Use of Opioids and Sedatives at End-of-Life

Shin Wei Sim, Shirlynn Ho, Radha Krishna Lalit Kumar

Department of Palliative Medicine, National Cancer Center, Singapore 11 Hospital Drive, Singapore

Address for correspondence: Ms. Shin Wei Sim; E-mail: shinwei.sim@mohh.com.sg

ABSTRACT

Despite their proven efficacy and safety, opioid and sedative use for palliation in patients afflicted with cancer in Singapore have been shown to be a fraction of that in other countries. This paper explores the various psychosocial and system-related factors that appear to propagate this conservative approach to care in what is largely a western-influenced care practice. A search for publications relating to sedative and opioid usage in Asia was performed on PubMed, Google, Google Scholar, World Health Organization, and Singapore's government agency websites using search terms such as "opioids," "sedatives," "palliation," "end-of-life-care," "pain management," "palliative care," "cancer pain," "Asia," "Singapore," and "morphine." Findings were classified into three broad groups – system-related, physician-related, and patient-related factors. A cautious medico-legal climate, shortage of physicians trained in palliative care, and lack of instruments for symptom assessment of patients at the end of life contribute to system-related barriers. Physician-related barriers include delayed access to palliative care due to late referrals, knowledge deficits in non-palliative medicine physicians, and sub-optimal care provided by palliative physicians. Patients' under-reporting of symptoms and fear of addiction, tolerance, and side effects of opioids and sedatives may lead to conservative opioid use in palliative care as well. System-related, physician-related, and patient-related factors play crucial roles in steering the management of palliative patients. Addressing and increasing the awareness of these factors may help ensure patients receive adequate relief and control of distressing symptoms.

Key words: Asia, End-of-life care, Opioids, Sedatives, Singapore

INTRODUCTION

A recent series of studies on the use of opioids, sedatives, and intravenous hydration amongst terminally ill cancer patients in Singapore by Krishna *et al.* have not only served to benchmark medical interventions at the end of life within the acute setting but has also sought to highlight the variations in care practices that exists within First World end of life care in the East and that of the West.[1-3]

In illustrating the vast differences in opioid and sedative use amongst the terminally ill, Krishna *et al.* evidenced the significant psychosocial factors that ought to be considered in an end of life evaluation.[1,2] Evidencing that the median daily dose of sedatives amongst local patients in the last 24 hours of life was a tenth of that expected in many western practices, whilst the mean daily dose (oral morphine equivalents) of opioids used locally over the same time frame was about 30% less than the 136-659 mg per day reported in the literature would only serve to perpetuate the belief that cancer pain is undertreated in the east.[4] The numbers it would seem only tell a part of story. Here, this article delves into the various psychosocial and system-related factors that appear to propagate this conservative approach to care in what is largely a western-influenced care practice. Due to the lack of data on the usage of sedation and opioids in community-based palliative care in Singapore, this commentary serves to explore only hospital-based palliative care in the local setting.

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System-related barriers

Looking at macroscopic factors at play within the realms of Singapore medical practice, current healthcare policies concerning the use of opioids and sedatives have been particularly restrictive.[5] This situation is compounded by an environment fraught with the stresses of legal repercussions and increasingly demanding patients and families.[5,6] Physicians may inadvertently exercise undue caution in their management of patient symptoms. This climate of caution, along with the dearth of specialized personnel and tools, would appear to serve only to reduce the quality of care for patients at the end of life.

Current medico-legal climate may encourage an overly cautious approach to symptom management at the end of life

Prevailing regulations on the conduct of physicians as well as the prescription of and access to certain medications deemed to have a potential for abuse have spawned a culture of conservative practice in applying these medications.[5,6] The Singapore Medical Council tough stance against medical malpractice in recent years and its deterrent sentencing has served merely to compound fears of many practitioners with regards to their conduct.[7]

A complaint culture, increasingly savvy and demanding family members, and a continued fear of opioid use have also contrived to reduce prescriptions of these medications even when indicated.[8-12]

An unwillingness to deal with the dissatisfaction of patients or their families, or inquiries by the authorities might thus be a reason for the underutilization of opioids and sedatives in the treatment of palliative patients in.[13-19]

Shortage of palliative medicine physicians and lack of training in palliative care limit patient access to good symptom control at the end of life

