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CASE REPORT

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Case report: sleep alterations associated with hypothyroidism

Reporte de un caso de alteraciones en el sueño asociadas a hipotiroidismo

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| Abstract |

This paper presents a case report of a perimenopausal woman who repeatedly attended health care institutions due to chronic insomnia, and underwent pharmacological treatments and psychiatric hospitalizations without achieving any positive result for nearly three years. After compiling all the information of the case, as well as analyzing previous and recent paraclinical studies, the patient was diagnosed with hypothyroidism.

The purpose of this paper is to draw attention on the adequate use of clinical diagnostic tools and processes to optimize the medical practice and to offer a better service to patients.

Keywords: Sleep Disorders; Hypothyroidism; Diagnosis; Sleep Initiation and Maintenance Disorders (MeSH).

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| Resumen |

Se presenta el caso de una mujer adulta perimenopáusica quien consultó múltiples veces al sistema de salud por presentar insomnio crónico y, durante cerca de tres años, recibió tratamientos médicos farmacológicos e incluso hospitalizaciones psiquiátricas sin lograr mejoría. Tras la integración de la información de la cual se dispuso, así como la toma y revisión de paraclínicos previos, se documentó hipotiroidismo.

En este estudio se intenta hacer un llamado a la utilización de las herramientas clínicas y a la implementación de adecuados procesos diagnósticos con el fin de optimizar la práctica médica y ofrecer un mejor servicio a los pacientes.

Palabras clave: Trastornos del sueño; Hipotiroidismo; Diagnóstico; Trastornos del inicio y del mantenimiento del sueño (DeCS).

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Introduction

This paper presents the clinical case of a patient who had consulted general and specialized physicians, several times, for about three years, without obtaining an effective solution to her ailments. For this reason, the possibility of illustrating the process experienced by the patient was considered; the patient, ultimately, received a comorbid diagnosis of hypothyroidism and dyslipidemia, and was provided with a treatment that evidently improved her symptoms.

In this study, all relevant precautions to protect the identity of the patient and maintain the confidentiality were taken. This paper makes reference to the patient in terms of sex and age, but no specific personal or contact information is provided.

Case presentation

This case is about a 51-year-old woman who consulted different doctors during the span of three years and felt that could never sleep nor obtain any rest. When explaining her sleeping habits, she explained that she woke up at 4:30 am, but got up two or three hours later; she did not take naps despite feeling tired and fatigued during the day, and went to sleep at 9:30 pm. She did not mention any difficulty to fall asleep. Sometimes during the week, she exercised at 8:00 am for about an hour, but she felt without energy. In order to sleep, and by medical order, she took Lorazepam 2 mg/night and Levomepromazine 50 drops/night (50 mg/night) without improvement. No related triggers of the symptoms were described.

Previously, the patient was hospitalized in a psychiatric clinic with a diagnosis of depression, and was administered zolpidem, zopiclone, lorazepam, levomepromazine, clonazepam and valproic acid; however, she felt that the treatment did not represent any improvement, and then, decided to self-medicate with amitriptyline, without any change. Due to her sleep difficulties, she consulted a general physician, and was again referred to psychiatry and a polysomnography (PSG) was requested; according to the patient, the result was normal, so her treating psychiatrist decided to continue the treatment with benzodiazepines.

The patient also reported a history of irritable bowel syndrome, an asymptomatic pituitary adenoma and frequent consultation to hospital services due to gastrointestinal issues. She also reported that her mother had died from breast cancer and had some nephews with thyroid malignancies.

During medical examinations, possible thyroid nodules were found, therefore, she underwent FNAB (fine-needle aspiration biopsy), and the result was normal. The patient did not remember if other paraclinical examinations had been taken.

A systems enquiry found dry skin, hair loss, brittle nails, milk discharge from breasts, menstrual irregularities prone to oligomenorrhea, frequent headaches treated with NSAIDs, nocturia and weight gain (about 10kg in two years).

