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LETTER TO THE EDITOR

Chemotherapy-induced peripheral neuropathy in the neuronal cells model

Nöronal hücre modelinde kemoterapiye bağlı periferik nöropati

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To the Editor,

Chemotherapy-induced peripheral neuropathy (CIPN) is a commonly occurring side effect of several chemotherapy drugs that can damage peripheral nerves[1]. The body's extremities and organs communicate with the central nervous system, which is made up of the brain and spinal cord, through peripheral nerves. Chemotherapeutic medications include vinca alkaloids (vincristine, vinblastine), taxanes (paclitaxel, docetaxel), and platinum-based medicines (cisplatin, oxaliplatin), among others, that are associated with chemotherapy-induced peripheral neuropathy (CIPN). The symptoms of CIPN can include tingling or numbness, searing or shooting pain, temperature sensitivity, poor balance and coordination, muscle weakness, and difficulties with fine motor skills[2]. The precise mechanism by which chemotherapy drugs induce damage to peripheral nerves remains incompletely elucidated. Nevertheless, it is postulated that these medications disrupt regular nerve function, precipitating nerve impairment and the onset of CIPN.

The known etiologies of chemotherapy-induced peripheral neuropathy (CIPN) include damage to neuronal cell bodies in dorsal root ganglia (DRG), axonal toxicity, dysfunction of axonal membrane ion (Na+) channels, mitochondrial damage[3], and central sensitization[4]. It is known that the cytotoxic activity of chemotherapy drugs impacts Schwann cells and axons, even though the pathophysiological mechanism of CIPN is not entirely understood[5]. Despite many chemotherapeutic agents being unable to cross the blood-brain barrier, they can affect dorsal root ganglia (DRG) by crossing the blood-nerve barriers. Therefore, they can reach capillaries surrounding DRG and contribute to the peripheral distribution of neurotoxins, playing a role in nutrient supply. The long nerve axons present in the peripheral nervous system (PSS) are more vulnerable to toxic drugs due to their sensitivity to external stimuli that affect cell function[6]. Neurotoxins spread along nerve fibers in DRG cells, causing damage to the axon structure, myelin sheath, and cell bodies. The mechanism of damage depends on the type of agents used[7].

The model of chemotherapy-induced peripheral neuropathy is generally studied in vitro using three different cell lines: DRG (dorsal root ganglion), PC12, and (SH)-SY5Y (Schwann-like cells)[8]. In vitro studies increase the reproducibility of the research. Especially, PC12 cell lines which are applied nerve growth factor (NGF) can be differentiated[9]. Thus, they can be transformed into mature human neuron cells, and in cells transformed into a neuron format, growth activity ceases, and they become electrically excitable.

My research focuses on developing comprehensive in vitro CIPN models to develop neuronal targeted therapeutics for preventing and treating peripheral neuropathy. In our prior investigation, our objective was to investigate the impacts of quercetin and low-level laser therapy (LLLT) on cisplatin-induced peripheral neuropathy[10]. The PC12 cell line was utilized in our investigation to create the CIPN

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model. The CIPN model was established in the study by treating NGF-differentiated and undifferentiated PC12 cells with cisplatin in isolation. The experimental groups were administered varying dosages of quercetin and Low-Level Laser Therapy (LLLT), and the impact on gene expressions related to Synapsin I, GAP43, mitochondria, apoptosis, and cell viability was examined. To examine the effects of quercetin and LLLT on the expressions of GAP-43 and Synapsin I, we used real-time PCR. The MTT assay was used to measure cell viability, while the Annexin and Dead assays were used to measure the induction of apoptosis. A Mitopotential Assay was used to assess changes in mitochondrial potential, and cell-level lactate dehydrogenase activity (LDH) was also measured. The study's findings demonstrated that CIPN benefited from the independent administration of LLLT and quercetin. Specifically, the upregulation of GAP43 and Synapsin I gene expression in NGF-differentiated PC12 experimental groups demonstrated a significant contribution of quercetin and LLLT treatment to neurite extension recovery. Moreover, it was shown that the CIPN-induced experimental groups showed higher levels of apoptosis rates, mitochondrial membrane potential, and LDH enzyme activity. Nonetheless, it has been demonstrated that the injection of quercetin with LLLT decreased apoptosis, alterations in mitochondria, and LDH enzyme activity.

To sum up, research has demonstrated the significance of quercetin and LLLT in the management of CIPN. Consequently, it is reasonable to assume that LLLT and quercetin may be utilized to treat CIPN. Future research may uncover fresh approaches to boost LLLT and quercetin's combined effectiveness.

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