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Editorial

Chemotherapy-induced peripheral neuropathy: bench to clinical practice

Eunsoo Kim[1,2]

[1]*Department of Anesthesia and Pain Medicine, School of Medicine, Pusan National University, Busan, Korea*
[2]*Department of Anesthesia and Pain Medicine, Biomedical Research Institute, Pusan National University Hospital, Busan, Korea*

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Correspondence
Eunsoo Kim
Department of Anesthesia and Pain Medicine, Pusan National University Hospital, 179 Gudeok-ro, Seo-gu, Busan 49241, Korea
Tel: +82-51-240-7274, Fax: +82-51-240-7466, E-mail: eunsookim@pusan.ac.kr

Continuing improvement in early diagnosis and treatment for cancer patients has led to an increase in cancer survival rates over the last decade. A recent population-based study described how cancer survival rates have increased across all cancer types, mainly in high-income countries [1]. As the number of cancer survivors increases, the health-related quality of life (HRQOL) for those patients is one of the biggest concerns. Many chemotherapeutic agents can cause chemotherapy-induced peripheral neuropathy (CIPN), characterized by tingling, numbness, and burning pain in both hands and feet. Those neuropathy-related symptoms have a negative impact on HRQOL in cancer patients and survivors [2]. Moreover, CIPN can lead to dose reduction or early cessation of chemotherapy because of the dose-dependent relationship of chemotherapeutic drugs on CIPN prevalence.

The incidence of CIPN is high, up to 68% within the first month, 60% at three months, and 30% at six months after chemotherapy [3]. The major chemotherapeutics that cause neuropathy include taxanes, platinum compounds, vinca alkaloids, proteasome inhibitors, and immunomodulating drugs. Although each drug has a different mechanism for causing neuropathy, the primary mechanism shared by these agents are morphologic and biochemical alterations in the dorsal root ganglion (DRG) and spinal cord [4]. Previous studies have demonstrated that the respective mechanism is as follows: disruption of axonal transport, ion channel dysregulation, mitochondrial and oxidative stress, neuroinflammation, and immunological processes [4,5].

Numerous pre-clinical studies have shown efficacy in the treatment of established CIPN or the prevention of CIPN. Modulation of ion channels, including the sodium [6,7], potassium [8,9], and calcium channel [10], have shown promising efficacy in pre-clinical studies. However, the clinical efficacy of these targeting drugs is still limited [11]. Duloxetine, a serotonin-norepinephrine reuptake inhibitor, is the only chemotherapeutic drug which has proven effective in a randomized clinical trial [12]. Topical menthol or capsaicin has been shown to improve neuropathy-related symptoms in a small non-randomized clinical study [13,14]. Therefore, there is still no well-defined treatment protocol.

Recent pre-clinical research has found novel preventive

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and therapeutic targets, including a specific organic anion transporting polypeptide [15], Sphingosine-1-phosphate receptor 1 [16], and an angiotensin II type 1 receptor [17]. These promising targets have the potential to be translated into clinical practice for the treatment of CIPN.

In this issue, Yin et al. [18] found that neurotensin receptor 1 (NTSR1), which is widely distributed in the spinal cord and DRG, plays significant roles in spinal- and supraspinal-level pain processing in a rat model of CIPN. NTSR1 agonist may also have an indirect effect on the serotonergic pathway. Therefore, NTSR1 could provide new therapeutic targets for a promising treatment for cancer survivors with CIPN.

There are several barriers to turning these laboratory discoveries into applications in clinical practice. The main problems include the lack of communication between basic scientists and clinicians, a lack of trained interdisciplinary researchers, a lack of access to shared resources, and complex ethical issues [19]. However, investigators working on translational research must continue their efforts to break these barriers down. It can lead them to a pathway for potential therapeutics. Therefore, under the guidance of the pre-clinical literature, we should continue to identify novel targets that may help improve CIPN and prove their clinical efficacy through the proper application.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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ORCID

Eunsoo Kim, https://orcid.org/0000-0001-9978-4973

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