat because it is difficult to increase proteins beyond a point.(19)

3-Low calorie diet:is typically between 1000 to 1500 calories and used to promote weight loss. It should be followed with guidance from professional to ensure all nutritional needs.(20)

Statistical analysis:

- Descriptive statistics and ANOVA-test were conducted for comparison of the mean age, weight and height between the three groups.

- Chi squared test was conducted for comparison of sex distribution between the three groups.

- ANOVA was carried out to compare BMI, WHR, PaO₂, PaCO₂ and pH between the three groups.

- Paired t test was carried out for comparison of BMI, WHR, PaO₂, PaCO₂ and pH between pre and post treatment mean values in each group.

- The level of significance for all statistical tests was set at $p < 0.05$.

- All statistical tests were performed through the statistical package for social studies (SPSS) version 25 for windows. (IBM SPSS, Chicago, IL, USA).

RESULTS

This study suggested that significance reduction of(BMI,WHR,Paco₂) and significance increase of(Pao₂,PH) after performing of ketogenic diet and IMT sessions. For Group A (IMT &ketogenic diet), percentage of improvement decrease of BMI was 14.12%,percentage of improvement decrease of WHR was 17.2%, percentage of improvement decrease of Pao₂ was 36.6%,percentage of Paco₂ was 14.52%,percentage of

improvement of PH was 0.82% shown in table(1)

For Group B (ketogenic diet only),percentage of improvement decrease of BMI was11.52 %, percentage of improvement decrease of WHR was 14.8%,percentage of improvement decrease of Pao₂ was21.2 %,percentage of Paco₂ was5.22 %, percentage of improvement of PH was 0.41 % shown in table(2)

For Group C (low calorie diet only), percentage of improvement decrease of BMI was 5.8%, percentage of improvement decrease of WHR was 8.13%, percentage of improvement decrease of Pao₂ was 15.7%, percentage of Paco₂ was 3.37%, percentage of improvement of PH was 0.54% shown in table (3)

Table (1): Comparison between pre and post according to all parameters in group A.

Parameters	Pre (n=15)	Post (n=15)	Diff.	Changed %	Paired- t test	P- value
PH	7.35 ± 0.04	7.41 ± 0.05	-0.06	0.82%	-4.92	0.0001
PACO ₂ (mmHg)	43.67 ± 1.8	37.33 ± 1.75	6.34	14.52%	10.12	0.0001
PAO ₂ (mmHg)	59.2 ± 7.93	80.86 ± 7.56	-21.66	36.6%	-8.97	0.0001
WHR	0.896 ± 0.05	0.742 ± 0.04	0.154	17.2%	15.95	0.0001
BMI	33.7 ± 2.36	28.94 ± 1.6	4.76	14.12%	11.06	0.0001

Table (2): Comparison between pre and post according to all parameters in group B.

Parameters	Pre (n=15)	Post (n=15)	Diff.	Changed %	Paired-t test	P-value
PH	7.37 ± 0.05	7.4 ± 0.04	-0.03	0.41%	-2.75	0.0001
PACO2 (mmHg)	44.46 ± 3.72	42.14 ± 3.23	2.32	5.22%	4.61	0.0001
PAO2 (mmHg)	58.53 ± 5.73	70.94 ± 9.31	-12.41	21.2%	-5.22	0.0001
WHR	0.885 ± 0.08	0.754 ± 0.09	0.131	14.8%	7.21	0.0001
BMI	33.41 ± 2.85	29.56 ± 2.42	3.85	11.52 %	8.49	0.0001

Table (3): Comparison between pre and post according to all parameters in group C.

