

MANAGEMENT OF PAIN WITH MORPHINE IN CANCER PATIENTS IN A TERTIARY CARE CENTRE OF NEPAL

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ABSTRACT

Pain is one of the most afflicting symptoms reported by cancer patients, mainly those with metastatic disease. The prevalence of cancer has increased, with an estimated projection of 17 million new cases in 2020. This means that there will be an increase in individuals with pain caused by the disease and by treatment. Morphine has been used to relieve pain in cancer patients for centuries. WHO, created a global health policy document for management of cancer pain entitled "Cancer Pain Relieve,¹ in which morphine was central. In a retrospective study of 1229 patients with cancer pain, the author reported that the analgesic ladder was effective in 71%. Many patients do not get adequate pain relief. Rationale of this study was to assess cancer related pain by using visual analogue pain scale and to prescribe optimal dose of morphine through dose titration to relieve pain and to improve quality of life. An interventional hospital-based study was done in fifty-two different types of cancer patients from 1st Jan, 2020 to 31st Dec, 2020 at Department of Oncology, Nepal Medical college and Teaching Hospital (NMCTH), Kathmandu. Among them 31 were male and 21 were female with mean age 63.87 and 58.19 respectively and SD +/- 12.10 in male and 16.07 in female with p value 0.152 significant. These patients were assessed for severity of pain through visual pain analogue. Improvement in daily activities after administration of morphine according to ECOG performance scale was done. Constipation was the most common complication induced by morphine 38.5%, sedation 32.7% and nausea in 25%. By understanding the context and social meaning surrounding the use of morphine to treat cancer pain, health care professionals can begin to anticipate, acknowledge and address some of the barrier to its use, thereby enhancing the pain control.

KEYWORDS

Morphine, pain, cancer, analgesic, Nepal

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INTRODUCTION

Pain is one of the most afflicting symptoms reported by cancer patients, mainly those with metastatic disease.¹ Pain prevalence in advanced cancer is about 70%, but rates vary according to cancer type and disease stage.² Over 80% of metastatic cancer patients suffer pain caused mostly by direct tumor infiltration.¹ Surgery, radiotherapy and/or chemotherapy contribute to, approximately, 20% of the cases of cancer-related pain (CRP).³

The prevalence of cancer has increased, with an estimated projection for 2020 of 17 million new cases.⁴ This means that there will be an increase in individuals with pain caused by the disease and by treatment.⁵

The World Health Organization (WHO) developed the analgesic ladder as a guideline for the treatment of cancer pain and recommended the use of non-steroid anti-inflammatory drugs (NSAIDs) for mild pain at first, weak opioids for moderate pain in the second and potent opioids for severe pain in the third step. Adjuvant drugs may be involved in all steps.

Morphine has been used to relieve pain in cancer patients for centuries. International developmental work, coordinated by WHO, created a global health policy document for management of cancer pain entitled "Cancer Pain Relieve," in which morphine was central.

In a retrospective study of 1229 patients with cancer pain, the author reported that the analgesic ladder is effective in 71%.⁶ Many patients do not get adequate pain relief.^{7,8}

Factors related to patients, healthcare institutions and regulatory policies on drug use contribute to the under treatment of pain.^{9,10} Many patients with moderate to severe pain do not receive analgesics and only 24% of those with severe pain are medicated with a potent opioid. In one study, 32% of patients reported that the discomfort was so great that they preferred death. Despite the evolution of knowledge about pain, more than 80% of patients with advanced cancer suffer from pain. In a systematic review, the authors suggest that pain is undertreated in approximately half of patients.¹¹

Few studies have proposed an alternative to the WHO ladder,¹¹ and suggested that opioids are prescribed inappropriately.¹² In a review, the authors suggest that the WHO protocol does not use evidence-based recommendations.¹³ Some authors criticize the restriction of potent opioids for the third step. In a study of 5084

patients, 56% had moderate to severe pain at least monthly. Better pain control and patient satisfaction could be obtained with the use of potent opioids as first medication.¹⁴

Because of these controversies, further studies are needed. The aim of this study was to determine whether the use of morphine in the first step of the WHO ladder can improve the outcome.

