Review Article

Cancer Pain Management in Developing Countries

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ABSTRACT

The World Health Organization estimated that more than 60% of the 14 million new cancer cases worldwide in 2012 were reported in the developing part of the world, including Asia, Africa, Central and South America. Cancer survival rate is poorer in developing countries due to diagnosis at late stage and limited access to timely treatment. Since the disease *per se* cannot be treated even with the best available treatment modalities, what remains important is symptom management and providing comfort care to these patients. The incidence of pain in advanced stages of cancer approaches 70–80%. Lack of preventive strategies, poverty, illiteracy, and social stigma are the biggest cause of pain suffering and patient presenting in advance stage of their disease. The need for palliative care is expanding due to aging of world's population and increase in the rate of cancer in developed and developing countries. A huge gap remains between demand and current palliative care services. Overcoming barriers to palliative care is a major global health agenda that need immediate attention. Main causes of inadequate pain relief remain lack of knowledge among physician and patients, lack of adequate supply of opioids and other drugs for pain relief, strong bureaucracy involved in terms of procurement, and dispensing of opioids. Beside this, poverty and illiteracy remain the most important factors of increased suffering.

Key words: Cancer pain, Developing countries, Opioid, Palliative care

INTRODUCTION

A developing country, also called a less-developed country or underdeveloped country, is a nation with an underdeveloped industrial base, and a low human development index relative to other countries.[1] This categorization does not necessarily reflect the development status of the following broad groups: East Asia and Pacific, Europe and Central Asia, Latin America and the Caribbean, the Middle East and North Africa, Sub-Saharan Africa, and South Asia.[2] The World Health Organization (WHO) estimated that more than 60% of the 14 million new cancer cases worldwide in 2012 occurred in the developing part of the world including Asia, Africa, Central and South America.[3] Over the years, the burden has shifted to less developed countries, which currently account for about 57% of cases and 65% of cancer deaths worldwide. In less developed countries, liver and stomach cancer among males and cervical cancer among females are also leading causes of cancer death.[4] It is known that many cancer patients present in an advanced stage. Cancer survival rate is poorer in developing countries due to diagnosis at later stage and limited access to timely treatment.[5] Since the disease *per se* cannot be treated even with the best available treatment modalities, what remains important is symptom management and providing comfort care to these patients. The incidence of pain in advanced

Access this article online

Quick Response Code:

Website: www.jpalliativecare.com

DOI: 10.4103/0973-1075.191742

How to cite this article: Saini S, Bhatnagar S. Cancer pain management in developing countries. Indian J Palliat Care 2016;22:373-7.

stages of cancer approaches 70–80%.[6] Lack of preventive strategies, poverty, illiteracy, and social stigma are the biggest cause of pain suffering and patient presenting in advance stage of their disease.[6] Unrelieved pain and other symptoms decrease the quality of life, place a burden on the family's economy, and on health-care system. It also influences patient's ability to endure treatment.[6-8]

PAIN: AN ASPECT OF PALLIATIVE CARE

The need for palliative care is expanding due to aging of world's population and increase in the rate of cancer in developed and developing countries. It is difficult to measure the scope of need for palliative care with existing research methodologies.[9,10] The WHO definition of palliative care is a "response to suffering" that includes physical, psychological, social, legal, and spiritual domains of care and is provided by an interdisciplinary team of professional and lay health-care providers.[11,12] In the world's most populous nations, China and India, palliative care development has advanced from localized service provision to some preliminary integration with the health-care system. However, large disparities in access to both curative and palliative medicine exist that are based on socioeconomic status.[13] Since fewer cancer prevention and screening services exist in these regions, as many as 80% of patients are diagnosed in advanced stages of illness. Palliative care ameliorates symptoms, most frequently, pain, and reduces the use of health-care services that is not beneficial for the quality of life or longevity, especially in the terminal phase of disease. The WHO estimates that in 80% of the world population, there is insufficient access to appropriate opioid analgesics.[9] Lack of proper pain medication prescription to the patient affects patients and the family and friends witnessing the patient's suffering. Therefore, globally, patients require aggressive pain management to prevent this suffering.

