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An Overview of the Pathophysiology and Therapeutic Approaches for Chemotherapy-Induced Peripheral Neuropathic Pain

Abstract

A cancer diagnosis and treatment can be a burden for patients. The chemotherapy can cause a neuropathic pain complication. CINP has become an increasingly prevalent issue among cancer patients, causing symptoms such as electrical sensations, tingling, pain, hyperalgesia, and allodynia. Neuropathic pain triggered by chemotherapy is a common and severely disabling adverse effect of cancer treatment. Some chemotherapy drugs have neurotoxic effects on the peripheral nerve system that leads to chemotherapy-induced neuropathic pain (CINP). These symptoms include burning, tingling, and numbness, as well as very intense, shooting pain, and it greatly decreases quality of life. This review will look at the key mechanisms of CINP, including neuroinflammation, oxidative damage, malfunctioning mitochondria, and disruption of ion channels. Also, it examines the disease's clinical features, elements of risk, and diagnostic methods. Neuropsychiatric patients suffering from convulsions are managed effectively with a combination of non-pharmacological techniques, acupuncture, cognitive behavioural therapy (CBT), physical therapy, etc. (CINP). Some medicines that are used are painkillers, anxiety pills and anti-epileptic ones. Preventive measures that are covered include protective drugs and the modification of doses of chemotherapeutic agents. Developments in therapy and creation of individualised medicinal strategies to further our understanding, prevention, and treatment of CINP will enhance patient outcome and quality of life.

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Introduction

Globally, cancer is a leading cause of disease and mortality, putting a significant burden on patients and healthcare systems. While chemotherapy is a cornerstone of cancer treatment, it often comes with severe complications such as chemotherapy-induced neuropathic pain (CINP)(Staff et al. 2017). This debilitating condition manifests as burning, tingling, and shooting pain, significantly impacting patients' quality of life and posing substantial challenges to their daily functioning and overall well-being. Approximately 50-90% of patients undergoing chemotherapy develop CIPN, with a high risk of chronicity in around 30-40% of these cases (Seretny et al. 2014). A systematic review and meta-analysis of 31 studies with 4,179 patients found that chemotherapy-induced peripheral neuropathy (CIPN) was 68.1% (57.7–78.4) in the first month, 60.0% (36.4–81.6) at three months, and 30.0% (6.4–53.5) at six months or later (Verstappen et al. 2005). A range of symptoms, from minor pain to severe discomfort, are associated with CINP including burning sensations, tingling, numbness, and sharp, shooting pains, often starting in the extremities and potentially progressing over time (Funabashi et al. 2022). These symptoms might limit patients' everyday activities and function, lowering quality of life (Megari 2013).

Pathophysiology

Neuropathic pain can arise from either impaired or undamaged sensory nerves. Multiple biochemical pathways are activated in the event of nerve damage, leading to pain(Kiguchi et al. 2019) . These pathways involve the release of inflammatory mediators, increased DAOO activity, mitochondrial dysfunction, ephrin activation, and Sigma-1 receptor activation **(Figure 1)** (Abbott et al. 2011).