Consumption of morphine in Nepal is 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). From 2007 there has 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). Though 6.445 kg of morphine has been consumed in 2008 (the highest level ever consumed) is more than 10 times the amount of morphine consumed in 2000. In 2011, Nepal reported consumption of 2.402 kg of morphine or 0.0802 mg per capita.¹⁶

MATERIALS AND METHODS

An interventional hospital-based study was done at the Department of Oncology, Nepal Medical College and Teaching Hospital (NMCTH), fifty-two different types of cancer patients from 1st Jan, 2020 to 31st Dec, 2020 were included in our study. Among them 31 were males and 21 were females, of age ≥ 18 years. The inclusion criteria included:

Diagnostic (histological or cytological) evidence of advanced / progressive / metastatic solid tumor and with pain of any degree of intensity assessed by numerical scale ranged from 0 to 10. The rate of intensity of pain in 24 hours along with monitoring of required analgesic treatment was done.²³ Individuals with medical conditions like psychiatric/mental illness, severe senile or Alzheimer' dementia, substance abuse and non-consenting patients were excluded from the study. The main aim of study was to assess the management of pain in cancer patients with morphine. Intensity of pain was assessed before and after use of morphine. An improvement in the daily activities was also studied along with morphine related complications.

Methodology: Operational definition: Self-management is almost always the first step

in a person’s journey to relieving pain, and is one that is returned to repeatedly. Because severe pain strongly influences virtually all aspects of a person’s quality of life, and because treatment often is insufficient and involves several specialties and professions, the burden of controlling pain falls most heavily on people in pain and their families.

1. Patients who came for follow up in OPD / ward or with complaint of pain were attended. The first step was to proceed to assess the pain by using visual pain analogue scale (0 to 10).

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|----|
| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|---|----|

Fig. 1: Visual Pain Analogue Scale

- As per the patients complaint the severity of pain was quantified (mild, moderate, severe).
- According to the severity of pain scale guided WHO, morphine was prescribed to the patients orally. The prescription was prescribed by authorized person with record being maintained in the register of the hospital.
- For the first time weekly follow up was done to know whether the pain subsided or not. Accordingly the doses were adjusted.
- Finally, the quality of life in daily activities was observed and noted, before and after the use of morphine recorded in form of table.²⁴

| Table 1: Comparative study of male and female cancer patients | | | | |
|---|-----------|--------------|--------------|---------|
| Sex | n | Mean | SD | p-value |
| Male | 31 | 63.87 | 12.10 | 0.152 |
| Female | 21 | 58.19 | 16.07 | |
| Total | 52 | 61.58 | 13.98 | |

RESULTS

Table 1 shows the total number 52 among which male are 31 and 21 were female, with mean of 63.87 and 58.19 respectively and SD ± 12.10 in male and ± 16.07 in female .

These 52 patients were assessed their pain through the visual pain analogue i.e scale starting from 0 - 10 (Fig. 1) where 0 means no pain; 1, 2 and 3 refers to mild pain 4, 5 and 6

Table 2: Comparative study of visual pain and pain scale in total patients

| Visual pain | Pain scale | n | % |
|---------------|------------|------------------|---------------|
| Before | 5 | 8 | 15.38 |
| | 6 | 24 | 46.15 |
| | 7 | 14 | 26.92 |
| | 8 | 5 | 9.62 |
| | 9 | 1 | 1.92 |
| | | Total= 52 | 100.00 |
| After | 1 | 10 | 19.23 |
| | 2 | 24 | 46.15 |
| | 3 | 15 | 28.85 |
| | 4 | 3 | 5.77 |
| | | Total= 52 | 100.00 |

for moderate pain and 7, 8, 9 and 10 means severe pain.

