EDITORIAL

Neuromodulation of the Response to Neuropathic Pain in Chronic Diseases

It is known that the pain occurs with different intensities depending on the pathology and the area where the damage occurs. The pain mechanisms involve different biochemical pathways and neurophysiological integration processes that are carried out in the nervous system and finally, the cerebral cortex. Derived from the fact that pain is the main cause of medical care and can be a cause of disability, in addition to the severity that occurs with the evolution of pathology such as bone tumors, there is a greater impact on the patient with pain, aggravating the symptoms, reflecting a greater effect of the disease on the patient. All these conditions generate a great negative impact on social and personal interrelationships, which leads to a great physiological and emotional affectation that has a serious impact on the patient, as well as a growing desertion of work that leads to a high economic cost.

In recent years, the number of patients with bone tumors and development of metastasis 60 to 85% of bone cancer patients have been increased, where the main symptom is pain [1]. In order to find new options to improve established treatments, Romero-Morelos and collaborators set out a broader neurysiological approach, analyzing the processes of inflammation, neuropathies and cognitive components to propose a new therapeutic approach that provides us with relevant information on the relationship of these processes that have been managed in isolation and not as a dynamic component that encompasses a single pathological process, so this work sought to identify the neurophysiology of mechanisms related to pain management in bone tumors [2].

Because the relationship of inflammatory processes with the development of bone metastases is not well established, it is of great importance to investigate the action of neurochemicals derived from inflammatory and tumor cells, while clarifying the function of peripheral sensitization caused by nerve compression and injury caused by tumor growth [3]. Based on the role played by different neurochemical substances, the authors propose that the bone tumor can cause neuropathic and inflammatory pain depending on the area where it is present and can affect both the peripheral nervous system as well as induce neurochemical changes at the neurological level [4]. The importance of pharmacological and non-pharmacological management can be inferred from the information provided by the authors according to the system involved.

On the other hand, trigeminal neuralgia is characterized mainly by chronic pain in the trigeminal nerve, affecting the face and brain, causing sudden unbearable pain. This condition is increasing and presents with an incidence of 2-13 per 100000 inhabitants per year and increases to 25 per 100,000 per year in people over 70 years of age [5], it is vitally important to address treatments that help reduce the painful process, so various treatments have been proposed to reduce pain. Garcia-Isidoro and collaborators performed a scientific evidence-based meta-analysis with the aim of evaluating the effectiveness of invasive and non-invasive electrical neuromodulation of trigeminal neuralgia, on pain and adverse effects. These articles have been searched and selected from the databases. In order to provide a new vision on the techniques used, the authors found that better results have been obtained using short- and medium-term continuous radiofrequency, although pulsed radiofrequency showed a smaller number of side effects after treatment, in addition to better results in the long term [6]. One of the main problems was performing the analysis, as the data were very heterogeneous, and no significant differences were found. However, what is shown in this study provides certain information regading the techniques to be used by clinicians [7].

Finally, Pérez-Neri and colleagues analyzed the therapeutic potential of low-intensity, high-intensity focused ultrasound neuromodulation for the management of neuropathic pain, which is especially useful in a group of chronic pain syndromes with a restricted response to conventional drugs [8]. The information presented is relevant, as it shows that low-intensity focused ultrasound may modify some mechanisms involved in neuropathic pain processes such as modulation of ion channels, glutamatergic neurotransmission, cerebral blood flow, inflammation and neurotoxicity, neuronal morphology and survival, nerve regeneration and remyelination, as well as minor side effects [9]. The authors propose that more clinical trials on safety and efficacy are needed, despite the evidence provided on the potential therapeutic use of low-intensity, high-intensity focused ultrasound for the management of neuropathic pain.

The information presented in this edition of Current Neuropharmacology provides an overview of current pain management as a fundamental aspect of clinical practice, treatment, therapy and research. The contribution offered is of high academic level that results in an interest of biomedical and clinical neurophasic and neuroscientists who work in research centers, hospitals, as well as in the industry, since it can provide new therapeutic strategies for the treatment and reduction of pain on the patient, to improve their quality of life.