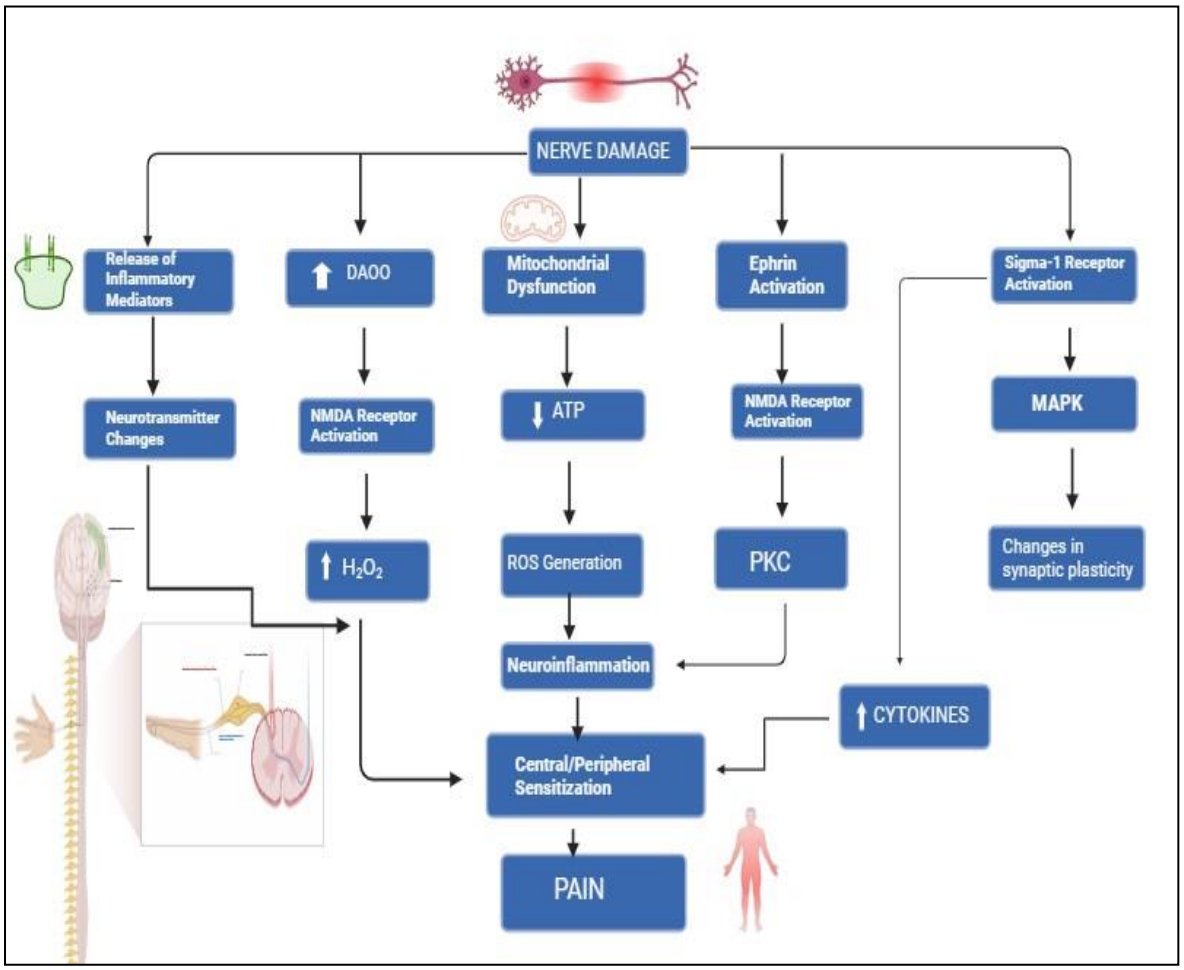


Figure 1 Different targets are involved in the development of NP. Protein kinase C (PKC), α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor (AMPA), N-methyl-D-aspartate receptor (NMDA), Microtubule-associated protein kinase (MAPK), D-amino acid oxidase (DAAO), and mitochondrial permeability transition protein (mPTP).

Each of these processes contributes to neuroinflammation and sensitization, ultimately resulting in pain (Warwick et al. 2021). Nerve injury triggers increased expression of ephrin-B and EphB, heightening the excitability of nociceptive neurons and synaptic plasticity, ultimately leading to neuropathic pain **(Figure 2)**. This process involves several signaling pathways, including PKCγ, MAPK, p-AKT, PI3K, c-Fos, and NMDA phosphorylation, each contributing to the development of neuropathic pain (Cui et al. 2023).

