WAYS TO IMPROVE TREATMENT EFFICACY IN OLDER ADULTS SUFFERING FROM NEUROPATHIC PAIN

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Abstract

Neuropathic pain is frequently seen in older adults. The treatment options include pharmacological and non-pharmacological strategies. Researchers have studied on the methods that can be used to improve therapy efficacy in older people who are suffering from neuropathic pain. These include, but are not limited to, accurate evaluation of positive and negative symptoms/signs, management of potential comorbidities or underlying diseases, mitigation of adverse events arising from therapeutic interventions, and personalized treatment. Clinical and biological markers are one of the most recent topics that have been proposed for personalized treatment. More studies are needed to improve our understanding on clinical and biological markers in the treatment of neuropathic pain. The current article aimed to review recent knowledge on the ways to improve treatment efficacy in older adults with neuropathic pain.

Keywords: biomarkers; elderly; neuropathic pain; older adults; pain; therapeutics

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Key Messages for Research and Practice

- A comprehensive approach is required to manage neuropathic pain in older adults.
- Personalized treatment, which involves accurate evaluation of symptoms, management of comorbidities, and consideration of individual responses to therapy paves the way towards more precise and tailored interventions.
- More research is needed to enhance understanding in exploring clinical and biological markers to refine treatment approaches and address the specific needs of older adults with neuropathic pain.
Introduction

Neuropathic pain impacts 7-10% of the overall population [1]. However, limited data exists regarding the prevalence of neuropathic pain in the elderly [2]. Akram and Malik conducted a cross-sectional survey, which indicated a notably high occurrence of neuropathic pain among individuals aged 60 and above who had experienced chronic pain for over 6 months [3]. Several prevalent neuropathic pain conditions among older adults include, but are not restricted to, central post-stroke pain syndrome, spinal stenosis and related myelopathy/radiculopathy, multiple sclerosis, transverse myelitis, traumatic spinal cord injury/brain injury, compressive neuropathic pain, post-herpetic neuralgia, diabetic neuropathic pain, complex regional pain syndrome type II, and chemotherapy-induced neuropathy [4-9].

Neuropathic pain is associated with damage or disease affecting the somatosensory system. Consequently, its treatment differs from that of other pain types (e.g. nociceptive pain) where the somatosensory nervous system remains unaffected [10]. Less than half of the patients with neuropathic pain exhibit a response to treatment. Moreover, the observed response tends to be moderate at best [11]. Since neuropathic pain significantly deteriorates an elderly individual’s quality of life, proper management is essential.

The aim of this narrative review was to discuss the ways to improve treatment efficacy in older adults with neuropathic pain.

What strategies can be employed to enhance treatment efficacy in elderly individuals suffering from neuropathic pain?

The optimal management of neuropathic pain encompasses several objectives, including: i) improvement in pain scores, ii) resolution of both positive and negative symptoms associated with the condition, iii) definitive treatment of concurrent comorbidities or underlying diseases, iv) mitigation of adverse events arising from therapeutic interventions, and v) personalized treatment.

Accurate evaluation of positive and negative symptoms/signs

Achieving all the above-mentioned objectives in their entirety can frequently pose a challenge. Adhering to the principles of individualized treatment can pave the way for a better treatment efficacy. In this regard, detailed anamnesis and physical examination evaluating potential negative (e.g. hypoalgesia, tactile thermal/punctate hypesthesia) and positive symptoms and signs (punctate hyperalgesia, allodynia, temporal summation) are essential [12]. In addition to clinical bedside assessments, quantitative sensory testing represents a valuable tool for assessing the functional status of the somatosensory system [13]. Accurate evaluation of the symptoms and signs enables physicians to develop individualized treatment strategies. Baron et al. introduced the categorization of patients with neuropathic pain based on sensory abnormalities related to pain as an initial stage towards implementing a stratified treatment paradigm [14]. The subtyping was performed on a cohort of 902 patients diagnosed with painful peripheral neuropathy and the method involved utilizing quantitative sensory testing followed by cluster analysis. The subgroups included thermal hyperalgesia, sensory loss, and mechanical hyperalgesia. The underlying pain mechanisms associated with the three subgroups were also delineated. In “thermal hyperalgesia” subgroup, there is an enhanced expression of receptors and channels on primary afferent nociceptors. The state of peripheral sensitization is expected to be responsive to sodium channel blockers, with a moderate response to antidepressants or gabapentinoids. In the “sensory loss” subgroup, degeneration of primary afferent fibers is the main mechanism. There is spontaneous pain due to ectopic action potentials proximal to injured nociceptors. A more pronounced response to antidepressants is anticipated. Regarding the “mechanical hyperalgesia” subgroup, there is selective degeneration of small primary afferents, central sensitization and spontaneous activity in both peripheral and/or central nervous systems. Such individuals are expected to be more responsive to gabapentinoids [14].

