

The Pharma Innovation

ISSN (E): 2277- 7695

ISSN (P): 2349-8242

NAAS Rating: 5.03

TPI 2018; 7(7): 819-824

© 2018 TPI

www.thepharmajournal.com

Received: 05-05-2018

Accepted: 07-06-2018

Preeti Wakode

Department of Hospital Management, Delhi Pharmaceutical Sciences and Research University, Pushp Vihar, Sector III, New Delhi, Delhi, India

Harvinder Popli

Dean and Professor, School of Pharmaceutical Sciences, Delhi Pharmaceutical Sciences and Research University, New Delhi, Delhi, India

Palliative care: A review

Preeti Wakode and Harvinder Popli

Abstract

The last quarter of the 20th century created broad advances in hospital and palliative care. Palliative care is an approach that elevates the personal satisfaction of patients and their families by challenging the issue related to perilous ailment. The objective is to avoid or treat the side effects or symptoms, at the correct time as conceivable that could be normal considering the present situation. This article provides an insight in the importance of palliative care and how various symptoms can be managed to enhance the quality of life in patients suffering from various life threatening diseases or malignancies.

Keywords: Palliative care, Pain, Fatigue, Sleep disturbances

Introduction

The word palliative originates from the Latin word *palliare*, meaning to “cloak”. In 2004, the World Health Assembly passed its first resolution on palliative care consequently Governments have a duty to prepare medicinal services experts, convey suitable and successful palliative care. Palliative care management emerged in the later part of the 20th century both as a social programme and medical specialty. Central to its modern development were the thoughts of Dr Cicely Saunders, whose vision for enlightening the care of the dying encompassed the physical, psychological, social and spiritual domains while emphasizing the importance of rigorous clinical practice, training and research. As palliative care advanced, it started to apply all-encompassing standards to the care of individuals earlier in their disease trajectory and in different settings, such as in hospitals and in community ^[1]. It is currently perceived as a field of medical specialization in a developing number of countries ^[2], some of whose legislatures now support national strategies for palliative care. However, around the world, palliative care is not consistently developed, and it needs to press hard to anchor full coordination into prevailing health policies. Palliative care still achieves a minor proportion maybe less than 10% of individual's benefits from it, particularly individuals with diseases other than cancer. The global challenge for palliative care in the 21st century is to create models and coverage appropriate to those in need, whatever their diagnosis, income or setting. There are signs that are being addressed by global health organizations and intergovernmental agencies, yet palliative care still faces real obstructions on the part of professionals, patients and the wider public. Palliative care is an approach that enhances the quality of life of patients and their families facing the problem related with life-threatening illness, through the prevention and relief of suffering by means of early identification, impeccable assessment and treatment of pain and other problems be it physical, psychosocial or spiritual. Palliative care not only addresses the ailment but the individual in general and facilitate complex decision making at any stage of a disease.

The World Health Organization (WHO) defines PC as

An approach that improves the quality of life of patients and their families facing the problem associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual ^[3]. As per the Centre to Advance Palliative Care (CAPC) palliative care is defined “focused on providing patients with relief from the symptoms, pain, and stress of a serious illness—whatever the diagnosis or prognosis. The goal is to improve quality of life for both the patient and the family”. Furthermore, according to American Society of Clinical Oncology Provisional Clinical Opinion, palliative care is “focused on relief of suffering, in all of its dimensions” ^[4]. The main objective is to prevent or treat the symptoms or side effects, as early as possible that could be expected under the circumstances. Systematic reviews support the effectiveness of palliative care for improving quality of life of

Correspondence

Preeti Wakode

Department of Hospital Management, Delhi Pharmaceutical Sciences and Research University, Pushp Vihar, Sector III, New Delhi, Delhi, India

patient, family satisfaction, and advance care planning for patients with cancer [5, 6]. Palliative care is given by palliative care specialists, medicinal services professionals who have got special and additionally affirmation in palliative care. Normally, palliative care experts function as a feature of a multidisciplinary group that may incorporate specialists, enrolled dieticians, drug specialists, ministers, clinicians, and social labourers. Palliative care specialists provide caregiver support, facilitate communication among members of the health care team. It is an active total care of patients and their families by a multi professional team when the patient's disease is no longer responsive to therapeutic treatment. Palliative care masters additionally give parental figure support, encourage correspondence among individuals from the social insurance group.