Physical examination found a hemodynamically stable patient, with vital signs within normal limits, overweight, dry skin, dull and thin hair, brittle nails, acrocyanosis, non-visible thyroid and no other relevant findings.

Mental examination exposed hypoprosia, bradypsychia and an overvalued somatic ideation related to the difficulty to sleep. After active exploration, no depressive overvalued ideation was found, but fatigability, constrained sadness and anxiety, lack of repairing sleep and preserved reality judgment were identified.

At the time, additional paraclinicals were requested. The gradual discontinuation of benzodiazepines and levomepromazine was indicated, and mirtazapine 15 mg/night during this period was prescribed. Sleep hygiene and habit structuring recommendations were given and the patient was scheduled for a control consultation with the paraclinical results requested, in addition to those previously taken.

Two weeks later, the patient attended consultation with the previous tests: a thyroid FNAB reporting goiter according to the Bethesda System category III and a PSG showing “no respiratory disorders during sleep” reported by a pneumologist; however, when reviewing other parameters and the hypnogram, a sleep destructure was found along with a significant increase in the superficial slow wave sleep, and multiple alertness periods at the expense of deep slow wave sleep without significant disturbances in the percentage of rapid eye movement (REM) sleep. A total sleep time of more than 350 minutes was reported, without respiratory events.

Among the tests requested on the initial consultation, hypothyroidism associated with dyslipidemia was documented, for which treatment was initiated, obtaining progressive symptomatic remission and instructions on changing habits were given. Finally, the patient was recommended to continue in treatment with endocrinology and attend a psychiatry control for follow-up, which she attended three months later with her bedmate and both, patient and companion, spoke about the improvement of symptoms according to their perception of sleep quality, day performance and parallel symptoms. In the same consultation, psychoeducation was provided to the patient and her companion.

Topic review

The relevance of this case is based on two important topics: the impact of hypothyroidism on sleep from the psychiatric point of view, which is not uncommon, and the necessary wake-up call that must be made regarding the diagnosis process in medicine, leading to consider this case for illustration.

Hypothyroidism and its impact on sleep from a psychiatric point of view

Hypothyroidism is a syndrome caused by a qualitative or quantitative decrease of the thyroid hormone, usually by alteration in any of the links of the hypothalamic-pituitary-thyroid axis; rarely, it may also be caused peripherally (1). It usually has an insidious course, so it is uncommon to have patients consulting in the early stages of the

disease. Diagnosis can take time and requires suspicion based on clinical and paraclinical confirmation.

This syndrome is characterized by metabolic, cardiovascular, reproductive, neurological, and osteotendinal alterations, and, in general, affects all bodily functions. Patients are more vulnerable to this disease at specific stages of life, like pregnancy or senior age (2-11).

Regarding the mental sphere, a slower course of thought, fatigability, asthenia, apathy, visuospatial construction skills and attention memory disorders are frequent, so the differential diagnosis often includes depression or dementia (2,12-16). However, although infrequent, there have been psychotic episodes called “malignant myxoedemas”, so the study of this pathology has been proposed in conjunction with others such as sleep apnea (17).

With hypothyroidism, sleeping habits may be altered including daytime sleepiness and prolonged nighttime sleep (18) that improves with the administration of the thyroid hormone (19). In addition, subclinical hypothyroidism has been documented in 10-15% of patients with symptomatic hypothyroidism and obstructive sleep apnea (OSA) in 5% of them; the occurrence of snoring and sleepiness was also reported. These respiratory events during sleep are explained from a pathophysiological perspective based on reduced thyroid activity which, in turn, produces anatomical changes and increases airway resistance, compromising significantly REM sleep with the appearance of sleep apnea.

Moderate to severe hypothyroidism causes central respiratory rhythm disorders with secondary alveolar hypoventilation. This supports the idea of the relation between hypothyroidism and increased resistance syndrome of the upper airway.

