Special Article

Opioid Availability and Palliative Care in Nepal: Influence of an International Pain Policy Fellowship

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Abstract

Globally, cancer incidence and mortality are increasing, and most of the burden is shifting to low- and middle-income countries (LMICs), where patients often present with late-stage disease and severe pain. Unfortunately, LMICs also face a disproportionate lack of access to pain-relieving medicines such as morphine, despite the medical and scientific literature that shows morphine to be effective to treat moderate and severe cancer pain. In 2008, an oncologist from Nepal, one of the poorest countries in the world, was selected to participate in the International Pain Policy Fellowship, a program to assist LMICs, to improve patient access to pain medicines. Following the World Health Organization public health model for development of pain relief and palliative care, the Fellow, working with colleagues and mentors, has achieved initial successes: three forms of oral morphine (syrup, immediate-release tablets, and sustained-release tablets) are now manufactured in the country; health-care practitioners are receiving training in the use of opioids for pain relief; and a new national palliative care association has developed a palliative care training curriculum. However, long-term implementation efforts, funding, and technical assistance by governments, philanthropic organizations, and international partners are necessary to ensure that pain relief and palliative care become accessible by all in need in Nepal and other LMICs. J Pain Symptom Manage 2015;49:110–116. © *2015 American Academy of Hospice and Palliative Medicine. Published by Elsevier Inc. All rights reserved.*

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Introduction

According to the World Health Organization (WHO), noncommunicable diseases (NCDs)—cancer, diabetes, cardiovascular disease, and chronic respiratory diseases—are the leading cause of death globally, totaling more than all other causes combined.[1] Low- and middle-income countries (LMICs) bear almost 80% of that burden.[1] Cancer alone claimed seven million lives in 2008, and 25 million more are living with the disease.[2] Complicating these dire statistics are healthcare systems and governments lacking adequate resources and expertise to care for their citizens. Despite good intentions, many countries lack basic palliative care services[3,4] and the essential medicines necessary to provide these services. Specifically, there is a lack of access to and, therefore, consumption of morphine in LMICs,[5–7] despite the medical and scientific literature that shows morphine to be effective to treat moderate and severe pain.[8,9] The WHO has included morphine in its Model List of Essential Medicines since 1977.[10]

Morphine and other opioid analgesics are internationally controlled substances because of their abuse potential. The Single Convention on Narcotic Drugs of 1961, as amended by the Protocol of 1972 (Single Convention), states that these substances are to be used for medical and scientific purposes only.[11] Although the Preamble of the Single Convention states that "the medical use of narcotic drugs continues to be indispensable for the relief of pain and suffering and (that) adequate provision must be made to ensure the availability of narcotic drugs for such purposes,"[11] these medications remain difficult for physicians in LMICs to obtain and prescribe for their patients.

Nepal has one of the lowest levels of development in the world, with a Human Development Index of 0.463, placing it 157th of 186 countries in 2012.[12] It also is struggling with a large burden of cancer, other NCDs, and AIDS. Most of its population of 27 million people live in rural areas, and almost a quarter live below the poverty level.[13] NCDs account for approximately 50% of total deaths in Nepal.[14] In 2008, there were an estimated 27,800 people diagnosed with cancer (most in an advanced stage) and 20,000 cancer deaths.[15] In 2012, there were approximately 49,000 people living with HIV/AIDS and 4600 deaths as a result of AIDS.[16] For the last decade in Nepal, the development of palliative care services has steadily increased,[3,4,17] but the availability of morphine has remained inconsistent and inadequate. The Government of Nepal is a signatory to the Single Convention and has a designated office, the Narcotic Drug Control Section of the Ministry of Home Affairs, that is responsible for meeting the treaty requirement to report annual narcotics consumption to the International Narcotics Control Board (INCB) and to submit annual estimates of requirements for narcotic medicines. These requirements provide an opportunity to work with governments to improve opioid availability.

The Pain & Policy Studies Group (PPSG), within the University of Wisconsin Carbone Cancer Center, is the home of the WHO Collaborating Center for Pain Policy in Palliative Care and has as its mission the improvement of global pain relief by helping LMICs to balance access to opioid analgesics for those in need with minimizing the risk of opioid diversion. In 2006, with funding from the Open Society Foundations, the PPSG developed the International Pain Policy Fellowship (IPPF) whose purpose is to assist LMICs to safely improve patient access to pain relief recommended by the WHO. United Nations bodies, including the WHO[18,19] and the INCB[20] have expressed concern about the low consumption of controlled pain medicines in the world, especially in developing countries. The IPPF is intended for health professionals, health-care administrators, policy experts, social workers, or lawyers from LMICs committed to improving the availability of

opioid analgesics for pain relief and palliative care. The IPPF program includes training, mentoring, action plan development, and an in-country pain policy project.

