Editorial

Neuropathic pain in cancer

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Abstract: Unrelieved neuropathic pain continues to be a substantial health problem in a cancer patient arises either due to disease itself or its treatment. Review of literature showed that neuropathic pain has high prevalence rate, greater severity and analgesic requirement with worse quality of life. Underreporting by patient and under treatment by physician is an important causative factor of indefinite persistence of neuropathic pain. Careful history taking, elaborated physical examination, patient's self report and diagnostic tools with high sensitivity and specificity are needed for accurate assessment of neuropathic pain. Neuropathic cancer pain is difficult to treat and also shows poor response to opioids so in this situation alternate a treatment strategy that also includes psycosocial and spiritual counseling with yoga and meditation exercises under the palliative care framework should be practiced. To find out the burden and estimation of resource generation of this widely recognized problem, accurate establishment of incidence, prevalence, severity, and effectiveness of treatment is quite mandatory. Complex phenomenon of neuropathic pain abolishes establishment of early diagnosis and accurate etiology of this symptom, emphasizes the need of sensitive and reliable clinical grading scale, international classification system and validated diagnostic tools that correspond with clinical assessment. Multiple studies towards this direction has been culminated and some are still going on, though the data and literature is very scant and require further research for the complete evaluation of neuropathic pain.

Keywords: Neuropathic pain; prevalence; diagnostic tool; international classification system

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That a new era in the cancer diagnosis and treatment is approaching leads to achievement of greater survival rate of many type of cancers. Increase in survival rate is often accomplished with compromise in quality of life of cancer patients. Pain is the most debilitating and disastrous experience encountered by cancer patient at one point of their illness and mostly remains underreported and undertreated (1).

Reason being, the reluctance of doctors to ask about pain or offer treatments and in patient part, reluctance to speak about pain, or to take treatment for pain relief already on polypharmacy (2,3) or fear of addiction or side effects.

Identification of source and clear cut classification of pain whether nociceptive or neuropathic is quite a complex phenomenon due to lack of validated diagnostic tools and an international classification system for cancer pain. In a crude manner, cancer patients have two types of pain nociceptive and neuropathic that derived from different etiologies.

Neuropathic pain is defined by the international association for study of pain as "pain caused by a lesion or disease of the somatosensory nervous system" (4).

According to literature non malignant neuropathic pain is more severe and debilitating then nociceptive pain (5-7). To evaluate the applicability of above theory in cases of malignant neuropathic pain, certain studies was done, even though the literature over cancer related neuropathic pain is scant.

The data from an international cross-sectional observational study that included, 1,051 patients from inpatients and outpatients, with incurable cancer revealed poorer performance status and more analgesic requirement

in patients suffer from neuropathic pain (8).

A combined analysis of the results from four controlled single-dose relative-potency studies was done over 168 cancer patients, received 474 administrations of either morphine or heroin to assess the analgesic response during a 6-hour period with visual analog scales , indicated in terms of total pain relief (TOTPAR) score. The result exhibited that the adjusted mean total pain score of the group with any neuropathic pain was significantly lower than that of the group with nociceptive pain only (26.1 versus 20.4, P=0.02) (9).

Management of intractable neuropathic pain, that arises from tumour invasion of the meninges, spinal cord and dura, nerve roots, plexuses and peripheral nerves is a challenge, requires in-depth knowledge and the formulation of a careful management plan usually multimodal therapy.

Accurate establishment of incidence, prevalence, severity, and effectiveness of treatment in cancer induced neuropathies is quite essential to find out the burden of this symptom and requirement of effective resource generation.

Bennett *et al.* reported the prevalence of neuropathic cancer pain ranged from 19% to 39% (10).

In an another prospective, cross-sectional, international, multicenter survey of pain specialists and their patients which was conducted by task force on cancer pain of the international association for the study of pain (IASP) over 1,095 patients with severe cancer pain revealed that neuropathic mechanisms occurred in 39.7% patients (11).

