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Systematic review

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Ozonetherapy in the treatment of Low Back Pain associated to Lumbar Disk Herniation – A systematic review

A utilização da Ozonioterapia no tratamento da lombalgia associada à hérnia de disco lombar – Uma Revisão Sistemática

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RESUMO | INTRODUÇÃO: Ozonioterapia é uma ferramenta terapêutica utilizada para o tratamento de dor lombar associada a hérnia de disco lombar. Objetivo: o objetivo dessa revisão sistemática foi ratificar a relevância desse tratamento na prática clínica e enfatizar sua possível utilização na fisioterapia. **MATERIAIS E MÉTODOS:** PRISMA e PICOS foram utilizados para analisar o desenho dos manuscritos. A seleção dos manuscritos foi realizada através de busca nas bases de dados PUBMED, Periódicos CAPES e Scielo. Quatro ensaios clínicos foram selecionados de acordo com os critérios de inclusão criado para essa estudo. **RESULTADOS:** Todos os autores confirmaram a eficiência da ozonioterapia como método terapêutico na reversão da sintomatologia álgica de pacientes com hérnia de disco lombar. Ozonioterapia associada ao tratamento fisioterapêutico pode contribuir no alívio da dor associada a dor lombar influenciando na qualidade de vida dos pacientes. **CONCLUSÃO:** Ozonioterapia é uma opção terapêutica efetiva para pacientes com dor lombar associada a hérnia de disco lombar.

PALAVRAS-CHAVE: Ozonioterapia. Dor lombar. Fisioterapia.

ABSTRACT | INTRODUCTION: Ozonetherapy is a therapeutic tool used in the treatment of low back pain associated to herniation of lumbar disks. **OBJECTIVE:** The objective of this systematic review was to ratify the relevance of this treatment in clinical practice, besides emphasizing its possible utilization on physiotherapy. **MATERIALS AND METHODS:** PRISMA and PICOS were used to analyze the manuscripts design. Manuscripts selection was made by a research in the PUBMED, Periódicos CAPES and Scielo databases. Four clinical trials were selected according to the inclusion criterias designer for the study. **RESULTS:** All the authors confirmed the efficiency of ozonetherapy as a therapeutic method in reversing the algic symptomatology of pacients whit lumbar disc herniation. Ozonetherapy associated to the physiotherapeutic treatment can contribute pain relief related to low back pain by influencing the improvement in patients quality of life. **CONCLUSION:** Ozonetherapy is an effective therapeutic option for patients whit low back pain associated whit lumbar disk herniation.

KEYWORDS: Ozonetherapy. Low back pain. Physiotherapy.

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Introduction

Ozonetherapy is a treatment performed by doctors and dentists that uses the oxidative potential of ozone. It has anti-inflammatory, analgesic and antioxidant properties, and involves a gaseous mixture of oxygen and ozone[1,2]. Its topical, subcutaneous, venous or rectal use is well documented, and it will generate local and systemic effects[2]. It has been used as a potent antiseptic in the treatment of infectious diseases; it also acts in the activation of the immune system, being able to reverse cases of immunosuppression; improves O_2 delivery to the tissue and the release of growth factors in case of vascular abnormalities and it also decreases pain and edema in osteoarticular disorders, with consequent increase in mobility[3].