Problems and Progress in Nepal

In 2008, an oncologist (B. D. P.) at Bir Hospital in the capital city of Kathmandu, was selected to participate in the IPPF program. Bir Hospital is not only the oldest and largest government hospital, but in 1991, it was the first hospital in Nepal to initiate an oncology service that includes curative and palliative care for cancer patients. In June 2008, after initial preparations, which included review of background information, the Fellow from Nepal (B. D. P.) joined eight other global Fellows to participate in a five day training program in Madison, Wisconsin. Fellows presented country reports detailing the level of palliative care development and the degree to which opioids were available in their country at the time. In 2008 in Nepal, there was a limited amount of immediate-release (IR) oral morphine tablets (10 mg) imported from Indian manufacturers. Because of the limited importation and delays in exportation from India, there were frequent shortages and stock-outs. Injectable morphine (15 and 10 mg) was available in major hospitals, typically for inpatient use. Transdermal fentanyl and oral morphine syrup were not available.

During the five day training session, the Fellow worked with his mentors to identify the following critical barriers to adequate pain relief and palliative care for cancer patients in Nepal: 1) low and irregular supply of IR oral morphine at hospitals throughout the country, despite increasing predicted demand; 2) severe lack of morphine availability outside major cities and for the very poor; 3) few morphine distributors in the country; 4) inappropriate and/or inadequate prescribing by physicians because of lack of clinical knowledge; and 5) limited support by the government for country-wide efforts in pain management and palliative care. The Fellow and mentors then developed an action plan with specific steps to address each barrier to opioid accessibility over the two year Fellowship. In 2010, after initial successes, the Fellow was awarded another two year IPPF to continue his work through 2012. Our approach to the barriers and progress to date in Nepal was guided by the WHO Palliative Care Strategy, which states that *medicine availability*, *education*, and *government policy* must all be addressed if adequate pain relief and palliative care are to be provided.[21]

Availability of Medicines

Consumption. Consumption of morphine in Nepal has consistently fallen below both the global and the regional means. For the eight years that Nepal reported morphine consumption statistics in the 10 year period 1996–2005, it ranked consistently among the bottom three reporting countries in the WHO Regional Office for Southeast Asia (SEARO) (Fig. 1). Only since 2007 has there been an increase in morphine consumption to a level above that for the SEARO regional mean in milligrams per capita but still far less than the global milligrams per capita mean (6.11 mg per capita for 2011). However, although the 6.445 kg of morphine consumed in 2008 (the highest level ever consumed) is more than 10 times the amount of morphine consumed in 2000 (Fig. 2), this amount would provide end-of-life pain treatment of 60 mg of morphine per day for 90 days[22] for only 1193 cancer patients, or less than 6%, of the estimated 20,000 cancer patients who died in Nepal that year. In 2011, the year for which the most recent data are available, Nepal reported consumption of 2.402 kg of morphine or 0.0802 mg per capita.

Lack of Oral Morphine. Starting in 2005, IR and sustained-release (SR) oral morphine tablets were available in Nepal via import from India but with an irregular supply because of export delays. Our efforts to find a way to avoid import delays and resultant stock-outs, although successful on occasion, did not lead to a sustainable solution. Ultimately, the Fellow, the Director of Drug Administration in the Ministry of Health and a private Nepalese manufacturer who was already manufacturing injectable morphine began discussions about the potential to manufacture morphine syrup in Nepal to overcome the problem of delays and stock-outs. Despite the very low profit margins of oral morphine and the burden of

