



Efficacy of Cognitive Behavioral Therapy for Habit Modification and Drug Adherence in Obesity

Eficacia de la Terapia Cognitivo Conductual para Modificación de Hábitos y Adherencia Farmacológica en Obesidad

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Abstract

The obesity is a global health problem, also it is increasing in adults and pediatric population, reducing life quality. Treatment must be interdisciplinary with elements of behavior modification on self-control, habit modifications, support networks and highlighting to adherence. Cognitive behavioral therapy, specifically on problem solving model, is efficient in treatment of anthropometric control, metabolic and behavioral indicators. Methods: Quasi-experimental, comparative, clinical and randomized study, n=100 adults of both sexes with an exogenous obesity diagnostic. The intervention was performed with an interdisciplinary treatment of cognitive behavioral therapy on problem solving model and 3mg. (0-0-1) of melatonin (50 subjects), comparing it with a group that only received the treatment by melatonin 3mg. (0-0-1) (50 subjects) per 8 months; the anthropometry and blood biochemical values (glucose, triglycerides, HDL and LDL) was evaluated after and before; dropout rate and adherence to the drug was evaluated every month. A bioimpedance machine was used. Results: The analysis demonstrated in eight months that the problem solving model with melatonin group got an adherence average of 80% (p= .05); in comparison with melatonin group that showed an average of 48% (p= .05). Relating to anthropometry and blood biochemical values, problem solving model and melatonin group got better effectiveness

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($p = .05$). Conclusions Cognitive behavioral therapy combined with melatonin, was more effective in anthropometric indicators, blood chemistry and mainly in adherence, confirming the importance of the incursion of effective psychological techniques that contribute to the management of obesity.

Keywords: Obesity, Adherence, Problem Solving Model, Melatonin, Biochemical Values

Resumen

La obesidad es un problema de salud que aumenta en la población, reduciendo la calidad de vida. El tratamiento debe de ser interdisciplinario, que incluya autocontrol de ingesta alimentaria, modificación de hábitos, redes de apoyo y manejo de adherencia. La terapia cognitiva conductual específicamente el modelo en solución de problemas es eficaz en el manejo de antropometría, indicadores metabólicos y conductuales, sin embargo no hay evidencia de su impacto en adherencia farmacológica. Método: estudio cuasiexperimental, comparativo, aleatorio simple y clínico. Participaron 100 adultos de ambos sexos con diagnóstico de obesidad exógena. Se aplicó intervención basada en el modelo en solución de problemas combinado con 3 mg. (0-0-1) de melatonina (50 sujetos), comparándola con un grupo que solo recibió melatonina 3 mg. (0-0-1) (50 sujetos) durante 8 meses; se evaluó antropometría (IMC y porcentaje de grasa), química sanguínea (glucosa, triglicéridos, HDL y LDL), tasa de abandono y adherencia al fármaco mensualmente. Se utilizó báscula de bioimpedancia. Resultados. El grupo de terapia y melatonina obtuvo un promedio de adherencia del 80% ($p = .05$); en comparación con el grupo de melatonina que mostró un promedio de 48% ($p = .05$). En la antropometría y química sanguínea, este grupo mostró mayor eficacia ($p = .05$). Conclusiones. La terapia cognitivo conductual combinada con melatonina, fue más efectiva en indicadores antropométricos, de química sanguínea y principalmente en adherencia, lo que confirma la importancia de la incursión de técnicas psicológicas efectivas que coadyuven en el manejo de obesidad.

Palabras Clave: Obesidad, Adherencia, Modelo en Solución de Problemas, Melatonina, Química Sanguínea

Obesity grows year after year in the world on a par with its comorbidities. On its being a multifactorial nosological entity, the regulations, and agreements, including Official Mexican Regulation (*Norma Oficial Mexicana*, NOM) for the treatment of obesity (SEGOB, 2010), the World Health Organization (WHO, 2004) and the SEEDO Consensus, among others (Gargallo et al., 2012) indicate that the treatment should be implemented with an interdisciplinary methodology, which includes, within the health team, the Psychologist, with competencies in the area, whose behavioral objectives comprise the increase in self-control of the ingestion of food, behavioral modification, (Foster, Sánchez-Collins & Cheskin, 2017), and the management of therapeutic adherence, which

includes pharmacological treatment (Hurren & Dunham, 2017).