Primary palliative care includes basic skills and competencies possessed by all physicians irrespective of specialty, whereas specialty palliative care includes secondary palliative care and tertiary palliative care. Secondary palliative care is provided by specialist consultants, whereas tertiary palliative care is provided at tertiary medical centres where specialists care for the most complex cases and clinical care, research, and educational palliative care practices exist simultaneously. In contrast to primary palliative care, specialty palliative care includes managing complex or refractory symptoms and facilitating communication in challenging situations. Primary palliative care skills consist of elements that are heart of palliative care, including management of basic symptoms, aligning treatment plan with patient goals, and addressing patient suffering. By exercising primary palliative care skills, primary care physician strengthens existing therapeutic relationships, whereas referring to specialist palliative care services for all basic symptom management and psychosocial support may further fragment care. Technological advances in both the pharmaceutical and medical device industries have improved medical care and resulted in the increased survival of individuals with multiple chronic conditions. Dementia and diseases previously considered terminal, such as heart failure, chronic obstructive pulmonary disease, HIV, end-stage renal disease, and cancer, are now chronic long-term health conditions managed by primary care physicians and health care teams [7].

Hence Palliative care:

- Provides relief from pain and other disturbing symptoms.
- Sustains life and regards dying as a normal process.
- Intends neither to hurry nor delay demise.
- Integrates the psychosocial and otherworldly parts of patient care.
- Offers an emotionally supportive network to enable the family to adapt amid the patient's sickness and in their bereavement.
- Uses a team approach to deal with the requirements of patients and their family including bereavement counselling, if indicated.
- Enhances quality of life and may also positively influence the course of illness.
- Is applicable early in the course of illness, in conjunction with other therapies that are intended to prolong life, such as chemotherapy or radiation therapy, and includes those investigations needed to better understand and manage distressing clinical complications [8].

Palliative Care can be dichotomous, overlapping, and concurrent. In the dichotomous model, Palliative Care is done only after the exhaustion of cancer treatment options. In case

of overlapping model, Palliative Care is focused when the curative treatment options become limited. Concurrent Palliative Care includes Palliative Care from the moment of cancer diagnosis and symptoms, is maintained during active treatment, and continues to support the family during the bereavement period following the death of patient [9]. Concurrent models of care have increasingly been embraced by oncology providers. In building relationships with patients over time, concurrent Palliative Care models may play a role in helping patients keep their decision making in the context of what matters most to them, including identification of appropriate timing to transition to end of life care.

The study, Economics of Palliative Care for Hospitalized patients with life threatening Illness, found, when palliative care was added to a patient's treatment, hospitals saved an average of \$3,237 per patient over the course of a hospital stay compared to patients who did not receive palliative care. Additionally, for cancer patients, hospitals saved an average of \$4,251 per stay. For non-cancer patients, hospitals saved an average of \$2,105 per stay. Compared with nonhospice care, hospice care saves at best 3% of total care costs. Advance directives done early in the disease course may save end-of-life care costs.

