ABSTRACT
The objective of this systematic review was to retrieve topics of relevance to the implications of leptin in modulating blood pressure and in the genesis, prevention and treatment of hypertension associated with obesity. Considering the hormone as a common link between the two pathological conditions, were identified actions to reduce the leptinemia, proposed and discussed in the literature. It was found that nursing lacks production of knowledge to subsidize the assistance to hypertensive obesity that present alterations in serum leptin. Were described signs and multifactorials symptoms dynamically interrelated and paradoxical in the manifestation of the clinical case studied, with effective management interventions in caring for those clients.

Keywords: Leptin; Blood pressure/therapy; Obesity; Hypertension

RESUMO
O objetivo desta revisão sistemática foi o levantamento de tópicos de relevância sobre as implicações da leptina na modulação da pressão arterial e na gênese, prevenção e tratamento da hipertensão arterial associada à obesidade. Considerando o hormônio como um elo comum entre as duas condições patológicas, foram identificadas as ações para a redução da leptinemia, propostas e discutidas na literatura. Constatou-se que a enfermagem carece de produção de conhecimento que subsidie a assistência ao hipertenso obeso com alterações nos níveis séricos de leptina. Foram descritos os sinais e sintomas multifatoriais que se interrelacionam de maneira dinâmica e paradoxal na manifestação do quadro clínico estudado, com ordenação de intervenções eficazes no cuidado a esses clientes.

Descritores: Leptina; Pressão arterial/terapia; Obesidade; Hipertensão

RESUMEN
El objetivo de esta revisión sistemática fue el levantamiento de tópicos de relevancia sobre las implicaciones de la leptina en la modulación de la presión arterial y en la génesis, prevención y tratamiento de la hipertensión arterial asociada a la obesidad. Considerando a la hormona como un eslabón común entre las dos condiciones patológicas, fueron identificadas las acciones para la reducción de la leptinemia, propuestas y discutidas en la literatura. Se constató que la enfermería carece de producción de conocimiento que subsidie la asistencia al hipertenso obeso con alteraciones en los niveles séricos de leptina. Fueron descritas las señales y síntomas multifactoriales que se interrelacionan de manera dinámica y paradojal en la manifestación del cuadro clínico estudiado, con ordenación de intervenciones eficaces en el cuidado a esos clientes.

Descritores: Leptina; Presión sanguínea/terapia; Obesidad; Hipertensión
INTRODUCTION

Universal prevalence rates of obesity are increasing at alarming proportions all over the world, as one of the main public health problems in modern society.(1)

Different epidemiological studies evidence the connection between obesity and different comorbidities, with a clear correlation between weight gain and overweight on the one hand and the occurrence of cardiovascular diseases on the other. Among obesity-associated diseases, arterial hypertension (AH) stands out, since weight gain has been appointed as an important risk factor for hypertensive disease. Studies demonstrate prevalence levels of hypertension about 50% higher in obese people.(2)

The concept that excess visceral adipose tissue is associated with the metabolic and hemodynamic complications involved in mechanisms leading to atherogenic cardiovascular disease and AH is not recent. For years, several research lines have shown the involvement of adipose tissue in the physiopathology of AH and its complications.(3-5)

The physiopathological mechanisms that favor the development of hypertension in cases of obesity are complex and involve multiple factors. In this context, systematic hemodynamic and renal alterations stand out, as well as insulin resistance with compensatory hyperinsulinemia, activation of the sympathetic nervous system and renin-angiotension system and effects of nitric oxide and plasma leptin.(6)

Clinical effects of leptin on obesity-associated arterial hypertension

Although hypertension is acknowledged as one of the most severe consequences of obesity, the physiopathology of increased pressure in obese people has not been fully clarified yet. Current concepts suggest that the recent Discovery of the leptin hormone can represent a common link between these two pathological conditions.(7-8)