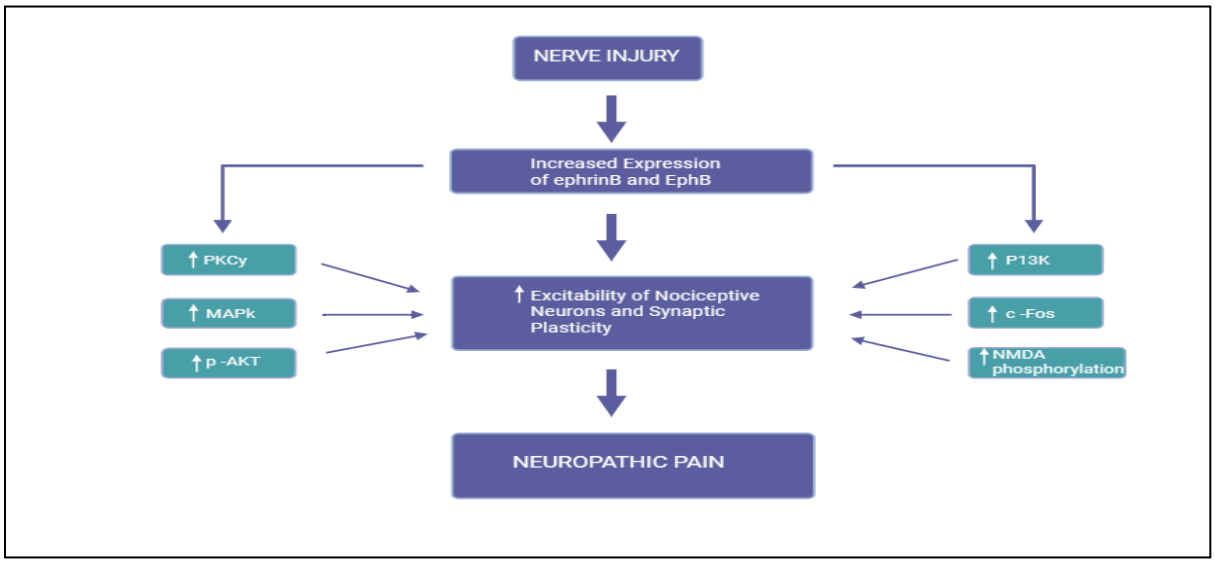


Figure 2 Ephrin and EphB receptor tyrosine kinase leads' function in NP. Elevated levels of PKY$_\gamma$, MAPk, p-AKT, P13K, and NMDA phosphorylation via ephrin-B and EphB pathways cause increased activity of pain-sensing neurons and synaptic flexibility after nerve loss, which contributes to neuropathic pain suffering

Pathogenesis of CINP

Although the precise mechanisms behind CINP are still complicated and not fully understood, a number of important processes have been identified (Kouli, Torsney, and Kuan 2018).

Mitochondria Dysfunction and Oxidative Stress

Oxidative stress and the generation of reactive oxygen species (ROS), such as peroxide and hydroxyl radicals, are caused by mitochondrial damage in both neuronal and non-neuronal cells. Neuropathic pain brought on by chemotherapy is exacerbated by this oxidative imbalance (CINP). Poor signal transmission results from this disruption of axonal transport (C. Guo et al. 2013). Raised reactive oxygen species (ROS) intensify neuropathic pain by inducing apoptosis, disrupting cell structure, and demyelinating cells. Furthermore, ROS triggers immunological responses, which in turn promote the synthesis of cytokines that promote inflammation (Z. Li, Chen, and Li 2019). Damage to mitochondria is sustained by this self-amplifying process. Research demonstrating the complicated processes behind chemotherapy-induced non-infectious pneumonia (CINP) has revealed mitochondrial swelling, vacuolation, and structural loss with these medicines (Oiki 2017).

Ion Channels

Both neuronal and glial cells' membrane excitability and neurotransmitter release are controlled by essential proteins called ion channels. Many channels are important in these activities, such as sodium (NaV) channels, potassium (KV) channels, and transient receptor potential (TRP) channels (Bhatti, Bhatti, and Reddy 2017). Specifically, action potential initiation and propagation in neurons depend on NaV channels. Mutations in the genes encoding NaV channel proteins can lead to a variety of neurological disorders (Kim et al. 2004). According to studies, variations in particular NaV channel genes may be able to predict whether cancer patients would develop peripheral neuropathy or how severe it will be. NaV channel function has also been found to be changed

in situations such as oxaliplatin-induced cold allodynia, indicating the importance of these channels in the genesis of neuropathic pain(de Lera Ruiz and Kraus 2015) .

Axon Degeneration

Axonal degeneration refers to the breakdown of nerve fibers, particularly those responsible for transmitting pain signals from the periphery. The process includes myelin loss, alteration of axonal structure, and hindrance of transport of essential materials along the axon (Koch and Lingor 2016). Chemotherapy agents like paclitaxel disrupt axons which leads to degeneration This damage disrupts microtubules (important parts of cells) and weakens axonal transport, and overall, the changes affect distal nerve segments and axonal membrane structure (the outer layer) (Yang et al. 2016). Cytokine and chemokine signaling may also affect axon degeneration. This leads to chemotherapy-induced peripheral neuropathy (CIPN), impeding sensory perception and nerve functioning. (Brandolini et al. 2019).

Calcium homeostasis

Calcium homeostasis is the process of regulating calcium (Ca2+) concentration in a cell which is important for several physiological processes. Drugs like vincristine, bortezomib and paclitaxel can injure neurons by disturbing calcium levels. This is often due to mitochondrial dysfunction (Rizzoli 2019). Cell damage frequently involves calcium influx, and improper handling of this process is linked to processes of cell death such as apoptosis. Since voltage-gated calcium channels are important in controlling nerve cell excitability, pain treatment techniques target them (Danese et al. 2020). Drugs that target these channels have demonstrated promise in mouse models for the relief of pain brought on by drug-induced nerve injury without impairing motor performance. All things considered, cellular health depends on maintaining an appropriate calcium balance, and disturbances in calcium homeostasis may exacerbate the condition of drug-induced peripheral neuropathy (Koivisto et al. 2024).