Before morphine administration visual pain analogue showed the severity of pain of 5 in 15.38% of patients, 6 in 46.15 %, 7 in 26.92%, 8 in 9.628% and 9 in only 1(1.92 %) patient.

After morphine administration, pain assessment was done with the same analogue and the result showed significant reduction in

Table 3: Severity of pain in patients before and after use of morphine

| Pain | Pain scale | N | % |
|---------------|------------|----|-------|
| Before | Moderate | 32 | 61.54 |
| | Severe | 20 | 38.46 |
| After | Mild | 49 | 94.23 |
| | Moderate | 3 | 5.77 |

Table 4: Improvement in daily activities of patients after morphine use

| Patients satisfaction | ECOG | n | % |
|-----------------------|------|----|------|
| Before | 1 | 2 | 3.8 |
| | 2 | 26 | 50 |
| | 3 | 15 | 28.8 |
| | 4 | 9 | 17.3 |
| After | 0 | 17 | 32.7 |
| | 1 | 19 | 36.5 |
| | 2 | 14 | 26.9 |
| | 3 | 2 | 3.8 |

severity of pain showing only moderate pain in 3 (5.77%) patients and mild pain in majority (94.23%) of patients.

Table 3 shows severity of pain before and after the pain management. Before the administration of analgesics 61.54% of patients had moderate pain, 38.46% had severe pain which has reduced after administration of morphine, showing mild pain in 94.23% and moderate pain in 5.77% of patients.

Table 4 shows improvement in daily activities after administration of morphine according to ECOG performance scale. Seventeen (32.7%) patient were fully active and were able to carry out on all pre disease performance without restriction, 1 (36.5%) had restriction in strenuous physical activity but ambulatory and was able to carry out daily activities. Only 3(3.8%) were confined to bed and was capable of only self-care.

Table 5: Side effects in patients after morphine use

| Complication | N | % |
|------------------|----|------|
| Constipation | 20 | 38.5 |
| Sedation | 17 | 32.7 |
| Nausea | 13 | 25 |
| No complications | 2 | 3.8 |

Before morphine 17.3% of patient had ECOG of 4 and post morphine there was an improvement in performance status with ECOG scale 3 being the maximum in only 2 patients

Table 5 shows that constipation was the most common (38.5%) complication induced by morphine, followed by sedation in 32.7% and nausea in 25% .

DISCUSSION

Morphine is the most commonly used opioid for cancer-related severe pain. Despite its established effectiveness, it is often used cautiously in clinical practice, particularly outside specialist palliative care. This study identifies the key social, contextual, and physical concerns held by patients and health care professionals when using morphine, which might explain the caution taken in its use. Some published literature argue for the appropriateness of Critical Interpretive Synthesis (CIS) for answering such questions. Using morphine is a balancing act and a trade-

off between pain relief and adverse effects. Deep-seated concerns regarding the symbolism of morphine, addiction, and tolerance are held by patients, care givers, and clinicians, which influence its prescription and use. Cancer pain is inferred subjective, with its perception and reporting influenced by those with whom the patient interacts.

The present study is a descriptive analysis of oral morphine prescriptions of 6 months duration, with prescription done between 2016 and 2017. All the prescriptions for the patients with pain under oral morphine in the hospital records were reviewed. The results showed that (53.6%) of all morphine prescriptions were from the Oncology Department/OPD, while the newly created Day Care Unit accounted for 43.9% of the prescriptions. Only 1.2% of all the prescriptions conformed to international guidelines. The results reflected that there was a need for more education and advocacy programs to increase awareness among doctors about morphine prescriptions. The cancer study revealed the useful information related to epidemiology of cancer among both the genders in Nepal which will prove to be useful in health planning and future research.¹⁷⁻¹⁸

