Journal of
Alzheimer's Disease & Parkinsonism

Tamae et al,. J Alzheimers Dis Parkinsonism 2020, 10:3

Research Article Open Access

Can the Associated Use of Negative Pressure and Laser Therapy Be A New and Efficient Treatment for Parkinson's Pain? A Comparative Study

Patrícia Eriko Tamae[1,2], Adriana Vital Dos Santos[1], Michelle Luise de Souza Simão[1,3], Ana Carolina Negraes Canelada[1], Kely Regina Zampieri[1,4], Tânia Vital Dos Santos[5], Antonio Eduardo de Aquino Junior[1,3]* and Vanderlei Salvador Bagnato[1,6]

[1]*São Carlos Institute of Physics, University of São Paulo, Brazil*

[2]*Centro Universitário Central Paulista/UNICEP-São Carlos, Brazil*

[3]*Clínica MultFISIO Brasil, Brazil*

[4]*LongeVida Physiotherapy Clinic, Brazil*

[5]*University Martin-Luther-Halle (Saale), Germany*

[6]*Hagler Institute for Advances Studies-Tamus, USA*

Abstract

Parkinson's disease is a chronic, progressive, neurodegenerative disease of the central nervous system, being the second most frequent movement disorder, affecting about 1% to 3% of the population aged over 60 years. Parkinson´s disease is characterized by three basic symptoms: Tremor, stiffness and bradykinesia. This study promotes the analysis of the combination of Laser Therapy with Vacuum Therapy which creates adequate conditions for a synergic effect of both together. 18 patients were selected, subjects with idiopathic Parkinson's Disease, diagnosed by a neurologist, of both genders, aged between 30 and 80 years, who use drugs to control Parkinson's disease and were classified according to reports of muscle pain and stiffness. The patients were divided into 3 groups (n=6): Experimental group (GE, n=6), control group 1 (GC1, n=6) and control group 2 (GC2, n=6). The analyses were realized in relation to visual analogue scale and quality of life. The results found point to a better effect for quality of life and pain through the synergistic action of therapies (Group Experimental). In conclusion, it is possible to affirm that the synergy of therapies (Laser and Vacuum Therapy) can improve the quality of life of the patient affected by Parkinson's disease.

Keywords: Parkinson's disease; Phototherapy; Vacuum; Negative pressure; Quality of life.

Introduction

Parkinson's disease is a chronic, progressive, neurodegenerative disease of the central nervous system, being the second most frequent movement disorder, affecting about 1% to 3% of the population aged over 60 years [1]. The cases of the disease that begin before the age of 40 are called early-onset parkinsonism [2]. Parkinsonism or idiopathic parkinsonian syndrome is demonstrated with four basic components: Muscle stiffness, tremor at rest, bradykinesia and postural instability (not caused by visual, vestibular, cerebellar or proprioceptive changes). Parkinson's disease has a devastating effect on its patients, especially if identified late, both in the physical-motor and psychosocial realms.

The clinical picture of this pathology, characterized mainly by involuntary movements, has been consistently associated with lesions on the compact part of the dark substance in the brain. Consequently, there is loss of adhesion to this region of the brain. These dopaminergic neurons, project to the striatum, where they are important for the control of the information processing from the Base Nucleus to the Thalamus and Motor Cortex. With dopamine depletion, there is inhibition of the direct pathway and activation of the indirect pathway, which stimulates the Internal Pale Globe and the Reticulated Dark Substance to produce the neurotransmitter acid gamma-aminobutyric acid (GABA). This inhibits the action of the thalamus. The inhibited thalamus does not produce the excitatory neurotransmitter glutamate (GLU) and there is a reduction in the activity of the motor areas of the Cerebral Cortex, pre-motor area and supplementary motor area. Such facts promote the triggering of the decrease in voluntary movements. There is also the loss of the cells of the peduncle-pontine nucleus, increasing its inhibition which disinhibits the reticulospinal and vestibulospinal pathways. This last fact produces an excessive contraction of the postural muscles, which are related to cholinergic deficits [3].

