NEUROPATHIC PAIN AS A CHALLENGING CLINICAL ENTITY IN OLDER ADULTS

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Abstract

Neuropathic pain is a challenging clinical entity in older adults. Certain clinical conditions such as diabetes mellitus, cerebrovascular diseases and infections may lead to neuropathic pain in the elderly. Recognizing neuropathic pain is essential for proper management. Neuropathic pain can be related to either peripheral or central conditions. A lesion or disease of the somatosensory system is required to define neuropathic pain. The assessment of neuropathic pain includes anamnesis, detailed physical examination, screening tools/questionnaires, quantitative sensory testing, and objective methods such as electroneuromyography, skin biopsy, and corneal confocal microscopy. The aim of this article was to review common neuropathic pain conditions in older adults and to provide an overview on the assessment tools.

Keywords: elderly, neuropathic pain, older adults, pain

Introduction

According to the revised definition proposed by The International Association for the Study of Pain (IASP), pain is “an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage” [1]. IASP and the Task force further added six keynotes describing in brief that: i) pain is a personal experience which is affected by biological, psychological, and social factors, ii) pain is different from nociception which is not inferred solely from sensory neuronal activity, iii) people learn the concept of pain from their experiences, iv) any report of an experience as pain deserves respect, v) pain not only has an adaptive role, but also may interfere with function and well-being, and vi) pain can be experienced regardless from verbal description [1].

Three main types of pain are nociceptive pain, neuropathic pain and nociplastic pain; particularly depending on the pathophysiology [1]. Nociceptive pain is caused by activation of nociceptors and tissue injury plays a certain role in nociceptive pain [2]. Nociplastic pain is a new definition of the IASP which refers to “pain that arises from altered nociception despite no clear evidence of actual or threatened tissue damage causing the activation of peripheral nociceptors or evidence for disease or lesion of the somatosensory system causing the pain.” [3]. Neuropathic pain, on the other hand, is related to a lesion or disease affecting the somatosensory system. Therefore, its management is different from other types of pain in which the somatosensory nervous system is not damaged [2]. Pain that cannot be designated as nociceptive, neuropathic, or nociplastic can be classified as “pain of unknown origin” [4].

Neuropathic pain is a challenging condition in elderly. Neuropathic pain can significantly deteriorate an elderly individual’s quality of life and is also related to the increased use of health care resources [5]. In this regard, proper assessment of pain in elderly is essential. The current article aimed to review common
neuropathic pain conditions in older adults and to provide a detailed description on the assessment tools.

Definition of neuropathic pain

The International Association for the Study of Pain (IASP) Special Interest Group on Neuropathic Pain (NeuPSIG) proposed a redefinition of neuropathic pain as “pain arising as a direct consequence of a lesion or disease affecting the somatosensory system” [2, 6]. Accordingly, a lesion or disease of the somatosensory system is necessary for considering any pain as “neuropathic”.

Prevalence and risk factors of neuropathic pain in elderly

The prevalence of neuropathic pain in the general population is between 6.9% and 10% [7]. Nevertheless, sparse data is available for the prevalence of neuropathic pain in elderly [8]. A cross-sectional survey by Akram and Malik revealed a very high frequency of neuropathic pain among patients above the age of 60 years who had chronic pain for more than 6 months [9]. Several clinical conditions/diseases, which are at increased prevalence among elderly population (e.g., cerebrovascular diseases), can increase the frequency of neuropathic pain in elderly. On the other hand, neuropathic pain in older adults may be underreported due to cognitive disorders or difficulties in completing questionnaires. Moreover, the perception of neuropathic pain can be altered among elderly individuals [7]. The frequency rates can also be affected by the screening questionnaire used. For instance, Sakai et al., by using the Neuropathic Pain Screening Questionnaire, identified 13 patients (43.3%) with neuropathic pain in a sample of elderly individuals with low back pain [10]. On the other hand, using the painDETECT questionnaire, 5 patients (15.6%) were assigned as having neuropathic pain [10]. Imagama et al. evaluated the risk factors of neuropathic pain in middle-aged and elderly individuals [11]. According to the results of this prospective longitudinal cohort study, poor gait ability, lumbar kyphosis, low body mass index, low percentage of the young adult mean, and low mental quality of life were appeared to be independent risk factors for the development of new neuropathic pain after five years [11]. Degenerative changes within the structures of the spine by aging can lead to neuropathic pain. For instance, facet hypertrophy and ligamentum flavum enlargement narrow the spinal canal and cause neurogenic claudication and radiculopathy [12].