A direct relationship between the severity of hypothyroidism, the presence of nocturnal snoring, daytime sleepiness and improvement after treatment with thyroid hormone was also documented (20-22).

Advanced hypothyroidism may lead to macroglossia, weight gain, muscle dysfunction or deposits of mucopolysaccharides in the upper respiratory tract and decreased ventilatory control, along with sleep apnea (23); however, no correlation was found between the severity of sleep apnea and thyroid hormone levels, so the recommendation for all patients with sleep apnea (24-27) or sleep disorders (28,29) is to undergo a thyroid study (30,31), even children (32), since the combination between hypothyroidism and sleep apnea is associated with pulmonary hypertension (33).

On the other hand, there have been studies on the quality of sleep of patients with thyroid disorders in which the measurement of objective (polysomnographic) and subjective (use of the Pittsburgh sleep quality index and Epworth Sleepiness Scale) parameters is included. Controversial results ranging from no correlation (34,35) to correlation between snoring and excessive daytime sleepiness with hypothyroidism, especially in the presence of obesity (28,36), were obtained.

Finally, some studies, such as Koehler *et al.* (38) have shown that acute and severe deficiencies of the thyroid hormone do not have a significant impact on the sleep architecture and no statistically relevant differences were found when comparing parameters such as the rate of apnea-hypopnea index (AHI), the average length of each of the stages of sleep, the duration of REM sleep, the latency of REM sleep, the total sleep time, the rate of leg movements and the alertness index in euthyroid persons. However, the effect of hypothyroidism on long-term sleep habits and structure was proven.

It is important to note that TSH is always high in primary hypothyroidism, but if tropine is within normal or low range, the existence of a sellar or suprasellar pathology should be considered; this may also correspond to the direct effect of a drug, usually a neuropsychiatric one, which prevents the rise of TSH levels.

Therefore, as a general recommendation in all cases, it is important to perform a complete clinical evaluation that includes paraclinical examination of the thyroid profile and taking into consideration the medical history.

Thus, from psychiatry, hypothyroidism is treated as a condition that often presents alterations in the sleep habits and sleep itself, and exploring and considering both conditions for diagnosis is advisable to provide a complete and appropriate treatment.

The diagnosis process in Medicine

Medicine is a probability science and an art for managing uncertainty (38), but it is also a discipline that follows the scientific method, described by The Real Academia Española (English: Royal Spanish Academy) as a “procedure followed by the sciences to find and teach the truth” (39).

The scientific method consists of several steps; the Oxford Dictionary defines it as “a method of procedure that has characterized natural science since the 17th century, consisting in systematic observation, measurement, and experiment, and the formulation, testing, and modification of hypotheses” (40). This means that, when facing a concern from a patient, the doctor makes a detailed study, formulates a hypothesis that is tested and acts accordingly, generally, proposing or offering treatment to seek relief or cure.

The “mechanics of clinical reasoning” or “intuition”, named after Beltran (41), is based on factors specific to the doctor as experience, learning, inductive and deductive logical reasoning, interpretation of information and high diagnostic suspicion. The quality of this reasoning—validity and reliability—, regardless of the scientific and technological baggage related to medicine, is what makes a good clinician. However, it is necessary to consider the different individual variations among physicians as the ones mentioned above, the intellectual analysis and synthesis skills, as well as the accumulation of knowledge and experience.

In order to achieve this “clinical reasoning”, which is the basis for the physician to start the research process and expand the information about the “history of the current illness”, the practitioner can follow one of the two methodological trends: the traditional, in which a predominantly algorithmic interrogation is used, and that which develops iterative hypotheses (42).

The development of other aspects of the clinical history—as the medical history and the review by systems of the life history—as well as the physical and mental examination seeks further information to confirm, discard or expand the hypotheses.

The way how this information is processed relates to the diagnostic process and the way it is taught and developed in the academic context, performing syndromic, topographic and etiologic diagnosis, that is, starting from the general to the specific, which can be narrowed with the use of diagnostic aids according to each case.