Taxanes, alkylating agents, vinca alkaloids, gemcitabine, anthracyclines, and capecitabine are common chemotherapeutic agents linked to neuropathy; the most common causes are vinca alkaloids, taxanes, and platinum agents (Dietrich 2020).

Chemotherapeutic Agents and their Mechanisms in CINP

Chemotherapeutic drugs can cause structural damage to the nervous system, resulting in demyelination, axonal damage, cranial neuropathies, autonomic dysfunction, and sensory or motor deficits. The frequency of chemotherapy-induced peripheral neuropathy (CIPN), a serious side effect, varies according to the kind of chemotherapy agent employed (Areti et al. 2014). For example, platinum-based drugs affect 70-100% of patients, taxanes impact 11-87%, thalidomide affects 20-60%, and ixabepilone affects 60-65%. Chemotherapy-induced peripheral neuropathy (CIPN) occurs in around 68.1% of cases during the first month after chemotherapy, drops to 60% after three months, and then drops to 30% at six months or later. (Shahlaei et al. 2024a). Common chemotherapeutic agents associated with neuropathy include taxanes, alkylating agents, vinca alkaloids, gemcitabine, anthracyclines, and capecitabine, with vinca alkaloids, taxanes, and platinum agents being the most frequent causes (Zajączkowska et al. 2019).

Platinum-based chemotherapeutic agents (Oxaliplatin, Cisplatin, and Carboplatin)

Chemotherapy medications based on platinum are essential for treating a variety of solid malignancies. In particular, advanced colorectal, stomach, oesophagus, liver, and pancreatic cancers are treated with oxaliplatin (Shahlaei et al. 2024b). On the other hand, cisplatin and carboplatin work well against a variety of tumor types, including small-cell lung malignancies, brain, ovarian, testicular, and bladder tumors. The manifestation of Cisplatin-induced peripheral neuropathy (CisIPN) occurs when the total dose surpasses 350 mg/m2. When the total dosage reaches 500-600 mg/m2, 92% of patients have CisIPNa (Ho, Woodward, and Coward 2016). Elevated PKC activity in areas above the spinal cord. Gamma/epsilon PKC isoforms are upregulated in the thalamus and periaqueductal region. Increased expression of pro-excitatory channels, particularly HCNs, is correlated with decreased levels of TRAAK and TREK1 inhibitory channel expression (Lieu, Tenorio, and Kerr 2013).

Taxanes

A class of drugs known as taxanes is used to treat cancer. It works by attacking microtubules and interfering with their regular processes of disintegration and reconstruction. This interference prevents cancer cells from proliferating, which eventually leads to cell death. Docetaxel, cabazitaxel, and paclitaxel are a few examples of taxanes (Mosca et al. 2021). The FDA has approved these medications for treating ovarian, prostate, breast, and non-small cell lung cancers, among other malignancies. Conversely, a significant number of chemotherapy-induced peripheral neuropathy (CIPN) cases have been associated with the use of taxanes; rates have been recorded ranging from 11% to 87%, with paclitaxel having the highest rates. Heat and cold allodynia are caused by the loss of certain A and C fibres that are warm and chilly (Das et al. 2021).

Vinca alkaloid

The plant known as the Madagascar periwinkle is the source of vinca alkaloid drugs. They function by interfering with the synthesis and disintegration of microtubules, which impedes the movement of materials within cells (Sharma et al. 2022). Vincristine, vinblastine, vinorelbine, and vindesine are often used as members of this pharmacological family. They are used to treat a number of cancers, including Hodgkin and non-Hodgkin lymphomas, non-small cell lung cancer, and testicular cancer. (Zhou and Rahmani 1992). The first three months of therapy are usually when symptoms appear. Hand and foot discomfort are among the early indicators. A rise in dorsal horn 5-HT2A and DRG receptors Peripheral nociceptive fibers and spinal dorsal horn neurons are sensitized (Wu et al. 2020).

Bortezomib

A drug called bortezomib (BTZ) is commonly used to treat solid tumors and multiple myeloma. When it was shown to be an effective cytotoxic agent, its initial recognition for anti-inflammatory qualities was swiftly superseded, and it was used to treat cancer (Scott et al. 2016). Despite being approved for single use at first, BTZ is now typically used in combination treatment regimens with other drugs Bortezomib disrupts normal protein degradation pathways, leading to the accumulation of damaged and misfolded proteins in neurons. In the end, this accumulation damages neurons by producing oxidative stress and mitochondrial malfunction (Dou and Zonder 2014). Additionally, bortezomib interferes with axonal transport and the function of Schwann cells, which are essential for myelin sheath maintenance. These disruptions collectively lead to demyelination, axonal

degeneration, and altered pain signaling, culminating in neuropathic pain (X. Li et al. 2020).