Issues in Palliative Care

Self-rule can be defined as the human capacity for self-determination. Several approaches are available to evaluate decision-making capacity. In the therapeutic setting, often utilized formal criteria incorporate the appraisal of a patient's capacity to (1) convey a decision, (2) comprehend the significant data, (3) value the circumstance and its outcomes, and (4) manipulate relevant information in a rational way [10]. Palliative care practitioners should be able to distinguish patients' basic decision making capability [11]. Advance care planning (ACP) can be defined as the process of planning for future medical care. ACP was developed in an attempt to address the problem of decision-making in patients and to improve care at the end of life [12]. The United Nations International Covenant on Economic Social and Cultural Rights enunciates the right to Ethical Issues in Palliative Care "enjoyment of the highest attainable standard of physical and mental health". Although pain is not overtly referred to, it has been argued that freedom from pain can be also inferred in this right. This view is gaining increasing acceptance as both developed and developing countries continue to struggle with the issue of undertreated pain. Despite high-quality palliative care some patient's experience intolerable suffering at the end of life. In such cases "Palliative sedation" is viewed as a contentious treatment of last resort, and is broadly defined as using sedative medications to relieve intolerable suffering caused by refractory symptoms via a reduction in patient consciousness [13]. Refractory symptoms are those symptoms that cannot be adequately treated using standard palliative interventions within an acceptable time frame. Suffering, intolerability, and adequate relief are of course subjective and can only be defined by the patient. The National Hospice and Palliative Care Organization (NHPCO) defines it as "suffering that arises from a sense of meaninglessness, hopelessness, fear and regret in patients who knowingly approach the end of life". Guidelines, such as those of the European Association of Palliative Care, include (1) the indications in which sedation may be considered, (2) the necessary evaluation and consultation procedures, (3) consent requirements, (4) medications and dose titration, (5) patient

monitoring, (6) guidance regarding hydration and nutrition during sedation, and (6) how to address the problem of using sedation for refractory existential distress.

Diseases requiring Palliative Care

Palliative care specialists treat people experiencing many serious disease types and chronic illnesses. Concentrating on the side effects of both the ailment and the treatment, palliative care helps you with an extensive variety of issues, including pain, depression, anxiety, fatigue, shortness of breath, constipation, nausea, loss of appetite and difficulty sleeping. It improves your ability to tolerate medical treatments. Palliative care helps patients who are suffering from various ailments as Alzheimer's Disease, Breast Cancer, Bone Marrow Transplant, Chronic Obstructive Pulmonary Disease (COPD,) Colon Cancer, Congestive Heart Failure, Dementia, Eosinophil Associated Disease (EAD), Head and Neck Cancer HIV/AIDS, Huntington's Disease, Kidney Disease, Leukaemia, Lymphoma, Liver disease, Lung Cancer, Multiple Myeloma, Multiple Sclerosis, Ovarian Cancer Pancreatic Cancer, Parkinson's Disease, Prostate Cancer, Sickle Cell Anaemia, Stroke etc.

Symptomatic management whether related to the disease or to the treatment, influences the quality of life of in patients having life threatening illnesses. Particularly in elderly patients, serious illness is often characterized by a high prevalence of untreated symptoms that ultimately results in progressive functional dependence. The focus on symptom management and maximization of functions provide the patients and their caregiver's relief from one of the largest sources of stress. Advanced age is also associated with physiologic changes that affect the pharmacokinetics and pharmacodynamics properties of medications, which further complicates the treatment. So age-related physiologic changes should be taken into consideration when making treatment decisions. In addition, cognitive impairment, functional difficulties, and caregiver issues play a role in errors and compliance. While prescribing the treatment for symptomatic management pharmacological as well as epidemiologic, social, cultural, and economic factors are considered. When

patient has a number of medical conditions that are unrelated to their palliative care diagnosis, they may be on numerous medications, the burden in terms of cost and discomfort of taking many drugs, as well as the escalating risk of drug interactions from polypharmacy, should be frequently viewed. Decisions about which medications to stop should be made by balancing the likely prognosis from the palliative care diagnosis, with short, medium, and long-term risks associated with stopping medications to manage co-morbidities. Patients receiving inpatient palliative care consultation are more likely to have follow-up services, for example, home care administrations, hospice care, and nursing home arrangement when compared to common care patients coordinated on age, mortality hazard, and ailment severity.

