


Nitric oxide as a vascular reactivity factor in dietary formulations consumed in menopause: Sanitary and nutritional surveillance of food: Case report

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ABSTRACT

Menopausal women, hypertension, dyslipidemia, sedentary lifestyle and stress as cardiovascular risk factors. Consult after consuming a dietary product containing L-arginine. With each consumption of the product, he reports intense vasodilation and palpitations, effects that subside when the intake is stopped and reappear with a new consumption. In Argentina, these products lack pharmacovigilance processes and are available for purchase without a prescription by the public. The compound L-arginine is a substrate for the production of nitric oxide, a vascular reactivity factor.

Keywords: Nitric Oxide (NO), Menopause, Suppl, Dietary, Pharmacovigilance (FVG).

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INTRODUCTION

CLINICAL CASE

Objective

Recognize that the presence of L-arginine in dietary products may be a factor of vascular reactivity when consumed as a supplement in the climacteric and/or menopause.

CLINICAL CASE

A 51-year-old patient, retired teacher. She has 2 teenage children who live with her and her husband. He has been diagnosed with hypertension for 1 year. Medicated with enalapril 10 mg/d in a single dose and atorvastatin 10 mg/d. You don't engage in physical activity.

She attended the Climacteric and Menopause Department for symptoms of hypoestrogenism, such as difficulty falling asleep and vaginal dryness. She stopped treatment with Tibolone (2.5 mg/d) so she sporadically feels hot flashes, but no longer as intense as at the beginning of her climacteric. She reports tiredness and feeling stressed.

She states that she does not want to perform hormone replacement therapy (HRT), so she self-medicates with dietary supplements. During his visit, he said that when he took them, he realized that he blushed in a way that drew the attention of everyone around him, he registered palpitations and low BP; He stopped taking it for a while and when he started consuming it again, the symptoms reappeared, so he got scared and decided to consult.

As a pathological family history, he comments that his father died of AMI at the age of 65 and his maternal family, mothers, aunts and grandmother are hypertensive.

Physical examination confirmed: BP: 154/98 mmHg. Weight 70 kg H 1.62 pcs: 105 cm

Estudios complementarios: Colesterol total 245 mg/dl, LDLc 160mg/dl; TG 160 mg/dl, HDLc 40 mg/dl y Glucemia 100mg/dl

Indications after the first consultation: scheduled physical activity, Mediterranean diet, daily BP control, and complete laboratory. Continue with your usual medication, incorporate therapy with local promestrien. Discontinue dietary product.

DISCUSSION

Menopause is characterized by the cessation of ovarian function and the permanent cessation of menstrual cycles. This period of life is determined by progressive hypoestrogenism and is clinically confirmed after 12 months of amenorrhea; It can start between the ages of 35 and 40 and extend until around age 65. Torres Jimenez, AP and Torres Rincón, JM, (2028). This event brings with it reduced estradiol production, as well as increased follicle-stimulating hormone (FSH) levels and decreased inhibin levels. (El Khoudary SR, Greendale G, et al, 2019).



In general, women in developed countries enter menopause later than those living in developing countries (Schoenaker, DA; Jackson, C et al. 2014.) (World Population Ageing; 2019). This later age in natural menopause has been associated with a reduced risk of cardiovascular disease (CVD). (Bolaños B, Ortega E; 2021)

Hypoestrogenism gives rise to the appearance of vasomotor symptoms, insomnia, vaginal dryness (urogenital syndrome), menstrual and mood disorders, among others, Gómez Alaya, AE. (2010) but the most significant in terms of its metabolic impact is the alteration of abdominal fat distribution, which leads to an increase in cardiovascular risk in these patients.

Hormone replacement therapy (HRT) is the first-line therapy for symptom relief and prevention of comorbidities (Trémollières FA, Chabbert-Buffet N; 2022) Among the ways of providing estrogen, the transdermal route in standard doses is the most indicated due to the reduction of thromboembolic phenomena that can accompany the oral administration of the hormone. (Level of evidence: 1A) (Renoux C, et al; 2010; Yana Vinogradova. 2019). This fear of adverse reactions (ADRs) typical of hormone therapy (HRT) and concern about improving health make it easier for some women to seek alternative therapies with natural estrogens (Guerrón Enríquez, SX et al; 2021). There are several treatment options available, both pharmacological and non-pharmacological, to relieve menopausal symptoms, especially vasomotor symptoms and many women are inclined towards natural products. (Belardo MA et. As of 2018)