The muscle stiffness present in patients with Parkinson's disease is responsible for muscle tension centered mainly at the level of the spine and the root of the limbs [4]. Some studies suggest that musculoskeletal pain seems to be related to the presence of muscle stiffness and akinesia. Muscle stiffness typically affects the muscles of the neck, arm, para-spinal or posterior leg [5]. As the involvement of the flexor musculature is predominant, there is a change in posture that becomes curved, with anteroflexion of the trunk and semiflexion of the limbs, contributing to postural instability [6]. This one being responsible for most of the falls common in patients with Parkinson's disease [7,8]. The stress caused by sustained muscle contraction and muscle spasm can induce the release of substances that sensitize nociceptors and generate localized pain, which can cause circulatory deficits and nutritional impairment, as well as affect muscle functional performance [9]. Musculoskeletal pain is triggered by the activation of peripheral nociceptors that are sensitized by algiogenic substances including bradykinin, histamine, potassium ions, prostaglandins, serotonin, tissue acidosis (pH below 6.1) and substance P. In tissues, there is a cascade of events, called neurogenic inflammation, which consists of the attraction and activation of leukocytes, and the activation and fibroblasts and Schwann cells that, in turn, release algiogenic substances in the tissues that enhance the sensitization of nociceptors [10].

***Corresponding author:** Antonio Eduardo De Aquino Junior, São Carlos Institute of Physics, University of São Paulo, São Carlos, São Paulo, Brazil, Tel: +55-16991721127; E-mail: antonioaquino@ifsc.usp.br

Received May 03, 2020; **Accepted** May 21, 2020; **Published** May 28, 2020

Citation: Tamae PE, Santos AVD, Simão MLS, Canelada ACN, Zampieri KR, et al. (2020) Can the Associated Use of Negative Pressure and Laser Therapy Be A New and Efficient Treatment for Parkinson's Pain? A Comparative Study. J Alzheimers Dis Parkinsonism 10: 488.

Fundaments for a Theraputical Approach Involving Negative Pressure and Laser

Pain in muscle spasm results from ischemia, which is the result from vascular compression in stressed muscles. Increased energy consumption under ischemic conditions results in less nutrient input and imbalance between ATP demand and synthesis.

One of the resources used with anti-inflammatory and analgesic action is laser therapy. Laser therapy acts in the cellular energy metabolism, in the mitochondria respiratory chain, increasing energy synthesis (ATP) and enabling several therapeutic effects, including the reestablishment of the metabolic balance [11]. Among the benefits resulting from laser therapy some can be cited: The analgesic effect on bone, muscle and acute or chronic tendon injuries [12]. Besides, vasodilatation and micro vessel proliferation, with possible increase in the amount of oxygen in the tissues are also observed [13]. In addition, there seems to be the release of cytokines that will reduce the inflammatory reaction [14]. Some hypotheses explain the analgesic action of laser therapy: Modulation of inflammatory processes, release of endogenous opioids, alteration of excitation and nervous conduction of peripheral neurons and increased serotonin synthesis[15-18]. It is also believed that the Low Intensity Laser can generate a systemic effect as metabolic changes occur in areas distant from the irradiated site, due to the fact that laser therapy promotes vasodilatation and increased blood flow and the substances are released into the blood circulation [19].

On the other hand, to improve muscle function and metabolic conditions the use of negative pressure is well applied. Negative pressure normally brings circulation to the regions and it is done with the use of vacuum. Negative pressure provides an improvement in the quality of blood and blood circulation and, consequently, improves cellular metabolism, allowing greater oxygenation of tissues and detoxification of the body, with the elimination of metabolic remains and algiogenic substances. These physiological effects of vacuum therapy contribute to the improvement of pain, muscle relaxation and the balance of bodily functions [20]. It is important to elaborate and implement strategies to favor the performance of people with Parkinson's disease, in carrying out daily activities, even in the initial stages of the disease, allowing the maintenance of independence, reduction of functional decline and better quality of life [21].

The combination of Laser Therapy with vacuum therapy creates adequate conditions for a synergic effect of both together. While the vacuum brings the essential nutrients (blood and oxygenation) for improvement of metabolic activity, laser stimulates the bio-reaction amplifying the effects. In a recent study carried out by our group, we have verified an outstanding effect of the combined therapies in Parkinson patients [22].

However, the aim of this study is to verify whether the combined use of negative pressure and local laser therapy attenuates muscle pain and stiffness, improving the quality of life of patients with Parkinson's disease, this time applying the technique in a large number of patients.