The field of palliative medicine in Singapore is still in its infancy, having been accredited as a subspecialty only in 2007. In the Report on the National Strategy for Palliative Care by Lien Centre for Palliative Care, Duke-NUS Graduate Medical School, a shortage of palliative medicine physicians was identified as a weakness of the current healthcare system in Singapore.[20] Physicians' lack of adequate training in the management of end-of-life issues may also contribute to the poor availability of palliative care in Singapore. While palliative medicine is currently represented in the undergraduate curriculum of medical schools in Singapore, studies nevertheless suggest that the training in medical school is inadequate.[21,22] Physician education on pain management is also largely limited to physicians within specific fields.[21,22]

Lack of instruments for symptom assessment of patients at the end of life

Yet another factor that may contribute to the under-treatment of symptoms in patients at the end of life is the lack of standardized symptom assessment instruments used in local practice, whilst the use of standardized symptom assessment instruments improve symptom treatment.[23] Instruments such as the M.D. Anderson Symptom Inventory (MDASI) and the Edmonton Symptom Assessment System (ESAS) were found to be useful for cancer patients under follow-up.[23] Specifically, the use of ESAS in 8 hospices in the United States helped the identification and subsequent treatment of patient symptoms.[24]

As such, these instruments may represent tools available for the routine assessment of palliative patients. They could better enable both medical and nursing staff to detect symptoms amenable to treatment, and thus improve symptom management at the end of life.

Physician-related barriers

Physicians play an integral part in the provision of good-quality care to patients at the end of life. However, physicians' misconceptions pertaining to the use of opioids and sedatives may hinder their prescription of these medications.[5,9] Timely referrals to palliative medicine physicians should minimize inappropriate or inadequate management of patient symptoms, although the effectiveness of palliative care teams in correcting erroneous beliefs of patients and their families remains to be seen.

Knowledge deficits and reluctant attitudes lead non-palliative medicine physicians to adopt a conservative approach in symptom management

Palliative medicine physicians are rarely the primary physicians of hospital inpatients in Singapore. More commonly, patients receiving palliative care are co-managed by a palliative medicine team and a primary healthcare team of another specialty. A referral to palliative medicine is usually made by the primary team before palliative medicine physicians join in the management of a patient requiring palliative care.

Hence, while palliative medicine physicians are generally recognized for their expertise in the management of terminally ill patients, there is a need for physicians both within and outside of the palliative medicine specialty to be knowledgeable and confident in the management of patient needs at the end of life, to ensure the good provision of care to the terminally ill.

To date, there have been no local studies on the knowledge and attitudes of non-palliative medicine physicians regarding the prescription of opioids and sedatives for patients at the end of life. However, many international studies have suggested that knowledge deficits and reluctant attitudes of physicians are common barriers to the adequate prescription of these medications for symptom management at the end of life.

A systematic review conducted in 2009 identified knowledge deficits, inadequate pain assessment, and misconceptions regarding pain management as significant barriers preventing adequate cancer pain management.[25] Similarly, a survey conducted on Taiwanese physicians (primarily from medical and surgical specialties) involved in the care of cancer patients revealed that inadequate knowledge and negative attitudes hindered the optimal prescription of opioids, and alluded to physicians' limited clinical experience in pain management as a possible cause.[21]

Given these findings, it is possible that misconceptions regarding the use of opioids are present among non-palliative medicine physicians in Singapore as well. Even if equipped with adequate knowledge of the clinical efficacy and safety profile of opioids, it is not unreasonable to expect that these physicians may be more reluctant in their prescription of opioids, given their limited clinical experience in doing so. Hence, while palliative medicine physicians provide clinical input and prescribe medications for inpatients requiring palliative care, the conservative approach of primary healthcare teams in executing the recommendations of palliative medicine physicians could still hinder optimal pain management.

Late referrals to palliative medicine delay access to palliative care

In Singapore, input from palliative medicine physicians is only provided after a referral has been sought. As such, late referrals to palliative medicine could contribute to inadequate symptom control for terminally ill patients, especially if non-palliative medicine physicians are more conservative or less knowledgeable in the management of these patients.