Pain is one of the most common symptoms experienced by patients with cancer. Malignancies and its treatments causes an assortment of various pain syndromes, including chemotherapy induced peripheral neuropathy, hormonal-related arthralgia, dyspareunia, myalgia, post mastectomy pain, and lymphedema identified with medical procedure or radiation. Adjustment in the dose of chemotherapeutic agent or switching to other agent is needed in severe cases. Patients with cancer develop several symptoms that impair comfort and quality of life. Such symptoms are managed by various pharmacological as well as by non-pharmacological interventions. Once the treatment is started patients are evaluated frequently until distressing symptoms subsides while looking out for the side effects caused by the medications. In case of older patients pain is difficult to evaluate and manage, many barriers exists which hinders the optimal and adequate management of pain. Up to two-thirds of all older patients develop pain as a result of the cancer or as a consequence of its treatment [14]. In elderly patients, pain may also be caused by non-cancer-related comorbidities, such as degenerative disk disease or osteoporosis-related fractures. One should be familiar with other common cancer pain syndromes such as plexopathies, peripheral neuropathy in order to identify the correct cause [15]. The standard pain management algorithm is based on the World Health Organization (WHO) analgesic ladder [16] (Table 1).

Table 1

WHO analgesic ladder and recommendations for elderly patients		
Step	Recommendations	Suggested Medications
Step 1: mild pain	Nonopioid ± Adjuvant	NSAIDs, acetaminophen Neurontin, pregabalin
Step 2: moderate pain	Weak opioid ± Nonopioid ± Adjuvant	Codeine NSAIDs, acetaminophen Neurontin, pregabalin
Step 3: severe pain	Strong opioid ± Nonopioid ± Adjuvant	Morphine, oxycodone, hydromorphone, fentanyl, methadone NSAIDs, acetaminophen Neurontin, pregabalin

Chemotherapy-induced peripheral neuropathy (CIPN), is one of the most common adverse effect of many chemotherapeutic agents. CIPN is likely to improve after cessation of therapy, but approximately half of patients who have received chemotherapy with CIPN have long-term symptoms. Patients may also have components of neuropathy related to other treatments, such as surgery or chronic cancer. Patients with CIPN should be reassessed periodically, as the neuropathic

symptoms often improve over time and medicaments used in the management of pain having significant side effects and can often be reduced or stopped [17]. Acetaminophen is used as a first line drug for the relief of mild to moderate pain in older patients with cancer [18]. Nonsteroidal anti-inflammatory drugs (NSAIDs) are also effective for the treatment of mild to moderate pain, especially bone pain. However, NSAIDs are associated with increased risks of side effects in older

patients, and have been linked to gastrointestinal bleeds, renal toxicity, myocardial infarction, and stroke. Patients who are on nephrotoxic agents and those with compromised renal function caused by aging or other comorbidities are at higher risk of NSAID-related renal toxicity. Side effects caused by NSAIDs dose and time dependent, because of this reason NSAIDs are recommended for short intervals only [19]. Although opioids are also used in cancer survivors' having chronic pain, but the addictive nature of opioids on patients and society warrants rethinking of this approach. Guidelines for chronic pain and neurologic conditions increasingly recommend a range of non-pharmacological approaches and no longer recommend chronic opioids, except in select refractory cases after full discussion of risks [20, 21]. A 2015 systematic review on long-term opioid therapy for chronic pain across conditions for a National Institutes of Health Workshop found no evidence of long-term effectiveness and significant adverse events, includes dependence (ranging from 3% to 26%), abuse (0.6% to 8%), misuse (6% to 37%), increased risk for overdose, sexual dysfunction, and motor vehicle crashes [22]. Addictive illnesses are also common in both patients and caregivers, and are often challenging to screen for and identify. The internist's cautious, attentive approach to opioid prescribing and management can help avoid the risks of long term use. Evidence-based guidelines on tapering of opioids are available [23], and similar approaches can often be used to wean benzodiazepines or sedative hypnotics used during the acute cancer treatment phase.

