

Scrambler Therapy for the Management of Chronic Oncologic Pain: Integrative Literature Review

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Scrambler Therapy no Controle da Dor Oncológica Crônica: Revisão Integrativa da Literatura

Scrambler Therapy para el Manejo del Dolor Oncológico: Revisión Integradora de la Literatura

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ABSTRACT

Introduction: Scrambler therapy is a novel, non-invasive pain modifying technique that utilizes transcutaneous electrical stimulation of pain fibers with the intent of re-organizing maladaptive signaling pathways. **Objective:** Evaluate the benefits of Scrambler therapy to manage the intensity of pain in oncologic patients. **Method:** Integrative literature review based on Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) in the electronic databases LILACS, PEDro, SciELO and PubMed. The descriptors “Scrambler therapy”, “cancer”, “pain” were randomly combined in addition to the Boolean operators AND, OR in Portuguese, English and Spanish with no time limitation. **Results:** For this review, 15 articles were found relevant. The Scrambler therapy machine is based on 5 artificial neurons controlled by an optimized algorithm to provide safety and effectiveness. The hardware receives information from the algorithm that creates the strings of “non-pain,” and processes them by transforming into potential flows of synthetic action (i.e. created by technology) functionally compatible with endogenous flows. Pain scrambler therapy had a potential to decrease pain in cancer patients. **Conclusion:** The positive findings from preliminary studies with Scrambler therapy endorses the benefits this device provides to manage oncologic pain.

Key words: neoplasms; transcutaneous electric nerve stimulation; pain management; cancer pain/therapy; chronic pain.

RESUMO

Introdução: A *Scrambler therapy* é uma nova e não invasiva modalidade de eletroanalgesia com a intenção de organizar a má adaptação dos sinais elétricos de nervos periféricos. **Objetivo:** Avaliar o benefício clínico da *Scrambler therapy* no controle de intensidade da dor em pacientes oncológicos. **Método:** Revisão da literatura conforme a metodologia *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (PRISMA) nas bases de dados eletrônicas LILACS, PEDro, SciELO e PubMed. Foram combinados aleatoriamente os descritores: “Scrambler therapy”, “cancer”, “pain”, assim como o uso dos operadores booleanos AND e OR, em português, inglês e espanhol, sem limite de tempo. **Resultados:** Foram incluídos 15 estudos que, após avaliação crítica, demonstraram benefício clínico na redução na intensidade da dor. A *Scrambler therapy* é baseada em cinco neurônios artificiais controlados por um algoritmo otimizado para fornecer segurança e eficácia. O *hardware* recebe informações do algoritmo que cria as sequências de caracteres “não-dor” e as processa, transformando-as em fluxos potenciais de ação sintéticos (isto é, criados pela tecnologia) funcionalmente compatíveis com os potenciais endógenos. **Conclusão:** Os resultados positivos encontrados nos estudos preliminares com a *Scrambler therapy* indicam benefícios no controle da dor oncológica. **Palavras-chave:** neoplasias; estimulação elétrica nervosa transcutânea; manejo da dor; dor do câncer/terapia; dor crônica.

RESUMEN

Introducción: *Scrambler therapy* es una modalidad nueva y no invasiva de electroanalgesia con la intención de organizar la pobre adaptación de las señales eléctricas de los nervios periféricos. **Objetivo:** Estudiar si la *Scrambler therapy* influye en la intensidad del dolor en pacientes con cáncer. **Método:** Revisión integradora de la Literatura según la *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (PRISMA), mediante búsqueda realizada en las bases de datos LILACS, PEDro, SciELO y PubMed, utilizando las palabras clave “terapia Scrambler”, “cáncer”, “dolor”, así como el uso de los operadores booleanos AND y OR, en portugués, inglés y español, sin límite de tiempo. **Resultados:** Se incluyeron 15 artículos relevantes para la revisión, que muestran una reducción en la intensidad del dolor. La *Scrambler therapy* se basa en cinco neuronas artificiales controladas por un algoritmo optimizado para proporcionar seguridad y eficacia. El *hardware* recibe información del algoritmo que crea las cadenas de “no dolor” y las procesa transformándolas en flujos de potenciales de acción sintéticos (es decir, creados por la tecnología) funcionalmente compatibles con los endógenos. **Conclusión:** Los resultados positivos encontrados en los estudios preliminares con la *Scrambler therapy* indican beneficios en el control del dolor por cáncer.

Palabras clave: neoplasias; estimulación eléctrica transcutánea del nervio; manejo del dolor; dolor en cáncer/terapia; dolor crónico.

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INTRODUCTION

Chronic pain is quite challenging for healthcare professionals. Complaints of chronic pain are already a major public health issue. It is hard to control, highly prevalent and expensive to treat. Approximately 100 million individuals were affected in the United States of America, accounting for US\$ 635 billion annually. For 140 million Europeans representing 19% of the adult population, chronic pain is considered the great public health problem of the continent. More than 70% of the patients with cancer suffer pain and in more than 50% of the cases, it is inadequately treated¹.