This study recruited a total of 62 patients but just 53 patients completing the study. Good analgesia was obtained with all 4 opioids. Morphine was associated with less negative impact of pain on the ability to walk and normal work, and tendency on activity (BPI-SF) and lower consumption of rescue morphine. All 4 opioids elicited similar adverse effects. According to ESAS, the intensity of nausea and drowsiness increased at the beginning but decreased as treatment continued. Appetite, well-being, anxiety, depression, and fatigue improved. No changes were seen in constipation, vomiting and dyspnea. Constipation was rarely observed with all opioids (BFI).²¹

In this study morphine was used in 52 patients during follow up, comprising 31 males and 21 females with mean 63.87 and 58.19 respectively and SD ± 12.10 in male and ± 16.07 female with p value 0.152. Before morphine administration visual pain analogue showed the severity of pain scale score was 5 in 15.38% of patients, 6 in 46.15%, 7 in 26.92%, 8 in 9.628% and 9 in only 1(1.92%) patient.

After morphine administration pain assessment was done with the same analogue and the result showed significant reduction in severity of pain, score of 3 moderate pain in 5.77%, and mild pain in majority of the patients. Before the administration of analgesics 61.54% reported

moderate pain, 38.46% reported severe pain. After the administration of morphine, 94.23% reported mild pain and 5.77% reported moderate pain.

According to ECOG performance scale, 17 (32.7%) patients were fully active and were able to carry out all activities normally without restriction. 1 (36.5%) patient had restriction in physically strenuous activity but was ambulatory and able to carry out normal daily activity. Only 3 (3.8%) patients were confined to bed and were capable of only self-care.

Before morphine 17.3% of patient had ECOG scale 4 and post morphine there was an improvement in performance status with ECOG scale 3. The maximum scale 5 being in 2 patients. The study also showed that constipation was the most common complication induced by morphine 38.5% followed by sedation in 32.7% and nausea in 25% patients.

A total of 1308 outpatients with metastatic cancer from 54 treatment centers in the Eastern Cooperative Oncology Group rated the severity of their pain during the preceding week, as well as the degree of pain-related functional impairment and the degree of relief provided by analgesic drugs. The results show sixty-seven percent of the patients (871 of 1308) reported to taking analgesic drugs daily during the week preceding the study, and 36 percent (475 of 1308) had pain severe enough to impair their ability to function. Forty-two percent of those with pain (250 of the 597 patients for whom we had complete information) were not given adequate analgesic therapy. Patients seen at centers that treated predominantly minorities were three times more likely than those treated elsewhere to have inadequate pain management. A discrepancy between patient and physician in judging the severity of the patient's pain was predictive of inadequate pain management (odds ratio, 2.3). Other factors that predicted inadequate pain management included pain that physicians did not attribute to cancer (odds ratio, 1.9), better performance status (odds ratio, 1.8), age of 70

years or older (odds ratio, 2.4), and female sex (odds ratio, 1.5). Patients with less adequate analgesia reported less pain relief and greater pain-related impairment of function.¹⁹

A total of 18 adult opioid-naïve patients with advanced cancer and 13 care givers (n = 31) were recruited at a private tertiary hospital via convenience sampling by prevalence study shows attitudes and perceptions of morphine were influenced by previous experiences. Many preferred morphine as a last resort because of concerns about side effects and dependence, and the perception that morphine was only used at the terminal stage. Caregivers' attitudes toward morphine did not affect patients' acceptance of morphine use.²⁰ This discrepancy may be related to epidemiology of cancer in Nepal and may provide insights for public health planning and future research.¹⁷⁻¹⁸

So, in our opinion the study modalities maybe different from the various authors. Nevertheless, our study showed significant changes with pain intensity experienced by patients and ideas regarding the use of morphine/opioids.

By understanding the context and social meaning surrounding the use of morphine to treat cancer pain, health care professionals can begin to anticipate, acknowledge, and address some of the barriers to its use, thereby enhancing pain control.¹⁵

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