They are specially formulated products designed to supplement the incorporation of nutrients into the diet of healthy people, who have basic dietary needs that are not met or greater than usual. They contain some of the following nutrients: proteins, lipids, amino acids, carbohydrates, vitamins, minerals, dietary fiber, and herbs. Dietary supplements can come in the form of tablets, capsules, tablets, powders, drops, etc. They should not be confused with medicines because, unlike medicines, they are intended for healthy people and should not be consumed in the hope of mitigating, curing or treating any ailment. (ANMAT, Food Health and Nutritional Surveillance. 2024)

The WHO defines pharmacovigilance as the science and activities related to the detection, evaluation, knowledge and prevention of adverse reactions and other potential drug-related problems. (Pharmacovigilance -PAHO/WHO, 2020)

It is a primary tool for monitoring drugs in their post-marketing phase, in order to detect adverse reactions that escape those reported during clinical trials. Dietary products or supplements, contrary to what the regulation indicates, are not covered by this activity in Argentina, so they escape the analysis of adverse reactions and therefore we do not have statistics in this regard.

Phytoestrogens are non-steroidal compounds derived from plants that possess weak estrogenic action. The most studied group is that of isoflavones mainly derived from soybeans, genistein and daidzein, which have a structure similar to estradiol. These compounds have an affinity

for the ER receptor β . They are administered by PO and metabolized in the intestine. (Monteiro, NES et al; 2028).

L-arginine (L-Arg) is a semi-essential amino acid (Woyka J; 2017), it can be combined with other prescription or over-the-counter medications. It is also found in seafood products such as fish or seafood. Its properties include: improving athletic performance, increasing the protection of the immune system, dilating blood vessels and improving circulation, since L-arginine is transformed into nitric oxide. On the other hand, taking L-arginine for a period of one month can increase vascularization, but after six weeks the effects are not so positive. This is called a chronic negative effect after supplementation and, in the case of L-arginine, may be due to a decrease in enzymes involved in nitric oxide synthesis.

Dietary supplements can be easily purchased on the market, predisposing patients to be able to use them at their own discretion and without any control (Borrelli F; 2010). This situation raises the possibility that the intake of nutritional supplements may lead to the occurrence of unwanted effects in the individual. In the particular case that concerns us, the only medication that the patient had included was the dietary supplement with L-arginine and the symptoms were related to its intake. This fact was reinforced the moment he took the compound for the second time and the signs (ruddy, palpitations) appeared again.

It is an unusual situation, but the ingestion of nutritional products has caused several dozen hospitalizations and at least 5 deaths in Japan. These are pills that contained red yeast rice and were sold as a supplement capable of lowering cholesterol. Red yeast rice is a food used in traditional Chinese medicine and has an active component that is potentially effective in lowering cholesterol levels (monacolin K), but it may also contain a type of toxin that causes kidney failure. (IFOBAE (2024). A nutritional supplement is a product taken orally that contains a "dietary ingredient" to supplement the diet. In the present case, the supplement was used for therapeutic purposes, homologating estrogen therapy with natural products in order to mitigate vasomotor symptoms (hot flashes). It can include a wide variety of non-pharmaceutical products such as, but not limited to, vitamins, minerals, proteins, amino acids, traditional medicine preparations, herbal extracts, essential fatty acids, prebiotics, enzymes and metabolites (Burke L and Deakin V. 2006) In recent years, the increasing number of dietary supplements offered via the Internet and by e-mail has been of concern to health authorities because, In such circumstances, the quality of the products purchased cannot be guaranteed. The Decision No. 4980/2005 of the ANMAT sets the ethical guidelines on product advertising. It should be clarified that, in order for a dietary supplement to be marketed in the country, it must have a registration (RNPA: National Registry of Food Products) granted by the corresponding health authority.



One of the main objectives of ANMAT is to promote food safety. To achieve this, it carries out actions that help prevent, detect and manage the risks transmitted by them. Food surveillance is used to detect problems with packaged foods, dietary supplements, food contact materials and packaging.

CONCLUSION

Health professionals must be vigilant and it is necessary to warn the community about the fact that many of these products are not properly registered, so they cannot be identified in a reliable and clear way with regard to their preparation, packaging and conservation. For this reason, and taking into account the risks involved in health, products of unknown origin that do not offer guarantees of safety and sanitary suitability should not be consumed.

The composition of L-arginine establishes the physiological basis for the production of Nitric Oxide (NO) and its impact on the endothelium, the vascular reactivity that characterized this case.



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