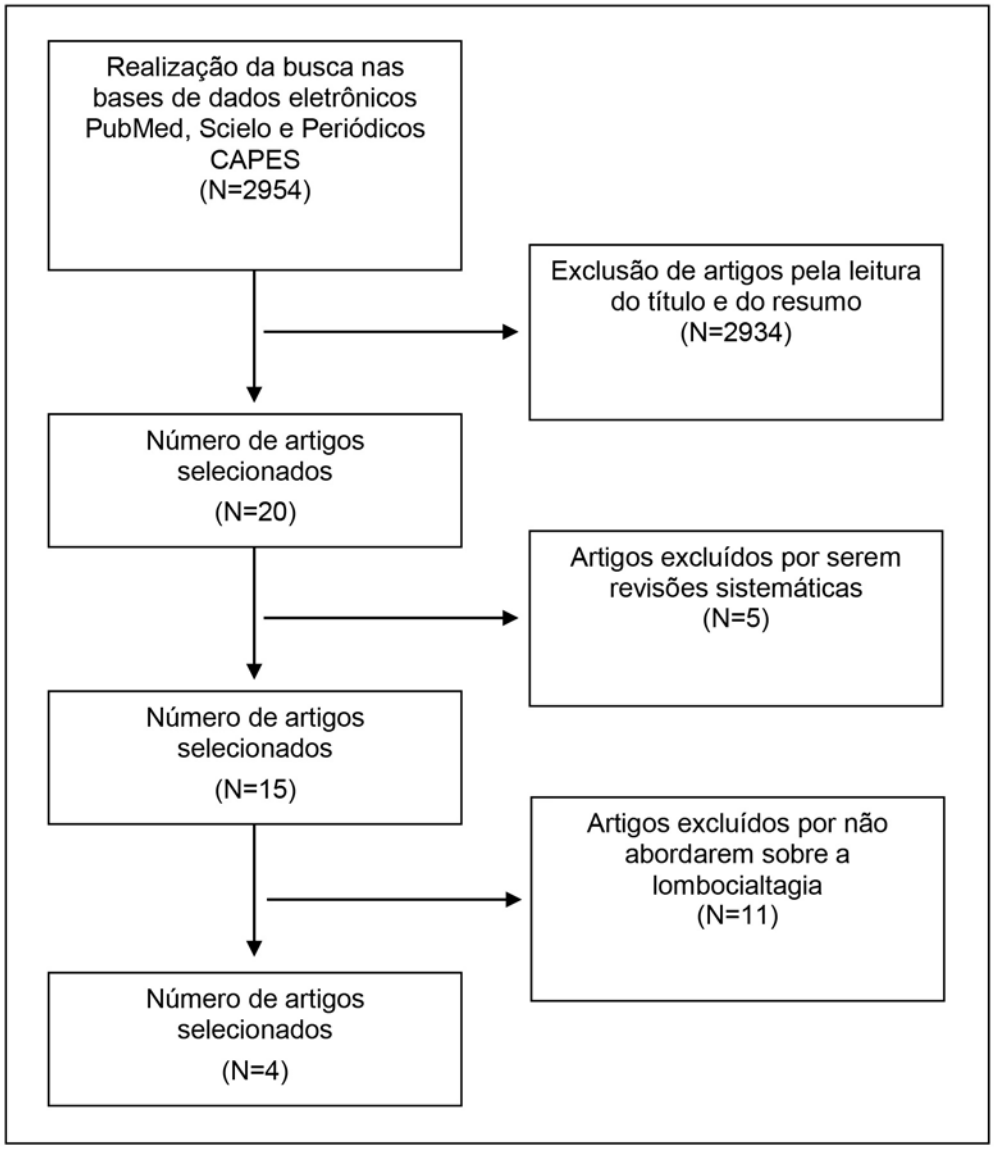
Among the indications for the use of ozonetherapy it is also included low back pain, which is characterized as a discomfort or painful sensation limited to the low back and buttocks, extending at most to the thigh. When the pain is radiated to the lower limbs, it is called sciatica, which means a pain along the sciatic nerve. If a patient experiences lumbar pain associated with pain radiating down to the lower limbs, this pain is called low back pain[2,4]. The main etiologic factors of low back pain are disc protrusions and hernias, vertebral canal stenosis, post-laminectomy syndrome and piriformis syndrome, which make the patient to experiment hyperalgesia, hyperpathia and allodynia. Such symptoms difficult to carry out everyday activities and may lead to patient incapacity to execute all of these activities[4].

The Ozonetherapy is a technique that has been, along with other conservative treatments and percutaneous techniques, an important tool for avoiding surgical procedures such as those used in the treatment of disc herniation in patients who develop low back pain. Prevents complications related to the post-surgical period[5], as it is a minimally invasive technique[1]. The objective of this systematic review is to ratify the relevance of ozonetherapy as an effective therapeutic tool for the treatment of low back pain. It will be emphasized its possible use in physiotherapeutic practice, mainly for the management of low back pain, originated from disc herniation.

Materials and Methods

PRISMA methodology was used as the basis for this systematic literature review. The databases from PUBMED, Periódicos CAPES and SciELO were searched for clinical trials characterized as randomized or not, written in English and Portuguese, published between 2007 and 2017 years. The thematic axis that guided this searching was the use of ozonetherapy in the treatment of low back pain. Twenty articles were selected, but only 4 were included according inclusion criteria. It was made an individual description of each one using PICOS flow chart (population, intervention, comparison, outcome and type of study)[6], (Figure 1).