Methodology

Approval and patients

This study was approved by the research ethics committee of Santa Casa de São Carlos, São Paulo, Brazil, under number CAAE 28065419.3.0000.8148. Were selected 18 patients, subjects with idiopathic Parkinson's disease, diagnosed by a neurologist, of both genders, aged between 30 and 80 years, who use drugs to control Parkinson's disease and were classified according to reports of muscle pain and stiffness. Volunteers who did not show symptoms of muscle pain and stiffness were excluded from the study, who were classified according to the degree of severity of the disease, in scores 2.5, 3, 4 and 5, as well as those who use drugs or substances that can have photosensitizing or analgesic and anti-inflammatory action, who are undergoing treatments with high-dose anticoagulants, pacemaker wearers, thrombosis, cancer, skin disorders. Patients were divided into 3 groups (n=6): Vacuum Laser (n=6), Laser Therapy (n=6) and Vacuum Therapy (n=6). To achieve the proposed objectives in this work, a longitudinal clinical study was carried out, consisting of 6 treatment sessions, twice a week, for 3 weeks.

Equipment

The Vacuum Laser equipment (MMO - São Carlos - SP - BRAZIL) uses the technique of vacuum-therapy through the uses of chambers of low pressure applied on the region to be treated, and simultaneously has Laser emitters operating in either red or infrared spectrum region (670 nm and 808 nm), composing a laser therapy. It consists of cabinet, hand piece and suction cups or chambers for low pressure application. Semiconductor lasers are located in the hand piece and penetrated to the cups, illuminating the region under low pressure. The suction cups have different sizes and are connected to the hand piece. The vacuum (negative pressure) is generated through a double piston vacuum pump, located in the interior. The system is presented in Figure 1.

Groups and protocols

The groups have included only the participants who are in the stages of 1.5 and 2 on the scale of Hoehn and Yarh, with stages between 0 and 5 [23]. To assess pain, the Visual Analogue Scale - VAS was used. It is an instrument used to check the patient's evolution during treatment and even at each visit, in a more reliable way, being an aid in measuring the individual's pain intensity. To use VAS, the individual will be asked about their degree of pain, with 0 meaning total absence of pain and 10 the maximum pain level that the patient can bear. To assess quality of life, the Quality of Life Questionnaire for Parkinson's disease (PSN) was used, an indicator of the individual's perception of social, physical and emotional health. This assessment tool consists of a questionnaire with 38 questions and two alternative answers (yes or no) [24]. Groups and Parameters given in Table 1.

Results

The data expressed in figure 2, shows the result of muscle pain, assessed using the Visual Analogue Scale, analyzed after the application for the different groups (Figure 2).

Figure 2 shows the comparison between the different therapies. It is observed that the Laser Therapy, when compared to the Vacuum Laser Therapy does not present statistical difference. However, it is important to note that there is a 50.3% percentage difference in this comparison. When Laser Therapy is compared to Vacuum Therapy there is a statistical difference ($p<0.02$) and when Vacuum Therapy compared to Vacuum Laser Therapy there is also a significant difference ($p <0.02$), respectively, showing a statistically significant improvement in muscle pain in parkinsonians, compared to the isolated use of therapies.

In relation to the data obtained in figure 3, when comparing the quality of life of parkinsonian patients after the application of different therapies, it was observed that the comparison between Laser Therapy and Vacuum Therapy did not show any difference statistics, although

Therapy	Parameters
Laser Therapy Group	Application sites consist of the paravertebral region, extending from the cervical spine to the lumbar spine and scapular waist bilaterally in the dorsal trunk, with the application being scanned, 5 min in the right region and left region of the cervical region and dorsal trunk. In the upper limbs, in an anatomical position, the application sites were 5 min on the arm and five minutes on the forearm and palm. Vegetable oil was used to slide the handle with the suction cup attached. The equipment was adjusted to the following parameters: negative pressure OFF, laser ON, 3 red emitters of 660 nm and 3 infrared emitters of 808 nm.
Vacuum Therapy Group	Application sites consist of the paravertebral region, extending from the cervical spine to the lumbar spine and scapular waist bilaterally in the dorsal trunk, with the application being scanned, 5 min in the right region and left region of the cervical region and dorsal trunk. In the upper limbs, in an anatomical position, the application sites were 5 min on the arm and five minutes on the forearm and palm. Vegetable oil was used to slide the handle with the suction cup attached. The equipment was adjusted to the following parameters: Pulsed mode MP7 (negative pressure-200 mbr) and laser OFF.
Vacuum Laser Group	Application sites consist of the paravertebral region, extending from the cervical spine to the lumbar spine and scapular waist bilaterally in the dorsal trunk, with the application being scanned, 5 min in the right region and left region of the cervical region and dorsal trunk. In the upper limbs, in an anatomical position, the application sites were 5 min on the arm and 5 min on the forearm and palm. Vegetable oil was used to slide the handle with the suction cup attached. The equipment was adjusted to the following parameters: pulsed mode MP7 (negative pressure-200 mbr), laser ON, 3 red emitters of 660 nm and 3 infrared emitters of 808 nm.