Adherence (ADH) is defined as the behavioral degree at which the patient, consciously and motivatedly, directs the taking of their medication in terms of the time, form, and grade it entails in order to carry out the guidelines of the treatment at the short, medium, and long term (OMS, 2004; Sieverink, Kelders & van Gemert-Pijnen, 2017). In chronic degenerative diseases, ADH is 30 and 50% at 4 months of treatment (OMS, 2004); however, these percentages could improve significantly with the use of Cognitive Behavioral Therapy (CBT), whose specific techniques are based on the problem-solving and decision-making model, with the addition of social reinforces,

the strengthening of self-confidence, self-control and self-efficacy, behavioral registries, and cognitive restructuring (Aguilera-Sosa et al., 2011; Murawski et al., 2009).

CBT through a meta-analysis showed to be efficient on diminishing the rate of treatment abandonment, in addition to improving motivation in terms of the change and in the prevention of relapse (Burgess, Hassmén, Welvaert & Pumpa, 2017). However, it is noteworthy that this work did not focus on data derived from the ADH evaluation concerning the medication, which is an important omission according to the World Health Organization (WHOOMS, 2004) and of the FEDNAD-SEEDO Consensus (Gargallo et al., 2012).

On its part, in medical environments, it is postulated as an intervention model for ADH; the psychoeducation that surrounds the importance of the treatment for controlling the signs and symptoms of obesity (Schaub, Hippius, Möller & Falkai, 2016). However, these methods have not exhibited therapeutic efficiency in the medium term

To evaluate ADH in terms of the medication, direct (specific metabolic measurement) and indirect (validated instruments) methods are employed; notwithstanding this, observation of the behavior can be more efficient utilizing indirect methods (Brown & Bussell, 2011; Nagpal, Prapavessis, Campbell & Mottola, 2017), being that of no taking of tablets in relation to the time, which is that recommended by the Mayo Clinic (Brown & Bussell, 2011).

The recent use of Melatonin (ML) has been increasing as a drug for the control of OB, mainly as a pathway of control of the harmful effects of inflammation and due to its antioxidant activity (Favero et al., 2015), as well as for its effect on the metabolism of the adipocytes, contributing to lipid diminution in blood, thus improving the Atherogenic Index (IAT) (Szewczyk-Golec et al., 2017; Valenzuela-Melgarejo, Caro-Díaz & Cabello-Guzmán, 2018). In comparison with other drugs, ML exhibits low adverse effects; therefore, the objective of the present work was to evaluate the effectiveness of an interdisciplinary intervention of CBT with treatment with ML alone in ADH of the medication, and the anthropometric and

blood-chemistry values. The hypothesis, is that CBT with ML will have greater statistical significance in the anthropometric, blood-chemistry and ADH, than the treatment of ML alone, in obese.

Method

Quasi-experimental research design, clinical, probabilistic, and comparative-efficiency study, between two groups.

Participants

Mexicans residing in Mexico City, Mexico, with a diagnosis of exogenous Obesity (Ob), of both sexes and without comorbidities: $n = 100$; between the ages of 25 and 55 years; who attended the meetings convened, and who complied with the inclusion criteria, comprising simple Ob, the signing of informed consent for participation in the study; not having received treatment for Ob for 6 months prior to study initiation; availability of the time required for attending a medical consultation and psychological treatment. Exclusion criteria included the following: the psychiatric diagnosis described in the patient's clinical history; gestational state; anomalies in the electrocardiogram; daytime hypersomnolence; diabetes; hypertension; metabolic syndrome; cirrhosis of the liver; cancer; smoking; alcoholism, and drug addiction (Figure 1).

