Cancer Pain Management: Is It Still Problematic?

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ABSTRACT

Objective: To evaluate the efficacy of pain management during 3-month follow-ups for outpatients with cancer pain.

Methods: A retrospective chart review was conducted and included all newly diagnosed cancer pain patients visiting the Siriraj Pain Clinic, Mahidol University, between January 2013 and June 2014. Demographic data, pain intensity at first visit, 1-, 2- and 3-month follow-ups, pharmacological therapy and co-treatments were collected. Good treatment response was defined as more than 30% pain reduction from baseline. Predictive factors associated with pain treatment response were also assessed.

Results: Out of 432 new patients, 118 cancer pain patients were included in the study with a mean age of 59.8±13.7 years (range 18-91 years). About half of patients had at least one comorbidity. Over 90% of all cancer patients presented with distance metastasis. Mixed neuropathic/nociceptive pain (53.4%) and nociceptive pain alone (43.2%) were common pain features in cancer pain patients. The mean initial pain intensity described by verbal numerical scales was 7.7±2.1 (range 3-10). The majority of patients (60.2%) received co-treatment. The main pharmacological therapies in all patients were opioids (99.2%) and anticonvulsants (90.7%). At 3-month follow-up, nearly half of patients achieved a good treatment response. However, 44.6% of good responders still had moderate and severe pain. No predictive factors associated with the pain treatment response was found.

Conclusion: Approximately half of patients with cancer pain in the pain clinic achieved a good treatment response whereas one-fifth of the patients had an increase in pain severity at their 3-month follow-up.

Keywords: Cancer pain; clinical response; pain management; predictive factor (Siriraj Med J 2019;71: 38-43)

INTRODUCTION

Pain is one of the most common symptoms in cancer patients (70-90%),[1] negatively affecting their functionality, emotion and quality of life.[2,3] Multiple factors are involved in the pain mechanism, including the disease itself, treatments, and comorbidities.[4] Although cancer pain treatment guidelines were developed by the World Health Organization (WHO) in the year 1986, and subsequently modified in 1996,[5] treatment outcomes still remain unsatisfactory.[6] For example, Deandrea reported 43% of cancer patients suffered from moderate to severe pain.[7] In addition, Yennurajalingam reported that only 45% of cancer patients in the United States receiving treatment experienced 30% pain improvement on a numerical rating scale.[8]

Regarding the difference of culture among the nations

which may affect to pain acceptance and factor-related to pain treatment response, the treatment outcome data of Thai patients is required to explore. However, there has been no study reporting the effectiveness of cancer pain management services in Thailand. Therefore, this study aimed to evaluate the efficacy of cancer pain management and identify factors associated with the pain treatment response during 3-month follow-ups at the Siriraj Pain Clinic.

MATERIALS AND METHODS

The study was approved by the Siriraj Institutional Review Board (Si 703/2014). The researchers retrospectively and manually reviewed outpatient records of all newly diagnosed cancer pain patients who visited Siriraj Pain Clinic from January 1st, 2013 to June 30th, 2014. Cancer patients with non-cancer pain conditions and patients who were lost before the 3-month follow-up were excluded. Demographic data including age, gender, living region, comorbidities (diabetes mellitus, hypertension, heart disease and chronic kidney disease), primary cancer site (gastrointestinal tract, respiratory tract, urogenital tract, breast, etc.), pharmacological therapy and co-treatments were recorded. Pain intensity using verbal numerical scales (VNS) at first visit, 1-, 2- and 3-month follow-ups were collected as the primary outcomes.

Pain severity was classified into three levels which were mild pain (VNS 0-3), moderate pain (VNS 4-6) and severe pain (VNS 7-10).

Responses to treatments varied from time to time, even for individual patients. The timing of pain evaluation was crucial. If pain was evaluated after a few weeks following treatment, the number subjects in the non-responding group may be appear elevated because it could be too early to see a response. Conversely, it is possible evaluating pain at distant time periods could allow the subjects' cancer to progress and cause more pain, reducing the number in subjects the responsive group. Therefore, the optimum time for evaluating the efficacy of pain treatment in this study was set at three months from the initial treatment. Factors associated with pain treatment responses were also analyzed.

Statistical analysis

The sample size was calculated based on the study of Yennurajalingam et al[8] and required 40% proportion of patients to achieve good treatment response at 3-month follow-up. We selected the confidence level 95% and allowable error 10% to calculate by Query program. Calculated sample size was 93 patients with 10% dropout. Therefore, at least 102 patients were included in this study.

The qualitative data, including gender and main site of cancer, was described as numbers and percentages. The quantitative data, consisting of the initial pain scores, numbers of visits, and age, was described using mean and standard deviation.

According to Farrar's study, the researchers defined good treatment response as the pain reduction of at least 30% using a verbal numerical scale.[9] To compare the good treatment response group and the poor treatment response group (VNS pain responses less than 30%), unpaired t-test (normality) or Mann-Whitney U-test (non-normality) were used to analyze quantitative data and Chi-square test or Fisher's exact test were used for qualitative data. Logistic regression analysis was applied when there were one or more statistically significant factors (p < 0.05). All parameters were analyzed by SPSS program version 15.0.

