

Neuropathic pain in elderly

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Ageing population is growing rapidly and by 2050, people who above 65 years old will nearly triple to 1.5 billion globally, representing 16% of the world population.(1) In Hong Kong, a local study reviewed that 35% people have chronic pain and elderly is even more prevalent.(2) Impacts of chronic pain in elderly include physical disability, mood disturbance, social isolation, poorer cognition and lower quality of life. It also posts a heavy socioeconomic burden to family and health care system that an early assessment and proper management are essential.

According to The International Association of Study of Pain, the definition of PAIN is *an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage*. For the mechanism, it can be divided into nociceptive pain and neuropathic pain. The former means pain arises from stimulation at nociceptors by direct issue injury, pressure and temperature etc. It is sometimes called physiological or inflammatory pain, which has protective function. The description of pain is usually sharp and well localized.

While neuropathic pain is pain that arises as a direct consequence of a lesion or diseases affecting the somatosensory system, including condition involving the nerve disruption either peripherally or centrally, e.g. diabetic neuropathy, post herpetic neuralgia. These conditions are usually more difficult to treat and multimodal analgesics may be required. The prevalence of neuropathic pain in general population is 7-10% while it composes to around 20-25% in chronic pain patients.(3) The following article focused in assessment and management of neuropathic pain in elderly.

Neuropathic pain is always pathological and features include burning and electrical shocking pain, as well as abnormal sensation such as ants-crawl. The mechanism is evolving from direct nerve injury e.g. amputation and neuroma formation, then there is abnormal firing of pain nerves, and changes in chemical signaling in the dorsal horn and abnormal nerve connections in the pain pathway, as well as loss of normal inhibitory function.

Neuropathic pain happens more in elderly because of the degeneration, systemic co-morbidities and increased risk of repeated trauma. Some examples of peripheral and central neuropathy are shown in the table below and highlighted diseases commonly seen in elderly will further be elaborated.(4)

Peripheral neuropathy		Central neuropathy
Focal	Generalized	
<ul style="list-style-type: none"> Phantom limb pain Post-herpetic neuralgia Complex regional pain syndrome Ischaemic neuropathy Trigeminal neuralgia 	<ul style="list-style-type: none"> Diabetic neuropathy Alcoholic neuropathy HIV neuropathy Hereditary sensory polyneuropathy 	<ul style="list-style-type: none"> Central post stroke pain Spinal cord injury Multiple sclerosis

1. Post-herpetic neuralgia (PHN)

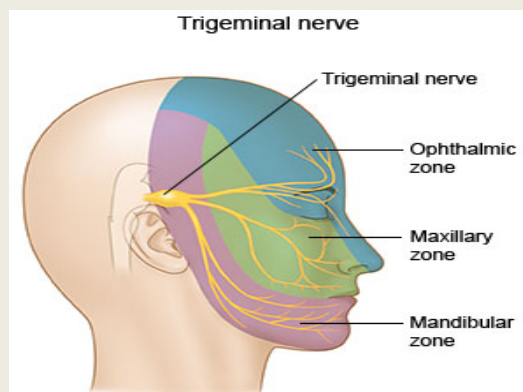
Acute herpes zoster is the reactivation of the varicella-zoster virus (VZV) from dorsal root ganglia of cranial or spinal nerve. It leads to hemorrhagic inflammation of the peripheral nerve, dorsal root, and dorsal root ganglion and in susceptible person, peripheral and central sensitization occur which then progress to PHN. The incidence of acute herpes zoster infection increases with impairment of the immune system due to age, disease, or chemotherapy. It is 5 to 10 times greater for those older than 80 years and the prevalence of PHN is 12% among the acute infection. There are risk factors of developing PHN such as elderly, immunosuppressed and greater severity in acute phase.

2. Diabetic neuropathy (DN)

DN developed in 50% of diabetic patient in 25 years' time. It usually starts at toes, feet and progress to hands with numbness and tingling, associated with loss of sensation. Some even can progress to burning and excruciating pain which is intolerable to patients. The pathophysiology involves the increased serum glycated product and protein kinase C which causing direct nerve injury and neuropathic pain.

3. Trigeminal neuralgia (TGN)

The prevalence of TGN is around 0.03-0.3% and it's more common for women and age more than 50. The pain is usually episodic lancinating, burning pain involving 5th cranial nerve with mandibular and maxillary branches are more commonly affected. The pain can be exacerbated by touching, wind blowing, eating and talking which can severely affect daily function, sleep and mood. The pathology can be a compressing vessel on trigeminal nerve, tumor or in case of multiple sclerosis. However, a substantial number of patients would have no abnormality in imaging.