Figure 1. PRISMA flowchart for the article searching to systematic review, the relevance of ozonetherapy as an effective therapeutic tool for the treatment of low back pain jun/2017



1.1. Searching strategy

The uniterms used were "ozonetherapy", "low back pain" and "physiotherapy". At least two authors went after the bibliographic research individually and identically, whose search results were later unified. In case there was any disagreement between the two authors regarding the inclusion of a specific manuscript, a third author would check the article in order to find a common sense.

1.2. Participants kind

The participants of the study should be adults aged at least 18 years old with low back pain reported for more than a month caused by spinal cord compression by disc herniation and who had undergone treatment with ozonetherapy.

1.3. Intervention type

The intervention type studied was the intradiscal application of therapeutic ozone guided by ultrasonography or tomography, associated or not to the use of steroids. There was also the presence of control groups, in which the treatment with ozone was simulated.

1.4. Measures types of results

The main measures evaluated were the pain sensation, life quality, posttreatment mobility, muscle capacity and intervertebral disc volume.

1.5. Side effects and adverse events

The side effects and adverse events reported by patients during the studies were analyzed and cataloged.

Results

The study made by Paoloni et al (2009), a sample of fifty-four patients with acute low back pain caused by disc herniation was checked. Fifty-eight patients were part of the sample of Lu et al study (2010), all of them with prominent lumbar disc hernia. This same condition was described by Fernández et al (2012), who evaluated 33 patients. In the study made by Lehnert et al (2012) the sample was broader and included a total of 283 patients submitted to ozone treatment for lumbar disc herniation. The total population covered by the four clinical studies was 428 individuals.

Each of the studies reported the effect of ozone injections applied at specific sites in the lumbar region, and only one of the manuscripts included the cervical region. In the study made by Paoloni et al (2009), fifteen intramuscular applications of a mixture of O2O3 (20 mL) were performed in the paravertebral lumbar muscles bilaterally[7]. The application of ozone in the study made by Lu et al (2010) was performed through intradiscal percutaneous injection, trough the posterolateral lateral margin of the facet joint. In this study, all patients received two injections of ozone within five days (8). Fernández et al (2012) performed applications twice a week for a total of twenty sessions in each patient. The ozone volume used was 10 mL in the lumbar disc hernia puncture and 5 mL for cervical disc herniation. The manipulation route was paravertebral, and ozone was injected at the points located in the paravertebral muscle, corresponding to the segment of the herniated disc, 2 cm calculated bilaterally to the spinous process[9].

In the study conducted by Lehnert et al (2012) all patients received an identical intradiscal injection of 3 mL of ozone and a periganglionar dose of 7 mL[10].

The cataloged authors analyzed different variables modulated by ozonetherapy (Graph 1). Paoloni et al. (2009) evaluated the patients considering the pain perception by the Visual Analogue Scale (VAS) and the inability related to acute low back pain, through the Backill questionnaire, which included 27 functional questions and 4 questions that qualified the type of pain, also observing the use of anti-inflammatory drugs at the end of the treatment. In GE (study group), 61% of the patients did not report any pain. During the course of the evaluation period, patients in the SG had a mean lower pain score and a significant improvement in the disability related to acute low back pain compared to the controls. About the drugs, patients in the GE had a shorter number of days using non-steroidal anti-inflammatory drugs, which lasted up to two weeks after the end of treatment[7].

Lu et al (2010) evaluated the efficacy of the treatment using the modified MacNab criteria. They rated the results as: Excellent (return to work, but with occasional low back pain or leg pain, no need of analgesics and no physical signs of nerve root damage, and good physical fitness); Good / Fair (general working ability, with intermittent mild pain or radiating pain, no need of analgesics and no physical signs of nerve root injury, and good physical fitness); or Bad (inability to work, with constant pain, the need of analgesics and limited physical activity with physical signs of nerve root damage). The authors found that in 63.8% of the cases the result was excellent, 27.6% was good / fair and 8.6% of the results was considered bad[8].