Table 1: Comparison of parameters of groups.

Figure 1: Vacuum-LASER, device that allows the simultaneous use of negative pressure and laser therapy on the same spot of application.

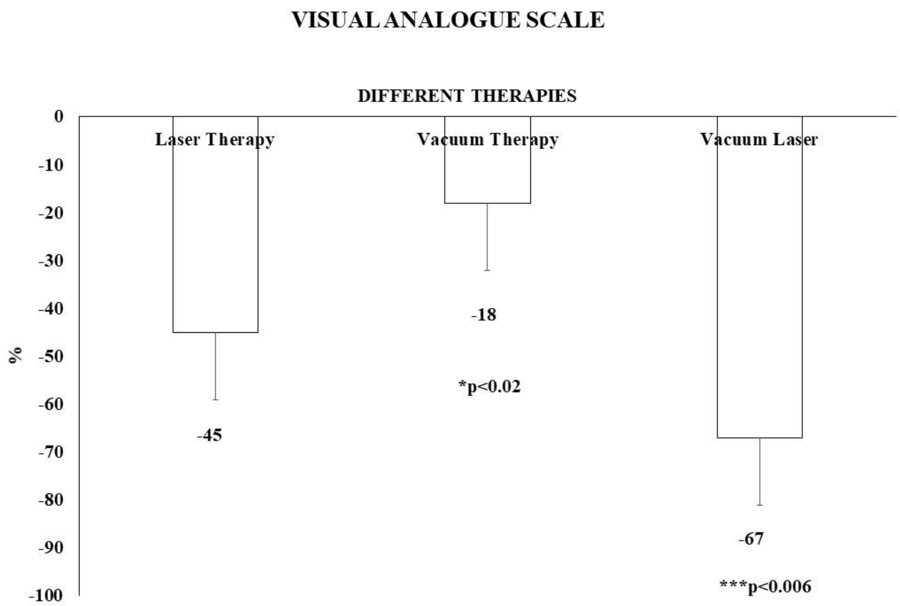

Figure 2: Comparison of the obtained result for different groups related to muscle pain score using the Visual Analog Scale. The comparisons used Mean and Standard Deviation. The statistical analysis used was the kolmogorov-Smirnov normality test and Anova two-way using the Tukey-Kramer post-hoc test for $p < 0.05$. The comparison between Laser Therapy x Vacuum Therapy (*$p<0.02$) and Vacuum Therapy x Vacuum Laser (***$p<0.006$).

