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Yoga and Physical Therapy: Integrating as a way of Life in Cancer Patients

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Introduction

The International Association for the Study of Pain defined neuropathic pain as "pain initiated or caused by a primary lesion or dysfunction in the nervous system". The prevalence of chronic pain is about 30-50% among patients with cancer and this rate increases to about 70-90% in patients with advanced disease [1]. The prevalence of neuropathic pain is estimated to be nearly 31.4% in patients with cancer pain [2,3].

The various factors that can lead to neuropathic pain in cancer patients can be classified as; (a) caused directly by cancer for instance tumour infiltration or compression of nerves, plexus, or roots, (b) caused by the treatment of cancer such as post-surgical neuropathic pain, damage due to radiation induced fibrosis and chemotherapy induced neuropathy [4].

With advancements in research, diagnostic tools, treatment modalities the life expectancy in cancer patients has been prolonged, thus increasing the need for a better quality of life. By controlling pain, we can improve the quality of life in patients with cancer and in those who are in need of palliative care.

Pharmacological Management of Neuropathic Pain

A successful treatment of neuropathic pain requires an appropriate diagnosis and assessment. The correct diagnosis of the neuropathic pain can be challenging as the diagnostic criteria are evolving and there can be other types of pain co-existing such as the nociceptive pain. Assessment of neuropathic pain should not only involve identifying the underlying cause but also assessing for other comorbidities such as anxiety, depression, sleep disturbances and adverse effects of neuropathic pain on the quality of life of patients. Thus we must establish a holistic approach towards pain management with realistic goals and involving care givers of the patients as well.

The mainstay of pain management in cancer patients is by giving analgesics as per the WHO analgesic ladder. This analgesic ladder is proven to be effective in 71% of the cases. But neuropathic cancer pain is more difficult to treat than nociceptive pain. Neuropathic pain requires higher doses of a broader range of analgesics to reduce the pain. Thus in addition to opioids antiepileptic and antidepressants need to be added [5,6].

First line medications

Three types of medications are included in the first line of management of neuropathic pain. These include antidepressants, anticonvulsants and topical lidocane [7,8].

1. Tricyclic antidepressants such as amitriptyline have proven to be effective in managing neuropathic pain in cancer patients [9]. But the most common side effects are the result of their anticholinergic activity, which are dry mouth, blurred vision, cognitive impairment, and lethargy. Therefore, they should be started cautiously in patients with cardiac problems and especially in the elderly [10,11].

Other antidepressant drugs that can be used are selective serotonin and norepinephrine reuptake inhibitors (SSNRIs) and among this group of medicine venlafaxine and duloxetine are the drugs of choice in neuropathic pain [12,13]. Venlafaxine has been found to be effective in post-mastectomy pain syndrome after breast cancer surgery [12]. Venlafaxine is also found to be effective in controlling hot flashes in post mastectomy patients but the frequent side effects experienced are nausea, decrease in appetite, dryness of mouth and constipation [14]. With respect to chemotherapy induced peripheral neuropathy, duloxetine is found to be effective, and can be considered in first-line therapy [13,15]. The frequent side effects experienced with duloxetine are nausea, dizziness, headache, constipation, fatigue and somnolence and increased sweating [16].

Antiepileptic drugs – gabapentinoids: The main antiepileptic drugs utilised are gabapentinoids (gabapentin and pregabalin). They act by inhibiting calcium channels and thereby decreasing the release of glutamate, norepinephrine and substance P [7].

Gabapentin has been shown to reduce neuropathic pain in palliative care setting. A randomised trial has shown that nearly 42% of the patients experienced pain relief after the 21st day of drug administration. The most common side effects encountered were somnolence, fatigue and cognitive disturbance [17].

Pregabalin has been effectively used to manage neuropathic cancer pain. The mechanism of action is same as that of gabapentin. The use of pregabalin either reduces the need for morphine dose escalation or allows the use of lower doses, resulting in less opioid-related adverse effects, such as constipation. It also improves sleep quality [18,19]. The side effects associated are dizziness, nausea, dry mouth, somnolence and peripheral oedema [19].

Other anti-epileptics such as carbamazepine and oxcarbazepine have been used in trigeminal neuralgia but they have a limited role in neuropathic cancer pain.

Topical antineuralgics: Lidocaine, capsaicin: Lidocaine relieves pain through nonspecific blocking of sodium channels on afferent fibers. It is convenient to use as there is no systemic absorption and thereby the side effects are reduced. Lidocane patches has shown pain relief in refractory neuropathic pain such as post thoracotomy pain, stump neuroma pain, intercostal neuralgia, diabetic polyneuropathy, meralgiaparesthetica, complex regional pain syndrome, radiculopathy, and post mastectomy pain [20,21].