Mechanism of combination chemotherapeutic drugs

Oxaliplatin, Paclitaxel, Vincristine and Bortezomib

In DRG neurons, elevated cytosolic calcium levels lead to reactive oxygen species, which generate free radicals that worsen neuronal cytotoxicity (Ma, Zhang, and Westlund 2009).

Paclitaxel, Vincristine and Oxaliplatin

DRG neurons' activation of the calcium-activated proteases caspases and calpains. Apoptotic cascade initiation that results in neuronal cytotoxicity (Metwally, Zhao, and Zhang 2021).

Vincristine, Paclitaxel, and Bortezomib

an increase in the skin's LC cell count. Increased production of TNF-alpha, IL-1, IL-6, and NO by glial cells, macrophages, and LC cells (Enk and Katz 1995).

Cisplatin, Oxaliplatin, Paclitaxel

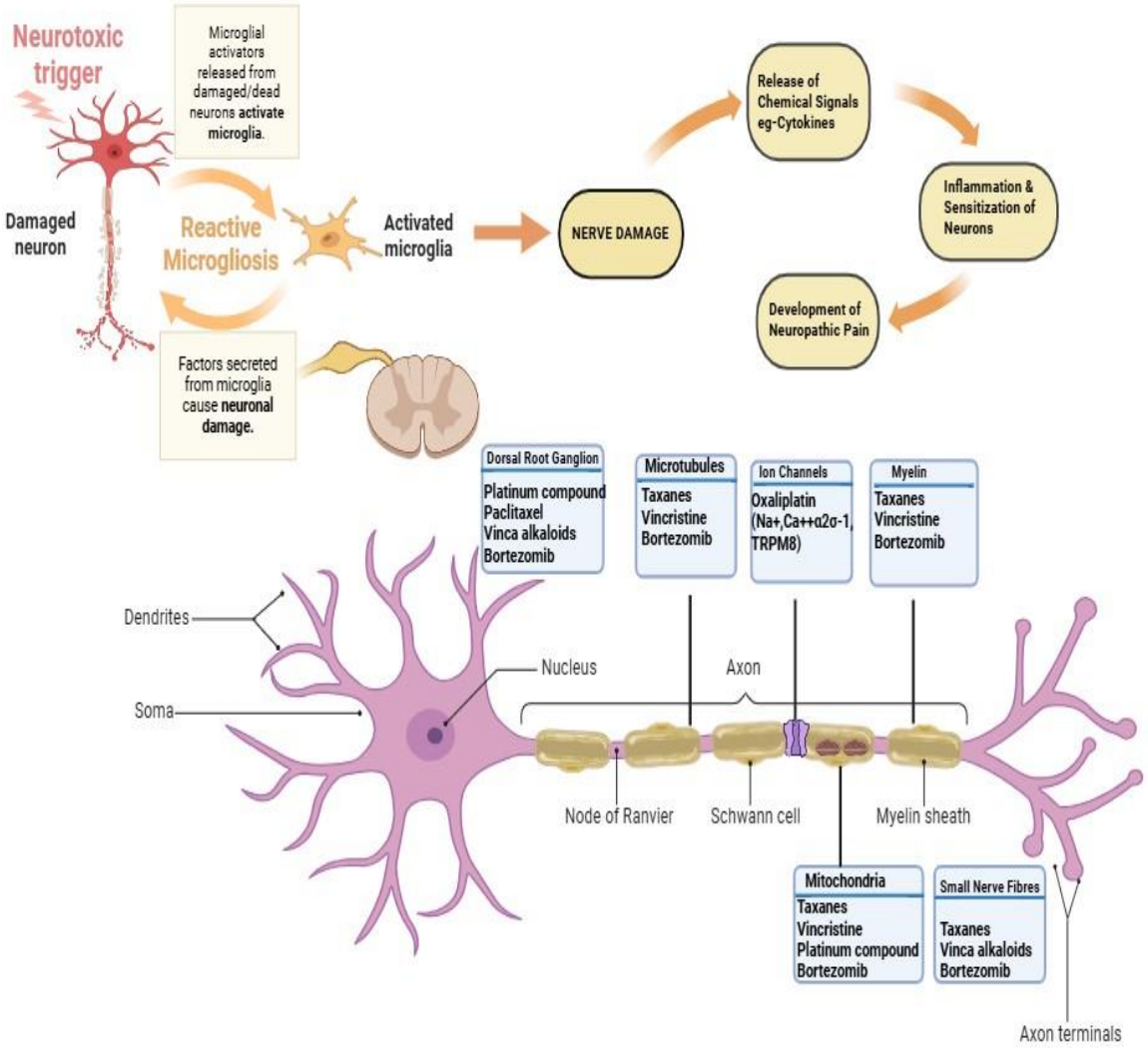
Nociceptor sensitivity is increased when DRG neurons produce more TRPV1, TRPA1, TRPM8, and TRPV4 (Crosson and Talbot 2022).