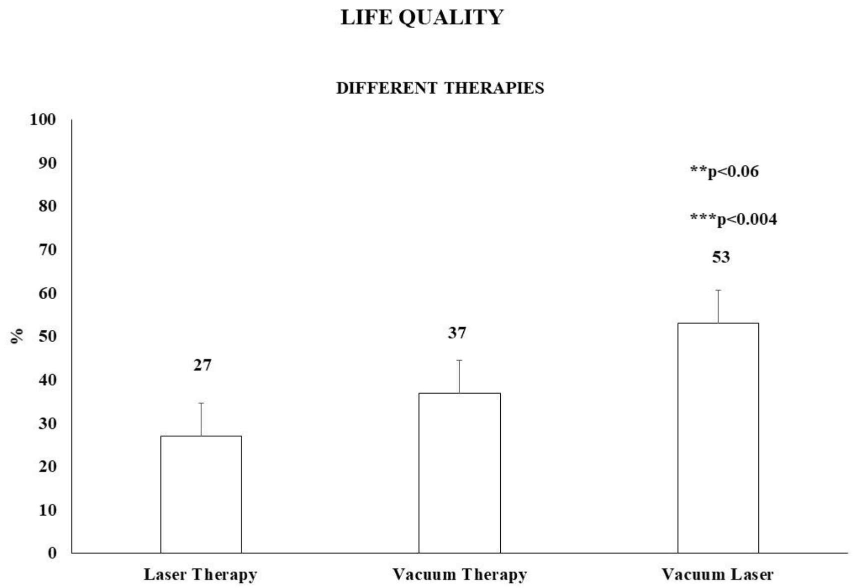

Figure 3: Comparative results for different groups using the quality of life score for the parkinsonian patients using the questionnaire of life quality for the Parkinson Disease (PSN). The comparisons used Mean and Standard Deviation. The statistical analysis used was the Kolmogorov-Smirnov normality test and Anova two-way using the Tukey-Kramer post-hoc test for p <0.05. The comparison between Vacuum Therapy x Vacuum Laser (**p<0.06) and Laser Therapy x Vacuum Laser (***p<0.004).

the percentage difference of 37% is observed in this comparison. However, when analyzing the comparison between Laser Therapy and Vacuum Laser Therapy, a significant difference was observed (p <0.004). When comparing the Vacuum Therapy and the Vacuum Laser Therapy, a significant difference was found (p <0.06). Thus, it was identified that the quality of life was positively affected with the combined use of vacuum therapy and laser therapy (Figure 3).

Discussion

Parkinson's disease, being a chronic and progressive disease, is incapacitating and impairs the quality of life of its patients. In the present study, it was found that pain affects the quality of life of parkinsonian patients, and is often more disabling than motor symptoms, affecting 80% of patients with the disease [25]. The pain that affects parkinsonian patients can have two characteristics: Nociceptive and neuropathic. Nociceptive pain is the most frequent pain with the evolution of the disease, being typically musculoskeletal and originating from abnormal postures, stiffness and akinesia causing motor fluctuations [26]. Neuropathic pain is a pain that originates of injury or dysfunction of the nervous system, as a result of abnormal activation of the nociceptive pathway (small-caliber fibers and spinothalamic tract) and represents 14% of painful syndromes in parkinsonian patients [27]. The neurophysiology of pain in Parkinson's disease is poorly understood. Animal studies suggest that dopamine probably plays a role in modulating central pain [28]. Neuroimaging studies in humans show that pain modulation involves dopaminergic D2 receptors [29]. These findings suggest that in parkinsonian patients, the abnormal function of the basal ganglia directly modulates pain, by increasing or decreasing the spread of the nociceptive signal [30]. Coriolano, et al. in their study, mapped the pain in the 24 participating volunteers and pointed out that the rigid-akinetic group had a greater number of regions of the body with pain [31]. The regions with the highest percentage of pain complaints are shoulders, arms and torso. The same found in the present study, these regions being selected, for the application of different therapies: Laser Therapy, Vacuum Therapy and Vacuum Laser Therapy.

Muscle stiffness leads to the onset of pain, although the causes of Parkinson's muscle stiffness have not yet been fully clarified, but co-contraction has been attributed, that is, to the increase in simultaneous contraction of the agonist and antagonist muscle pairs [32]. Therefore, in the present study, parkinsonian patients were selected, who presented muscle stiffness and pain for the application of different therapies. The onset of pain in the stiff muscles results from the metabolic stress generated by the constant contraction. There is ischemia resulting from vascular compression, resulting in less nutrient input, increased energy consumption and imbalance in ATP production, compromising the reception of calcium in the sarcoplasmic reticulum, a necessary condition for muscle relaxation. In addition, localized hypoxia stimulates the production of vasoactive substances that sensitize nociceptors [9]. In the present study, the three applied therapies (Laser Therapy, Vacuum-Therapy and Vacuum Laser) were effective in reducing pain intensity in patients with Parkinson's Disease according to the Visual Analog Scale, one of the most used one-dimensional scales for measuring pain in clinical studies [33]. These findings are justified by the theories surrounding the mechanism of action, of both therapies in pain control, which when applied in a combined way, enhance the therapeutic effects.