Detailed assessment of potential comorbidities or underlying diseases

The decisive management of concurrent comorbidities or underlying diseases stands as a pivotal step in addressing neuropathic pain effectively [15]. For instance, the stability of glycemic control is important in managing painful diabetic peripheral neuropathy. In this context, alongside optimal pharmacological approaches, non-pharmacological interventions such as health behavior modifications are recommended. These interventions encompass exercise, reduction of sedentary habits, and dietary adjustments [16].

Comorbidities such as sleep disorders demand special consideration, as they influence the selection of medications. For instance, patients experiencing insomnia may benefit from
pharmacological interventions aimed at enhancing nighttime sleep quality. A comprehensive approach to addressing comorbid clinical conditions would enhance treatment efficacy, as well as the quality of life in patients experiencing neuropathic pain. One of the ways to improve management of neuropathic pain in older adults is being aware of the co-medications. Given the high frequency of multimorbidity in the elderly, duplicate drugs should be avoided. The physician should also be aware of the pharmacological agents that may interact with the drugs that will be prescribed for neuropathic pain medications [17, 18]. This approach is also helpful to prevent from adverse reactions.

**Personalized treatment**

Recent literature particularly highlights personalized treatment in neuropathic pain. In such approach, all the issues mentioned above should be taken into consideration. Patient’s comorbidities, co-medications, needs, and preferences should be evaluated meticulously.

There are several predictors of treatment response that are proposed for developing personalized management strategies. These are categorized as clinical and biological predictors. Clinical predictors of treatment response can be evaluated by detailed anamnesis, bedside sensory testing, quantitative sensorial test, and patient reported outcome measures [11].

Biological predictors of treatment response include molecular, functional, and structural markers, that is to say, biomarkers. In terms of molecular biomarkers, genetic and genomic markers, proteomics and metabolomics have been studied. NAv1.7, which is a voltage-gated sodium ion channel, is encoded by SCN9A gene. Targeted inhibition of Nav1.7 is expected to pose little risk of misuse or addiction, central nervous system or cardiac adverse effects. Metabolomics provides a very accurate biochemical representation of a patient’s clinical phenotype. Metabolomics has considerable potential as a source of new clinical biomarkers [19, 20]. Proteomics can complement metabolomics by identifying proteins and peptides that act as signaling agents in pain-related processes [21, 22]. Functional biomarkers include peripheral and central markers. Centrally, quantitative electroencephalography can be used as a biomarker for mu-opioid receptor activity; non-invasive magnetic resonance spectroscopy imaging can quantify metabolite levels in the brain. Functional magnetic resonance imaging (MRI) and magnetoencephalography can also be used to predict treatment responsiveness. Peripherally, microneurography can depict nerve fiber activity and threshold tracking techniques can show axonal excitability. Regarding the structural biomarkers, anatomic MRI evaluates density and volume in brain areas; diffusion MRI accesses white and grey matter integrity; skin biopsy shows intra-epidermal nerve fiber density [22]. Markers are regarded as objective predictors of treatment response. Therefore, the topic warrants further studies.

**Concluding remarks**

Neuropathic pain is common in older adults and treatment approaches vary. Several strategies can be employed to enhance treatment efficacy in elderly individuals suffering from neuropathic pain. One of the most recent strategies depends on the evaluation of markers of treatment response. Further trials are needed to enhance the knowledge on clinical and biological markers and to pave the way for adopting those into daily clinical practice.

**CONFLICTS OF INTEREST**

The author declares no conflicts of interest regarding the publication of this article.

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