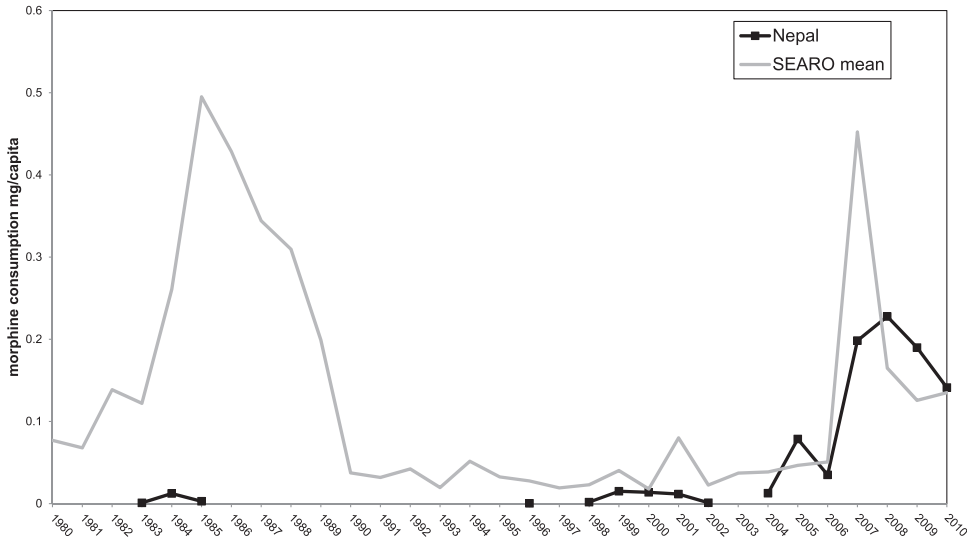

Fig. 1. Annual morphine consumption (milligrams per capita) in Nepal and the mean morphine consumption (milligrams per capita) for the World Health Organization Regional Office for Southeast Asia (SEARO).

paperwork required to manufacture or import internationally controlled substances, the manufacturer decided to proceed based on the humanitarian conviction that relief of moderate and severe pain with oral morphine was essential for the well-being of the Nepalese people.

In 2009, the Nepalese company received a license to manufacture morphine solution in Nepal and began to provide this solution to Nepalese hospitals and pharmacies the same year. In early 2011, it began importing morphine powder from Switzerland and India and began to manufacture 10 mg IR oral morphine tablets.

The opposite problem occurred with the importation of SR morphine tablets from India. Importers of 30 mg SR oral morphine tablets reported large unused stocks, in part because of a lack of predictability of the timing of the shipment and large quantities received all at one time. Similar reports from hospitals and hospices throughout Nepal suggested that the available morphine was not being consumed. Regrettably, in 2011, 97,000 of 200,000 (49%) SR morphine tablets expired

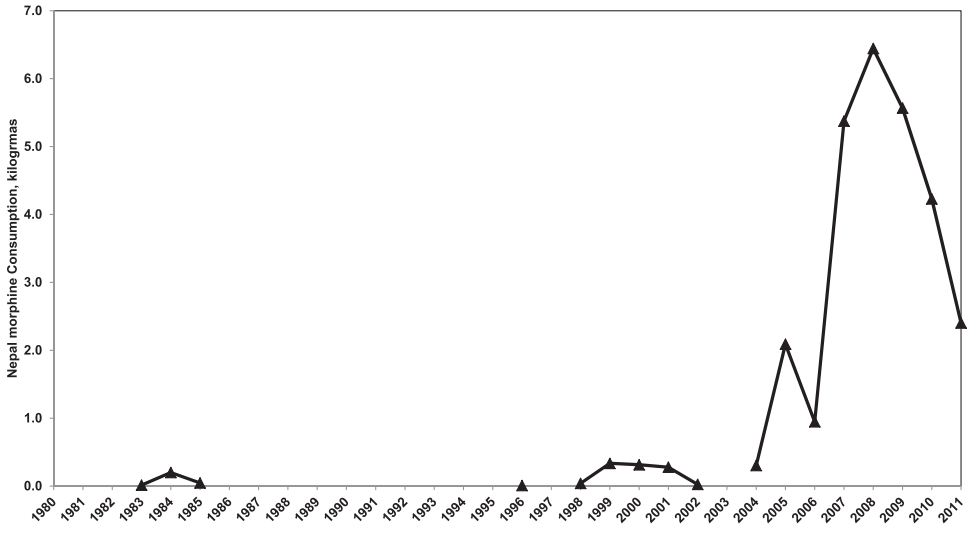

Fig. 2. Nepal morphine consumption (kilograms) from 1980 to 2011.

because of lack of demand. This illustrates another potential barrier to patient access to opioids: physicians are reluctant to prescribe because of a lack of education and training in pain management.

However, despite the challenges with consuming 30 mg SR morphine tablets, there remained a need for 10 mg SR tablets in Nepal. The Fellow collected data on consumption and found that 300,000 SR morphine tablets (10 mg) were imported in February 2010 and consumed by the end of 2011. Finally, the Nepalese company began to manufacture a small batch of SR morphine tablets in 2012, which provided a local more sustainable supply of SR tablets than when they were imported.