OPIOID AVAILABLITY IN DEVELOPING COUNTRIES

Adequate pain relief is considered to be a human right by many organizations of health professionals.[14-21] There is a basic need to make these opioid analgesics available to those patients who need it and at the same time strict regulations to control the illicit use of these drugs. Global Opioid Policy Initiative (GOPI)[22] reported the opioid formulations that are available for cancer patients in developing countries which are in the form of codeine, morphine immediate release (MIR), morphine injection (M_{inj}), oxycodone immediate release, methadone per oral (MPO), and fentanyl transdermal (FTD). Most commonly available formulation is codeine and morphine. China, Malaysia, and the Philippines had all seven formulations available while five other countries (China-Hong Kong, Japan, South Korea, Thailand, and Vietnam) had six of seven formulations. Immediate release formulation of Oxycodone was not available in these countries. Few countries such as Afghanistan, Bangladesh, Bhutan, Cambodia, Kazakhstan and Laos did not have oral MIR formulation available. Some other countries such as Afghanistan, Bangladesh, Bhutan, Myanmar, had access to only three formulations which are codeine, M_{inj}, MPO. Many countries had access to FTD. It is an irony that a cheap drug such as oral morphine is not available, but an expensive formulation such as FTD is available.

In most of the countries, these medicines are provided either at no cost or <25% of the cost. However, in countries such as Bangladesh, Cambodia, Indonesia, Laos, Nepal, and the Philippines, patients have to pay full cost of all medicines.

STATUS OF OPIOID CONSUMPTION IN DEVELOPING COUNTRIES

Reliable access to strong opioid, such as morphine, is a prerequisite to deliver quality palliative care, a crucial component of global cancer control.[23-25] However, despite its designation as a WHO essential medicine, "Morphine" is drastically limited, or absent, in many low- and middle-income countries, such as India.[26-29] According to the WHO data from 2003, 6 developed countries accounted for 79% of global morphine consumption while developing countries only accounted for 6% of global opioid consumption despite improved access to pain treatment over the past two decades.[30-33] To put this into a global context, figures for the USA (750 mg/capita), Australia (427 mg/capita), Germany (396 mg/capita), and the UK (253 mg/capita) are even higher than that of South Korea.[34] Furthermore, the consumption of opioids in most Asian countries continues to increase at a slower rate than global averages.[34]

BARRIERS TO PALLIATIVE CARE

A huge gap remains between demand and current palliative care services. Overcoming barriers to palliative care is a major global health agenda that need immediate attention. Most of the low-income countries where the majority

of cancer patients are diagnosed with advanced-stage disease, the only realistic treatment option is pain relief and palliative care. Barriers that interfere with adequate pain management have been broadly classified as problems related to health-care professionals, to patients, and to the health-care system.[8] Regarding health-care professionals, there are no separate slots for cancer pain management in nursing and medical school curriculum. Lack of awareness about assessment and management of pain with available medicines has always remained a major barrier in providing pain relief. Even though foundation of palliative care has been laid down with availability of services in few areas, many patients in developing countries, especially in Africa and Asia, approach traditional healers and take other medications. They recognize the burden of pain as their deeds and tend to live with it. Many health-care systems in most of the developing countries lack palliative care policy guidelines. Palliative care teams are nonexistent in many countries. Patients with cancer receive inadequate opioid therapy for their pain. They are often too ill to travel to cancer facilities and possess limited financial capacity for opioid treatment.[35]

Opioid consumption is an indicator of palliative care services in a country. Opioid availability in a region does not mandate opioid availability to the patients. Developing countries face many barriers at each step to make this essential drug available to the patients. There are many eligibility criteria to prescribe morphine which are not readily met. While some formulations are always available and accessible to patients in some countries, few countries such as Afghanistan, Bangladesh, Cambodia, and Myanmar report opioid accessibility with special authorization only. Afghanistan, Bangladesh, Kazakhstan, Myanmar, Pakistan, and the Philippines require registration for all patient categories such as outpatients, inpatients, and hospice.[22] In China and Vietnam, special authority or registration is mandatory only for outpatients while Mongolia requires registration for both outpatients and hospice patients. Many countries have restrictions on prescription forms. While some (Cambodia, China, Laos, Mongolia, Myanmar, Pakistan, the Philippines, and Thailand) have restrictive access to these forms, few (Cambodia, Mongolia, Pakistan, and the Philippines) require payment for prescription.[22]

In Afghanistan, pharmacists are allowed to prescribe in emergency situations such as pain crisis at night or public holiday. Bhutan, Indonesia, Laos, Malaysia, and Pakistan allowed opioid prescription on fax or phone.[22]

Hence, main causes of inadequate pain relief remain lack of knowledge among physician and patients, lack of adequate supply of opioids and other drugs for pain relief, strong bureaucracy involved in terms of procurement and dispensing of opioids.[6,8] Beside this, poverty and illiteracy remain the most important factors of increased suffering.