Fatigue

Cancer-related fatigue (CRF) as defined by the National Comprehensive Cancer Network is a distressing, persistent, subjective sense of physical, emotional, and/or cognitive tiredness or exhaustion that is related to cancer or cancer treatment, which interferes with usual functioning, and that is not proportional to recent activity. CRF significantly affects the physical, psychosocial, and economic status of patients and caregivers, as well as patients' overall quality of life [24]. Fatigue has been observed to be related with nausea, trouble, misery, nervousness, and low execution status, and in addition different manifestations, for example, sickness, regurgitating, absence of craving, dyspnoea, dry mouth, restlessness, and issues with concentration [25]. Fatigue usually occurs alongside and interacts with other issues, particularly pain, distress, and decreased functional status. Symptoms generally improve after the cessation of treatment, but improvement is often slow, but in some cases fatigue and associated issues frequently persist after completion of therapy [26, 27]. In spite of the fact that weakness is frequently multifactorial or is identified with tumour or its medicines, the challenge to the internist is to decide if fatigue indicates progression of underlying disease, the beginning of new therapeutic condition, interaction with other symptoms or issues or the symptoms from current treatment. It is also important to identify whether there is any contribution from sleep disturbances; deconditioning, depression, anxiety, psychosocial distress, dyspnoea, and uncontrolled pain or any other symptoms [28].

Meta-analyses [29] and guiding principle [30, 31] suggests a small but significant impact of aerobic exercise programs and yoga for fatigue, predominantly if the disease is in early-stage. In some patients exercise may be challenging or impossible due to the burden of disease. In these situations, one should focus

on energy conservation and rest to achieve goals; rehabilitative programs can sometimes assist with maximizing functions. Psychosocial interventions, including educational programs on fatigue, training in self-care and activity management, may also be effective [32]. Trials of pharmacologic agents and supplements for fatigue have not generally shown evidence of benefit for patients with cancer or survivors, particularly multiple randomised controlled trials (RCTs) of methylphenidate, dexamphetamine, and modafinil, and adverse effects are common, particularly anxiety and insomnia. Aerobic exercise is considered beneficial for individuals with CRF, specifically those having solid tumours during and after cancer therapy [33, 34].

Sleep disturbances

Poor sleep can be detrimental to survivor's quality of life which affects other symptoms hence deserves careful evaluation and treatment. Insomnia is considered difficulty in falling asleep or awakening during the night, which should be distinguished from general complaints about fatigue, distress, or depression. Other sleep disturbances also impact survivors sleep pattern, such as sleep apnoea and restless legs syndrome. Insomnia occurs in 30% to 59% of cancer survivors at different times during the course of their disease. In breast cancer after 2 to 5 years of diagnosis, 14% of patients reported sleep disturbance. In case of prostate cancer patients, insomnia affected up to 40% as late as 2 years post treatment. Managing sleep disturbances starts with assessing patients for symptoms that may be interfering with their ability to rest or sleep. Insomnia may be aggravated by excessive sleeping during the day, uncontrolled symptoms (eg, pain or dyspnoea), medications, caffeine, or alcohol. Psychosocial and spiritual issues and anxiety can be most bothersome in the evening and may contribute to patients being unable to sleep, interventions such as counselling may be helpful in some cases. Helping patients with good sleep hygiene interventions is important. Managing pain and depressive symptoms such as sadness and anxiety can be initial steps toward improving sleep. If patients taking medications for other purposes (eg, depression, neuropathy), clinicians can consider whether medication has a side effect of drowsiness, if yes then that can be taken at night, and can be effective as a dual aid for insomnia. The NCCN Survivorship Guidelines include specific guidelines for sleep disorders. In addition to standard recommendations for promoting good sleep hygiene, the guidelines also include cognitive behavioural treatments such as cognitive therapy, relaxation training and stimulus control, in addition to pharmacologic recommendations. An evidence-based review of RCTs of interventions for sleep disturbances in patients with cancer found substantial evidence to support cognitive behavioural therapy, with some evidence for exercise and mindfulness-based stress reduction³³. There is insufficient evidence for use of medications for sleep disturbances in patients with cancer [35]. Both the Oncology Nursing Society's Putting Evidence into Practice and evidence-based non cancer practice guidelines from the American College of Physicians (strong recommendation) recommend the use of cognitive behavioural therapy for insomnia as initial treatment. Cognitive behavioural therapy includes a combination of cognitive therapy, behavioural interventions (eg, daytime sleep restriction and reducing stimuli) and education on sleep hygiene, and is available through print materials, individual or group therapy or Web-based methods. Engaging cancer