Leptin is a peptide hormone with 167 amino acids, mainly released by adipose tissue and to a lesser extent by bone marrow, placenta, stomach and hypothalamic tissue. Leptin concentrations are proportional to the volume of fat cells and increase proportionally to the increase in the body fat percentage, that is, leptin levels are positively correlated with the degree of obesity in animal and human models.(9)

Historically, leptin was originally described as the fat cell hormone(10-12). Since 1994, the discovery that a mutation in the leptin gene causes severe obesity in rodents suggested that the physiological function of leptin is to avoid obesity during excessive food consumption.(12-13)

Among other actions, leptin activates hypothalamic receptors, inhibiting the secretion of neuropeptide Y (NPY), which is an important neurotransmitter in body weight control, released by hypothalamus neurons. The inhibition of NPY decreases appetite and increases thermogenesis through the activation of the sympathetic nervous system.(14). Leptin deficiency (mutation in the leptin gene) or resistance against leptin action (mutation in the leptin receptor gene), results in increased NPY in the hypothalamus. NPY, which increases appetite, also causes hypersecretion of insulin and glucocorticoids, with subsequent leptin secretion. When leptin is ineffective to reduce NPY production, a vicious circle will be established, giving rise to a phenotype marked by fat deposition or obesity, depending on the food intake(13,15-16)

Based on this and other studies, it is inferred that leptin inhibits the orexigenic – appetite inducing – route and stimulates the anorexigenic – satiety inducing – route. We know today that fat cells are not only considered protection and support structures, but as an actual organ with intensive endocrine and metabolic activity.(7,15)

Plasma leptin levels are increased in case of obesity, entailing multiple actions that are potentially relevant not only to control appetite and body mass, but also to regulate the cardiovascular system.(16)

Among the implications of this hormone for the pathogenesis of cardiovascular diseases, the effects of leptin on blood pressure (BP) modulation stand out, through its potential pressure-raising actions and depressing effects(5). To give an example, it exerts direct action on the kidneys, increasing renal sodium release and nitric oxide production, which can result in decreased pressure levels. It also increases sympathetic tonus in the kidneys, adrenal glands and heart, which can raise BP. Experimental research shows that, while leptin infusions are natriuretic in the short term, sodium retention emerges through the reduction in the renal blood flow and increases renal vascular resistance during prolonged infusions. This and other evidence involve leptin in some obesity-associated hypertension models(19)

Despite reports on leptin’s pressure increasing and decreasing actions, the former seem to predominate.(20). Moreover, in pathological conditions associated with increased sympathetic activities, such as congestive heart failure, hypertension and obesity, the renal diffusion of norepinefrin is correlated with plasma leptin after adjustments to the fat mass(21).

In view of these explanations, conclusive evidence about leptin actions on BP in human still seems to be lacking. Although the actual importance of this hormone for blood pressure regulation has not been fully established yet, it seems plausible that interventions to reduce leptin concentrations are convenient and desirable in hypertension treatment. High leptin concentration seems to play an important role in the physiopathological mechanisms of obesity-associated AH and can be considered an independent risk factor for this and other cardiovascular diseases.(22)

Reflecting on the importance of nurses’ role in AH patient care, the researchers aimed to carry out a systematic literature review about actions to reduce leptin concentrations in care delivery to patients with obesity-associated pressure alterations.

METHODS

The systematic literature review method was used, in which earlier research is summarized and conclusions are established. The selected articles were based on the question: “What nursing actions have been proposed or put in practice to reduce leptin concentrations in care delivery to patients with obesity-associated
pressure changes.

The search was carried out through on-line access to scientific publications indexed in the following electronic databases: LILACS (Latin American and Caribbean Health Science Literature), SciELO (Scientific Electronic Library Online) and MEDLINE (Medical Literature Analysis).

Initially, the investigated key words were “leptin”, “hypertension”, “obesity”, “arterial pressure” and “nursing”, using descriptors in Portuguese, English and Spanish. The criteria adopted to select the papers were: to address the theme; be indexed in the abovementioned databases; be available in full versions in the languages of the descriptors used for data survey. No restriction was established as to the research period and design.