Capsaicin is a naturally occurring irritant compound that binds to

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neurons and reduces their response to a broad range of stimuli, i.e., leading to desensitization. This effect is utilised for the therapeutic purpose [22]. Though studies have shown its efficacy in management of neuropathic pain but caution must be followed while prescribing because literature also shows its carcinogenic attributes [22-24].

Second line medications

When the patients do not respond satisfactorily to the first line medications alone or in combination, opioid analgesics and tramadol are considered.

Tramadol is a weak opioids analgesic and it also inhibits the reuptake or noradrenaline and serotonin. Tramadol has shown significant benefit in cancer pain. Tramadol leads to less constipation and nausea than other weak opioids such as codeine.

Morphine has been shown to be an effective analgesic and is recommended as first line opioid. Studies have shown morphine, transdermal fentanyl and oral methadone to be equally effective in controlling cancer pain. The side effects associated with morphine are constipation, nausea, vomiting and confusion. Fentanyl and methadone however had reduced propensity to induce constipation [25-28].

Role of alternative therapies in managing cancer pain and other treatment related effects: As discussed the pharmacological agents used for cancer pain management are associated with a number of side effects. The intensity of side effects may vary from mild to moderate or at times might become severe to interfere with the compliance of the drugs. But complementary and alternative therapies such as yoga, physical therapy, music therapy and acupuncture can be used to improve quality of life by decreasing the adverse effects of anticancer treatments or through alleviating the symptoms of cancer [29,30].

Yoga: Texts indicate that yoga originated in India and has been practiced for approximately 4,000 years . The term yoga is derived from the Sanskrit verb yug, which means to bind or join. This refers to the goal of yoga, which is to unite the mind and body in a way that promotes health. The key elements of yoga include breathing exercises (pranayama), postures (asanas), and meditation (dhyana). Literature shows promising results of yoga in pain management from a biological, social and psychological perspective [31]. Yoga in cancer patients has shown positive effects such as improving the psychological well-being, reducing stress, anxiety and improving quality of life [29].

A recent randomised control trial shows positive influence of yoga on depression in breast cancer patients. The experimental group received yoga session which included a set of asanas, breathing exercises, pranayama, meditation, and yogic relaxation techniques with imagery. All the patients had undergone surgery and were receiving chemotherapy and radiotherapy. Yoga intervention decreased depressive symptoms more than the controls from their baseline. The antidepressant effects of yoga intervention could be explained by reduction in the levels of psychophysiological arousal such as decrease in sympathetic activity, balance in the autonomic nervous system responses, alterations in neuroendocrine arousal, and decrease in morning cortisol [32].

Yoga has an important role to play in palliative settings as well. As shown by Carson et al. through a pilot study on metastatic breast cancer. The study included a novel yoga based palliative intervention, the Yoga Awareness Program. The session lasted for 8 weeks and showed a decrease in pain and fatigue and a greater acceptance of the condition and relaxation. Thus the results support the role of yoga in life limiting conditions such as metastatic breast cancer [33].

In an attempt to demonstrate the efficacy of Sudarshan Kriya and Pranayam a randomised control trial was conducted by Dr. Sushma Bhatnagar (Professor and Head of Department) in the Department of Onco-anaesthesia and Palliative Medicine, at DR B.R.A IRCH in All India Institute of Medical Sciences (AIIMS), New Delhi. Breast cancer patients with advanced disease were enrolled and given 18 h workshop on sudarshan kriya and pranayama. They were advised to practise the same at home daily for 20 min. This was in adjuvant to the standard pharmacological management as per the WHO analgesic ladder. The patients were assessed for pain using VAS and serum cortisol levels. The assessment was done at baseline, 3rd and 6th month. The results showed significant reduction in both the parameters as compared to the control group. Thus the study further strengthens the use of yoga in the management of neuropathic cancer pain [34] (Table 1).

Physiotherapy

Physiotherapy means a system which includes comprehensive examination, treatment, advise and instructions to any persons preparatory to or for the purpose of or in connection with movement/functional dysfunction, bodily malfunction, physical disorder, disability, healing and pain from trauma and disease, physical and mental conditions using physical agents, activities and devices including exercise, mobilization, manipulations, electrical and thermal agents and other electro therapeutics for prevention, screening, diagnosis, treatment, health promotion and fitness [35].