survivors in therapy for sleep disturbances may be challenging, and in-person cognitive behavioural therapy for insomnia is not widely accessible, although evidence-based online programs are now available [36]. Given the significant adverse effects of medications for insomnia (eg, amnesia, drowsiness, and rebound insomnia), they are best used as second-line therapy and for acute episodes rather than chronically. When necessary for short-term use, evidence-based clinical practice guidelines from the American Academy of Sleep Medicine and the American College of Physicians (weak recommendation) agree on use of selected non-benzodiazepine hypnotics (zaleplon, zolpidem, and eszopiclone) and the tricyclic antidepressant doxepin. When the treatment is determined to be too burdensome or harmful in proportion to the likely outcome, clinicians should initiate discussions with patients and families regarding withholding and withdrawing life-sustaining treatments.

Palliative Care in India: Current Progress and Future Needs

The idea of palliative care is relatively new in India, introduced only in the mid-1980s. In 1975, the Government of India introduced a National Cancer Control Program. By 1984, this plan was altered to make relief from pain as one of the elementary services to be delivered at the primary health care level [37]. In India, the earliest facilities to deliver palliative care within cancer centres were established in some places like Ahmedabad, Bangalore, Mumbai, Trivandrum, and Delhi in the late 1980s and the early 1990s [38]. McDermott *et al.* recognized 138 organizations as of now providing hospice and palliative care services in 16 states or union territories. These services are usually concentrated in urban cities and regional cancer centres, except for Kerala, where facilities are more widespread [39]. It is estimated that less than 3% of India's cancer patients have access to adequate pain relief [40]. Insufficient consideration regarding pain relief is equivalent to moral and legal negligence and is a violation of the principle of beneficence. The medicinal use of opioids such as morphine is highly regulated by the Indian Narcotic Drugs and Psychotropic Substances Act (NDPS), and to distribute morphine to patients the hospitals must be registered with the government and adhere to a set procedure [41]. Procurement of oral morphine for treatment of pain in cancer patients is another problem because of cumbersome legislation [42]. These standards fluctuate from state to state and include separate licensing agencies, each with abundant levels of review and approval in the bureaucracy. In spite of some success in increasing availability, progress is slow and opioid accessibility continues to remain a constant problem for the providers of palliative care in India. There are various complications in fulfilling patients' and their families' hopes because of the heterogeneity of various geographical, social and medical backgrounds among the various districts. Considering the diversity in India, each state will have to develop its own policy that suits the need of patients and their social and cultural background. Central government should develop a policy which should provide guidelines for general application and provide an umbrella of support, especially in matters relating to opioid availability and education.

Conclusion

Palliative care is substantial in patients having malignancies or life threatening diseases. Palliative care specialists can improve symptom management and improve the quality of

life, while avoiding non beneficial care that is misaligned. Symptoms can be managed by a combination of non-pharmacological and pharmacologic interventions. After initiation of treatment, patients should be reassessed frequently until the distressing symptoms are controlled while looking out for medication side effect. Caregiver should be educated what to expect in the final hours thereby significantly lessens stress.