Procedure

An announcement was made in electronic networks, flayers were given in the immediate vicinity of the *Lázaro Cárdenas* Unit and the subways, patients from the schools' clinics were invited (Figure 1). The study subjects were randomly divided into two groups by picking numbers from a bowl: 1) the experimental group submitted to CBT and to pharmacological treatment with ML ($n = 50$), and 2) the treatment group with ML alone with ML alone (3 mg daily) (Cronocaps®) ($n = 50$). The average age of the

CBT+ML group was 35.53 ± 10.22 years and, in the ML alone group, this was 35.33 ± 8.90 years. A total of 46.9% of the patients were married, and 44.9% were single. The duration of the study was 8 months, and it was carried out at the installations of the *Escola Superior de Medicina del Instituto Politécnico Nacional* (ESM-IPN). The procedures were approved by the Institution's Committee (CEI-CICS-010); similarly, the patients' personal data were managed in a confidential manner, and those who participated in the study received the complete intervention and the medication without cost.

Evaluations and Instruments

We evaluated the following: (I) number of returned tablets monthly in the study groups; (II) percentage of treatment abandonment during the 8 study months; (III) differences in the Body Mass Index (BMI); (IV) percentage of fat by means of the bioimpedance scale (Tanita, model BC533), as well as (V) the blood chemistry of glucose, lipids, triglycerides, cholesterol, and High-Density Lipoproteins (HDL) and Low-Density Lipoproteins (LDL). We carried out the medical clinical and psychological history of each of the patients

medical (based on the Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders of the DSM-V). The first group attended a 2½-h session weekly during 8 months to receive the CBT intervention. The consultations for medical control and for returning the unused tablets were held monthly or in case of the need of the patient. The percentage of returned tablets was evaluated monthly, anthropometric measurements were performed prior to the initiation of the intervention and at 8 months, and blood-chemistry measurements were being conducted at the beginning of the intervention and at 8 months. The psychological therapy was carried out by four Psychologists who had received their formation in the Psychology of Health and in CBT.

The CBT program followed the line of a previously developed program (Aguilera-Sosa, Leija, et al., 2009; Leija-Alva et al., 2011), with the addendum of ADH management. The CBT-group assistants were provided with a participant's manual that included the contents of the 32 sessions. Every 2 weeks, the Psychologists met to supervise and homogenize the system of psychological intervention. The framework for the application of the problem-solving therapy was based on the elements by Murawski et al. (2009) (Table 1).

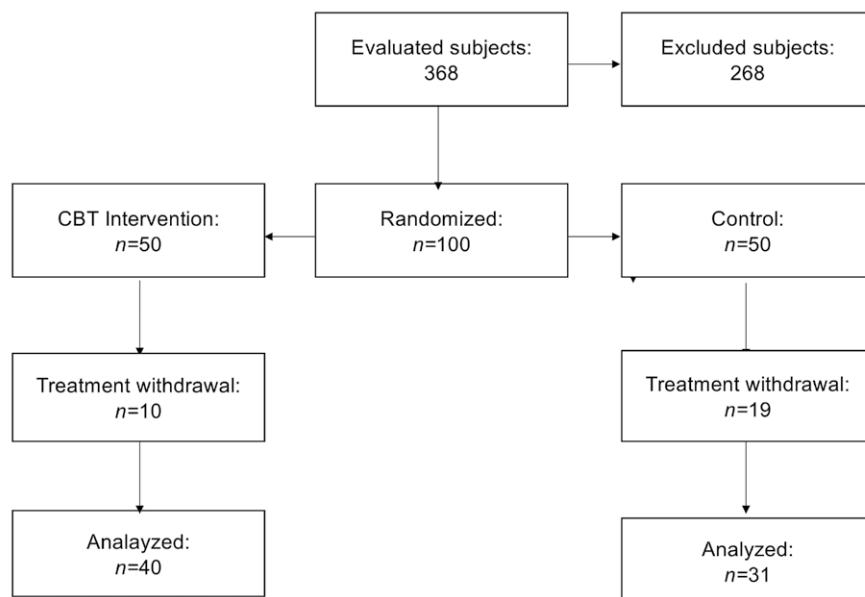


Figure 1. Proces diagram. Process Flowchart from selection of n to application of instruments at end of treatment.