Fernández et al. (2012) considered different variables, such as pain intensity, redox markers as indicators of oxidative stress, plasma levels of phospholipase A (PLA), fructolysin, malondialdehyde (MDA), peroxidation potential (PP), total hydroperoxides), and advanced oxidation protein products (AOPPs) as lesion markers[9]. They concluded that the treatment with ozone could reduce pain and osteotendinous reflex in the patient, even though the mechanisms of this interaction were not fully verified by the authors. Ozone also restored the

REDOX balance. It reduced the oxidative process in the region where it was administered and avoided the pathological cascade that induces the protein injury of the intervertebral discs. The main variable checked by Lehnert et al (2012) was disc volume, measured before and after the intervention, Figure 2. The authors found that the volume of the herniated disc was reduced in 96.1% of the cases after treatment with ozone[10].

All studies concluded that ozonetherapy was effective for the treatment of lumbar disc herniation. Most of them had as main objective improving the patients' pain symptomatology, considering that this is a factor that limits the patients daily and work activities, Table 1/ Figure 2.

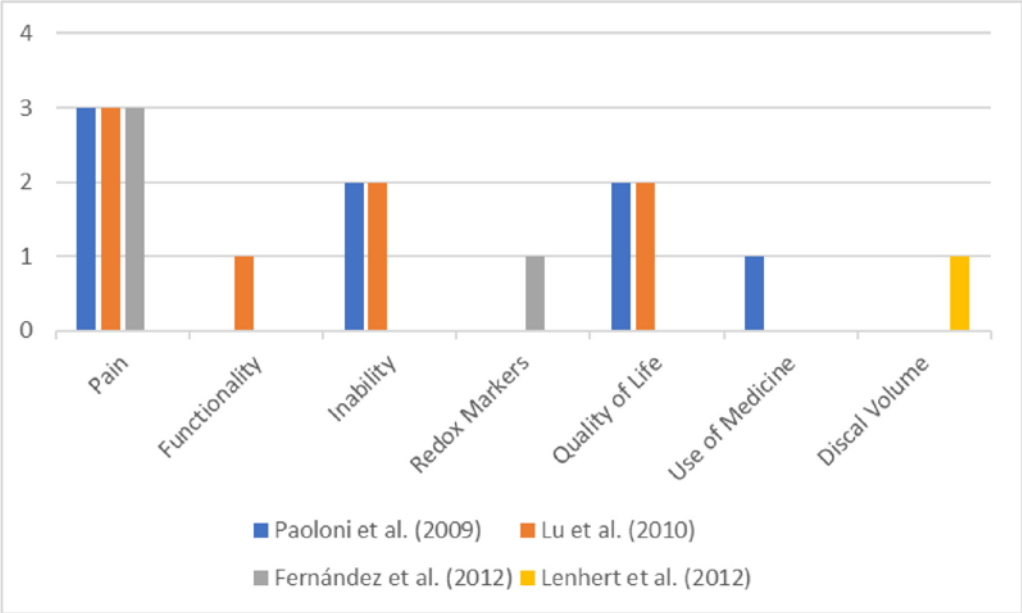
Table 1. Data of the selected manuscripts: Ozonetherapy; Low Back Pain; Lumbar Disk, jun/2017 (to be continued)