Pain and deconditioning accounts for nearly 90% of the functional disabilities in a palliative care setup and if utilised physiotherapy can benefit 50% of the patients. Physiotherapy in cancer patients is aimed at achieving symptom control, maximizing remaining functional abilities, providing education to care givers and contributing to interdisciplinary team communication. The various physical therapy agents used in achieving these goals are exercise therapy, massage, transcutaneous electrical nerve stimulation (TENS) and scrambler therapy [36].

Literature shows the efficacy of exercise in reducing fatigue, improving cardiovascular fitness, quality of life and physical function in patients with breast cancer, lung cancer, Hodgkin's disease and prostate cancer [37-39]. In an attempt to demonstrate the efficacy of exercises in improving the immune status in cancer, Hutnick et al. enrolled breast cancer patients post chemotherapy and radiotherapy for an exercise regime. The exercises were continued for 6 months and consisted of resistance training, aerobic exercise, stretching exercise, upper and lower body training. These patients showed improvements in fitness as well as immunological status as depicted by greater proliferation of CD4, CD69 and T-helper cells. These findings are clinically significant as patients post chemotherapy and radiotherapy often gets secondary infections. So a moderate level of exercise regime can be effective in boosting immunity [40].

Similar results were observed by Waart et al., were they utilised exercises to minimise the decline in cardiorespiratory fitness, muscle strength and fatigue while undergoing chemotherapy. There was a decrease in chemotherapy associated side effects such pain, nausea and vomiting. All these factors helped in improving the chemotherapy completion rates. Patients in the exercise group were more likely to return to work after a 6 month follow up, thereby enhancing the quality of life as well [41].

The reduction in the functional capacity and activity level is also seen in patients post operatively. Studies have shown beneficial effects of exercise post operatively. Literature suggests that patients post lung

S. no	Author, year	Type of study	Diagnosis of patients	No. of patients	Type of intervention	Results
1	Mohan and Rao et al. (2015) [32]	Randomized control trail	Stage II and III breast Cancer patients post-operative undergoing radiotherapy/chemotherapy	N=98	A 24 weeks yoga intervention consisted of a set of asanas, breathing exercises, pranayama, meditation, and yogic relaxation techniques with imagery	Yoga intervention decreased depressive symptoms more than the controls from their baseline means by 42% following surgery, 28.1 and 28.5% during and following RT, respectively, and 39.5 and 29.2% during and following CT, respectively.
2	Carson et al. (2007) [33]	Pilot study	Metastatic breast cancer	N=13	8 weekly group sessions of yoga that consisted of asanas, breathing exercise, meditation, study of pertinent topics and group discussions	The intervention was significant increase in boosting daily invigoration and acceptance. There were improvements in pain and relaxation
3.	Kumar and Bhatnagar et al. (2013) [34]	Randomized control trial	Breast cancer stage IIb, III, IV post treatment and in follow up for pain management	N=147	Cognitive and behavioral stress management module of Sudarshan Kriya and pranayam	There was significant reduction in blood cortisol levels and pain perception levels in patients after sudarshan kriya and pranayama.
4	Hutnik et al. (2005) [40]	Comparative study design	Breast cancer patients	N=49	6 month exercise program consisting of resistance training and aerobic activity at 60-75% of functional capacity for three times in a week with personal trainer	Exercising group showed greater increase in maximal oxygen uptake and upper body strength. There was a greater percentage of CD4+CD69+ cells and greater levels of titrated thymidine incorporation in exercising group.
5	Wart et al. (2015) [41]	Randomized control trial	Primary breast or colon cancer patients	N=230	Moderate to high intensity combined resistance and aerobic training under supervision of the physical therapist for	Exercise group showed fewer declines in cardiorespiratory fitness, better physical functioning, less nausea and vomiting and less pain. Also the exercise group returned earlier to work than control group.
6	Granger et al. (2012) [42]	A pilot randomized control trial	Lung cancer patients	N=15	Exercise consisted of aerobic, resistance and stretching training. The exercise session was given twice daily until discharge and then twice weekly for 8 weeks on outpatient basis	Exercises were found to be safe and feasible. The exercise group had greater improvements in 6 min walk test and health related quality of life post operatively
7	Haren et al. (2013) [42]	Systematic review and meta-analysis of randomized control trial.	Cancer patients undergoing hematopoietic stem cell transplantation (HSCT)	11 studies were included and the total number of patients =734	Exercise sessions consisted of endurance, resistance, progressive relaxation and relaxation training. Exercises were performed before, during and after hospitalization for HSCT	Quality of life, psychological well-being, distress and fatigue were assessed. Exercises led to better quality of life and less fatigue
8	Loh et al. (2015) [43]	Retrospective cohort study	Cancer patients including breast, sarcoma, lymphoma, lung, renal and cervical, etc.	N=87	High frequency TENS was applied for 30 min to 1 h 4-6 times in a day by the patients at home for 2 months	Patients were assessed on visual analog scale (VAS), numerical rating pain scale (NRP) and short form McGill questionnaire. The results showed decrease in VAS and NRP scores
9	Fiorelli et al. (2012) [44]	Randomized control trial	Lung cancer patients undergoing thoracotomy for lung resection.	N=50	TENS therapy was given at a frequency of 80 pulses/s. It was applied after every 4 h for 30 min in the first 48 post-operative h. Then TENS was applied twice daily for 5 post-operative days	Serum cytokines levels, pain, respiratory function and intake of narcotic medication were assessed. Serum IL-6, IL-10, VAS scores were significantly lower in TENS group. Recovery of FEV1 was better and morphine requirement were lower in TENS group.
10	Searle et al. (2009) [45]	Case study	Metastatic lung cancer with bone pain.	N=1	TENS therapy was applied at 80Hz for 1 h. Patient then continued TENs at home and was reviewed after 48 h	Visual analog scale, numeric rating scale and verbal rating scale were assessed both at rest and with movement. Short McGill questionnaire was also use at the end of treatment. VAS score reduced from 4 at rest and 7 on movements to 1 at rest and 2 on movements. McGill pain reduced from 8 at base to 1 after treatment.
11	Tilak et al. (2015) [47]	Randomized control trial	Phantom limb pain	N=26	Group 1 received mirror therapy which lasted for 20 min daily for 4 days. Group 2 received TENS therapy which was given using Burst TENS for 20 min daily for 4 days.	Visual analog scale (VAS) and universal pain score (UPS) were used foe assessment. Significant reduction in pain levels was seen within both the groups but there was no difference between the two groups.
12	Mulvey et al. (2012) [48]	Single center pilot study	Patients with trans tibial amputation persistent moderate to severe pain.	N=10	TENS therapy was given using conventional TENS at a strong but comfortable sensation for 60 min.	Numeric rating scale (NRS) was used to assess pain intensity. A telephone follow up after 48 h of treatment was done to know of any adverse events. Significant reduction in NRS scores from 2.6 at rest and 5.7 on movement to 0.8 at rest and 1.8 on movement after treatment.
13	Darnall (2009) [50]	Case study	Left above knee amputation with phantom pain.	N=1	Self-delivered mirror therapy for 20 min daily for 3 months.	VAS score reduced from 4 to 0 after 3 months of mirror therapy