In Europe cross-sectional, multi-centre study on 951 adult patients with cancer identified 32.60% prevalence of neuropathic pain (1).

Above research signifies the great burden of neuropathic pain in cancer patients and requirement of good diagnostic tool for early identification of symptom and sufficient resource development for facing off this complex pain.

Though the prevalence of neuropathic pain is lesser than nociceptive pain but severity of pain and requirement of analgesic is higher.

Study over 1,100 patients from 11 palliative care sites of different country stated that patients with cancer induced neuropathic pain required more days to achieve stable pain and higher final opioid doses and adjuvants as compare to neuropathic pain (12).

Mercadante *et al.* conducted study over 167 cancer patients and observed that patients with definite neuropathic pain required more intensive treatment (13).

An another observational study over 1,051 patients with incurable cancer reconfirmed that patients with neuropathy have severe pain and greater analgesic requirement (8).

Neuropathic cancer pain is difficult to treat and also shows poor response to opioids so in this situation alternate treatment strategies (14) included antidepressants, sodium channel-blocking agents, steroids, anti-inflammatory drugs (NSAIDS), N-methyl-D-aspartate (NMDA) antagonists, calcium channel antagonists, clonidine, neural blockade, physiotherapy, psychological, spiritual interventions with yoga and meditation should be exercised. Thus pain management should be embedded in palliative care framework and multimodal approach should be implemented.

In cancer patients to elucidate the incidence, prevalence, severity, and potential economic impact of cancer in multiple studies, various method of clinical assessment and certain diagnostic tools were being practiced but none of them were ideal method of assessment.

Study conducted by Rodríguez *et al.* (1), used painDETECT (PD-Q) screening tool to identify potential neuropathic component of cancer-related pain by physician. Shifts in diagnosis before and after the use of this tool indicate that it may help physicians identify CRNP but not all the physician, who used (PD-Q) screening tool were interested to use it in future. When compare with Edmonton Classification System of Cancer Pain (ECS-CP), the authors calculated the sensitivity and specificity of PD-Q for the detection of cancer-related neuropathic pain is 53% and 77%, respectively. Garcia *et al.* (15) exercised Douleur Neuropathic 4 questionnaire (DN4) test to find out the prevalence of neuropathic pain in Spanish population and found that DN4 reports only about half the cancer NP cases diagnosed by clinicians. Thus DN4 test shows the lower values of neuropathic pain than the established cut-off points evaluated in patients clinically. Mercadante *et al.* (13) stated that for the evaluation of the different symptoms of NP, established Neuropathic Pain Questionnaire (NPQ) complete and Neuropathic Pain Questionnaire short form (NPQ-SF), also provide lower cut off point than assessed clinically.

Another study conducted by Clare *et al.* (8) revealed that for identification of neuropathic cancer pain, the self-reported pain DETECT tool showed poor sensitivity against the clinical assessment (using the ECS-CP) and less accurate also when compared with non-cancer pain.

Cruccu and colleagues (16) present a pain assessment tool called Standardized Evaluation of Pain (StEP) that combines six interview questions and ten physical tests. For the validation of back pain StEP is a novel tool but applicability of this test in cancer pain patients is still to be

evaluated.

Since neuropathic cancer pain has high prevalence and causes more suffering and analgesic requirement, but due to limitations of diagnostic tool, despite the intensive and repeated investigations, in certain cases, the cause of neuropathic pain often remains unknown, thus treatment gets hamper and patient develop frustrated hopes and become reluctant to further treatment. Thus careful assessment that combines physical examination, patient's self report and diagnostic tools with high sensitivity and specificity is needed.

Finally there is major requirement of accurate observing criteria for assessing the severity of cancer induced neuropathic pain, sensitive and reliable clinical grading scale, international classification system and validated diagnostic tools that corresponds with clinical assessment.

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