Three strategies complementary to the development of the cognitive diagnostic process are proposed: the deterministic strategy, causal reasoning and the probabilistic strategy. Thus, when combining clinical and laboratory findings in the form of probabilities, a rigorous definition of the disease is required based on the diagnostic criteria, which usually include the gold standard, in addition to clinical or paraclinical diagnostic aids such as radiological, histological, biochemical tests, among others.

The diagnostic process is a probabilistic estimate that includes several sources of information, among them, the doctor-patient dyad; this means that it is a dynamic process that is adjusted from the start allowing the approach to diagnostic certainty.

Discussion

This clinical case takes into consideration the difficulties faced by patients who, for various reasons, have weakened the diagnostic processes based on clinical practice. This case references a person who consulted general and specialized practitioners that offered treatments that did not provide solutions. However, during the consultations, the information was not obtained in a complete, adequate and meaningful manner, therefore, conclusions, different from those initially considered, could not be reached.

This case included a more extensive medical history, which took into consideration anamnesis and heteroanamnesis; clinical and paraclinical diagnostic aids were also considered, and the patient and her partner received therapeutic and psychoeducational interventions, with the subsequent strengthening of the doctor-patient relationship.

After establishing the specific complaint of the patient, a detailed characterization showed that her main issue was the perception of poor sleep and rest more than the lack of it, was established in detail. After a review of other portions of the medical history, some general health difficulties surfaced, as well as relevant family and personal medical history; also, physical and mental examinations were performed. Based on this preliminary information, the diagnostic hypotheses considered possible affective disorders (depressive/anxious) and their related differential (metabolic, endocrinological or rheumatoid) somatic or psychiatric diagnoses. Because of this, the patient required other clinical and paraclinical assistance. Finally, additional information was integrated with available information, reaching the diagnostic conclusions described above, and a treatment plan was proposed, which eventually proved useful for the expressed complaint.

This is the time to recognize that hypothyroidism is a relatively common condition that affects physiologically all body systems, and can even induce anatomical changes in people with this condition; this is evident in the results of the corresponding paraclinical examinations, but, as in this case, FNAB and PSG may be unspecific, therefore, this is not to be considered a typical or illustrative case.

While psychiatry considers hypothyroidism as a differential diagnosis when facing the possibilities in any given case, it is interesting that, for this specific case, the main ailment of the patient consisted of sleep difficulties that were perpetuated in time, despite being accompanied by a parallel array of symptoms.

The review of the topic sought to illustrate that the association between hypothyroidism and sleep disturbances is not unusual and its manifestations are varied, so recognizing and identifying a relation or a simultaneous occurrence requires a high diagnostic suspicion, as well as complete medical history and the use of an appropriate diagnostic algorithm.

In addition, the case shows the need for integration and implementation of a diagnostic process that allows to offer an effective therapeutic approach as soon as possible, since, after a long journey, the end result is that after years of subjective insomnia, multiple consultations, psychiatric hospitalizations, pharmacotherapy and paraclinical examinations, the patient was diagnosed with hypothyroidism and dyslipidemia, and an improvement in the habit of sleep was obtained with the recommendations of sleep habits and hygiene, the prescription of antidepressants in hypnotic doses—indicated in chronic insomnia to preserve sleep architecture—and the initiation of hormone replacement therapy.

It is worth noting that the pathology related to sleep disorders is multiple, but it is not uncommon that the symptoms mentioned

in other pathologies involving qualitative or quantitative alterations in sleep, lead to consultations due to the discomfort or interference this causes in the patients' lives. The reason for consultation is not always the real reason of the discomfort, therefore, it is necessary to perform a complete medical history and examination before opting for a symptomatic treatment.

It is important to ask whether the patients are no longer seen as a whole, full of medical complexities because of the medical specialization and, hence, they are simplified according to each medical specialty.

