



Casos Clínicos

■ Dos casos de calambres nocturnos en las piernas que mejoraron con ingesta suplementaria de remolacha (*Beta vulgaris rubra*) en la dieta

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Eduardo Romero-Vecchione

MD, PhD
Arterial Hypertension Outpatient
Consult, JM Vargas School of Medicine.
Central University of Venezuela.
Caracas

Dos casos de calambres nocturnos en las piernas que mejoraron con ingesta suplementaria de remolacha (*Beta vulgaris rubra*) en la dieta

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Alicia Martin-Hirsel

MD Gyn
Gyn Obstetrics Ultrasonographer
Kansas City area, Missouri. USA.

Los pacientes con calambres nocturnos de las piernas se quejan del dolor intenso que esta patología produce, con alteración del ritmo de sueño y deterioro de la calidad de vida. Describiremos dos casos de pacientes con calambres nocturnos de las piernas que mejoraron notablemente sus síntomas después de comer remolacha (*Beta vulgaris rubra*) cocida al vapor, diariamente. Ambos casos tienen en común la disfunción endotelial que se observa durante la posmenopausia (casi 1) y en la enfermedad hipertensiva. La remolacha contiene grandes cantidades de nitratos (NO₃⁻) y su conversión a nitritos (NO₂) y a óxido nítrico ((ON) puede aumentar el aporte de sangre a los músculos estriados y mejorar los calambres nocturnos. Ambos pacientes cumplían con los criterios de calambres nocturnos de las piernas de la Academia Americana de Medicina del Sueño. La terapia complementaria consistió de una taza (aproximadamente 120 g) de remolacha cocida al vapor, ingerida durante la comida de la noche, por cuatro semanas, con evaluaciones en las semanas 2 y 4. La intensidad del dolor por los calambres nocturnos, evaluada con la escala visual analógica 0- 10 cm, disminuyó 50-100 % al final de las semanas 2 y 4 de tratamiento, respectivamente, la frecuencia de los calambres disminuyó de manera similar y la calidad del sueño mejoró concomitantemente. No se observó hipotensión ni algún otro efecto adverso con la administración de la remolacha. La ingesta de remolacha cocida durante la cena es aparentemente un suplemento dietético eficaz y seguro para el alivio de los calambres nocturnos de las piernas en pacientes posmenopáusicas y en hipertensos. No obstante, es necesario un estudio controlado y aleatorizado con remolacha en forma cocida, en jugo, o deshidratada en cápsulas, para establecer con precisión el porcentaje de eficacia de este suplemento dietético en el control de los calambres nocturnos de las piernas.

María Eugenia Acosta

Pharm PhD
Dept. Toxicology, School of Pharmacy,
Central University of Venezuela.
Caracas. Venezuela

Palabras Claves: *Beta vulgaris rubra*, nitratos

Title

Two clinical cases of nocturnal leg cramps that improved with supplementary beetroot (*Beta vulgaris rubra*) intake in the diet

Abstract

Nocturnal leg cramps is a pathology that deteriorates quality of life in patients because it can produce intense pain that disrupts their sleep pattern. Nocturnal leg cramps are more frequent after 60 years of age and slightly more frequent in women. As its pathophysiology is not completely understood, they are classified as idiopathic 1. On the other hand, differential diagnosis should be made because some neurological pathologies can induce leg cramps, and

several prescription medicines can also cause them as an adverse event ². Patients with idiopathic nocturnal leg cramps have been treated with many prescription medicines; in some cases showing moderate control of symptoms, lack of efficacy or dangerous adverse events; the list includes quinine ^{3, 4, 5}, gabapentin ⁶, naphthidrofuryl ^{7, 8}, and over the counter products such as magnesium ^{9, 10}, vitamin E ¹¹, vitamin B ¹² and vitamin D with calcium ¹³. Patients also have received treatment with physical therapy as leg stretching exercises before sleeping ^{14, 15}, leg muscles electrical stimulation ^{16, 17}, leg warming with heating pads or massages; all of them demonstrating to be useless or showing poor results ¹⁸.