Paclitaxel, Vincristine, Bortezomib, Cisplatin

The mitochondria of axons are larger and vacuolated. The activation of caspases, initiation of the apoptotic pathway, opening of the mitochondrial permeability transition pore (mPTP), and release of intracellular calcium occur (Webster 2012).

Paclitaxel, Cisplatin

Antagonists of NMDA receptors counteract NP produced by anticancer drugs. A neurotoxic trigger lead to nerve damage through a series of events starting with the activation of microglia(Wilcox et al. 2022)This process involves the release of microglial activators from damaged neurons, which cause reactive microgliosis. The activated microglia secrete factors that induce neuronal damage, further leading to nerve damage (Lull and Block 2010). This sequence results in the release of chemical signals, such as cytokines, which contribute to inflammation and sensitization of neurons, ultimately developing neuropathic pain.



Chemotherapy-induced peripheral neuropathy involves various mechanisms and targets within neuronal cells. As depicted in (Table 1), the neurotoxic effects of different chemotherapeutic agents are mediated through several pathways (Carozzi, Canta, and Chiorazzi 2015). Illustrates the complex mechanisms involved in the development of neuropathic pain, particularly focusing on the impact of anti-cancer drugs. It shows how these drugs can influence various cellular and molecular pathways, leading to cytotoxicity and neuropathic pain. Chemotherapy (Pellacani and Eleftheriou 2020).

Table 1 Cancer chemotherapy-induced neuropathy is caused by several different ways

Drug	Targets	Mechanism	References
Vincristine, Paclitaxel, Bortezomib, and Cisplatin	Mitochondrial changes	Release of intracellular calcium by the opening of mPTP, activation of the apoptotic pathway Enlarged and filled with fluid mitochondria within axons.	(Jaggi and Singh 2012a)

Oxaliplatin, Paclitaxel, Vincristine and Bortezomib		DRG neurons' reactive oxygen species.	(Jaggi and Singh 2012b)
	neuronal cytotoxicity	The production of free radicals results from an increase in cytosolic calcium and causes neuronal cytotoxicity.	(Lipton and Nicotera 1998)
Vincristine Oxaliplatin Paclitaxel	Sodium channels	Paraesthesia is predisposed by an increase in sodium ions in the DRG.	(Geisler et al. 2019)
Vincristine	5-HT receptors	Elevated levels of 5-HT2A receptors observed in the dorsal horn and DRG neurons	(Thibault et al. 2008)
Paclitaxel Vincristine Suramin	Calcium	Enhanced 2-1 subunit expression in the DRG and dorsal horn	(Jaggi and Singh 2012c)
Oxaliplatin	Protein kinase C (PKC)	Pk C activity is elevated in supraspinal areas	(Sanna, Ghelardini, and Galeotti 2016)

DIAGNOSIS

The diagnosis of CIPN is multifaceted and cannot rely solely on a single, definitive test due to its varied presentation. Clinical judgment plays a crucial role in conjunction with specific assessment tools. Tests to confirm nerve damage, qualitative sensory evaluation, and skin biopsies are essential in confirming CIPN (Jaggi and Singh 2012d). Additionally, bedside assessment of sensory indicators and confocal microscopy of the cornea can provide valuable insights into neuropathic damage. Several screening instruments have been developed over the past decade to aid in the evaluation of CIPN (Kundu et al. 2022). The purpose of these evaluation instruments is to examine specific symptoms and indicators associated with neuropathic pain. These include the Neuropathic Pain Scale, Neuropathic Pain Questionnaire, Leeds Assessment, Douleur Neuropathies Questionnaire, Questionnaire on Neuropathic Pain, Pain DETECT, and ID Pain They evaluate various sensory indicators, pain types, and discomfort levels, aiding in the comprehensive assessment of CIPN in clinical settings (Herr 2004).