Conclusion

This case serves to illustrate the close link between sleep disorders with other pathologies, as common as hypothyroidism that can manifest with symptoms ranging from the presence of unspecific sleep alterations to complex clinical entities related to breathing disorders during sleep or even with episodes of psychosis. In consequence, it is important to perform a complete diagnostic exercise, a process based on the scientific method in which the clinical skills are challenged for the sake of the welfare of patients.

Conflicts of interest

None stated by the author.

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References

1. López JM. Hipotiroidismo. *Boletín de la Escuela de Medicina*. 2000 [cited 2016 Jul 21];29(3). Available from: <http://goo.gl/OU0Ga2>.
2. Kvetny J, Heldgaard PE, Bladbjerg EM, Gram J. Subclinical hypothyroidism is associated with a low-grade inflammation, increased triglyceride levels and predicts cardiovascular disease in males below 50 years. *Clin. Endocrinol*. 2005;61:232-38. <http://doi.org/cn645j>
3. Meier C, Staub JJ, Roth CB, Guglielmetti M, Kunz M, Miserez AR, et al. TSH-controlled L-thyroxine therapy reduces cholesterol levels and clinical symptoms in subclinical hypothyroidism: a double blind, placebo-controlled trial (Basel Thyroid Study). *J. Clin. Endocrinol. Metab*. 2001;86(10):4860-6. <http://doi.org/bmt5>.
4. Hak AE, Pols HA, Visser TJ, Drexhage HA, Hofman A, Witteman JC. Subclinical hypothyroidism is an independent risk factor for atherosclerosis and myocardial infarction in elderly women: The Rotterdam Study. *Ann. Intern. Med*. 2000;132(4):270-8. <http://doi.org/wh2>.
5. Zoncu S, Pigliaru F, Putzu C, Pisano L, Vargiu S, Deidda M, et al. Cardiac function in borderline hypothyroidism: a study by pulsed wave tissue Doppler imaging. *Eur. J. Endocrinol*. 2005;152(4):527-33. <http://doi.org/fg82xs>.
6. Luboshitzky R, Aviv A, Herer P, Lavie L. Risk factors for cardiovascular disease in women with subclinical hypothyroidism. *Thyroid*. 2002;12(5):421-5. <http://doi.org/bmf2ft>.
7. Christ-Crain M, Meier C, Guglielmetti M, Huber PR, Riesen W, Staub JJ, et al. Elevated C-reactive protein and homocysteine values: cardiovascular risk factors in hypothyroidism? A cross-sectional and double-blind, placebo-controlled trial. *Atherosclerosis*. 2003;166(2):379-86. <http://doi.org/c4m8qh>.
8. Dattilo G, Crosca S, Tavella S, Marte F, Patanè S. Pericardial effusion associated with subclinical hypothyroidism. *Int. J. Cardiol*. 2011;153(3):e47-50. <http://doi.org/c7r4wn>.
9. Lincoln SR, Ke RW, Kuttah WH. Screening for hypothyroidism in infertile women. *J. Reprod. Med*. 1999;44(5):455-7.
10. Baldini M, Colasanti A, Orsatti A, Airaghi L, Mauri MC, Cappellini MD. Neuropsychological function and metabolic aspects in subclinical hypothyroidism: the effects of L-Thyroxine. *Prog. Neuropsychopharmacol Biol. Psychiatry*. 2009;33(5):854-9. <http://doi.org/d98q7p>.