Key Word

leg cramps, beetroot, *Beta vulgaris rubra*, nitrates

Introduction

Nocturnal leg cramps is a pathology that deteriorates quality of life in patients because it can produce intense pain that disrupts their sleep pattern. Nocturnal leg cramps are more frequent after 60 years of age and slightly more frequent in women. As its pathophysiology is not completely understood, they are classified as idiopathic ¹. On the other hand, differential diagnosis should be made because some neurological pathologies can induce leg cramps, and several prescription medicines can also cause them as an adverse event ².

Patients with idiopathic nocturnal leg cramps have been treated with many prescription medicines; in some cases showing moderate control of symptoms, lack of efficacy or dangerous adverse events; the list includes quinine ^{3, 4, 5}, gabapentin ⁶, naphthidrofuryl ^{7, 8}, and over the counter products such as magnesium ^{9, 10}, vitamin E ¹¹, vitamin B ¹² and vitamin D with calcium ¹³. Patients also have received treatment with physical therapy as leg stretching exercises before sleeping ^{14, 15}, leg muscles electrical stimulation ^{16, 17}, leg warming with heating pads or massages; all of them demonstrating to be useless or showing poor results ¹⁸.

Patient selection and methods

The diagnostic criteria of nocturnal leg cramps established by the American Academy of Sleep Medicine ¹⁹ was applied for clinical case selection. We will describe two clinical cases of patients suffering nocturnal leg cramps that improved after receiving supplementary daily treatment with cooked beetroot (*Beta vulgaris rubra*) in their regular night meals, during four weeks. We hypothesized that beetroot dietary treatment, because of its high nitrate (NO₃⁻) content can be transformed to nitrite (NO₂⁻) and therefore to nitric oxide (ON) that in turn, can induce vasodilation ²⁰ and better oxygen supply to the lower limbs striated muscles ²¹ to provide leg cramp relief. The clinical cases we shall describe all have in common the endothelial dysfunction observed both in postmenopause (case 1) ²² and in arterial hypertensive disease (case 2) ²³. Pain intensity perception during leg cramp episodes were evaluated with the analogic 0 – 10 cm analogic visual scale.

Treatment. Supplementary therapy with steam-cooked beetroot (*Beta vulgaris rubra*) was prescribed to prevent nocturnal legs cramps, in a cup daily amount (approximately 120 grams) with dinner meals, during four weeks and evaluations at the end of weeks 2 and 4.

Clinical case 1 (AM)

She was a postmenopausal, overweight, 71 year old patient that during her routine cardiovascular evaluation complained about painful nocturnal leg cramps in both legs, predominantly in the right side, 3-4 times per week and of 5-20 min duration. She found relief after standing, stretching and walking a few steps. Clinical history: right hip osteoarthritis, osteopenia. Medications received: magnesium chloride 71.5 mg/ daily, vitamin C 500 mg every other day and leg warming with a heating pad during the night. She also received calcium chloride 300 mg plus vitamin D 200 IU on a daily basis for osteoporosis prevention and naproxen 250 mg twice daily in case of hip joint pain.

Physical examination. Systolic blood pressure (SBP) and diastolic blood pressure (DBP): 125/78 mm Hg, heart rate: 82 beats/min, respiratory frequency: 14 breaths/min. Body mass index (BMI): 29.5 kg/m². S1 and S2 heart sounds were normal without murmurs. Lungs auscultation: no wheezes, rhonchi or rales. Peripheral arteries pulses: normal. Abdomen: soft, non-tender, without organomegaly. Osteotendinous reflexes were normal, touch and pain skin sensitivity unaltered. Routine hematological laboratory tests were within normal range. Resting ECG was normal and thoracic X-ray exam only showed osteopenic changes. Results. Basal pain perception intensity was 8-10 points in the 0-10 visual analog scale. At the end of the second week of beetroot intake, the score diminished to 5 and also the cramp frequency. At the end of week 4, painful cramps disappeared completely; blood pressure was 132/80 mm Hg and heart rate 68 beats/min.