Preventative treatment strategies for CIPN

Chemotherapy-induced neuropathic pain (CINP) poses a significant challenge in cancer treatment due to its debilitating effects on patients' quality of life. To mitigate the development and severity of CINP, several preventative treatment strategies have been explored (Miltenburg and Boogerd 2014). For patients suffering from neuropathic pain brought on by chemotherapy, preventive treatment methods can significantly improve their

quality of life and results. (Jheng et al. 2024).

Pharmacological Interventions

Nutraceutical

According to a study done by Cochrane and also according to ASCO (American Society of Clinical Oncology) expert panel of various interventions: omega-3 fatty acids use in patients on paclitaxel/carboplatin chemotherapy, vitamin C, vitamin E, N-acetylcysteine-carnosine, and glutathione (GSH) use were not recommended (Cumpston et al. 2019). Moreover, ALC (acetyl-L-carnitine) did not have any effect on CIPN after 12 weeks but did increase it after 24 weeks. In different research, getting vitamin E supplements lowered peripheral neurotoxicity in people getting the chemotherapy drug cisplatin. At the animal level, vitamin E and silibinin have both demonstrated resolution of oxaliplatin-induced pain and improvement of motor coordination in CIPN rats. Consequently, clinical trials have been conducted to evaluate the vitamin E effects in managing CIPN development (Di Cesare Mannelli 2012; et al. 2012). The oral administration of alpha-lipoic acid (ALA) has failed to prevent oxaliplatin or cisplatin-induced neurotoxicity due to considerable dropout and poor compliance with the dose suggested (Y. Guo et al. 2014).

Calcium and Magnesium Infusion

According to the most comprehensive retrospective study (Knijn et al. 2011), Ca/Mg infusions reduced the severity of oxaliplatin-induced neurotoxicity of all grades. To be more specific, the severity of acute symptoms caused by oxaliplatin were remarkably decreases and the occurrence of cumulative neuropathy may be late, particularly at an oxaliplatin dosage of 85mg/m (2). Surprisingly, Ca/Mg infusion helps to reduces the nruotoxicity, but the efficacy remained unchanged. These findings recommended that Ca/Mg infusions may help a favourable method of managing chemotherapy induced peripheral neuropathy in cancer patients receiving oxaliplatin based treatment (Wolf et al. 2008) and possibly other chemotherapies, without losing the effect of the treatment.

Symptomatic Treatments

There are a various of drugs agents present now to manage neuropathic pain. Randomized controlled trials (RCTs) have been assumed on the two important classes of drugs ie antidepressants and anticonvulsants (Attal 2019). Most reviews and meta-analyses suggest that tricyclic antidepressants are the best. Substances like duloxetine, venlafaxine, and gabapentin have been found to have neuroprotective effects against CIPN (Baethge et al. 2022). Right now, it's still difficult to prevent chemotherapy-induced peripheral neuropathy (CIPN). Recent studies does not suggest any drug to prevent this situation. It’s not recommended to use acetyl-l-carnitine for this purpose (Loprinzi et al. 2020). If severe neuropathy or functional impairment occurs in a patient, the clinician may delay, reduce the dose, switch drugs, or stop chemotherapy. Of the available treatment options for established painful CIPN, duloxetine has the best evidence despite this, its effect is still moderate (Desforges et al. 2022). Over the years, a lot of research have been done to find that various drugs acting on CIPN do not have a proper consensus. This could be due to the diversity of the various manifestations and complex drug interactions occurring in antineoplastic agents. New treatments need to be looked into a little better to see if they are working (Anand et al. 2023). The pharmacological management of neuropathic pain involves a variety of drugs, each with distinct

mechanisms of action and associated side effects. These treatments are typically categorized into first-line, second-line, and third-line options based on their efficacy and safety profiles (Table 2) (Saini and Twelves 2021).

Table 2 Pharmacological treatments for neuropathic pain, including their mechanisms of action and side effects

	Drugs	**Mechanisms of action**	**Side effects**	**Reference**
First line	Tricyclic antidepressants: Nortriptyline, Amitriptyline	Inhibition of monoamine reuptake, blockade of sodium channels, and suppression of cholinergic activity.	Somnolence, anticholinergic effects and weight gain	(Kamp et al. 2024)
	Serotonin noradrenaline reuptake inhibitors: Duloxetine, Venlafaxine	Serotonin and noradrenaline reuptake inhibition	Nausea, abdominal pain, constipation, Nausea and hypertension at high doses	(Baldwin 2006; Marcum, Duncan, and Makris 2016)
	Ca^{2+} channel α2δ ligands: Gabapentin, Pregabalin	Act on the voltage-gated calcium channels, which decrease central sensitization	Sedation, peripheral edema	(Patel and Dickenson 2016; Thorpe and Taylor 2007)
Second line	Lidocaine 5% plaster:	Sodium channel blockade	Local erythema, itching and rash	(Goddard and Reaney 2018)
	Capsaicin high concentration 8% patch:	Transient receptor potential cation channel subfamily V member 1 agonist	Pain, erythema, itching	
Third line	Neurotoxin Botulinum toxin A	Ach release inhibitor and neuromuscular-blocking agent	Pain at the injection site	(Montecucco et al. 1996)