Parameters	Pre (n=15)	Post (n=15)	Diff.	Changed %	Paired-t test	P-value
PH	7.36 ± 0.05	7.4 ± 0.05	-0.04	0.54%	-4.46	0.001
PACO2 (mmHg)	42.72 ± 2.15	41.28 ± 2.01	1.44	3.37%	4.11	0.001
PAO2 (mmHg)	59.06 ± 7.65	68.33 ± 9	-9.27	15.7%	-3.54	0.003
WHR	0.898 ± 0.06	0.825 ± 0.07	0.073	8.13%	3.44	0.004
BMI	33.35 ± 1.81	31.42 ± 1.56	1.93	5.8%	13.91	0.0001

DISCUSSION

The objective of this study was to determine the effect of combined respiratory muscle training and ketogenic diet on obese patients risky to obesity hypoventilation syndrome. p values less than 0.05 was considered statistically significant. The results of this study showed that there was significant effect of combined respiratory muscle training and ketogenic diet on obese patients risky to obesity hypoventilation syndrome.

The following measurements were done for 3 groups (Body mass index, Waist /Hip ratio, $Paco_2$, Pao_2 , PH).

These variables measured initially before starting the treatment and after the end of the sessions in 3 groups ,the study duration was three months.

To our knowledge few studies addressed the effect of combined respiratory muscle training and ketogenic diet on obese patients risky to obesity hypoventilation syndrome. This study showed a significant decrease in (BMI, W/H ratio, $Paco_2$) and showed increase in (Pao_2 , PH) in all groups but the improvement in group A is more than group B & C.

These results came in accordance with a study conducted by (Blair O'Neill and Paolo Raggiain 2020) . The ketogenic diet induces a rapid weight loss .It is

not entirely clear if the loss is due to water loss, a special effect of the diet itself (i.e. fat burning) or a reduction in total calorie intake ; in fact ,the keto diet is known to induce a quick sense of satiety that has a potential to reduce total calorie intake. In-house, controlled studies comparing low-fat versus low-carbohydrate diets did not demonstrate the superiority of either dietary approach for weight loss. Other potentially relevant effects of the keto diet are the improvement in glycemic control and reduction in triglycerides and small dense LDL lipoprotein particles concentration attainable with this nutritional approach.(21)

In this context, there is study fulfilled by (Alessandro et al, 2015) demonstrated that the KD may significantly decrease carbon dioxide body stores, which may theoretically be beneficial for patients with increased carbon dioxide arterial partial pressure due to respiratory insufficiency or failure.(22)

Other study by (Inoue et al, 2019) has shown that it is possible to achieve a preoperative mean weight loss of 4.5% (3.2 kg) and a 16.8% decrease in visceral fat using a short-term (20 day) VLCD program for patients with obesity before laparoscopic gastrectomy for gastric cancer. Theoretically, an aggressive reduction in the preoperative dietary

intake could be associated with loss of skeletal muscle mass.(23)

This study conducted by(Blanco et al,2019)Although the ketogenic diet with or without periods of fasting might yield short-term weight loss, it has potentially dangerous side effects, including ketoacidosis. It is recommended that people, especially those with comorbidities such as diabetes mellitus type II, consult their physicians before initiating this diet. Clinicians must keep a broad differential when evaluating acute metabolic acidosis.(24)

Other study conducted by(Casali et al,2011) has assessed the effects of IMT on lung function, muscle strength, and muscular endurance in obese patients submitted to bariatric surgery. The results showed that IMT improved muscle strength and endurance and accounted for an earlier recovery of pulmonary airflow in the trained patients, comparing to controls. This is the first study to demonstrate the effects of an IMT program on obese patients treated by bariatric surgery.(25)

Other study conducted by(Souza et al,2014)suggested that Inspiratory muscle training of moderate intensity improves respiratory muscle strength, diaphragm thickness, and diaphragm mobility in elderly women and it should be considered to minimize changes associated with senescence. After training, in TG maximal

inspiratory pressure, maximal expiratory pressure, diaphragm thickness, and mobility increased by 37%, 13%, 11%, and 9% respectively, and their values were significantly higher than CG ($p < .005$, $p = .013$, $p = .001$, and $p = .001$). (26)

Other study By(Edwards et al,2016)suggested that the main finding of this study was that a 4-week period of inspiratory muscle training(IMT) appears efficacious for improving inspiratory muscle strength and the functional fitness of obese and overweight participants.(27)