No articles were found that complied with the criteria. Then, nursing was excluded as a descriptor and the search was refined to include only papers whose methodological design would classify the research as a review article. In this second step, i.e. the critical analysis of the texts this review was based on, the researchers considered the possibility that the ideas the authors presented would answer the guiding question.

Fifty-six articles were selected, published between 1997 and 2009, in international journals indexed in MEDLINE and SciELO. No nursing journal or specific publication was identified. This finding shows that nurses lack information and investments in the theme, opening up a range of possibilities to produce nursing knowledge about care delivery to obese hypertensive patients with alterations in serum leptin levels.

Below is a synthesis of the selected texts, in addition to excerpts of other kinds of scientific publications, with a view to supporting nursing professionals’ clinical practice by listing the main recommendations about the topic.

**Nursing actions to reduce leptin concentration**

Research appoints that long-term multidisciplinary treatments, including lifestyle changes, are fundamental for the follow-up of obese hypertensive patients.

Multidisciplinary intervention models without medication have demonstrated their efficiency to improve patients’ metabolic health, reducing fasting glucose and circulating insulin concentrations. According to some authors, circulating glucose and insulin concentrations explain 86% of the variation in circulating leptin concentrations. This means that leptin concentrations can be strongly modified, depending on glycemic homeostasis and insulinemia, suggesting that identifying leptin concentration adaptations can support clinical and public health strategies.

Interventions to reduce circulating leptin can exert cardiovascular and renal effects in hypertensive obese patients. Interventions are needed in the prevention and control of risk factors that affect circulating glucose and insulin concentrations, including food and increased body mass index (BMI), as well as the treatment and control of blood pressure alterations.

Nurses play an extremely important role in prevention, treatment and pressure control actions in the hypertensive population. Strategies that can help professionals to achieve significant BP reductions include the establishment of effective and pertinent blood pressure control and hypertension treatment actions.

Primary prevention of hypertension, obesity and factors related to these morbidities is accomplished by intercepting pre-pathogenic factors and includes health promotion and specific protection, which should be directed at the removal of risk factors. Secondary intervention involves patients, the pathogenic agent’s action, and the level of the disease and is related to diagnosis, early treatment and prevention of sequelae. Tertiary prevention, then, involves preventing disability through rehabilitation measures. Health promotion should be performed at all health care levels for hypertensive patients, but nurses and other health professionals should focus on primary care, avoiding the establishment and progression of the disease.

With regard to nutritional orientations, long-term diet treatment, through moderated calorie consumption and salt intake, is the most effective and safe treatment for obesity-associated hypertension. The use of different calorie limitation treatments should be considered with care. Energy-consuming or appetite-reducing drugs can increase blood pressure levels and are inadequate for use in AH patients.

Among all strategies described though, weight reduction may be the primary and fundamental measure to manage obesity-associated hypertension. Special considerations for obese patients, in addition to adequate BP control, include the correction of metabolic abnormalities and renal protection.

Obesity can be diagnosed through different methods, but anthropometric measures are the easiest, harmless, low cost and most indicated for daily practice. The form the World Health Organization (OMS) most recommends to diagnose obesity is body weight assessment through the BMI.

To classify obesity, it should be taken into account that the disease is heterogeneous and involves multiple factors, either due to its etiopathogenic, anatomopathological characteristics, the clinical situation and its evolution, as well as the concomitance of health risk factors or not. As a result, the disease is classified in different ways, depending on the factor that needs to be considered.

Basic obesity treatment rests on the modification of alimentary behavior and the increase of physical activity. Research appoints a decrease in circulating leptin concentrations after systemized exercise, with long-term interventions, probably due to the increased production of non-sterified fatty acids while exercising, reflecting a catabolic state of adipose tissue and, thus, less leptin secretion.