Table 1
Objectives and contents of the CBT intervention in problem solving

Sessions	Objective	Contents
Session 1-4	Training in the objectives of BCT and problem solving.	<ul style="list-style-type: none"> - Psycho-education in obesity and ADH; cognitive distortions, irrational beliefs and ADH. - General orientation towards the problem of Ob and ADH. - Definition and formulation of the ADH problem. - Self-efficacy in ADH and habits.
Session 5-7	Identification of ADH proximal elements, obesity and its cognitive products.	<ul style="list-style-type: none"> - Generation of differential alternatives for ADH and habits; barriers interfering on medication intake. - Management of "ideal weight" fallacy. - Family, Ob and ADH.
Session 8-13	Training on detection and deviation of dysfunctional thoughts, use of differential reinforcers in food and Socratic and empirical debates for ADH.	<ul style="list-style-type: none"> - Self-control and social reinforcers for ADH and change of habits. - Family, Ob and ADH. - Cognitive restructuring and self-efficacy. - Verification of the complete process for ADH and habits.
Session 14-23	Discussion of dysfunctional cognitive products related to Ob and ADH; achievement evaluation of the solution process.	<ul style="list-style-type: none"> - Management of "ideal weight" fallacy. - Acceptation, self-confidence and self-control. - Cognitive restructuring.
Session 23-32	Evaluation of the whole process and the application of group debate.	<ul style="list-style-type: none"> - Self-control. - Barriers that interfering on medication intake. - Cognitive restructuring - Verification of the complete process for ADH and habits. - Closure.

Statistics

For the statistical analysis performed by means of the SPSS ver. 22.0 statistical software program, we used central trend measurements, dispersion, frequencies, and percentages. We applied the Kolmogorov-Smirnov test to evaluate data distribution; in the comparative analysis, we applied the Student t test for independent samples, and the Student t test for related samples; for the monthly analysis of the number of returned tablets with regard to the type of intervention, we employed the Analysis Of Variance (ANOVA) assay of repeated measurements. We established a value of $p = 0.05$ as statistically significant.

Results

Dropout percentages were taken, from users that did not finish in the eight months. With respect to the percentage of treatment abandonment, in the CBT+ML group, 20% (10/50) did not finish the intervention vs. 48% (19/50) of the ML group ($p = 0.0047$) (Table 2). One hundred percent of the men of both groups did

not finish the treatment. With respect to the ADH, we may observe in Table 3 the average of tablets returned to the treating physician and its comparison between the groups (CBT+ML vs. ML alone), taking the monthly evaluation into account. It can be observed that the CBT+ML group exhibited a significant diminution of returned tablets between the initial and the final month (2.93 ± 1.54 vs. 1.62 ± 1.18 ; $p = 0.0001$), while the ML alone group presented an increase (2.73 ± 1.21 vs. 9.11 ± 1.14 ; $p = 0.0001$); it is also shown that the average number of returned tablets was different ($p = 0.005$) between both treatments from month 3, this less in the CBT+ML group (2.18 ± 0.89 vs. 3.30 ± 1.73 ; $p = 0.05$); this tendency was maintained until month eight.

Table 2
Percentages by sex of the groups

	Women	Men
CBT+ML ($n = 50$)	86% (43)	14% (7)
ML ($n = 50$)	88% (41)	12% (9)

Note: CBT = Cognitive Behavioral Therapy; ML = Melatonin

Table 3

Comparison of the repeated measurements of the number of tablets returned to the treating physician in relation to the treatment group and the monthly evaluation

Measurement	CBT+ML Mean \pm SD (n = 50)	ML Mean \pm SD	p	F
September	2.93 \pm 1.54 (50)	2.73 \pm 1.21 (50)	0.58	0.30
October	2.71 \pm 1.22	3.15 \pm 1.75	0.27	1.22
November	2.18 \pm .89	3.30 \pm 1.73	0.002	10.03
December	2.37 \pm 1.80	3.53 \pm 1.67	0.01	6.32
January	1.68 \pm 1.28	4.23 \pm 1.53	0.0001	47.45
February	1.56 \pm 1.10	5.15 \pm 2.14	0.0001	67.604
March	1.53 \pm 1.52	6.53 \pm 2.17	0.0001	105.76
April	1.62 \pm 1.18 (n = 40)	9.11 \pm 1.14 (n = 31)	0.0001	591.83

Note: CBT = Cognitive Behavioral Therapy; ML = Melatonin; SD = Standard Deviation. n = 50 initially for each group. F = variance estimation.