11. Lee WY, Oh KW, Rhee EJ, Jung CH, Kim SW, Yun EJ, et al. Relationship between subclinical thyroid dysfunction and femoral neck bone mineral density in women. *Arch. Med. Res*. 2006;37(4):511-6. <http://doi.org/bzscq>.
12. Dugbartey A. Neurocognitive aspects of hypothyroidism. *Arch. Intern. Med*. 1998;158(13):1413-8. <http://doi.org/d32gm8>.
13. Haggerty JJ Jr, Evans DL, Prange AJ Jr. Organic brain syndrome associated with marginal hypothyroidism. *Am. J. Psychiatry*. 1986;143(6):785-6. <http://doi.org/bmt6>.
14. Mennemeier M, Garner RD, Heilman KM. Memory, mood and measurement in hypothyroidism. *J. Clin. Exp. Neuropsychol*. 1993;15(5):822-31. <http://doi.org/dsdvpv>.
15. Osterweil D, Syndulko K, Cohen SN, Pettler-Jennings PD, Hershman JM, Cummings JL, et al. Cognitive function in non-demented older adults with hypothyroidism. *J. Am. Geriatr. Soc*. 1992;40(4):325-35. <http://doi.org/bmt7>.
16. Lass P, Slawek J, Derejko M, Rubello D. Neurological and psychiatric disorders in thyroid dysfunctions. The role of nuclear medicine: SPECT and PET imaging. *Minerva Endocrinol*. 2008;33(2):75-84.
17. Neal JM, Yuhico RJ. "Myxedema madness" associated with newly diagnosed hypothyroidism and obstructive sleep apnea. *J. Clin. Sleep Med*. 2012;8(6):717-8. <http://doi.org/bmt8>
18. Yanes-Quesada M, Rodríguez-Fernández L, Cruz-Hernández J, Turcios-Trista S, Yanes-Quesada MA. Hipotiroidismo subclínico, ni tan asintomático, ni tan inofensivo. *Rev. Cubana Endocrinol*. 2009;20(2).
19. Shinno H, Inami Y, Inagaki T, Kawamukai T, Utani E, Nakamura Y, et al. Successful treatment with levothyroxine for idiopathic hypersomnia patients with subclinical hypothyroidism. *Gen. Hosp. Psychiatry*. 2009;31(2):190-3. <http://doi.org/ft5hh5>.
20. Ferro R, Sánchez A. Manifestaciones neurológicas y neurocognitivas del hipotiroidismo. In: Niepomniszcze H, Novelli JL, editors. Hipotiroidismo. Rosario: UNR Editora; 2009.
21. Misiolek M, Marek B, Namyslowski G, Sciarski W, Zwirska-Korczala K, Kazmierczak-Zagorska Z, et al. Sleep apnea syndrome and snoring in patients with hypothyroidism with relation to overweight. *J. Physiol. Pharmacol*. 2007;58(Suppl 1):77-85.
22. Resta O, Carratù P, Carpagnano GE, Maniscalco M, Di Gioia G, Lacedonia D, et al. Influence of subclinical hypothyroidism and T4 treatment on the prevalence and severity of obstructive sleep apnoea syndrome (OSAS). *J. Endocrinol. Invest*. 2005;28(10):893-8. <http://doi.org/bmt9>.
23. Takeuchi S, Kitamura T, Ohbuchi T, Koizumi H, Takahashi R, Hohchi N, Suzuki H. Relationship between sleep apnea and thyroid function. *Sleep Breath*. 2015;19(1):85-9. <http://doi.org/bmvb>.
24. Ozcan KM, Selcuk A, Ozcan I, Ozdas T, Ozdogan F, Acar M, et al. Incidence of hypothyroidism and its correlation with polysomnography findings in obstructive sleep apnea. *Eur. Arch. Otorhinolaryngol*. 2014;271(11):2937-41. <http://doi.org/bmvc>.