When to refer pain as “neuropathic pain”?

There are some distinct features of neuropathic pain. The following criteria lead us to name any pain as definite, probable or possible neuropathic pain: i) The history of the patient indicates a relevant lesion/disease of the peripheral/central somatosensory system, ii) pain is inside a neuro-anatomically plausible area, iii) ≥ 1 pathological sensory finding in the neuro-anatomically plausible area, and iv) detection of a relevant lesion/disease of the peripheral/central somatosensory system by using ≥ 1 examination method [2, 6, 13, 14].

Common neuropathic pain conditions in older adults

Neuropathic pain in elderly can be classified according to the etiological origin. Central post-stroke pain syndrome (CPSP) is a common type of central neuropathic pain in elderly. Central spinal stenosis and related myelopathy can lead to neuropathic pain, as well. Other central conditions include -but not limited to- multiple sclerosis, transverse myelitis, and traumatic spinal cord injury/brain injury [7]. Peripheral conditions can be related to neuronopathy, radiculopathy, plexopathy, mononeuropathy, mononeuropathy multiplex, or polyneuropathy [15]. In this regard, peripheral neuropathic pain conditions include - but not limited to - diabetic neuropathic pain, compressive neuropathic pain, post-herpetic neuralgia, chemotherapy-induced neuropathy, complex regional pain syndrome type II, and post-amputation neuropathic pain [7].

Several painful conditions such as diabetic painful peripheral neuropathy, post-herpetic neuralgia and central post-stroke pain are frequent in elderly population. Post-herpetic neuralgia persists for ≥ 3 months following acute herpes zoster, which is associated with the reactivation of the dormant varicella zoster virus [16]. Post-herpetic neuralgia is persistent and often refractory neuropathic pain; shows unilateral distribution in 1 or more spinal dermatome [16, 17].

Diabetes mellitus is a common cause of painful neuropathy in older adults. However, underdiagnosis and undertreatment/mistreatment of diabetic sensorimotor polyneuropathy in clinical practice are also

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common [18]. A large sample-sized study revealed that the prevalence of painful diabetic peripheral neuropathy was 43.3% in patients with type 2 diabetes (aged 18-85 years) [19]. As an important finding, 54.3% of these patients were undiagnosed. The researchers also showed that the adjusted odds ratios for painful diabetic peripheral neuropathy were higher with increasing diabetes duration [19]. Painful peripheral neuropathy is typically felt in the feet (and often lower limbs) and hands in a glove and stocking distribution [12, 17]. Lower extremities are more likely to be affected than upper limbs [12].

Central post-stroke pain occurs following a cerebrovascular accident [20]. Pain is contralateral to the affected hemisphere. In case of lateral medullary infarction, pain can also be present in the ipsilateral side of the face [17]. There may be proximal referral of pain; pressure over a distal site in hand/foot may be felt in the shoulder/proximal thigh [12]. Sensory loss and hypersensitivity in the painful area may indicate the combination of deafferentation and the development of neuronal hyperexcitability. It is hard to determine the exact prevalence of central post-stroke pain, as it is also difficult to distinguish central post-stroke pain from other pain types that can be observed in stroke survivors (e.g., hemiplegic shoulder pain, painful spasticity, persistent headache) [20].

**How to assess neuropathic pain?**

In medical history, clues of neuropathic pain should be searched. The nature of the pain, its localization and density are important.

**The nature of pain**

Neuropathic pain can be discriminated from nociceptive pain in several ways. In this regard, evaluating the nature of pain is essential. Neuropathic pain is often spontaneous, radiates distally and not related to physical movements. It has a burning, shooting and/or stubbing feature. Electrical-like sensations, and pain resulting from non-painful stimulations (e.g., light touch) are typical for neuropathic pain. It is also important to assess whether pain is located in a neuroanatomically plausible area [17].

There are validated questionnaires to screen/assess neuropathic pain such as Leeds Assessment of Neuropathic Symptoms and Signs, Douleur Neuropathique 4 questions, Neuropathic Pain Questionnaire, painDETECT, ID pain, and Neuropathic Pain Symptom Inventory [17]. Screening questionnaires are useful for identification of patients with neuropathic pain; to distinguish neuropathic pain from non-neuropathic pain [17, 21]. Yet, screening questionnaires have several limitations: they do not provide information about history of the pain, and sensory examination is succinct or absent. Assessment questionnaires are used to measure the characteristic neuropathic pain symptoms and to complement screening questionnaires [21].