14	Foell et al. (2013) [51]	Prospective interventional study	Chronic phantom limb pain after unilateral arm amputation	N=13	Mirror therapy was given for 4 weeks.	Phantom limb pain was measured using VAS.an average decrease of 27% was seen after 4 weeks of mirror therapy.
15	Brenda et al. (2007) [52]	Randomized control trial	Phantom limb pain after amputation of limb or foot	N=22	Mirror therapy was given for 4 weeks.	Pain decreased from 30 mm to 5 mm on VAS after 4 weeks of treatment.
16	Marineo et al. (2012) [53]	A pilot randomized controlled trial	Chronic neuropathic pain on a VAS score of more than 6 with unsatisfactory pain management.	N= 52	Scrambler therapy was given daily for 45 min for 5 days in a week for 2 weeks. Patients were followed up monthly for 3 months.	Pain reduced from 8 to 0.7 at 1 month and to 1.4 and 2 at 2nd and 3rd month. No adverse effects were observed.
17	Marianna et al. (2012) [54]	Prospective interventional study	Cancer and non-cancer pain with unsatisfactory pain management.	N=73 Cancer patients (40) and non-cancer patients (33)	Scrambler therapy was given daily for 30 min for 5 days in a week for 2 weeks. A 2 weeks follow up was done at the end of treatment.	Pain was assessed using VAS scores. The VAS score reduced from 6.2 to 1.6 at the end of 2nd week and 2.9 at the end of 4th week.
18	Pachman et al. (2015) [55]	Pilot study	Patients with chemotherapy induced peripheral neuropathy (CIPN)	N= 37	Scrambler therapy was given daily for 10 sessions for 30 min each. A follow up of 10 weeks was done after end of therapy	Pain, tingling and numbness were assessed at the baseline, at the end of therapy and after 10 weeks of follow up. The mean pain intensity reduced from 5.7 to 2.6, tingling sensation reduced from a mean of 6 to 3.3 and
19	Coyne et al. (2013) [56]	Single arm clinical trial	Patients with CIPN	N=39	Scrambler therapy was given for 45 min daily for 5 days for 2 weeks. Followed up to 3 months.	Pain was assessed using NRS scale. Secondary measures were Brief Pain Inventory and European Organization for Treatment and Cancer QLC-CIPN-20. Pain scores reduced from 6.6 before treatment to 4.5 at 14th day and 4.6 at 3rd month.