References

- Clark D. From margins to centre: a review of the history of palliative care in cancer. *Lancet Oncol.* 2007; (8):430-8.
- Clark D. International progress in creating palliative medicine as a specialized discipline. In: Hanks G, Cherny NI, Christakis NA, Fallon M, Kaasa S, Portenoy RK, eds. Oxford textbook of palliative medicine.4th edn. Oxford: Oxford University Press, 2010, 9-16.
- <http://www.who.int/cancer/palliative/definition/en/>. Accessed August 18, 2016.
- Smith TJ, Temin S, Alesi ER *et al.* American Society of Clinical Oncology provisional clinical opinion: the integration of palliative care into standard oncology care. *J Clin Oncol.* 2012; 30(8):880-7.
- Singer AE, Goebel JR, Kim YS *et al.* Populations and interventions for palliative and end-of-life care: a systematic review. *J Palliat Med.* 2016; 19(9):995-1008.
- Kavalieratos D, Corbelli J, Zhang D *et al.* Association between palliative care and Patient and caregiver outcomes: a systematic review and meta-analysis. *JAMA.* 2016; 316(20):2104-14.
- Mor V, Joyce NR, Cote DL *et al.* The rise of concurrent care for veterans with advanced cancer at the end of life. *Cancer.* 2016; 122:782-90.
- Palliative Care: An Evolving Field in Medicine Serife Eti. 2011; 38(2):159-71.
- LeBlanc TW. Addressing end-of-life quality gaps in hematologic cancers: the importance of early concurrent palliative care. *JAMA Intern Med.* 2016; 176(2):265-6.
- Beauchamp TL, Childress JF. Principles of biomedical ethics. Oxford (NY): Oxford University Press, 1989.
- Messinger-Rapport BJ, Baum EE, Smith ML. Advance care planning: beyond the Living will. *Cleve Clin J Med* 2009; 76(5):276-85.
- Patient Self-Determination Act, 42 1990.
- De Graeff A, Dean M. Palliative sedation therapy in the last weeks of life: a literature review and recommendations for standards. *J Palliat Med.* 2007; 10(1):67-8.
- Rao A, Cohen HJ. Symptom management in the elderly cancer patient: fatigue, pain, and depression. *J Natl Cancer Inst Monogr.* 2004; (32):150-7.
- Makris UE, Abrams RC, Gurland B *et al.* Management of persistent pain in the older patient: a clinical review. *JAMA.* 2014; (312):825-36.
- Zech DF, Grond S, Lynch J *et al.* Validation of World Health Organization guidelines for cancer pain relief: a 10-year prospective study. *Pain.* 1995; (63):65-76.
- Hershman DL, Lachetti C, Dworkin RH *et al.* Prevention and management of Chemotherapy induced peripheral neuropathy in survivors of adult cancers: American Society of Clinical Oncology clinical practice guideline. *J Clin Oncol.* 2014; 32(18):1941-67.
- Taylor Jr R, Lemtouni S, Weiss K *et al.* Pain