PALLIATIVE CARE: STATUS OF INDIA

Home to one-sixth of the World's population, India has a huge burden of suffering from life-limiting diseases. Less than 1% of its population has access to pain relief and palliative care.[36] Provision for health care and for opioid access varies from state to state. This created difficulties, especially when one state had to depend on a manufacturer of opioids in another state or when palliative care provisions had to be made a part of government's health system.[37] Opium is grown in India in the three Northern states of Uttar Pradesh, Madhya Pradesh, and Rajasthan, and India exports the raw materials used to manufacture opioid analgesics around the world. Paradoxically, very little is produced for local medical use, and India has had very low opioid consumption.[36] In the late 1990s, several new palliative care initiatives were started. India had formed, in 1985, the Narcotic Drugs and Psychotropic Substances (NDPS) Act.[38] In 13 years which followed the enactment of the NDPS Act, morphine consumption in the country fell by an alarming 92% – from around 600 kg to a mere 48 kg. In 1997, India's per capita consumption of morphine ranked among the lowest in the world (113th of 131 countries). During the same period, global consumption of morphine had increased by 437%.[38] Various societies were formed for encouraging palliative care. Many activists struggled together for the same cause for years and fought to provide a very basic human right. Finally, in February 2014, the parliament passed the NDPS Amendment Act. The new Act transferred the powers for legislation on "Essential Narcotic Drugs" from the state governments to the central government. It is necessary now for the Government of India to announce the uniform simplified state rules. These rules and the standard operating procedures were already prepared by the government, in consultation with the department officials, with the support lawyers and palliative care activists collectively. In May 2015, the Government of India concluded the process with notifications regarding the rules to be followed by the state governments. It is up to palliative care activists and state governments to ensure that the amended rules are implemented.[37] If we weigh improvement in palliative care services by looking at the opioid consumption, after so much struggle a rise in the consumption of morphine has been seen over a period of decade.[39]

As per GOPI[40] report, MIR is available throughout all the states of India. TDF is available in all but two states (Jammu and Kashmir and Tripura). More than 50% of the cost of medications has to be paid by the patients. In most of the states, primary care physicians require special authorization to prescribe opioids and in four states (Bihar, Haryana, Punjab, and Tamil Nadu), it could be prescribed in an emergency situation only. Generally, the maximum number of days for prescription is 30 days.[40] Laws are changing to make opioid accessible to patients in need and improve palliative care services in India.

The Medical Council of India has approved a postgraduate course in palliative care, but the lack of teaching at the undergraduate level has seen few physicians develop careers in of palliative care.[41] Very few medical colleges in India have incorporated palliative care in their curriculum. These bold steps will help develop an attitude of students toward palliative care as their careers.

PAIN RELIEF STRATEGIES

Cancer pain can be managed successfully utilizing a holistic approach which includes an understanding of the type of pain, psychosocial issues involved, the pathophysiology of the pain, and the pharmacology of the pain-relieving drugs. Drug treatment helps curbing the cancer pain management 70% and 90% with oral medication.[42] Adequate pain relief can be achieved in more than 75% of patients who receive optimal analgesic management using simple techniques such as opioids, nonopioid analgesics, and adjuvant medications as suggested by the WHO analgesic ladder.[43,44] However, a patient in moderate cancer pain, there is no role of weak opioids and the second step can be omitted.[45] These weak opioids are more expensive in many developing countries, where they are not manufactured. Here, patients started on strong opioids as a first-line analgesic may have better pain relief, but morphine availability and accessibility is the major hurdle. Along with opioids, adjuvant drugs such as Tricyclic antidepressants, anticonvulsants play an important role too in managing complex pain syndromes. Pain can also be relieved by the modification of the disease process, when appropriate, with surgery, chemotherapy, and radiotherapy, but these therapies are expensive and inaccessible to many patients, especially in rural communities.[2] Nondrug methods including psychological interventions, physical therapy, and complementary medicine are also employed for pain relief, sometimes by nonspecialists.[2]

FUTURE RECOMMENDATIONS FOR DEVELOPING COUNTRIES

- National policies and strategies to develop resource-based palliative care guidelines based on the socioeconomic conditions of the region
- Strict implementation of these guidelines with supervision
- Government should undertake a thorough review for the inclusion of palliative care at all levels
- Health-care professionals should get training for providing palliative care
- Monitoring and reporting of availability, accessibility, and opioid consumption at regular interval.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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