In the literature there are reports of two hypotheses of the action of Vacuum Therapy in pain: The metabolic hypothesis assumes that Vacuum Therapy decreases muscle tension activity, resulting in decreased pain. Some studies on the application of Vacuum Therapy in cervical pain suggest that the visible reddening of the skin in the treated area, local vascular dilation, reports better local microcirculation and consequently in the metabolic conditions of the muscle, promoting its relaxation. The Neural hypothesis recognizes that Vacuum-therapy influences chronic pain by altering the signal processed at the donor acceptor level. It is expected that the activation of non-acceptors by Vacuum therapy can stimulate the A-delta and C fibers, with involvement of via espino-thalamic. Therefore, according to Emerich, et al. the Metabolic and Neural hypotheses may be interconnected, since nociceptors are sensitized by metabolic factors such as lactate, adenosine triphosphate, cytokines, among others [34].

Laser Therapy with its special characteristics provide important therapeutic properties. According to Karu, when offering the cell a low energy with the use of low intensity laser, as used in the present study, it will induce a biomodulation, that is, the cell will seek a state of normalization of the affected region [11]. The photon energy of a laser radiation absorbed by a cell will be transformed into biochemical energy and used in the respiratory chain, which will result in an increase in the concentration of ATP, reflecting an increase in the cellular metabolic process. Carnevalli, et al. in his study observed that 24 and 48 h after laser irradiation in cells, there is an intense cluster of mitochondria in the peri-nuclear region, there are changes in the morphology of the mitochondria from a filamentous to granular appearance in the 72 h after proliferation and greater distribution in the cytoplasm when compared to the non-irradiated control group [35].

In addition, the Laser Therapy, with its analgesic and anti-inflammatory action, characterized by the high production of B-endorphins and the control of prostaglandins, allows the reduction of pain and muscle spasm [36]. At the same time, Laser-therapy promotes an increase in local microcirculation, favoring the drainage of catabolic resulting from the maintained muscle contraction metabolism. One of the theories proposed for pain control with the use of laser therapy suggests a systemic effect causing a decrease in the perception of pain in the treated area, by altering the sensory input to the central nervous system [37]. Another theory proposes that the increased circulation induced by the irradiation of Laser Therapy leads to a greater blood supply to cells in hypoxia, that is, an increase in the oxygen supply, which may be responsible for breaking the pain-spasm-pain cycle [38]. The comparison of quality of life before and after six sessions of the application of different therapies was performed by analyzing the results of the questionnaire on quality of life for Parkinson's disease. This questionnaire has a high level of reliability obtained through the test-retest (0.75-0.88) and defined validity in individuals with chronic diseases [39]. The instrument was applied in the form of an interview in order to avoid misinterpretation and emphasize the main question.

When correlating pain and quality of life in patients with Parkinson's disease, we can see in Figure 3 of the present study that quality of life was positively affected with the combined Vacuum-Laser therapy. Still, in a percentage of 37% in comparison between Laser-therapy versus Vacuum-therapy. With this, we demonstrate in a scheme before and after the treatment of six sessions of combined therapy, the relative increase in quality of life, occurring in part by the improvement of pain and muscle stiffness, since both contribute to the development of muscle weakness and this correlates with greater fatigue caused by mitochondrial dysfunction in Parkinson's disease [40]. However, it was observed that after an interval of fifteen days from the sixth session, without the combination of Vacuum Laser therapy, there was a return of complaints of pain and negative perception as to quality of life, however to a lesser extent, when compared to the treatment with the combined Vacuum Laser therapy.

Silva FS, et al. in their study observed that the greater the impairment of the disease the greater the physical damage including pain, which affects the perception of quality of life, and the same was observed in this study [41]. In addition, Martinez-Martin P, et al. considers that not only motor symptoms, including muscle stiffness, determine the quality of life of parkinsonians, but also non-motor ones, which compromise other dimensions of quality of life with the evolution of the disease [42].