- management in the elderly: an FDA safe use initiative expert panel's view on preventable harm associated with NSAID therapy. *Curr Gerontol Geriatr Res.* 2012; 196159.
19. American Geriatrics Society Panel on Pharmacological Management of Persistent Pain in Older Persons. Pharmacological management of persistent pain in older Persons. *J Am Geriatr Soc.* 2009; (57):1331-46.
 20. Franklin GM. American Academy of Neurology. Opioids for chronic non cancer Pain: a position paper of the American Academy of Neurology. *Neurology.* 2014; 83(14):1277-84.
 21. Qaseem A, Wilt TJ, McLean RM *et al.* Clinical Guidelines Committee of the American College of Physicians. Non-invasive treatments for acute, subacute, and chronic low back pain: a clinical practice guideline from the American College of Physicians. *Ann Intern Med.* 2017; 166(7):514-530.
 22. Chou R, Turner JA, Devine EB *et al.* The effectiveness and risks of long-term Opioid therapy for chronic pain: a systematic review for a National Institutes of Health Pathways to Prevention Workshop. *Ann Intern Med.* 2015; 162(4):276-86.
 23. Berna C, Kulich RJ, Rathmell JP. Tapering long-term opioid therapy in chronic non-cancer pain: evidence and recommendations for everyday practice. *Mayo Clin Proc.* 2015; 90(6):828-42.
 24. Hofman M, Ryan JL, Figueroa-Moseley CD, *et al.* Cancer-related fatigue: the scale of the problem. *Oncologist.* 2007; (12):4-10.
 25. Tsai LY, Li IF, Lai YH *et al.* Fatigue and its associated factors in hospice cancer patients in Taiwan. *Cancer Nurs.* 2007; (30):24-30.
 26. Husson O, Mols F, van de Poll-Franse LV *et al.* The course of fatigue and its correlates in colorectal cancer survivors: a prospective cohort study of the profiles registry. *Support Care Cancer.* 2015; 23(11):3361-71.
 27. Vardy JL, Dhillon HM, Pond GR *et al.* Fatigue in people with localized colorectal cancer who do and do not receive chemotherapy: a longitudinal prospective study. *Ann Oncol.* 2016; 27(9):1761-7.
 28. Ebede CC, Jang Y, Escalante CP. Cancer-related fatigue in cancer survivorship. *Med Clin North Am.* 2017; 101(6):1085-97.
 29. Cramp F, Byron-Daniel J. Exercise for the management of cancer-related fatigue in adults. *Cochrane Database Syst Rev.* 2012; (11):CD006145.
 30. Bower JE, Bak K, Berger A *et al.* Screening, assessment, and management of fatigue in adult survivors of cancer: an American Society of Clinical oncology clinical practice guideline adaptation. *J Clin Oncol.* 2014; 32(17):1840-50.
 31. Oncology Nursing Society. Fatigue, 2017. Available at: <https://www.ons.org/> Practice-resources/pep/fatigue. Accessed June 19, 2017.
 32. Goedendorp MM, Gielissen MF, Verhagen CA *et al.* Psychosocial interventions for reducing fatigue during cancer treatment in adults. *Cochrane Database Syst Rev.* 2009; (1):CD006953.
 33. Cramp F, Byron-Daniel J. Exercise for the management of cancer-related fatigue in adults. *Cochrane Database Syst Rev.* 2012; (11):CD006145.
 34. Van Waart H, Stuiver MM, van Harten WH *et al.* Effect of low-intensity physical activity and moderate to high intensity physical exercise during adjuvant chemotherapy on physical fitness, fatigue, and chemotherapy completion rates: results of the paces randomized clinical trial. *J Clin Oncol.* 2015; 33(17):1918-27.
 35. Oncology Nursing Society. Sleep-Wake Disturbances, 2017. Available at: <https://www.ons.org/practice-resources/pep/sleep-wake-disturbances>.
 36. Ritterband LM, Thorndike FP, Ingersoll KS *et al.* Effect of a Web-based cognitive behaviour therapy for insomnia intervention with 1-year follow-up: a randomized clinical trial. *JAMA Psychiatry.* 2017; 74(1):68-75.
 37. Rajagopal MR, Venkateswaran C. Palliative care in India: Successes and limitations. *J Pain Palliat Care Pharmacother.* 2003; (17):121-8.
 38. Mohanti BK. Research focus in palliative care. *Indian J Palliat Care.* 2011; (17):8-11.
 39. McDermott E, Selman L, Wright M, Clark D. Hospice and palliative care development in India: A multimethod review of services and experiences. *J Pain Symptom Manage.* 2008; (35):583-93.
 40. Rajagopal MR, Joranson DE, Gilson AM. Medical use, misuse, and diversion of opioids in India. *Lancet.* 2001; (358):139-43.
 41. Sharma DC. Poor palliative care in India. *Lancet Oncol.* 2008; 9:515.
 42. Ghooi RB, Ghooi SR, Chaturvedi HK. Pain relief in India. *Lancet.* 1999; 354:677.