Clinical case 2 (CA)

He was a male, 84 year old patient with stage 2 arterial hypertension²⁴, controlled with valsartan 80 mg/day, hydrochlorothiazide 25 mg/day, carvedilol 6,25 mg/day and spironolactone 25 mg/day for blood pressure control. Basal SBP/DBP: 134/73 mm Hg, heart rate: 60 beats/min. Respiratory rate: 13 breaths/min. BMI: 25.30 kg/m². He had been suffering nocturnal and early morning painful legs cramps for several months. Pain intensity score was 8 in a 0-10 analogical visual scale, daily or every other day in frequency, relieved after sitting or standing for some minutes. Preventive cramps treatment with 71.5 mg/day magnesium capsules that he received were unsuccessful. Heart auscultation: Normal S1 and S2 heart sounds without murmurs. Lungs auscultation: No wheezes, rhonchus or rales. Abdomen: soft, non-tender, no visceromegaly. Peripheral arterial pulses were unaltered. Legs with grade I pretibial edema. Plasma electrolytes (mmol/L): Na⁺137, K⁺ 3.9, Cl⁻ 103 and Mg⁺⁺ 0.85. Resting ECG: sinus rhythm with premature atrial complexes. Thorax X-ray: No remarkable findings. His routine blood tests were within normal limits.

Results. At the end of weeks 2 and 4 of supplementary steam-cooked beetroot (*Beta vulgaris rubra*) administration, in a cup daily amount (approximately 120 grams) with dinner meals, during four weeks; the intensity of leg cramp pain decreased to score 3 in the 0-10 visual analog scale, and leg cramps frequency was reduced to one episode per week. SBP/DBP at the end of week 4 was 127/82 mm Hg, heart rate: 58 beats/min, respiratory rate: 16 breaths/min. ECG: premature atrial complexes did not change related to basal findings.

Discussion

Beetroot is an inorganic nitrate-rich vegetable and its NO₃⁻ content may be transformed *in vivo* to NO₂⁻ and then to nitric oxide by the activity of many NO₂⁻ reductases present in organ tissues,²⁵ and also through non-enzymatic reduction²⁶. It has been demonstrated that beetroot juice can increase forearm reactive vasodilation, most probably through beetroot generated nitric oxide²⁰ that can improve organs and muscle blood perfusion.

In the two clinical cases we report, the nitrate content of cooked beetroot was not analyzed; however, it has been demonstrated that nitrate concentration does not change with cooking and its bioavailability in its crude or cooked form is 100 %²⁷; in the referred bioavailability study, 500 mg of intravenously administered sodium nitrate were compared to 300 g of ingested cooked beetroot; then we can roughly estimate that NO₃⁻ content in 120 grams (one cup) of cooked beetroot is approximately 200 mg. Beetroot juice used in human studies differs in a broad range of NO₃⁻ content, between 7.5 mmol/250 mL to 23 mmol/ 500 mL²⁸.

Considering blood pressure changes, beetroot juice, when administered to normotensive, 57-71 years old healthy volunteers, acutely increased plasma NO_3^- and NO_2^- , reaching the maximum in 3 hours and returning to basal values in 6 hours' time, accompanied by an acute systolic and diastolic blood pressure decrease of 7.9 and 5.7 mm Hg respectively²⁹. In hypertensive patients, a similar amount of beetroot juice administered during 4 weeks, demonstrated to reduce SBP, DBP and arterial stiffness³⁰. The cooked form of beetroot we administered during a 4 week period did not diminish blood pressure, neither in the postmenopausal nor the hypertensive patient; and as we did not measure plasma nitrates and nitrites in them, it is unknown if this effect is related to lower plasma levels of both compounds. In relation to this finding, a similar result of no long-term hypotensive effect of beetroot juice administration has been reported in hypertensive³¹ patients.