Conclusions

The combined application of the two therapies (Vacuum and Laser), can be an interesting and very satisfactory alternative for the treatment of muscle pain in patients with Parkinson's disease. In this work, we could identify the individual contribution of each of the elements involved (laser and negative pressure), while the combination produces a synergic effect that goes beyond the addition of individual contribution. Observations clearly indicate that both had different beneficial effects in improving the level of muscle pain and quality of life, which are extremely important for the restoration of the function of muscle-bearers with this pathology. We conclude that the effective management of pain, with the use of the combined Vacuum Laser therapy, in patients with Parkinson's disease, significantly improves their quality of life, with pain being a little recognized and treated symptoms in this pathology. Our analysis is in line with current thinking, which identifies Parkinson's disease, as much more of a multisystemic disease with non-motor symptoms than previously thought. The advance of new therapies like the one promoted with the vacuum-laser type can bring significant improvement for the quality of life of the parkinsonian patients.

Acknowledgement

This work was supported by FAPESP- program CEPID (under the grants 2013/07276-1, 2014/50857-8 and 2018/09191-7) and CNPq under the grant 465360/2014-9. We also acknowledge the company MMOptics-São Carlos-Brazil for providing equipment's adding support.

References

1. Lang AE, Lozano AM (1998) Parkinson's disease. First of two parts. N Engl J Med 339: 1044-1053.
2. Paulson HL, Stern BM (2004) Clinical manifestations of Parkinson's disease. In: Watts RL, Koller WC (eds), Movement disorders neurologic principles and practice. New York: MacGraw. Pp: 233-246.
3. Teive HAG (2005) Etiopatogenia da doença de Parkinson. Ver Neurocienc. 13: 201-214.
4. Nascimento ICB, Santos RDCOD, Guerreiro CF, Costa ACND, Camelier FWR (2016) Postural evaluation in people with Parkinson's disease: A state of art. RPF 6: 56-64.
5. Goetz CG, Tanner CM, Levy M, Wilson RS, Garron DC (1986) Pain in Parkinson's disease. Mov Disord 1: 45-49.
6. Davie CA (2008) A review of Parkinson´s disease. Br Med Bull 86: 109-127.
7. Clarke CE (2007) Parkinsons disease. BMJ 335: 441-445.
8. Beitz JM (2014) Parkinson´s disease: A review. Front Biosci (Schol Ed) 6: 65-74.
9. Simons DG, Travell JG, Simons LS (1999) Myofascial pain and dysfunction. The trigger point manual. 2nd edition, Baltimore, William & Wilkins, Volume 1: Upper half of body.
10. Mense S (1997) Pathophysiologic basis of muscle pain syndromes: An Update. Phys Med Rehabil Clin Nort Am 8: 23-53.
11. Karu TI (1988) Molecular mechanism of the therapeutic effect of low-intensity laser irradiation. Dokl Akad Nauk SSSR 291: 1245-1249.
12. Hawkins D, Abrahamse H (2007) Phototherapy-a treatment modality for wound healing and pain relief. Review. African J Biomed Res 10: 99-109.
13. Ihsan FRM (2005) Low-level laser therapy accelerates collateral circulation and enhances microcirculation. Photomed Laser Surg 23: 289-294.
14. Medrado AR, Pugliese LS, Reis SR, Andrade ZA (2003) Influence of low-level laser therapy on wound healing and its biological action up on myofibroblasts. Lasers Surg Med 32: 239-244.

15. Lopes-Martins RA, Albertine R, Martins PSLL, Bjordal JM, Neto HCCF (2005) Spontaneous effects of low-level laser therapy (650 nm) in acute inflammatory mouse pleurisy induced by carrageenan. Photomed Laser Surg 23: 337-381.

16. Hagiwara S, Iwasaka H, Hasegawa A, Noguchi T (2008) Pre-irradiation of blood by gallium aluminum arsenide (830 nm) low-level laser enhances peripheral endogenous opioid analgesia in rats. Anesth Analg 107: 1058-1063.

17. Hadian M, Moghagdam B (2003) The effects of low-power laser on electrophysiological parameters of sural nerve in normal subjects: A comparison between 670 and 780 nm wavelengths. Acta Med Iran 41: 138-142.

18. Ceylan Y, Hizmetli S, Silig Y (2004) The effects of infrared laser and medical treatment son pain and serotonin degradation products in patients with myofascial pain syndrome. A controlled trial. Rheumatol Int 24: 260-263.

19. Sandoval-Ortiz MC, Mattiello-Rosa SM, Soares EG, Parizotto NA (2003) Low power laser influence on the plasmatic proteins levels in rabbits. Braz J phys ther 7: 187-194.