REFERENCES

- [1] Ma, VY.; Chan, L.; Carruthers, K. Incidence, prevalence, costs, and impact on disability of common conditions requiring rehabilitation in the United States: stroke, spinal cord injury, traumatic brain injury, multiple sclerosis, osteoarthritis, rheumatoid arthritis, limb loss, and back pa. Arch. Phys. Med. Rehabil., 2014, 95, 966-995.
- http://dx.doi.org/10.1016/j.apmr.2013.10.032
- [2] Romero-Morelos, P.; Ruvalcaba-Paredes, E.; Garciadiego-Cázares, D.; Pérez S.M.; Reyes-Long, S.; Salcedo, M.; Mancilla-Ramírez, J.; Bandala, C. Neurophysiological mechanisms related to pain management in bone tumors. *Curr. Neuropharmacol.*, 2020, 19, 308-319.

http://dx.doi.org/10.2174/1570159X18666201111112748 PMID: 33176655

- [3] Ge, C.; Huang, H.; Huang, F.; Yang, T.; Zhang, T.; Wu, H.; Zhou, H.; Chen, Q.; Shi, Y.; Sun, Y.; Liu, L.; Wang, X.; Pearson, R.B.; Cao, Y.; Kang, J.; Fu, C. Neurokinin-1 receptor is an effective target for treating leukemia by inducing oxidative stress through mitochondrial calcium overload. *Proc. Natl. Acad. Sci. USA*, 2019, *116*(39), 19635-19645. http://dx.doi.org/10.1073/pnas.1908998116 PMID: 31488714
- [4] Feller, L.; Khammissa, R.A.G.; Bouckaert, M.; Ballyram, R.; Jadwat, Y.; Lemmer, J. Pain: Persistent postsurgery and bone cancer-related pain. J. Int. Med. Res., 2019, 47(2), 528-543.
 - http://dx.doi.org/10.1177/0300060518818296 PMID: 30632434
- [5] Feller, L.; Khammissa, R.A.G.; Fourie, J.; Bouckaert, M.; Lemmer, J. Postherpetic neuralgia and trigeminal neuralgia. *Pain Res. Treat.*, 2017, 2017, 1681765.
 - http://dx.doi.org/10.1155/2017/1681765 PMID: 29359044
- [6] Garcia-Isidoro, S.; Castellanos-Sanchez, V.O.; Iglesias-Lopez, E.; Perpiña, M. S. Invasive and not invasive electrical neuromodulation in trigeminal nerve neuralgia: a systematic review and meta-analysis. *Curr. Neuropharmacol.*, 2020, 19, 320-333. http://dx.doi.org/10.2174/1570159X18666200729091314 PMID: 32727329
- [7] Gambeta, E.; Chichorro, J.G.; Zamponi, G.W. Trigeminal neuralgia: An overview from pathophysiology to pharmacological treatments. *Mol. Pain*, 2020, *16*, 1744806920901890.
 - http://dx.doi.org/10.1177/1744806920901890 PMID: 31908187
- [8] Pérez-Neri, I.; González-Aguilar, A.; Sandoval, H.; Pineda, C.; Ríos, C. Therapeutic potential of ultrasound neuromodulation in decreasing neuropathic pain: clinical and experimental evidence. *Curr. Neuropharmacol.*, 2020, 19, 334-348. http://dx.doi.org/10.2174/1570159X18666200720175253 PMID: 32691714
- [9] Gregory, N.S.; Terkawi, A.S.; Prabhakar, N.K.; Tran, J.V.; Salmasi, V.; Hah, J.M. Peripheral nerve stimulation for pudendal neuralgia: A technical note. *Pain Med.*, **2020**, *21*(Suppl. 1), S51-S55. http://dx.doi.org/10.1093/pm/pnaa171 PMID: 32804222

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