In clinical case 1, a postmenopausal woman, she outstandingly improved her leg cramps after the daily beetroot intake, an effect possibly due to the supply of inorganic nitrates. It has been demonstrated that in the postmenopausal condition, the endothelial dysfunction these patients have is due to loss of the cardiovascular protective role exerted by estrogens²². This dysfunction can be restored by estrogen hormone replacement³², but estrogens cannot be used in leg cramp treatment because estrogen replacement therapy can induce leg cramps as an adverse event, as it has been observed in women treated with these hormones^{33, 34}. In our postmenopausal patient, it is possible that the endothelial dysfunction resulted in a lower nitric oxide production by the endothelial lining of her vessels, with decreased vasodilation and lower oxygen delivery to striated muscles that contributes to the nocturnal leg cramp symptoms; a condition apparently corrected by the nitrates load absorbed after nightly beetroot intake. On the other hand, it is unlikely that the anti-inflammatory compounds betalaines of beetroot are responsible for the improvement of nocturnal leg cramps, because in clinical experiments done with nitrate-free *Beta vulgaris rubra* it does not induce any vasodilatory effect²⁹, furthermore, as leg cramps are not an inflammatory disease, betalaines are hardly the explanation of the observed therapeutic action. It is interesting that neobetanines contained in beetroot have demonstrated to reduce glucose absorption and insulinemia³⁵; it remains to be explored if this effect can have some influence in its anti-cramp action.

In clinical case 2, a hypertensive patient, the nitric oxide production by endothelial cells has been demonstrated to be reduced in hypertensive disease, due to the lower activity of blood vessels nitric oxide synthase²³. Blood pressure figures in this patient remained within normal range after four weeks of receiving beetroot in his diet. In relation to this finding, a similar result was found in a randomized controlled trial in which long term administration of beetroot juice did not diminish PAS and PAD in hypertensive patients, although plasma nitrites increased by 3 and 7 fold in saliva and intestines respectively, after beetroot juice administration³¹. Actually, beetroot is devoid of antihypertensive properties; and hypertensive patients receiving supplementary beetroot treatment must adhere to the treatment prescribed by their physician, based on acknowledged treatment guidelines²⁴; as was the case in this patient. We think that plasma transitory nitrate increases produced by beetroot intake in dinnertime, promoted striated muscles vasodilation with better blood perfusion and oxygenation that reduced nocturnal leg muscle cramp symptoms. A similar effect of beetroot was observed in patients with peripheral artery disease in whom the nitrates absorbed from this vegetable increased exercise performance and gastrocnemius muscle oxygen extraction²⁸.

Basal plasma electrolytes concentration were within normal range in this patient receiving combined treatment with diuretics, an angiotensin II blocking agent, a beta-alpha blocker and spironolactone; all indicating that administered doses of these antihypertensive agents were within safe and efficacious limits. Regarding this finding, it is worth mentioning that in long distance runners, leg cramps occur without changes in plasma electrolytes at the end of strenuous physical effort, so, potassium and magnesium plasma ions do not seem to play a role, at least in these kind of cramps³⁶.

As formerly mentioned, the betalaine content of beetroot, having anti-inflammatory and antioxidant properties^{37, 38} could have some role in its anti-cramp action; however, as this pathology is not of inflammatory in origin, it is quite unlikely that betalaines are responsible for the observed improvement in nocturnal cramps; on the other hand, non-steroidal anti-inflammatory (NSAID) agents do not seem to be good for nocturnal leg cramp relief because naproxen, a NSAID compound has been associated to nocturnal cramp symptoms as an adverse event³³.

We acknowledge there are several limitations in the two clinical cases presented here. The self-report of symptoms improvement, pain intensity and cramp frequency, would be subjected to bias of up- or underestimation and an objective neurophysiological or leg activity measurement would

provide a better estimate of symptom changes. Another limitation is that a nitrate plasma assay was not done before and after the beetroot supplementary treatment, to correlate plasma levels with clinical efficacy. Our observations require a randomized controlled trial in order to know, more precisely, the percent efficacy and probable mechanism of action of beetroot in nocturnal idiopathic leg cramps; in its cooked, dehydrated or juice form.

In conclusion, the beetroot supplementary diet seems to be a self-prepared, natural, safe, and efficacious treatment for idiopathic nocturnal leg cramp control in postmenopausal and hypertensive patients.

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