20. Cunha AA (2001) Ventosaterapia: Tratamento e prática. São Paulo: Ícone.

21. Foster ER (2014) Instrumental activities of daily living performance among people with Parkinson's disease without dementia. Am J Occup Ther 68: 353-362.

22. Santos AVD, Santos TVD, Zampieri KR, Tamae PE, de Aquino Junior AE, et al. (2019) Negative pressure and phototherapy: Use of combined and localized therapy to improve life's quality in Parkinson disease in a case study. J Alzheimers Dis Parkinsonism 9: 471.

23. Hoehn MM, Yahr MD (1967) Parkinsonism: Onset, progression and mortality. Neurology 17: 427-442.

24. Hunt SM, McEwen J, Mckennas SP (1985) Measuring health status: A new tool for clinicians and epidemiologists. J R Coll Gen Pract 35: 185-188.

25. Mc Dowell I (1987) Measuring health: A guide to rating scales and questionnaires. New York: Oxford University Press.

26. Sage JL (2004) Pain in Parkinson's disease. Curr Treat Options Neurol 6: 191-200.

27. Wasner G, Deuschl G (2012) Pains in Parkinson disease-many syndromes under one umbrella. Nat Rev Neurol 8: 284-294.

28. Merskey H, Bogduk N (1994) Classification of chronic pain. Seattle: IASP Press.

29. Dennis SG, Melzack R (1983) Effects of cholinergic and dopaminergic agents on pain and morphine analgesia measured by three pain tests. Exp Neurol 81: 167-176.

30. Hagelberg N, Jääskeläinen SK, Martikainen IK, Mansikka H, Forssell H, et al. (2004) Striatal dopamine D2 receptors in modulation of pain in humans: A review. Eur J Pharmacol 500: 187-192.

31. Truini A, Frontoni M, Cruccu G (2013) Parkinson's disease related pain: A review of recent findings. J Neurol 260: 330-334.

32. Meunier S, Pol S, Houeto JL, Vidailhet M (2000) Abnormal reciprocal inhibition between antagonist muscles in Parkinson's disease. Brain 123: 1017-1026.

33. Farrar JT, Young JP Jr, LaMoreaux L, Werth JL, Poole RM (2001) Clinical importance of changes in chronic pain intensity measured on an 11-point numerical pain rating scale. Pain 94: 149-158.

34. Emerich M, Braeunig M, Clement HW, Ludtke R, Huber R (2014) Mode of action of cupping--local metabolism and pain thresholds in neck pain patients and healthy subjects. Complement Ther Med 22: 148-158.

35. Carnevalli CMM, Soares CP, Zângaro RA, Pinheiro ALB, Silva NS (2003) Laser light prevents apoptosis on Cho K-1 cell line. J Clin Laser Med Surg 1: 193-196.

36. Tuner J, Hode L (1988) It's all in parameters: A critical analysis of some well-known negative studies on low-power laser therapy. J Clin Laser Med Surg 16: 245-248.

37. Brousseau L, Welch V, Wells G, Tugwell P, de Bie R, et al. (2000) Low-level laser therapy for osteoarthritis and rheumatoid arthritis: A metanalysis. J Rheumatol 27: 1961-1969.

38. Simunovic Z, Ivankovich AD, Depolo A (2000) Wound healing of animal and human body sport and traffic accident injuries using low-level laser therapy treatment: A randomized clinical study of seventy-four patients with control group. J Clin Laser Med Surg 18: 67-73.

39. Coriolano MGWS, Balbino JMS, da Silva BRV, Cabral ED, Asano AG, et.al. (2014) Characterization of pain in patients with Parkinson's disease. Rev Dor 15: 78-82.

40. Vanitallie TB (2008) Parkinson disease: Primacy of age as a risk factor for mitochondrial dysfunction. Metabolism 57: S50-55.

41. Silva FS, Pabis JVPC, Alencar AG, Silva KB, Peternella FMN (2010) Evolution of the Parkinson's disease and impairment of quality of life. Rev Neurosci 18: 463-468.

42. Matinez-Martin P, Rodrigues-Blazquez C, Kurtis MM, Chaudhuri KR (2011) The impact of non-motor symptoms on health-related quality of patients with Parkinson's disease. Mov Disord 6: 399-407.