RESULTS

After screening outpatient charts, 432 cancer pain patients were reviewed; of these 314 were excluded due to attrition or incomplete follow-ups during the 3 months. A total of 118 cancer patients were included in this study (Table 1), 50.8% of which were males with the median age of 60 years old (range 18-91 years old). About half of the patients had at least one comorbidity. Most of the patients presented with advanced stage of cancer, accounting for 91.5% of the total number. The majority of patients suffered from nociceptive and mixed pain. The most common adjuvant treatment (apart from pain medication) was radiation (28.8%) while only two patients underwent the pain intervention. Regarding pharmacological treatment, almost all of the patients (117 patients) were prescribed opioids (Table 2). The most common opioid used was morphine (54.7%), while the most common adjuvant drugs were anticonvulsants (90.7%). Dosages for opioid therapy in each visit have been presented in Table 3.

The overall outcome after cancer pain treatment found that the mean VNS decreased from 7.7±2.1 to 5.7±2.6 at the 1-month follow-up and maintained at this level until 3-month (Table 3). Moreover, there were 47.5% of the patients achieving good treatment response while 44.6% of which still suffered from moderate to severe pain at three months after treatment (Fig 1). However, 19.5% of the patients got worse even after 3 months of pain treatment.

Many potential factors associated with treatment outcome were analyzed, including age, gender, comorbidity, primary organ tumour, stage of cancer, initial pain intensity, types of pain, adjuvant therapy, type and dose

TABLE 1. Demographic data.

Patient characteristics	N=118
Age (yrs)	60 (18-91)
Gender M:F	60 (50.8):58 (49.2)
Comorbidity	
0	62 (52.5)
1	34 (28.8)
≥ 2	22 (18.6)
Primary tumor	
Gastrointestinal system	26 (22.0)
Respiratory system	20 (16.9)
Others	72 (61.0)
Stage of cancer	
Local invasion	10 (8.5)
Distant metastasis	108 (91.5)
Initial pain intensity (verbal numerical scale)	8 (3-10)
Types of pain	
Nociceptive	51 (43.2)
Neuropathic	4 (3.4)
Mixed pain	63 (53.4)
Co-treatment	
Radiation therapy	34 (28.8)
Chemotherapy	24 (20.3)
Surgery	10 (8.5)
Pain intervention	2 (1.6)

Data are presented as median (range), n (%)

TABLE 2. Medications used in pain treatment on 3-month follow-up visit.

| Drugs	N=118
Opioids	117 (99.2)
Strong opioid	78 (66.1)
morphine	64 (54.7)
fentanyl	12 (10.3)
methadone	2 (1.7)
Weak opioid	39 (33.1)
codeine	4 (3.4)
tramadol	35 (29.9)
Acetaminophen	49 (41.5)
NSAIDs	37 (31.4)
Antidepressant	70 (59.3)
Anticonvulsant	107 (90.7)

Data are presented as n (%), NSAIDs = Non-steroidal anti-inflammatory drugs

TABLE 3. Opioid dosage and average pain intensity in each visit for 3 months.

Opioid	1st visit	1-month	2-month	3-month
Morphine (mg/day)	20 (10-180)	20 (10-200)	20 (10-180)	35 (10-180)
Fentanyl (mcg/hr)	12 (12-25)	25 (12-100)	25 (12-50)	25 (12-37)
Methadone (mg/day)	10 (10-10)	10 (10-15)	20 (10-30)	10 (10-10)
Codeine (mg/day)	60 (45-90)	60 (45-90)	45 (45-60)	45 (30-60)
Tramadol (mg/day)	150 (50-400)	150 (50-300)	150 (100-300)	150 (100-200)
VNS	7.7±2.1	5.7±2.6	5.8±2.9	5.7±3.1

Data are presented as median (range), mean±SD
Abbreviation: VNS = verbal numerical scales
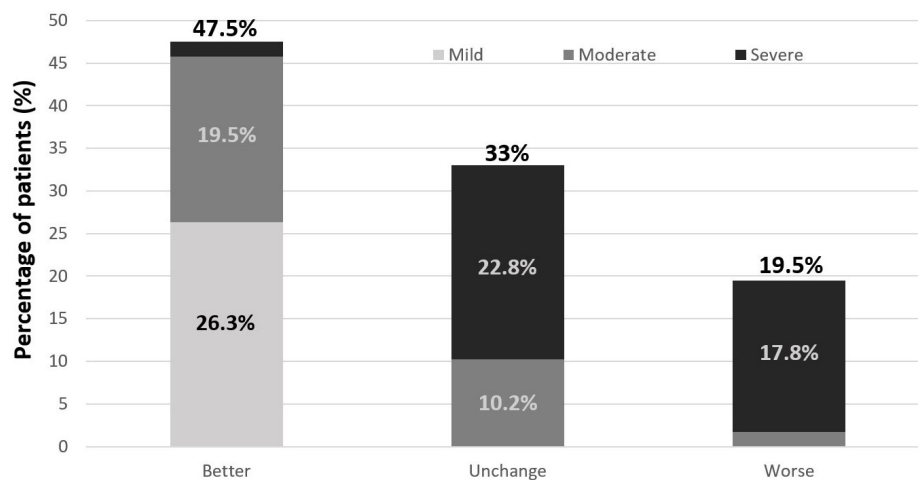
Fig 1. Pain treatment response at 3-month follow-up.

of opioids, etc. However, there were no predictive factors significantly associated with the pain treatment response (Table 4).