In Tables 4 and 5, the results are presented of Body Mass Index (BMI) and the percentage of initial and final fat, as well as the results of glucose, triglycerides, HDL, and LDL, before and after the 8-month intervention.

In the initial anthropometry evaluation, which involves BMI and the percentage of fat, significant results were not found in measurements between the groups, while in the final measurements of these values, we identified significant results in favor of the CBT+ML; however, in the ML alone group, the final differences were significant, although less than those of the CBT+ML group.

Table 4
Comparison of the anthropometric measurements

Measurement	CBT+ML Mean \pm SD	ML Mean \pm SD	p
Initial BMI	34.13 \pm 2.85 (n = 50)	34.02 \pm 2.67 (n = 50)	0.8425
Final BMI	30.24 \pm 2.97 (40)	33.15 \pm 2.96 (31)	0.0001
	p = 0.001	p = 0.005	
% Initial body fat	42.33 \pm 4.23 (50)	42.27 \pm 3.24 (50)	0.93
% Final body fat	33.27 \pm 3.92 (40)	40.88 \pm 5.07 (31)	0.0001
	p = 0.0001	p = 0.01	

CBT = Cognitive Behavioral Therapy; ML = Melatonin; SD = Standard Deviation; BMI = Body Mass Index

On performing the Analysis of Variance (ANOVA) of the blood-chemistry measurements, we found significant differences (p < 0.05) in the final measurement between groups, especially in CBT+ML, in which the levels of triglycerides and LDL diminished, while those of HDL increased in this group. In both groups, the levels of glucose and HDL increased significantly.

Table 5
ANOVA of the means of glucose, triglycerides, cholesterol, HDL, and LDL before and after the intervention

	CBT+ML (n = 50/40) Mean \pm SD	ML (n = 50/31) X \pm SD	p
Glucose Initial	84.81 \pm 7.27	88.04 \pm 11.51	0.09
Glucose Final	90.33 \pm 5.94	108.64 \pm 23.23	0.04
	p = 0.0003	p = 0.001	
Triglycerides Initial	152.81 \pm 77.48	161.08 \pm 117.51	0.75
Triglycerides Final	134.09 \pm 43.20	192.68 \pm 100	0.004
	= 0.14	p = 0.39	
HDL Initial	31.81 \pm 8.76	36.12 \pm 10.34	0.09
HDL Final	88.20 \pm 0.20	40.68 \pm 14.59	0.001
	p = 0.0001	p = 0.05	
LDL Initial	104.31 \pm 32.80	114.36 \pm 27.37	0.22
LDL Final	101.47 \pm 18.96	119.72 \pm 28.60	0.006
	p = 0.64	= 0.09	

Note: CBT = Cognitive Behavioral Therapy; ML = Melatonin; SD = Standard Deviation; ANOVA = Analysis of Variance; HDL = High-Density Lipoprotein; LDL = Low-Density Lipoprotein