4. Central post stroke pain

The prevalence is around 32-42% at 4-6 months and 11-21% at 1 year post stroke. The pain can be spontaneous or evoked pain localized in the affected extremities, usually described as aching, burning or sensory disturbance eg temperature change, dysesthesia and hypersensitivity. The pain can be alleviated with relaxation and worsened with emotional and physical stress.

Assessment

Pain should be assessed multi-dimensionally, which includes firstly, sensory dimension such as intensity, nature and site, secondly the emotion and thirdly the impact on daily function or sleep. While self report is "gold standard" for assessment because pain is a subjective experience, elderly with cognitive impairment imposes difficulties for health care worker during interview.

Common assessment tools such as Verbal descriptor scales (none, mild, moderate, strong, severe), Numeric rating scales (0-10), Visual analogues scales and **faces scales** (eg Baker Wong/ Faces Pain Scale) are usually adequate for initial assessment. Other multidimensional pain scale e.g. Brief Pain Inventory, McGill Pain Questionnaire are also readily available. For elderly with dementia, **PAINAD(Pain Assessment in Advanced Dementia)**, a 5-item observational tool can be adopted. The observations included breathing independent of vocalization, vocalization, facial expression, body language and consolability. The pain is more severe if patient score higher marks. Another tool named **MIBOD (Mobilisation-Observation-Behaviour-Intensity-Dementia Pain Scale)** adopted similar approach can also be used.

Management

The principle for managing neuropathic pain in elderly should be multidisciplinary with multimodal analgesia for synergistic effect and minimizing complication. Physical treatments e.g. exercises, ultrasound and transcutaneous electrical nerve stimulation (TENS) are essential for patients not tolerate side effect of drug. Other non-pharmacological methods such as psychological approaches, e.g. cognitive behavioral therapy (CBT) and mindfulness meditation are also helpful in selected cases. For some isolated neuropathy, pain interventional procedures which targets localized source of pain may spare adverse effect of systemic drugs.(6)

For pharmacological treatment in neuropathic pain, most studies are based on post-herpetic neuralgia and diabetic neuropathy. There are multiple guidelines e.g. IASP, NICE and generally recommended as below: (7)

- 1st line: gabapentinoid, tricyclic antidepressant (TCA), serotonin noradrenaline re-uptake inhibitor (SNRI)
- 2nd line: opioid, topical (lignocaine/ capsaicin)
- 3rd line: Na channel blocker/ anticonvulsant
- Disease specific: Carbamazepine for TGN, TCA for PHN

Age related pharmacological changes must be alerted when prescribing treatment to elderly. The progressive changes should be considered in patients >70 years old with extra caution with >85 years old and frail patients. Pharmacokinetic changes including absorption, distribution, metabolism and clearance are discussed:



Absorption

Oral absorption is affected by the decreased gastric secretion, slower gastric emptying, diminished splanchnic blood flow in elderly. This can increase the time to reach peak plasma concentration after intake a solid form of medication. Besides, the comorbidities and concomitant use of medications may further reduce gastrointestinal transit, such as chronic constipation and chronic laxative use.

Distribution

Aging is associated with decreased lean body mass, increased fat mass and decreased total body water. Therefore, volume of distribution of *hydrophilic* drugs (Panadol/Hydromorphone) is decreased, resulting in higher plasma concentration. While that of *lipophilic* drugs (Benzodiazepine, antipsychotics, antidepressants) is greater so increasing the drug's half-life and favors accumulation. The decreased serum albumin, thus increasing the unbound fraction of drug may impose danger to elderly, especially for those highly protein bound drug (>90%) with narrow therapeutic index.

Metabolism and Clearance

Liver mass and hepatic blood flow decrease with age so hepatic clearance of drugs would be reduced, especially for phase one reaction (oxidation, reduction, hydrolysis). Renal mass and tubular secretion also decrease in elderly, leading to potential accumulation of renally excreted drugs.

For pharmacodynamic changes, elderly usually has increased sensitivity of cholinergic receptors, therefore, more side effect from anticholinergic drug, e.g. Tricyclic anti-depressant. There is also increased risk of delirium, memory impairment, falls with benzodiazepine and increased opioid related sedation due to the increased drug sensitivity.

In conclusion, neuropathic pain in elderly is more and more common as the progressive ageing and associated co-morbidities. Multi-disciplinary and multi-modal approach of treatment plan should be adopted as to improve synergistic effect and reduce potential side effects. While pharmacodynamic and pharmacokinetic properties of elderly are varied from normal adult, caution should be given when prescribing multiple analgesics to elderly patients.

Reference:

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