DISCUSSION

This study evaluated outcomes of cancer pain treatment at the Siriraj Pain Clinic at three months after treatment. Even though after following regimens provided by guidelines for cancer pain management[5], average pain score was reduced from 7.7 to 5.7 which was about 26% pain reduction. Also, 42.3% of patients were still in severe pain and less than half achieved good treatment response. However, this data was comparable to Yennurajalingam's study, in which the responsive group was accounted for 45% of subjects.[8] Regarding the treatment outcome in this study revealed that cancer pain is still problematic even in the tertiary pain center.

Considering about one-fifth of patients in this study and one-third of patients in the Yennurajalingam's study developed worse pain over 3 months,[8] this could be attributed to either rapid cancer progression or the duration of the visits per month was perhaps too long, particularly in advanced stage cancer patients. Therefore, more frequent follow-up visits should be set in the case of uncontrolled pain. To address some of the difficulties that were encountered, for example, remoteness from the hospital or physical limitations, a telephone interviewing program is advisable. In addition, some patients might not well tolerated to higher dose of opioids or doubted about using opioid therapy which could be another hindrance to increase opioid dosage. Interestingly, mean opioid dosage appeared to be stable from the first visit to 3-month visit, which should have been increased in the following visits if the pain could not be controlled

TABLE 4. Factors associated with pain treatment outcomes.

Factors	Good treatment response n=56	Poor treatment response n=62	P-value
Age	58.7±13.5	60.8±14.0	0.418
Female	28 (50)	30 (48.4)	0.861
Living outside Bangkok and metropolitan area	27 (48.2)	35 (56.5)	0.371
Comorbidities	25 (44.6)	31 (50)	0.561
Primary organ tumor			
Gastrointestinal system	12 (21.4)	14 (22.6)	
Respiratory system	9 (16.1)	11 (17.7)	0.949
Others	35 (62.5)	37 (59.7)	
Advanced cancer stage	50 (89.3)	58 (93.5)	0.515
Initial pain intensity	8.0±2.1	7.4±2.1	0.976
Types of pain			
Nociceptive	28 (50)	23 (37.1)	
Neuropathic	2 (3.6)	2 (3.2)	0.348
Mixed	26 (46.4)	37 (59.7)	
Co-treatment			
Radiation therapy	13 (23.2)	21 (33.9)	0.202
Chemotherapy	13 (23.2)	11 (17.7)	0.461
Surgery	4 (7.1)	6 (9.7)	0.746
Pain intervention	0 (0)	2 (3.2)	0.497
Opioid dosage			
Morphine	45.0±36.5	46.8±35.3	0.803
Fentanyl	24.8±8.8	28.3±9.4	0.492
Tramadol	145±35.9	153±35.2	0.793

Data are presented as mean±SD, n (%)

(Table 3). Nevertheless, the poor treatment response group seemed to consume only a little more opioids than the good response group (Table 4), presenting that opioids might not help in the poor response group or they experienced some problems to increase opioid consumption.

The previous study found that high initial pain intensity was a factor associated with good clinical response in outpatients.[8] In contrast, another retrospective study in inpatients demonstrated that high pain intensity on the first day of consultation was related to poor treatment response.[10] However, there was no association between initial pain intensity and the pain treatment response in this study. In addition, no significant association of any potential factors to the treatment response was observed.

Although this study was a retrospective study, all data were obtained by pain specialists and well-trained nurses in pain management, which made the data more reliable. However, there were some limitations in this study. Firstly, some data were not documented in some included charts, for instance, the side effects, the frequency of incidental pain or effects of pain on emotion and function, which may affect the treatment outcomes. Therefore, we decide not to present and analyze those data in this study. Secondly, the number of patients may not be enough to detect significant factors associated with the

treatment response. Although there were a large number of cancer patients consulted the pain clinic, about 73% of reviewed charts were excluded from this study mainly due to incomplete follow-up in three months, which may cause by patients' death within three months after the first visit or some difficulty of traveling to-and-from the hospital. Despite the limitations, the results of this study serve as baseline data for cancer pain treatment and further development of guidelines for cancer pain management.

Future prospective studies should be conducted to compare the effectiveness of treatments between different cancer service centers. However, future prospective research with cancer pain management protocol should be developed to improve the effectiveness of cancer pain treatment. Also, the psychological aspects played an important role in cancer patients and could not be solved only by pain medications. Multidisciplinary teams, including psychiatrists and behavioral therapists, could offer better care and help improve the treatment's efficacy.

CONCLUSION

Approximately half of patients with cancer pain in the pain clinic achieved a good treatment response whereas one-fifth of the patients had an increase in pain severity at 3-month follow-up. There is no significant factor that associated with treatment response.

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