Discussion

One of the greatest challenges for the treatment of chronic disease, is the management of ADH; thus, it has been suggested that these diseases be cared for by means of an interdisciplinary vision (SEGOB, 2010). To this effect, the FESNAD-SEEDO Consensus mentions that the behavioral treatment be directed by means of self-control, eating habits, and physical exercise, and the strengthening of the ADH at the short, medium, and long terms (Gargallo et al., 2012). However, despite there being diverse models and the empirical evidence of the effectiveness of CBT and its effect on anthropometry many of the reports have been unidisciplinary or short-term, and not combined with the use of drugs for the control of Obesity (Ob). On the other hand, in hospital environments, the majority of the medical interventions for ADH do not have technically well-defined behavioral elements, such as the work conducted by Ford et al. (Ford, Haskins & Nahar, 2017), which obtained an ADH percentage of 51% (2017), in contrast with that obtained in this investigation in the CBT+ML at 8 months of 80%. This result was achieved through a behavioral model, structured by four general objectives: behavior modification; self-control; the establishment of social limits, and the control of ADH. Problem-solving therapy impacted positively on the percentage of tablets of ML returned monthly, which was observed as decreasing, with statistically significant high levels, in contrast with the ML alone group, which demonstrated an inverse response, with an average ML tablet return in the last month of nearly seven tablets.

As correctly pointed out by Jacob & Isaac (Jubbin & Rajesh, 2012), the successful management of ADH is based on the promotion of consciousness of the disease, analysis, and the search for novel solutions to the contingencies that curtail the treatment and that importantly impact motivation. Problem-solving therapy for the treatment of Ob is effective for control of the anthropometry, as demonstrated by Murawski et al. (2009); however, unidisciplinary interventions fail in the medium and long term. Contrariwise, the sum of the components of our intervention that combined ML and CBT in the problem-solving method

strengthened behavioral adherence by the users, who learned to solve, in an efficient manner, contingencies related with their habits, ingestion control, the management of social networks, of assertive limits, and in primordial fashion their ADH behavior on taking the medication, whose results exerted an impact on anthropometry, triglycerides, HDL, and LDL (Leija-Alva et al., 2011).

In the present study, we determined that the interdisciplinary intervention, which combines the use of ML and CBT, is effective for maintaining the reduction of returned tablets with an index above 90% in ADH at 8 months. For the case of the management of anthropometric and blood chemistry levels, we also demonstrated that CBT in combination with ML results effective; notwithstanding this, we were able to observe that, on its own, ML exerted a positive effect on anthropometry and HDL. Therefore, it is suggested as a pharmacological treatment for Ob, in combination with behavior modification.

Limitations: it is necessary to expand the sample, follow up to one year and evaluate with drugs of greater potency but with more side effects.

Referencias

Aguilera-Sosa, V.R., Leija, A.G., Rodríguez, J.D., Trejo, M.J. & López, D.M. (2009). Evaluación de cambios en esquemas tempranos desadaptativos y en la antropometría de mujeres obesas con un tratamiento cognitivo conductual grupal. *Rev. Colomb. Psicol.*, 18(2), 157-66.

Aguilera-Sosa, V.R., Leija-Alva, G., Eleazar, P.E., Rodríguez-Choreño, J., López, C.S., Matamoros, M.R., López de la Rosa, M. & Trejo-Martínez, J. (2011). Tratamiento cognitivo conductual grupal vs. ejercicio aeróbico para el manejo de la obesidad, estrés oxidante celular y química sanguínea. *Rev. Elec. Psicol. Izt.*, 14(1), 236-6.

Brown, M. & Bussell, J. (2011). Medication Adherence: WHO Cares? *Mayo Clin. Proc.*, 86(4), 304-14.

Burgess, E., Hassmén, P., Welvaert, M. & Pumpa, K.L. (2017). Behavioural treatment strategies improve adherence to lifestyle intervention programmes in adults with obesity: a systematic review and meta-analysis. *Clin. Obes.*, 7(2), 105-114.

Favero, G., Stacchiotti, A., Castrezzati, S., Bonomini, F., Albanese, M., Rezzani, R. & Rodella, L.F. (2015).

Melatonin reduces obesity and restores adipokine patterns and metabolism in obese (ob/ob) mice. *Nutr. Res.*, 35(10), 891-900.

Ford, M.A., Haskins, M.A. & Nahar, V.K. (2017). Does adherence to a motivational counseling program impact weight loss? *Int. J. Health Sci. (Qassim)*, 11(4), 13-17.