Table 1: Summary of studies.

resection due to malignancy can benefit from resistance training, aerobic exercise and stretching exercise. These exercises also help in reducing post-operative pain and fatigue [39].

Exercises have also been used to benefit patients undergoing hematopoietic stem cell transplantation. Haren et al. concluded through a systematic review of trials that exercises are safe and feasible in these patients. The exercises that were included were aerobic exercise, resistance training stretching exercises, progressive relaxation training and activities of daily living training. Positive outcomes were observed on the quality of life, muscle strength, physical functioning and fatigue [42].

Transcutaneous Electrical Nerve Stimulation (TENS) can be used to relieve cancer pain. TENS works on the principle of pain gate mechanism. This modality provides electrical impulses that stimulate A-beta nerve fibers. These fibers further inhibit transmission via A-delta and C- fibers and thereby it reduces pain. Loh et al. demonstrated the efficacy of TENS in cancer patients. TENS when used daily over a period of 2 months showed beneficial effects. TENS can be used as an adjunct to pharmacological agents and help in reducing their associated side effects [43]. Once the pain is reduced patients' functional capacity also increases.

Fiorelli et al utilised TENS therapy in lung cancer who have undergone lung resection via postero-lateral thoracotomy. The results show that in comparison to control group those receiving TENS have greater reduction in pain and further reduced consumption of analgesics. With the reduction in pain patients demonstrated an increase in the pulmonary ventilation parameters. Thus the results support the use of TENS therapy to reduce pain and improve functional status of the patients [44].

Searle et al have made an attempt to highlight the efficacy of TENS by means of a case study. They reported the use of TENS in a 63 year old female with metastatic lung cancer. The female presented with upper extremity arm pain due to bony deposits in the proximal humerus. She had received radiotherapy for the same. The analgesics requirement were: modified release morphine sulphate 1200 mg daily, ketamine 400 mg daily, gabapentin 1800 mg daily and oral morphine for breakthrough pain. TENS was applied for 60 min and the visual analog score (VAS) reduced from 4 at rest and 7 with movement to 1 at rest and 2 with movement. The results therefore provide promising evidence for the use of TENS in cancer bone pain [45].

Phantom limb pain is prevalent in cancer patients post amputation. In addition to the pharmacological management other alternatives such as TENS and mirror therapy can be utilised to reduce this type of pain. TENS has been shown to be an effective modality to reduce phantom limb pain [46]. Tilak et al. conducted a trial to compare the efficacy of mirror therapy and TENS. Their results showed no significant difference between the two groups. However both the groups showed significant improvements from the baseline VAS score. Thus they demonstrated both the therapies to be equally effective [47]. Similar findings were observed by Mulvey et al. in their pilot study, where they used TENS for phantom limb pain in trans-tibial amputation patients. There was significant reduction in pain scores post TENS application [48].

In the mirror therapy the patients exercise in front of the mirror in such a manner that the reflection of the intact limb appears to be the missing limb. This information tricks the brain to interpret it as coming from the amputated part and helps in reducing the phantom pain [49]. This therapy does not require very expensive equipment, it can be taught to the patient to be practised at home. Thus this therapy can give a low cost treatment option [50-52].

A novel approach for management of neuropathic pain is scrambler therapy. This therapy works on the principle of mixing or "scrambling" non-painful stimuli with pain information and thereby reducing pain intensity. It consists of a multiprocessor with five channels or set of electrodes that are placed on the skin beyond the painful site. The therapy is usually given foe 30-45 min for 10 consecutive days.

Literature provides evidence for its use in neuropathic cancer pain and chronic chemotherapy induced peripheral neuropathy along with pharmacological agents [53-56].

Conclusion

Pain in cancer patients is difficult to manage because of many associated complexities such as physical co-morbidities, psychological symptoms, treatment and drugs related side effects, functional decline, financial burden and spiritual distress. When addressing pain issues all the aforesaid factors have to be kept in mind. Therefore a holistic approach involving both pharmacological and non-pharmacological agents should be followed for a successful pain control.

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