TITLE AND AUTHORS	STUDY TYPE AND POPULATION	DISCHARGE	RESULTS
Intramuscular Oxygen-Ozone Therapy in the Treatment of Acute Back Pain with Lumbar Disc Herniation: A Multicenter, Randomized, Double Blind, Clinical Trial of Active and Simulated Lumbar Paravertebral. **Paoloni, et al (2009). Spine. Impact factor: 2439. Qualis: A2.**	Multicenter Study Randomized, double-blind - cohort simulation of 60 patients of both sexes with acute low back pain caused by lumbar disc herniation.	Reduction of pain, functional disability and analgesic ingestion.	In the Study Group, 61% of the cases reported absence of pain, versus 33% of the Control Group. Patients in the Study Group had a mean lower pain score and a significant improvement in disability related to acute low back pain when compared to Control Group subjects. Patients in the Study Group had a shorter number of days of non-steroidal anti-inflammatory drug use up to two weeks after the end of treatment.
Treatment of large lumbar disc herniation with percutaneous ozone injection via the posterior-lateral route and inner margin of the facet joint **Lu, et al (2010). World Journal of Radiology. Impact factor: not available. Qualis: B4.**	Randomized, non-blind and uncontrolled clinical trial - Percutaneous ozone punctures in 58 patients with large disc herniation.	Reduction of pain, improvement in the ability to work performance tasks and decrease the use of analgesics.	In 63.8% of the cases, the result was excellent, 27.6% was good / fair and for only 8.6%, the result was considered bad.
Ozone oxidative post-conditioning reduces oxidative protein damage in patients with disc hernia **Fernández, et al (2013). Neurological Research. Impact factor: 1376. Qualis: B1**	Non-Randomized, uncontrolled clinical trial with 33 patients separately into two groups according to their pathologies, 16 patients with intervertebral disc protrusion and 17 patients with disc prolapse.	Regulation of the redox state, protection against damage by oxidative proteins, blockade of the progression of oxidative damage.	In 73% of patients, treatment with intradiscal ozone improved or reestablished the values of the redox markers analyzed in the study, including pain and protection markers. 73% of patients also reduced their pain levels to 41.9%. Were also observed the increasing muscle strength and a significant decrease in the osteotendinous reflex.

Table 1. Data of the selected manuscripts: Ozonetherapy; Low Back Pain; Lumbar Disk, jun/2017 (conclusion)

TITLE AND AUTHORS	STUDY TYPE AND POPULATION	DISCHARGE	RESULTS
Analysis of Disk Volume before and after CT-guided intradiscal and Periganglionic Ozone–Oxygen injection for the Treatment of Lumbar Disk herniation **Lehnert, et al (2012). Journal of Vascular and Interventional Radiology. Impact factor: 2.780. Qualis: B1**	Prospective Clinical Trial with a /population of 238 patients of both sexes with subacute or chronic pain due to disc herniation that did not respond to conservative treatments.	Reduction of herniated disc volume.	There was a reduction of the herniated disc volume in 96.1% of the cases after treatment with ozone.

Graphic 1. Variables evaluated in patients submitted to ozonetherapy in the selected studies. Ozonetherapy; Low Back Pain; Lumbar Disk, jun/2017



Discussion

Ozonetherapy is based on the application of a mixture of oxygen and ozone, which has been used for therapeutic purposes for many years. More recent studies that have sought to better understand the performance of ozone have concluded that its use, when done in a brief and calculated way, can generate an oxidative stress capable of correcting a permanent imbalance caused by acute or chronic oxidative damage. Treatment with ozone may increase the activity of some antioxidant enzymes, which can neutralize the excessive formation of reactive oxygen species. In this way, it is possible to induce adaptation to stress and promote important therapeutic effects[3]. Ozone therapy is considered a minimally invasive and safe technique, which presents few complications[11].

Choosing a suitable treatment for the herniated disk is a great challenge, due to the need to consider several aspects that allow to identify the magnitude of the problem, such as the location of the disc herniation, its size and the possible compression of structures. These difficulties in the search for the ideal treatment, the concerns with the surplus of surgeries performed unnecessarily, the fear of opting for conservative therapeutic practices, cause that studies are made out with the objective of identifying safe and effective alternatives for the treatment of this condition, minimally invasive techniques such as ozonetherapy[12].

One of the main symptoms associated with lumbar disc herniation is low back pain, which arise with nerve compression caused by the herniated disc region[2]. Several studies have shown that treatment with ozone generates positive effects in reducing this type of pain[7-10].

Depending on the effects to be achieved with ozonetherapy, including local, regional or systemic, a specific route of application of the ozone and oxygen mixture is used. This application can be topically, subcutaneously, intra-articular, muscular, venous and / or rectal. Except for the topical, in the other routes the gas mixture of O_3 / O_2 or ozonized blood is injected or insufflated. In the treatment of spinal anesthesia, the application can be done by intradiscal, subcutaneous regional, paravertebral supralaminar muscle, rectal insufflation and through muscular or venous autohemotherapy. The most recommended route regarding the treatment of disc herniation is the intradiscal route[2].