Education

Lack of Training in Pain Relief and Palliative Care. Across Nepal, since 2009, approximately 500 doctors, residents, nurses, pharmacists, and volunteer health workers have been trained about morphine use by colleagues from Kasih Hospice Malaysia, OZQuest Medical Team of Australia, U.S. experts, Bhaktpur Cancer Hospital, Hospice Nepal, and the Nepal Network for Cancer Treatment and Research (NNCTR), which is a branch of the International Network for Cancer Treatment and Research (INCTR). In 2009, a four week palliative care training program was started with the help of INCTR. In 2010 and 2012, the B.P. Koirala Memorial Cancer Hospital (BPKMCH) conducted a one month palliative care training program for physicians and nurses with joint collaboration of the Nepalese Association of Palliative Care (NAPCare) and NNCTR. The National Academy of Medical Sciences, the medical school based at Bir Hospital, also conducted palliative care training for resident doctors in 2011 and 2013. In all these trainings, the Fellow's (B. D. P.) responsibility was to conduct the session on pain management with balanced use of opioids. It is expected that the BPKMCH and National Academy of Medical Sciences/Bir Hospital trainings will be held annually. The Ministry of Health has accepted the importance of palliative care training for doctors and nurses and has already conducted a one month palliative care training with the help of NAPCare in September 2013. In some instances, nurses who have received basic pain management training are allowed to initiate morphine treatment under physician supervision. In some countries, such as Uganda, specially trained nurses are permitted to prescribe morphine,[23] and several other countries with insufficient prescribers or with a large rural population are considering this as an option to improve accessibility.

To fully address the lack of clinicians trained in pain relief and palliative care in Nepal, well-trained Nepali trainers will be needed. Training of trainers will require that either Nepali clinicians committed to pain relief and palliative care go abroad for intensive training or expert foreign trainers come to Nepal specifically to intensively train trainers.

Government Policy

National Drug Policy. The stated goal of the 1995 Nepalese National Drug Policy is "To maintain, safeguard, and promote the health of people by making the country self-reliant in drug production; ensuring the availability of safe, effective, standard, and quality drugs at affordable price in quantities sufficient to cover the need of every corner of the country; and to manage effectively all the drugs-related activities including production, import, export, storage, sale, supply, and distribution."[24] In addition, a stated policy goal is "to be able to produce 80% of the essential drug formulations in the coming 10 years."[24] Although the policy promotes the "rational use of drugs" and appropriate drug monitoring, there is no specific mention of opioids for pain relief.

National Palliative Care Development Efforts

Palliative care has been developing gradually for nearly two decades in Nepal and has involved many different institutions providing palliative care over the years. These include Pashupati Temple, Maiti Nepal, and Hospice Nepal, which started their palliative care activities in 1995, 1999, and 2000, respectively. In 2002, the NNCTR began working with global palliative care experts to form a national palliative care group to begin addressing the three key WHO foundational measures of palliative

care: government policy, education, and opioid availability.[17] Likewise, Bhaktpur Cancer Hospital and Shechen Clinic launched separate palliative care wings in 2004, and BPKMCH initiated their wing in 2005. Finally, Thankot Hospice was started in 2007 for cancer patients. This work was continued and strengthened by the Fellow's activities.

In February 2009 and April 2012, International Palliative Care Conferences were held in Nepal. Experts and supporters from Canada, Ireland, and India participated in these conferences along with representatives of various Nepali health institutions. The Fellow spoke at both conferences on the importance of opioid availability and accessibility in all parts of the country for pain management.

To further the development of palliative care in Nepal, a group of 22 palliative care providers collaborated to launch in December 2009 the NAPCare, a multidisciplinary, nonpolitical, nonprofit organization with the sole purpose of advancing palliative care by training, research, and promoting a good standard of care. NAPCare activities include providing educational opportunities for medical and nursing students and developing policies related to palliative care such as a Pain Management Protocol in Palliative Care, released in 2011, which guides clinicians in best pain treatment practices. In April 2012, a second International Palliative Care Conference was held jointly by NAPCare and INCTR.

Conclusion

Developing and integrating a new discipline such as palliative care into the health system of any country is a challenge. The task is even more daunting for those countries with few resources. However, as the increasing prevalence of NCDs and the lack of access to palliative care and opioid analgesia gain increasing attention from global health and political bodies, there is growing pressure to ensure that they are addressed. Following the WHO public health model, efforts in Nepal have begun to bear fruit: three forms of oral morphine (SR tablets, IR tablets, and syrup) are now manufactured in the country, health-care practitioners are receiving training in the use of opioids for pain management, and the new national palliative care association is conducting a one month palliative care training on an annual basis, with the help of the Ministry of Health. However, nascent progress should not be mistaken for long-term success. Systemic change requires long-term attention and implementation efforts. We have identified some of the tools, including the IPPF, which can be helpful to facilitate opioid availability and palliative care development. What is needed now is sustained funding and technical assistance by governments, philanthropic organizations, and international partners to ensure that global efforts to make pain relief and palliative care available to all those in need come to fruition. Long-term sustenance of these efforts is especially imperative in this time of global economic austerity, marked by shrinking budgets, increased need caused by the growing incidence of NCDs, and competing priorities.

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