In other hand , there is study conducted by (Hoffmeister et al,2019) suggests that obese individuals have similar hemodynamic responses to inspiratory muscle metaboreflex activation as lean individuals. Fatiguing resistive inspiratory muscle work, performed with a constant load of 60% MIP, leads to the accumulation of metabolites that stimulate the metaboreceptors to induce sympathetic activation and peripheral vasoconstriction, increasing BP suggesting that the increase in BP found in our study was mediated by inspiratory muscle metaboreflex.(28)

CONCLUSION:

It was concluded that combination of Respiratory muscle training and Ketogenic diet showed significant improvement in ABG parameters, WHR and BMI on

patients at risk to develop obesity hypoventilation syndrome.

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تأثير التدريب العضلي التنفسي مع النظام الغذائي الكيتوني علي المرضي البدناء المعرضون للاصابة بمتلازمة سمنة نقص التهوية

الخلفية العلمية: تعد السمنة من اخطر امراض هذا الزمن علي الانسان لما لها من تاثيرات جانبية وامراض مزمنة تؤثر تأثيرا كبيرا علي الجهاز التنفسي واذا لم يتم علاجها والتخلص منها ستؤدي الي قصور في وظيفة الرئتين.

الهدف من البحث: هو دراسة تأثير استخدام التدريب العضلي التنفسي مع النظام الغذائي الكيتوني علي المرضي البدناء المعرضون للاصابه بمتلازمة سمنة نقص التهوية.

الطريقة: تم إجراء هذه الدراسة علي ٤٥ شخصا يعانون من صعوبة في التنفس من كلا الجنسين (١٥ ذكور و ٣٠ اناث) وكانت اعمارهم تتراوح بين (٤٠-٣٠) عاما تم اختيارهم من عيادات تاهيل بسلطنة عمان واخرون من عيادات بالمهندسين بمصر

وقد اشتملت هذه الدراسة فقط علي المرضي كبار السن المعرضين للاصابه بمتلازمه سمنة نقص التهوية الذين ضغط ثاني اكسيد الكربون الجزئي يتراوح بين (٤٥-٤٠) مم زئبق والذين ضغط الاكسجين الجزئي اكبر من ٧٠ مم زئبق ومؤشر كتلة الجسم تتراوح بين ٣٥-٤٠ كج/متر مربع
تم تكليفهم بثلاث مجموعات:

المجموعة الاولي: تألفت من ١٥ شخصا، تلقوا تدريبات التنفس من قبل مدرب العضلات التنفسي
بالاضافة الي النظام الغذائي الكيتوني لمدة ١٢ اسبوع.(IMT)

المجموعة الثانية: تألفت من ١٥ شخصا، تلقوا النظام الغذائي الكيتوني فقط لمدة ١٢ اسبوع.

المجموعة الثالثة: تألفت من ١٥ شخصا، تلقوا نظام الوحدات الحرارية منخفضة السعرات فقط
لمده ١٢ اسبوع.

القياسات: وقد تم قياس غازات الدم لكل من الثلاث مجموعات قبل بدأ البرنامج واعيدت بعد ثلاثة اشهر وتم قياس مؤشر كتلة الجسم ونسبه تحسن الخصر الي الورك قبل بدا البرنامج واعيد قياسها بعد ثلاثة اشهر.

النتائج: قد أظهرت النتائج فروق ذات دلالة احصائية تشير الي تحسن في غازات الدم بين مرضي المجموعة الاولي (مجموعة أ) أكثر من المجموعة الثانية (مجموعة ب) والمجموعة الثالثة (مجموعة ج) مما يؤدي الي ضرورة استخدام التدريب العضلي التنفسي والنظام الغذائي الكيتوني مع المرضي البدناء المعرضون للاصابة بمتلازمة نقص التهوية.

الاستنتاج: في حدود الدراسة الحالية ، وجد انه توجد علاقة بين التدريب العضلي التنفسي مع النظام الغذائي الكيتوني علي المرضي البدناء المعرضون للاصابه بمتلازمة سمنة نقص التهوية