The four manuscripts analyzed in this study evaluated the application of ozone through different routes. In the study made by Paoloni et al (2009) the applications were in the paravertebral lumbar muscles bilaterally, without the use of anesthesia[7]. Lu et al. (2010) used the intradiscal route, posterolateral to the vertebrae and the internal margin of the facet joint[8]. Fernández et al (2012) used paravertebral route and the ozone was injected at the points located in the paravertebral muscle corresponding to the segment of the herniated disc[9]. And in the study conducted by Lehnert et al (2012) the patients received an intradiscal injection and a periganglionar injection, accompanied by an anesthetic agent application[10].

The four manuscripts concluded that ozonetherapy is an effective therapeutic technique for the treatment of lumbar disc lesions caused by lumbar disc herniation. In addition, the conclusions of two of them (Fernández et al (2012) and Lehnert et al (2012)) confirmed that ozone is also capable of inducing a decrease in the size of disc herniation, through the adaptations generated to oxidative stress.

Other researchers have proposed studying the action of ozonetherapy in the treatment of lumbar disc herniation. Buric et al. (2005) evaluated thirty patients with uncontained lumbar disc herniation, and the ozone was applied by the intradiscal route. They used as parameters of analysis the volume of the disc, the pain and the functionality of the patients. About 90% showed significant improvement in pain and function with respect to the morphological alterations of the herniated disc, and in 50% of them the disc volume decrease was significant[13].

In his Study, Magalhães el at (2012 systematic review and meta-analysis, were evaluated eight observational studies and four randomized trials. In the studies analyzed, the ozone applications were performed by the intradiscal, paravertebral and periforaminal routes. They concluded that ozone therapy appears to produce positive results and is a method that can be considered as an option

to treat lumbar disc herniation related to lumbar disc herniation that did not respond to conservative treatment[14].

Physiotherapy has in its practice to see the patient well beyond their physical disability, seeks to identify the functional disabilities presented by the individual, and how these impacts on the accomplishment of basic activities of daily living and restrictions on social participation. It searches the development of its evaluation and intervention activities, considering a specific functional profile for each individual. Therefore, Physiotherapy is important in the therapeutic action of pathologies that interfere with the performance of these functional activities, as well as low back pain caused by lumbar disc herniation[15].

In individuals with low back pain, it is common to have functional limitations of daily activities, in addition it restricts their participation in society (leisure, work, school). Treating this lumbar disc herniation and associated complications positively influences the quality of life and the functional gain on the part of these individuals, which is precisely what physiotherapy aims in its practice[16]. The studies analyzed demonstrate the positive effects of ozonetherapy in the treatment of lumbar disc herniation, with a significant decrease in low back pain. This information demonstrate that the use of ozone therapy associated with physiotherapeutic treatment could further contribute to the treatment efficacy by influencing the improvement of the quality of life of individuals with this disorder.

Even with evidence on the effectiveness of ozone treatment, its practice is still not regulated and authorized in Brazil, and there are many discussions about the proper use of the method and about which health professionals are trained and able to use the resource. According to the Brazilian Association of Ozonetherapy (ABOZ), in several Eastern European countries, besides countries like Cuba, Egypt, Israel, Australia and thirteen US states, the medical use of ozone is already regulated and practiced by doctors and dentists[17]. Because it is an invasive treatment, ozonetherapy is practiced exclusively by doctors and dentists. However, according to the veto carried out in 2016 on Law 12.842, dated July 10, 2013, piercing-cutting procedures with or without substance application are no longer exclusive to medical practice[18]. Thus, since that due to training and qualification, other health professionals could benefit their patients with this technique, like physiotherapists.

However, among the limitations detected during the development of this systematic review, the small number of studies available that obeyed the inclusion and exclusion criteria can be highlighted. Low methodological level of the articles was also observed, showing the need of better protocols of study in this area. All the included articles have a good number of participants, but none of them were applied to the Brazilian population.

Conclusion

The studies evaluated in this systematic review ratified the efficacy of ozonetherapy as part of the treatment for patients with low back pain. The use of ozone can be considered a promising tool for the control of pain in patients with chronic inflammatory processes associated with some pathologies.

Author contributions

Sampaio NSR participated in the data collection and analysis, and writing of the manuscript; Cruz LRO participated in the collection / analysis of the data and revision of the manuscript; Medrado AP participated in the study design, review of the manuscript and supervised the research.

Competing interests

No financial, legal or political competing interests with third parties (government, commercial, private foundation, etc.) were disclosed for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc.).

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