Foster, D., Sanchez-Collins, S. & Cheskin, L. J. (2017). Multidisciplinary team-based obesity treatment in patients with diabetes: current practices and the state of the science. *Diabetes Spectr.*, 30(4), 244-249. DOI: 10.2337/ds17-0045

Gargallo, M., Breton, I., Basulto, J., Quiles, J., Formiguera, X., Salas-Salvadó, J. & FESNAD-SEEDO Consensus Group, (2012). FESNAD-SEEDO Consensus summary: Evidence-based nutritional recommendations for the prevention and treatment of overweight and obesity in adults. *Endocrinol. Nutr.*, 59(7), 429-37.

Hurren, K.M. & Dunham, M.W. (2017). Pharmacokinetic drug evaluation of extended release Lorcaserin for the treatment of obesity. *Expert Opin. Drug Metab. Toxicol.*, 13(8), 891-6.

Jubbin, J.J. & Rajesh, I. (2012). Behavioral therapy for management of obesity. *Indian J. Endocrinol. Metab.*, 16(1), 28-32.

Leija-Alva, G., Aguilera-Sosa, V.R., Lara-Padilla, E., Rodríguez-Choreño, J.D., Trejo-Martínez, J.I. & López-de la Rosa, M.R. (2011). Diferencias en la modificación de hábitos, pensamientos y actitudes relacionados con la obesidad entre dos distintos tratamientos en mujeres adultas. *Rev. Latinoamer. Med. Conduct.*, 1(2), 19-28.

Murawski, M.E., Milsom, V.A., Ross, K.M., Rickel, K.A., DeBraganza, N., Gibbons, L.M. & Perri, M.G. (2009). Problem solving, treatment adherence, and weight-loss outcome among women participating in lifestyle treatment for obesity. *Eat. Behav.*, 10(3), 146-151. DOI: 10.1016/j.eatbeh.2009.03.005

Nagpal, T.S., Prapavessis, H., Campbell, C. & Motolla, M.F. (2017). Measuring adherence to a nutrition and exercise lifestyle intervention: Is program adherence related to excessive gestational weight gain? *Behav. Anal. Pract.*, 10(4), 347-354. doi: 10.1007/s40617-017-0189-5.

OMS (2004). Adherencia a los tratamientos a largo plazo. Pruebas para la acción. *Proyecto sobre Adherencia Terapéutica a Largo Plazo*. Available in: <http://www.farmacologia.hc.edu.uy/images/WHO-Adherence-Long-Term-Therapies-Spa-2003.pdf>

Schaub, A., Hippius, H., Möller, H.J. & Falkai, P. (2016). Psychoeducational and cognitive behavioral treatment programs: implementation and evaluation from 1995 to 2015 in Kraepelin's Former Hospital. *Schizophrenia Bull.*, 42(1), 81-9. doi: 10.1093/schbul/sbw057

SEGOB, Norma Oficial Mexicana NOM-008-SSA3-2010 (2010). Para el tratamiento integral del sobre peso y la obesidad. *Diario Oficial de la Federación*. Available in: http://www.dof.gob.mx/nota_detalle.php?codigo=5154226&fecha=04/08/2010

Sieverink, F., Kelders, S.M. & van Gemert-Pijnen, J.E. (2017). Clarifying the concept of adherence to eHealth technology: systematic review on when usage becomes adherence. *J. Med. Internet Res.*, 19(12), e402. doi: 10.2196/jmir.8578

Szewczyk-Golec, K., Rajewski, P., Gackowski, M., Milla-Kierzenkowska, C., Wesołowski, R., Sutkowy, P., Pawłowska, M., & Woźniak, A. (2017). Melatonin Supplementation Lowers Oxidative Stress and Regulates Adipokines in Obese Patients on a Calorie-Restricted Diet. *Oxidative medicine and cellular longevity*, 8494107. <https://doi.org/10.1155/2017/8494107>

Valenzuela-Melgarejo, F.J., Caro-Díaz, C. & Cabelllo-Guzmán, G. (2018). Potential crosstalk between fructose and melatonin: a new role of melatonin-inhibiting the metabolic effects of fructose. *International Journal of Endocrinology*, 11 pages. <https://doi.org/10.1155/2018/751576>