25. **Lanfranco F.** Sleep apnea syndrome and hypothyroidism. *Endocrine*. 2013;44(3):551-2. <http://doi.org/bmvd>.
26. **Carratù P, Dragonieri S, Resta O.** Lack of association between OSAS and hypothyroidism. *Endocrine*. 2013;44(3):821. <http://doi.org/bmvf>.
27. **Mete T, Yalcin Y, Berker D, Ciftci B, Guven Firat S, Topaloglu O, et al.** Relationship between obstructive sleep apnea syndrome and thyroid diseases. *Endocrine*. 2013;44(3):723-8. <http://doi.org/bmvg>.
28. **Krishnan PV, Vadivu AS, Alappatt A, Kameswaran M.** Prevalence of sleep abnormalities and their association among hypothyroid patients in an Indian population. *Sleep Med*. 2012;13(10):1232-7. <http://doi.org/bmvh>.
29. **Sridhar GR, Putcha V, Lakshmi G.** Sleep in thyrotoxicosis. *Indian J. Endocrinol. Metab*. 2011;15(1):23-6. <http://doi.org/ctppwj>.
30. **Bozkurt NC, Karbek B, Cakal E, Firat H, Ozbek M, Delibasi T.** The association between severity of obstructive sleep apnea and prevalence of Hashimoto's thyroiditis. *Endocr. J.* 2012;59(11):981-8. <http://doi.org/bmvj>.
31. **Bahammam SA, Sharif MM, Jammah AA, Bahammam AS.** Prevalence of thyroid disease in patients with obstructive sleep apnea. *Respir. Med*. 2011;105(11):1755-60. <http://doi.org/cnv9j8>.
32. **Sakellaropoulou AV, Hatzistilianou MN, Emporiadou MN, Aivazis VT, Rousso I, Athanasiadou-Piperopoulou F.** Evaluation of thyroid gland function in children with obstructive apnea hypopnea syndrome. *Int. J. Immunopathol. Pharmacol*. 2011;24(2):377-86.
33. **Araz O, Yilmazel Ucar E, Yalcin A, Pulur D, Acemoglu H, Tas H, et al.** The incidence and severity of pulmonary hypertension in obstructive sleep apnea with hypothyroidism. *Med. Sci. Monit*. 2013;19:883-7. <http://doi.org/bmvk>.
34. **Akatsu H, Ewing SK, Stefanick ML, Fink HA, Stone KL, Barrett-Connor E, et al.** Association Between Thyroid Function and Objective and Subjective Sleep Quality in Older Men (MrOS) Study. *Endocr. Pract*. 2014;20(6):576-86. <http://doi.org/bmvm>.
35. **Ulas T, Buyukhatipoglu H, Eren MA, Dal MS, Torun A, Aydogan T, et al.** Evaluation of sleeping energy expenditure using the SenseWear Armband in patients with overt and subclinical hypothyroidism. *Clin. Invest. Med*. 2012;35(3):E126-31.
36. **Levy Andersen M, Tufik S.** Is thyroid screening of sleep clinic patients essential? *Sleep Med*. 2012;13(10):1215-6. <http://doi.org/bmvn>.
37. **Koehler C, Ginzkey C, Kleinsasser NH, Hagen R, Reiners C, Verburg FA.** Short-term severe thyroid hormone deficiency does not influence sleep parameters. *Sleep Breath*. 2013;17(1):253-8. <http://doi.org/bmvp>.
38. **Young P, Finn BC, Bruetman JE, Emery JD, Buzzi A.** William Osler: el hombre y sus descripciones. *Rev. Med. Chile*. 2012;140(9):1218-27. <http://doi.org/bmvq>.
39. **Diccionario de la lengua española.** Madrid: Real Academia Española; 2014 [cited 2015 Apr 22]. Método. Available from: <http://goo.gl/Ne6utp>.
40. **Oxford English Dictionary.** Oxford: Oxford University Press; [cited 2015 Apr 22]. Scientific. Available from: <http://goo.gl/3oRTOI>.
41. **Beltrán-Galvis OA, Torres DP.** El proceso diagnóstico (Primera parte). *Rev. Colomb. Gastroenterol*. 2004;19(3):213-20.
42. **Peña-Martínez JL.** El enfoque por Problemas en la Sistematización de la Práctica Clínica y el la Formación Médica. Bucaramanga: Ed. UIS; 1998.