Currently, the algorithm of pain management and peripheral neuropathy in oncologic patients is in constant evolution. Scrambler therapy is a novel electro-analgesia therapy based in artificial neurons, different from the gate control therapy. The active principle is the transmission of synthetic “non-pain” information by C fiber surface receptors².

In the Scrambler therapy, the qualitative element of the electric stimulation is essential, different from transcutaneous electric nerve stimulation (TENS) which activates the nervous system through electric impulses transmitted by alpha and beta fibers to block pain. These elements are coded neurophysiologic information where pain blocking is not enough, but to transform the information of pain in “non-pain”³.

Information becomes the central point of control of the plasticity of the pain system, both in the genesis of chronicity (induced by endogenous information of pain repeated over time) and in its regression (induced by synthetic information of “non-pain” repeated over time) in the Scrambler Therapy model. The therapeutic approach is no longer to inhibit the transmission of pain, which is transitory on its own but to transform the information of pain into “non-pain”. The theoretical expectation is therefore that of an immediate and complete analgesic effect in treatment, and of a return to normal physiological response after one or more cycles of treatment².

The objective of the Scrambler therapy is to reduce the complexity of the electric signal of the pain through artificial intelligence. The Scrambler Therapy machine is based on 5 artificial neurons controlled by an optimized algorithm to provide safety and effectiveness. Typically, a neuron receives, processes, and transmits information. Artificial neurons from Scrambler Therapy perform the same functions through the hardware and software synergy specifically designed for pain control⁴. The information is synthesized from 16 different types of action potentials with variable geometry, producing 256 combinations, quite similar to the endogenous kind which produce

different perceptions depending on the string-sequence selected. The algorithm dynamically generates the type of “non-pain” information in order to try to achieve the goal of immediate and complete analgesia causing the modulation of the pain system with high level of safety and long-term efficacy².

In this context, this study was aimed to evaluate whether the Scrambler therapy influences the intensity of the pain in oncologic patients.

METHOD

Integrative review based in original scientific articles published about Scrambler therapy in oncologic patients found in the databases LILACS, PEDro, SciELO and PubMed. The descriptors “Scrambler therapy”, “cancer”, “pain” were combined randomly in Portuguese, English and Spanish. All the articles which utilized the Scrambler therapy in oncologic patients regardless of the study design were included. As search strategy, the Boolean operator AND was utilized with the descriptors mentioned. The articles were analyzed by title and abstract to find relevant and pertinent studies; the inclusion criteria were original articles which responded to the research question: does Scrambler therapy influence chronic oncologic pain management? Review articles were excluded. The search occurred in December 2020, all the original articles found were included and not cutoff date was established due to the low number of studies available.

RESULTS

78 original articles were found. After the exclusion of duplicates and evaluation by two reviewers, 15 articles were eligible (Figure 1). The studies are described in Chart 1.

DISCUSSION

The use of Scrambler therapy significantly relieves the intensity of pain in oncologic patients, in addition to reduced use of opioids and morphine. No side effects were found in the studies completed. Studies with follow-up were not discarded and none of them presented adverse events showing that the technique is fully effective.

The Scrambler therapy is approved by the Food and Drug Administration (FDA)². It is prescribed for stable nerve lesions that provoke chronic pain. One of the advantages is the plasticity of the electric stimulation. The Scrambler therapy is well tolerated, nearly pleasant similar to a massage, a sensation attributed to tactile stimulation of fibers C².

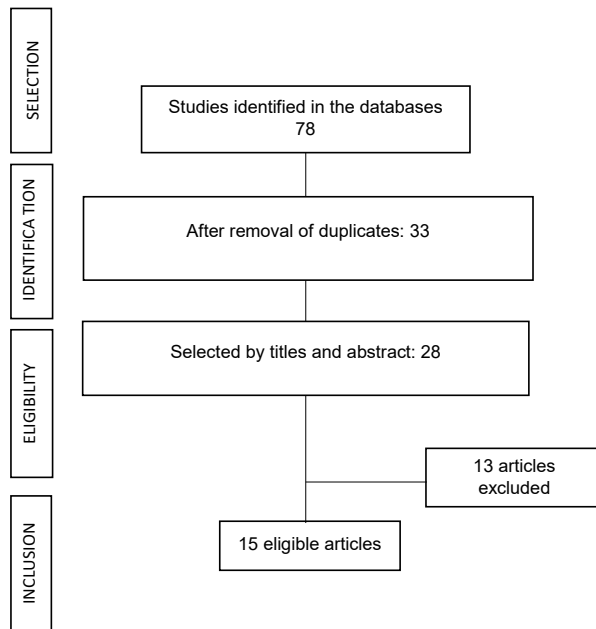


Figure 1. Flowchart of search in electronic databases

Nerve integrity is essential to reach the results. It requires careful positioning of the electrodes always guided by patient feedback. It is important to use only nerve pathways that do not represent alterations and/or interruptions capable of degrading the synthetic information of “non-pain”. The action of analgesic drugs can confuse the perception of pain by incorrectly positioning the electrodes. Anticonvulsants inhibit the Scrambler therapy and muscle relaxants affect its effectiveness². Two studies followed-up the use of drugs and noticed the reduction of morphine and opioids but the utilization of drugs that may inhibit the therapy was not controlled.