Topical therapies

Some topical applications that can provide relief in neuropathic pain are: -

Lidocaine Patch: Lidocaine patches provide local analgesia by blocking sodium channels in peripheral nerves, offering relief from neuropathic pain (Dahlhamer et al. 2018).

Amitriptyline Cream: Amitriptyline, a tricyclic antidepressant, has been formulated into a cream for topical application and has shown a theoretical advantage in reducing neuropathic pain intensity (Moore et al. 2015).

Capsaicin Cream: Capsaicin, a compound derived from chili peppers, has been used topically to relieve neuropathic pain by desensitizing nociceptive nerve fibers. Capsaicin may provide moderate pain in neuropathic

pain (Hayman and Kam 2008).

NSAIDS gel: NSAIDs in gel form, such as diclofenac gel, Ibuprofen can be applied topically to reduce inflammation and alleviate pain associated with Neuropathic pain.

However, more studies are needed to conclude the effectiveness of the use of topical therapies, especially in CIPN (Wade et al. 2019).

Non-Pharmacological Approaches

Physical Therapy

Techniques such as exercise, massage, and stretching can effectively improve nerve function and alleviate neuropathic pain in cancer patients. Exercise, in particular, has shown significant benefits in clinical, functional, and survival outcomes across different cancer types, making it a recommended intervention (Leitzelar and Koltyn 2021). However, precautions and screening are necessary for patient safety. There's a growing need to standardize reporting in clinical trials, establish guidelines, and integrate exercise and rehabilitation services into cancer care systems. Studies have demonstrated that exercise can reduce sensory symptoms in chemotherapy-induced peripheral neuropathy (CIPN), especially in older patients, males, or those with breast cancer (Lee and Henderson 2018). Recent reviews also support the effectiveness of exercise interventions in improving CIPN symptoms and reducing postural stability loss induced by CIPN (Huang et al. 2024).

Acupuncture

Acupuncture shows promise in relieving neuropathic pain, particularly in cancer patients, although further research is needed for conclusive evidence. A recent systematic review involving 19 randomized controlled trials (RCTs) and 1174 patients revealed that acupuncture not only reduced pain but also improved nerve conduction velocity, indicating potential benefits beyond pain management (Friedemann et al. 2022a). Pilot studies exploring electro-acupuncture and laser acupuncture have also demonstrated positive outcomes in self-reported measures and sensory testing for chronic chemotherapy-induced peripheral neuropathy (CIPN), highlighting acupuncture's potential as a complementary therapy in managing neuropathic pain in cancer patients (Friedemann et al. 2022b).

QUALITY OF LIFE

Chemotherapy-induced neuropathic pain can significantly impact a patient's quality of life, affecting physical, emotional, and social well-being. The persistent pain, often accompanied by sensory disturbances like tingling or numbness, can impair daily activities, disrupt sleep patterns, and lead to fatigue and mood changes (Mandal et al. 2023). These symptoms may contribute to decreased mobility, limitations in self-care, and challenges in maintaining social relationships and work productivity. Furthermore, the psychological distress caused by chronic pain can exacerbate anxiety and depression, further impacting the overall quality of life (Cunha, Tavares, and Costa-Pereira 2024; Liu et al. 2023). Enhancing patients' quality of life and promoting general well-being before and after cancer treatment requires a comprehensive approach to chemotherapy-induced neuropathic pain that includes pain management techniques, psychological support, and rehabilitation programs (Liu et al. 2023) .

Conclusions

Chemotherapy-induced neuropathic pain is a significant concern in cancer treatment, impacting patients' quality of life and treatment outcomes. This review has highlighted the mechanisms underlying this pain, including neuronal damage, inflammation, and altered ion channel activity. To reduce symptoms and improve patients' quality of life, many pharmacological and non-pharmacological strategies have been investigated. However, challenges such as limited efficacy and adverse effects persist, emphasizing the need for further research and innovative approaches in managing this debilitating condition. Integrating multidisciplinary strategies and personalized care can contribute to enhancing the quality of life for cancer patients experiencing chemotherapy-induced neuropathic pain.

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