**Negative and positive symptoms**

The coexistence of negative and positive symptoms is a peculiar feature of neuropathic pain, which reflects loss-of-function and gain-of-function of the somatosensory system, respectively [22]. The anamnesis should include questions evaluating potential negative and positive symptoms/signs. Hypoalgesia, tactile hypesthesia, hypopallesthesia, thermal hypesthesia and punctate hypesthesia are negative symptoms or signs of neuropathic pain. On the other hand, positive symptoms include paroxysmal pain, superficial/deep pain, and paresthesia. Positive signs include heat/cold hyperalgesia, punctate hyperalgesia, mechanical allodynia, temporal summation of pain and after-sensations [22].

**Comorbid conditions**

The presence and/or history of comorbid conditions such as diabetes, infections (e.g. varicella zoster virus infection), neurological disorders (e.g. cerebrovascular diseases, neurodegenerative diseases) should be evaluated. Comorbidities, which are frequent in elderly, can have direct association with neuropathic pain (e.g. diabetes mellitus and diabetic neuropathic pain; varicella zoster virus infection and postherpetic neuralgia).

**Medications**

Past therapies and co-medications are of great importance. For instance, pain experienced by a patient receiving/has received chemotherapy, might be chemotherapy-induced neuropathic pain. Older adults tend to develop chronic chemotherapy-induced polyneuropathy more frequently than younger adults [7, 23].

Co-medications are also important during the management of neuropathic pain. Certain drugs may interact with neuropathic pain medications. As a matter of fact, multimorbidity and polypharmacy are common in elderly [24]. In this
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regard, extra effort should be given to avoid combination of drugs with similar active ingredients and/or mechanisms of action [25].

**Physical examination**

A detailed physical examination (e.g., motor and sensory exam, deep tendon reflexes, pathologic reflexes) is essential in order to recognize neuropathic pain. On bed-side examination, sensory disorders should be recorded in much detail, preferably on body sensory maps. In order to evaluate tactile sense, a piece of cotton wool can be used. Pinprick sense can be evaluated by using a wooden cocktail stick, whilst warm and cold objects such as metal thermorollers are used for the assessment of thermal sense. Vibration sense is examined by a tuning fork [26, 27]. Bed-side examination is preliminary to any quantitative assessment [27].

**Quantitative sensory testing**

Quantitative sensory testing is a psychophysical test method, which is used to evaluate the functional state of the somatosensory system [28]. The response to standardized mechanical and thermal stimulus is assessed by quantitative sensory testing. This test can detect positive and negative signs; is helpful in quantifying mechanical and thermal allodynia and hyperalgesia in painful neuropathic syndromes [26]. The test set includes needle stimulators (pinpricks) of different intensity and Q-tip, cotton swab and brush, von Frey filaments, a tuning fork, a thermal testing set, and a pressure algometer [28].

**Neurophysiological tests**

Electroneuromyography (ENMG) is used to verify a lesion of peripheral large nerve fibers. It can also locate and classify the lesion (axonol or demyelinating) [29]. Laser-evoked potentials can be used in the diagnosis of neuropathic pain. Laser-evoked potential amplitudes are objective markers of damage to the nociceptive pathways. Due to the high technical and time expenditure involved, laser-evoked potentials are not routinely used. Pain-related evoked potentials, a simple, inexpensive and non-invasive procedure, can also be used in the diagnosis of neuropathic pain at specialized centers [2].

**Skin biopsy**

Skin punch biopsy is an objective procedure for neuropathic pain syndromes with suspected small-fiber pathology. A few millimeters of skin are obtained in order to detect a potential somatosensory lesion [2].

**Corneal confocal microscopy**

Corneal nerve fibers of the subbasal plexus (corneal nerve fiber length, nerve fiber density, and number of nerve branches) are evaluated by corneal confocal microscopy [2]. It is a rapid and non-invasive nerve imaging technique [30]. When conventional electrophysiological methods do not reveal any abnormalities and/or there is a suspicion of small fiber neuropathy, skin biopsy and corneal confocal microscopy can be used [2].

**Concluding remarks**

Neuropathic pain is a common clinical entity in elderly. It interferes with quality of life and general well-being in older adults. The recognition of neuropathic pain is, therefore, of great importance. Detailed anamnesis and physical examination are essential. Quantitative sensory testing can provide information on the functional state of the somatosensory system. Electrophysiological tests can identify the damage to the somatosensory system. Skin biopsy and confocal corneal microscopy are certain methods that can be further used.

**CONFLICTS OF INTEREST**

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

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