Medication treatment for obesity is indicated in cases of body mass index higher than 25 kg/m2 or central or android adiposity, with other obesity-associated diseases (including AH) or in patients with BMI over 30 kg/m2 when non-medication treatment alone fails. For didactical purposes, drugs for obesity treatment can be divided in three basic groups: centrally acting anorexiant drugs, thermogenic drugs and drugs affecting nutrient absorption. Although anti-obesity drugs offer powerful pharmacotherapy for obese hypertensive patients, their use should be limited and additional research is fundamental to test these agents’ safety and efficacy. The association with other cardiovascular risk factors, besides BP rise, needs to be considered.
when choosing the anti-hypertensive drug for obese patients. The psychological approach needs to be highlighted, which is a fundamental branch in treating this disease, in a biopsychosocial conception of health that contributes to guarantee successful treatment. Studies have demonstrated that the use of a joint clinical approach, combining clinical treatment with an intervention program to control different risk factors through educative orientations or behavioral interventions, is more effective to reduce cardiovascular morbidity and mortality rates than an exclusively pharmacological treatment. According to some authors, clinical treatment associated with psychological interventions in patients’ lifestyle is useful for hypertensive patients with two or more cardiovascular risk factors, including stress, overweight/obesity and dyslipidemia, as this strategy showed to be able to change a large number of risk factors. Nurses should collaborate to put in practice strategies needed for patients’ proper psychological follow-up, including the proposal of therapies by health professionals trained for this purpose.

With a view to contributing and adding efforts to improve nursing care, nurses can perform the following actions, in cooperation with the health team, to assess hypertensive and obese patients and detect possible abnormalities related to leptin concentrations. These include clinical intervention through diagnostic clinical assessment of the general health state (family and obesity history); nutritional intervention, through patient forwarding to nutritional consultations for specific food re-education goals; interventions related to physical activity, including the assessment of habitual physical activity and forwarding to professionals who are trained to determine what activities are indicated; information about lifestyle changes and stimulation to perform the changes; BP monitoring; measurement and follow-up of anthropometric measures, including BMI assessment and periodical patient weight evaluation; nursing consultations; plasma analysis and monitoring through hormone and glucose dosage, preferably including the assessment of insulin resistance ratios and insulin sensitivity; psychological intervention, according to the patient’s agreement and will.

**FINAL CONSIDERATIONS**

Obesity-associated hypertension should be considered a chronic disease that is difficult to manage, with multiple characteristics that involve the interaction of metabolic, physiological, behavioral, social and molecular influences. Hence, it becomes a great concern for health professionals, and interventions should originate in routine consultations at primary care units.

Nurses play a crucial role in the control of obese hypertensive patients’ treatment, which is similar to treatment indicated for metabolic syndrome patients. Diet, exercise and lifestyle modifications represent the gold standard for these patients’ treatment. If these measures fail, medication treatment and even more drastic interventions, including surgical procedures, can be considered.

Nursing professionals should accompany health system users or perform interventions in the community. With a view to adequate prevention, orientations about disease risks should always be focused on. After the disease has installed, nurses should provide counseling about the benefits of adequate treatment, avoiding unfavorable consequences, besides guiding the multidisciplinary team about indicated therapeutic approaches with a view to integrated therapy, to achieve a more effective prognosis.

Although the understanding about the physiopathology of obesity-associated hypertension has substantially progressed in recent years, treatment for obese hypertensive patients remains empirical and should be assessed in controlled experiments and large randomized studies.

Nursing professionals need to expand their knowledge about the physiological determinants of this pathological condition. In this perspective, researchers should pay great attention to leptin, as it is an important marker of body adiposity and stands out as a signal and modulator of obesity. And obesity, as one of the main risks for the development of hypertension, should not be considered a simple cardiovascular risk predictor, but should be acknowledged as a primordial element in the pathogenesis of hypertension.

By distinguishing the physiopathological mechanisms associated with the diseases addressed in this study, nurses can act more effectively in health promotion, protection and recovery. Together with their knowledge, they become increasingly able to act in the fight against the great evils of this century: arterial hypertension and obesity.

**REFERENCES**