Despite the lack of local studies on the prevalence of late referrals in Singapore, studies conducted overseas acknowledge the existence of such an issue. An audit in a United Kingdom hospital showed that 49% of patients were recognized as dying only 24 hours or less before death.[26] This implies that only a small proportion of dying patients were able to benefit from end-of-life care pathways. A similar phenomenon was observed in Japan, where a survey of bereaved family members of cancer patients showed that 47% of family members and 44% of patients considered the timing of referrals to palliative care units as late.[27]

It is heartening to note that an overwhelming majority of the families in the Japanese study evaluated the palliative care team as useful. Specifically, 93% of families indicated that the palliative care team was useful in symptom control and 90% of families indicated that the palliative care team was useful in providing emotional support.[27] This reinforces the need to minimize late referrals, so that patients and families can benefit from the palliative care received at the end of life.

Care provided by palliative care teams not necessarily ideal

Although palliative medicine physicians are widely recognized for their expertise in the management of terminally ill patients and their symptoms, the care provided by palliative care teams may nonetheless be imperfect. An audit of morphine prescription in a local hospice revealed varied and even inappropriate prescription within a palliative care institution,[28] thus hinting at the possibility of suboptimal care provided by specialized palliative care teams.

While palliative care teams have been recognized for their value in symptom control and provision of emotional support to patients and their families, among other things, the effectiveness of palliative care teams in changing erroneous perceptions of patients and their families remains unknown. Given the presence of unique patient concerns within the local setting, good communication between palliative care teams, patients, and their families may hold the key to heightened levels of acceptance for the use of opioids and sedatives in patient care.

Patient-related barriers

Many studies have described patient-related barriers that contribute to inadequate pharmacological management of cancer symptoms, and in particular, cancer pain. The most commonly cited patient-related barriers include fears of addiction, tolerance, side effects, and a tendency to underreport symptoms.[29-32] In the discussion that follows, we aim to present these barriers in the context of modern Singaporean society.

Fear of addiction and tolerance

Various fears regarding opioids have been described in the literature.[31,32] Such "opioid phobia" appears to be cross-cultural and is common among patients and, to a lesser extent, healthcare professionals.[29] However, we believe these misconceptions may also affect local patients' perceptions of other medications, specifically in this context, traditional sedatives.

Singapore's experience with opioids may be traced to the opium wars of the 1800s. Chinese immigrant laborers of the time often turned to smoking opium to escape the harsh reality of their lives, and it was estimated that at the peak of the problem, one in three adult Chinese were active opium users.[33] While these largely historical accounts may fade into relative obscurity, the continued existence of a small group of aging opium addicts in Singapore serve as a reminder of the dangers of narcotic drug addiction.

In 1971, heroin (diacetylmorphine) abuse rates were on the rise and the Singaporean government set up the Central Narcotics Bureau to combat what was being seen as a growing threat against the society at large.[33] A multi-pronged approach was employed, with the amendment of legal acts to level stiffer penalties against drug abuse, drug possession, and drug trafficking, as well as a series of public education campaigns about the consequences of drug abuse and addiction. The latter was targeted at a wide demographic range, with school-going children aged 10 years and above being identified as a priority population.[33] Increasingly, drug abuse was depicted as not merely a state of physical degeneracy, but also one of moral decrepitude.[34]

A study of the general population in 1991 showed the results of these interventions. More than 80% of the population surveyed believed that drug abuse was a serious social problem, which placed it above other "social problems" such as sexual promiscuity, smoking, and alcohol. The awareness of anti-drug abuse activities was correspondingly high at 85.[35] Thus, it is not surprising that patients may have an excessive fear of morphine, which is classified as a drug of abuse with all of its legal, social, and moral implications.

With the turn of the millennium, the media limelight turned onto a relatively new group of abused drugs. These included buprenorphine (Subutex), a drug intended to treat opioid dependence; midazolam (Dormicum), nimetazepam (Erimin-5), and other sedatives of the benzodiazepine class; as well as codeine and dextromethorphan, both active ingredients that are found in cough mixtures.[36,37]

The main difference between these new drugs of abuse and their traditional counterparts was that in many cases reported in the media, the abuser had no particular demographic characteristics and was first prescribed the medication for specific medical indications.[38] This was clearly opposed to that of the traditional drugs of abuse where potential abusers were typified in government campaigns to be young men from lower socioeconomic backgrounds and broken families, who first came into contact with drugs through acquaintances of questionable repute.[33,34] Against this backdrop of increasing public concern regarding the addictive potential of even seemingly innocuous medications, it is possible to understand how patients may be as wary of using traditional sedatives as they are of using opioids.