Studies addressing Scrambler therapy in non-oncologic patients with chronic pain can be found and all of them with satisfactory pain relief⁹⁻²³. It is a novel therapy still unavailable in Brazil that may contribute for oncologic pain relief with benefits already described in several randomized clinical trials. The daily application from 30 to 60 minutes for 10 to 14 days is the standard use, prescribed for patients with chemotherapy-induced peripheral neuropathy and to

Chart 1. Description of the studies encountered

Author	Sample	Intervention	Results
Marineo ³	11 oncologic patients in palliative care	Once a day for 45 minutes during 10 days	Reduction of opioids due to improvement of pain ($p < 0.0001$)
Lee ⁵	1 patient with lymphedema secondary to breast cancer	Once a day for 45 minutes during 10 days	Reduction of 6 points in VAS, with no increase of limb volume
Smith et al. ⁶	3 patients with post-mastectomy pain syndrome	Once a day for 45 minutes during 10 days	Significant reduction of pain in VAS in the three cases
Tomasello et al. ⁷	9 adolescents with cancer and CIPN	Once a day for 45 minutes during 10 days	Significant reduction of pain. Some patients needed additional sessions
Notaro et al. ⁸	25 oncologic palliative patients (visceral and bone metastasis)	Once a day for 30-40 minutes during 10 days	All the patients improved more than 50% (8.4 to 2.9). Duration of pain control 7.7 (5.3) weeks. Sleeping hours 4.4 ± 1.2 to 7.5 ± 1.1
Pachman et al. ⁹	37 patients with cancer and CIPN	Once a day for 30-40 minutes during 10 days	53% reduction in pain score; 44% reduction in hyperesthesia and 37% reduction of numbness. Benefit lasted for 10 weeks
Kashyap et al. ¹⁰	20 oncologic patients with bone pain or CIPN higher than 4 in VAS	-	Improvement of pain after each session and after 2 weeks of follow-up ($p < 0.001$)
Loprinzi et al. ¹¹	Randomized clinical trials with 25 patients with CIPN in each group (Scrambler x TENS)	Once a day for 30 minutes during 10 days	Significant pain relief

to be continued

Chart 1. continuation

Author	Sample	Intervention	Results
Park et al. ¹²	1 adolescent with CIPN by leukemia	Once a day for 40 minutes during 4 days	Pain-free after each session and significant pain relief. Continuous analgesia for 4 weeks
Lee et al. ¹³	20 oncologic patients with bone pain or CIPN or post-operative neuropathic pain	-	Reduction of opioids due to significant pain relief
Coyne et al. ¹⁴	39 patients with CIPN with VAS >5	Once a day for 45 minutes during 10 days	Significant pain relief (p<0.0006)
Ricci et al. ¹⁵	Prospective study with 73 patients with refractory chronic pain to the treatment (40 with several types of cancer and 33 controls)	Once a day for 45 minutes during 10 days	After 10 days of treatment, pain relief of 74% (p<0.0001). 81% of the patients reported continued analgesia after 2 weeks (p<0.0001)
Kashyap et al. ¹⁶	40 patients with chronic pain by thoracic and head and neck cancer using morphine and tramal	Once a day during 40 minutes for 10 days	Pain relief after the 3 rd days (p<0.0001). Morphine reduced after the 7 th day (p<0.05)
Smith et al. ¹⁷	16 patients with CIPN who used taxanes, platinum by-products and bortezomib	Once a day during 60 minutes for 14 days	Significant pain relief (p<0.0001)
Childs et al. ¹⁸	50 patients with CIPN	Once a day during 60 minutes for 14 days	Improvement of more than 60% of the pain in more than 50% of the patients

Captions: VAS = Visual analogic scale; CIPN = chemotherapy-induced peripheral neuropathy; TENS = transcutaneous electric nervous stimulation.

reduce analgesia for chronic pain, but long-term follow-up studies need to be carried out.

The present article in Portuguese is shedding light to a new resource yet unknown by healthcare professionals to enable them, as opposed to other electrophysical devices when is possible to determine the frequency, duration of the pulse and intensity. The hardware receives information from the algorithm that creates the strings of “non-pain” and processes them by transforming into flows of synthetic action potentials functionally compatible with endogenous ones. The resulting emission is calibrated to synchronize the surface receptors of C fibers to propagate the artificial electric signal². This represents a novel perspective about how electrophysical agents are used for pain relief in oncologic patients.

Long-term clinical follow-up studies for the Brazilian population are necessary and authorization to apply the Scrambler therapy in the country. For such, healthcare professionals need to be acquainted with this therapy.

CONCLUSION

The Scrambler therapy appears to be a promising resource for pain relief in oncologic patients despite the necessity of more randomized controlled clinical trials.

Artificial intelligence for electroanalgesia is a technological innovation to be considered by healthcare professionals. The absence of the equipment in Brazil, its high cost abroad and necessity of skilled professionals are obstacles for its dissemination.

CONTRIBUTIONS

All the authors contributed for the study design and/or conception, data acquisition, analysis and interpretation, wording and critical review; they approved the final version to be published.

DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interests to declare.

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