Recent advancement in the treatment of neuropathic pain: A valid Strategy for the discovery of novel therapeutics

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ABSTRACT

Neuropathic pain (NeP) is an enervating state resulting from certain diseases, damage, and dysfunction of the peripheral or central nervous system. The crosstalk of neurons and interactions between pro-and anti-inflammatory cytokines, glial cells, and inflammatory immune cells are responsible for the occurrence and maintenance of NP. It is caused by various nerve-affecting mechanisms that affect the somatosensory system, such as trauma, infectious diseases, diabetes, postherpetic neuralgia, and chronic inflammation. The therapeutic suggestions for neuropathic pain vary depending on the different causes and underlying molecular mechanisms necessitating the development of generally effective and standardized therapy. However, accentuation of non-pharmacological treatment approaches like yoga therapy and cognitive behavioral therapy draws attention due to their long-term effectiveness in controlling the pain with negligible detrimental effects when used alone or in combination with conventional pharmacological medications.

BACKGROUND

- Peripheral neuropathic pain (PNP) is the condition in which the parts of nerves branching off the spinal cord or peripheral nervous tissues get damaged due to certain stimuli that are greater than the capabilities of the nervous system, resulting in chronic neuropathic pain, which is often difficult to cure.
- The clinical symptoms of PNP are frequently considered in terms of their positive aspects, such as paraesthesia, dysesthesia, hyperalgesia and spasm and negative aspects, including decreased neural impulse conduction hypoesthesia or anaesthesia, as well as weakness.
- Peripheral neuropathy includes inflammatory, metabolic, toxic, and mechanical nerve lesions that could all be its causes.
- Also, several studies have found that immune cells and proinflammatory mediators play an important role in the generation of NP following peripheral nervous system injury.
- NP can be caused by a number of medical conditions seen in psychiatric practice, such as infection, traumatic nerve injury, metabolic abnormalities and nerve compression.

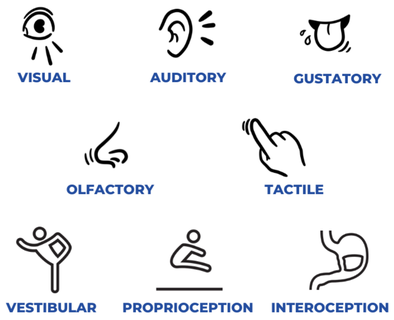
OBJECTIVES

- To demonstrate the postures, breathing, and meditation enhance the alleviation of stress, anxiety, and depression association with Nep.
- To update the knowledge of the fundamental processes leading to the creation of NeP it was established that gene target is one of the best techniques to produce the treatment for neuropathic pain.
- To understand the major genome sequencing programs and considerable breakthroughs in microarray and target validation procedures, new treatment approaches are being rigorously explored.
- To discuss the ancient to novel therapeutics strategies used to treat the neuropathic condition and also interpret the pro and cons of the different treatments.

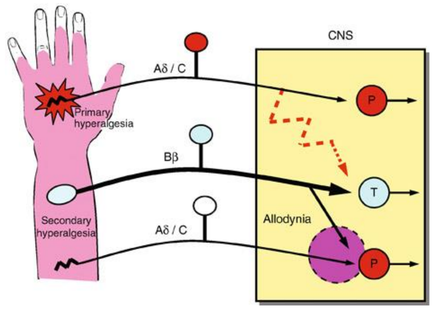
PERIPHERAL NEUROPATHY

Analysis of certain clusters showed that patients with PNP can be sub grouped into:

1. Sensory loss



2. Hyperalgesia



TREATMENTS

For sensory loss

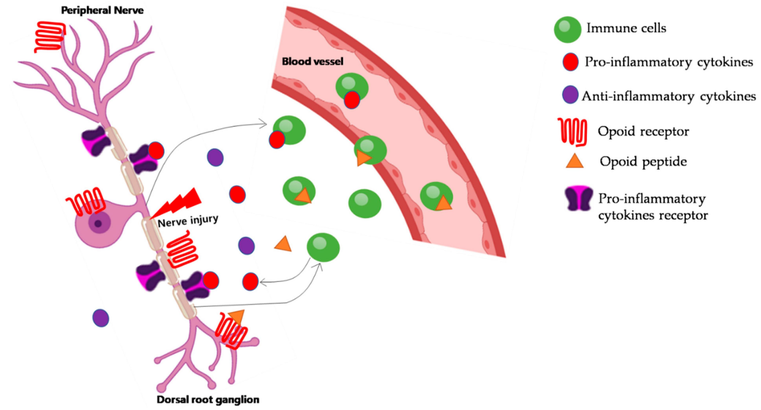
- Patients having NP associated with sensory loss (one of the most common profiles in PNP) were more likely to take tricyclic antidepressants, also resulting in an elevated incidence of depressive symptoms while anticonvulsants were commonly used for NP related to thermal hyperalgesia.
- In a prospective randomised placebo-controlled trial (PCT) with oxcarbazepine, in a prearranged analysis of a PCT with botulinum toxin, and in a meta-analysis study using topical capsaicin patches without a placebo arm, patients with a baseline QST (quantitative sensory testing) profile similar to thermal hyperalgesia showed higher efficacy, while the efficacy of lidocaine was reviewed to be poor in a PCT.

For hyperalgesia

- In a PCT with oral opioids, patients having sensory loss showcased higher efficacy on the other hand oxcarbazepine had a decreased efficacy while in PCTs with oral pregabalin, topical lidocaine, lamotrigine, or intravenous lidocaine, patients with mechanical hyperalgesia had a higher effectiveness.
- oxcarbazepine was found highly effective in relieving pain for patients with PNP with irritable than in patients with non-irritable nociceptor phenotype in a double-blind placebo-controlled phenotype-stratified study.

CURRENT THERAPEUTICS

- Currently available therapeutic aspects consist of drug therapy such as anticonvulsants, the lidocaine patch 5%, antidepressants, opioids, tramadol, etc., and other interventions include peripheral or neuraxial nerve blockade, implanted spinal cord stimulators, implanted intrathecal catheters, etc.
- Current treatments have a narrow therapeutic index and have side effects which are poorly manageable by patients. The limited efficacy and compatibility of available PNP treatments affects the working lives of patients as it affects them physically as well as mentally. This scenario demonstrates the need for better PNP treatment to maintain and improve the quality of one's life.



- **Figure:** Current stem cell therapeutic for modulating Neuro-inflammation in neuropathic pain

CONCLUSIONS

- Although several therapeutic approaches have been introduced in clinical practice but the pharmacological treatment of PNP remains a challenge for clinicians.
- Potential targeting sites should be discovered which directly ameliorate PNP. In future, novel therapeutic agents working at the level of mitochondrial metabolic control are likely to further improve the management of PNP.
- Natural sources, for the treatment of PNP, should be explored in order to provide safe and cost effective treatment to the patients.
- Alteration of metabolic pathways is directly involved in th epathogenesis of PNP, thus exploration of drugs acting through these pathways and conducting extensive clinical trials, may lead to evolution of curative therapy for PNP rather than a symptomatic relief with conventional therapy available.

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