Fear of side effects

The most common side effects of opiate drugs include constipation, nausea, and sedation.[39] It has been reported in the literature that up to 20% of patients who are prescribed opioids for treatment of chronic non-cancer pain may discontinue treatment due to side effects.[40] However, there is a lack of similar data for the use of opioids in treating cancer pain.

As Krishna *et al.* studied the patients' use of opioids and sedatives in only the last 48 hours of life, sedation - as a side effect of opioids and the primary effect of sedatives - may be of particular concern to both the patient and the patient's family, given the cultural and religious considerations in the region.[41]

In Singapore, more than 85% of the population has a religion and the main religious affiliations are Buddhism, Christianity, Islam, Taoism, and Hinduism.[42] Near or at the end of life, these religions each have diverse beliefs, customs, and rituals that may further differ based on ethnic influences, community norms, and individual preferences.

To Buddhists, life and death are parts of a cycle of reincarnation, and it is important to remain lucid till the time of death, for the content of the last conscious thought will determine the outcome of reincarnation. Hindus also believe that the patient's final thoughts determine the outcome for his soul, and hence similarly, consciousness up to the time of death is preferred. For Muslims, a clear mind is valued because the recitation of daily prayers should continue up to the point of death. Additionally, the patient and his family members traditionally ask for each other's forgiveness as the time of death draws near; hence ideally, the patient should remain conscious and alert as death approaches.[41,43]

Interestingly, a recent qualitative study of Singaporean patients and family caregivers shows that while patients prefer to die quickly or to die in their sleep, family caregivers emphasized the importance of being able to bid a final farewell to the patient (Lee 2013).[44] However, the authors made reference to the relevant literature, and suggested that these preferences expressed by the patient may represent a desire to escape from pain. In the absence of pain, it is possible that patients may then prefer to remain conscious.

As can be seen, the maintenance of consciousness appears to be a relatively important aspect of a good death. Therefore, it is possible that the fear of sedation could represent a barrier to the management of cancer symptoms.

Underreporting of symptoms

The literature reports several reasons for patients underreporting or understating the pain that they are experiencing. These include a sense of fatalism in which they believe their pain is inevitable and untreatable, a belief that increased levels of pain implies disease progression, a fear of distracting the physician from treating the main problem of cancer, and a worry that complaining of pain precludes one from being a "good" patient.[29-32]

A recent meta-analysis of patient-related barriers assessed by the validated Barriers Questionnaire (BQ) showed that Asian patients perceive more barriers to cancer pain management, as indicated by a higher mean BQ score than their Western counterparts. Also, specifically they are more likely to have fatalistic beliefs regarding cancer pain, as well as beliefs that increased pain levels imply disease progression.[45] The authors were of the opinion that these differences could result from a common failure in Asian societies to share the disease prognosis with the patient. They explained that in the absence of knowledge regarding the extent of disease and thus also knowledge of treatment options for their pain, patients might attribute unfounded significance to their symptoms, and even view pain as an innate and unavoidable part of their condition.[45]

While the above explanations are logically sound, we would like to highlight several culture-specific differences in emotional styles that could contribute to Asian patients being less likely to report their physical symptoms compared to those in the West.

Cross-cultural studies have shown that Asians tend to be dialectical in their emotional repertoire, meaning that they experience a fairly balanced mix of both positive and negative emotions, as opposed to Americans who often exhibit a non-dialectical emotional style - experiencing more positive than negative emotions, or vice versa, over time.[46-48] Furthermore, Asians were described to seek the "middle way" emotionally, avoiding the extremes of emotion that were more common among the Americans.[46] In studies conducted on well individuals within the community, these more inhibited styles of emotional experience and expression were associated with fewer reported psychological and physical symptoms.[48,49] While admittedly these findings may not be fully generalizable to palliative patients, they reflect unique cultural mindsets that may affect patients' willingness to report symptoms and should be considered when managing their symptoms.

CONCLUSION

The appropriate use of opioids and traditional sedatives for amelioration of symptoms among cancer patients near the end of life have been shown to be both efficacious and safe.[50-56] However, the frequency and dosages of opioids and traditional sedatives used in Singapore are lower than in similar international studies.[1-3] System-related, physician-related, and patient-related barriers to the use of these medications in symptom management were examined and discussed against the backdrop of the local socio-cultural circumstances. These pose unique challenges to the palliative care teams in the management of distressing symptoms in their patients near the end of life.

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