

นิพนธ์ต้นฉบับ

ปัจจัยที่เกี่ยวข้องกับความปวดลดยากในผู้ป่วยระยะท้ายช่วง 48 ชั่วโมงแรกของการรับปรึกษาประคับประคอง

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บทคัดย่อ

ที่มา: ความปวดเป็นอาการที่ทำให้ผู้ป่วยระยะท้ายไม่สุขสบาย หากปล่อยไว้นานอาจทำให้ความปวดจัดการได้ยาก ทีมประคับประคองจึงมุ่งเน้นการลดความปวดใน 48 ชั่วโมงแรกหลังรับปรึกษา อย่างไรก็ตามผู้ป่วยบางรายลดปวดยาก ผู้วิจัยจึงต้องการศึกษาปัจจัยที่เกี่ยวข้องกับความปวดลดยากในช่วงแรกของการรับปรึกษาประคับประคอง

แบบวิจัย: การศึกษาจากเหตุไปหาผลแบบย้อนหลัง

วัตถุประสงค์และวิธีการ: ผู้ป่วยประคับประคองที่มีความปวดปานกลางขึ้นไปจะถูกนำเข้าการศึกษาหลังคัดผู้ที่ไม่สามารถประเมินความปวดด้วยตนเองออกแล้ว จึงทบทวนข้อมูลพื้นฐาน การรักษาความปวด และคะแนนปวดใน 48 ชั่วโมง ปัจจัยที่เกี่ยวข้องกับความปวดลดยากใช้วิธีวิเคราะห์แบบถดถอยโลจิสติก

ผลการศึกษา: ผู้ป่วยประคับประคอง 997 คน ร้อยละ 11.03 มีความปวดลดยาก พบปัจจัยที่เกี่ยวข้อง ได้แก่ อายุ การกลืนลำบาก อาการต่อไปนี้ที่มีระดับรุนแรง ได้แก่ คลื่นไส้ ชิมเศร้า วิดกกังวล ง่วงซึม เบื่ออาหาร และไม่สบายกายและใจ ส่วนปัจจัยที่เกี่ยวข้องโดยตรงได้แก่ อายุ การกลืนลำบาก และชิมเศร้ารุนแรง (OR 0.98, 95%CI 0.97-0.99, p-value 0.007, OR 1.83, 95%CI 1.03-3.27, p-value 0.040, และ OR 1.73, 95%CI 1.04-2.89, p-value 0.035 ตามลำดับ)

สรุป: อายุ การกลืนลำบาก และชิมเศร้ารุนแรง เป็นปัจจัยที่เกี่ยวข้องโดยตรงกับความปวดลดยากในผู้ป่วยประคับประคอง จึงควรมีการจัดการภาวะชิมเศร้าอย่างเหมาะสมควบคู่การจัดการความปวดเพื่อช่วยให้ผลลัพธ์ดีขึ้น

คำสำคัญ: ปัจจัย ความปวดลดยาก ประคับประคอง ผู้ป่วยระยะท้าย

ORIGINAL ARTICLE

Factors Associated with Challenging Pain Management in Terminally Ill Patients Within 48 Hours of Palliative Care Consultation

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ABSTRACT

Background: Pain is one of the most common distresses for palliative care patients. Prolonged pain is increasingly difficult to manage. For this reason, early pain management within the first 48 hours is of utmost importance and is the focus of the palliative care team. However, despite our best attempts, some patients do not respond to initial management. This study aimed to identify the factors associated with challenging pain management in palliative patients during their initial palliative care consultation.

Design: A retrospective cohort study

Methods: Palliative care patients with moderate to severe pain were recruited for the study. Patients who could not report pain scores by themselves were excluded. Patients' characteristics, pain management, and pain score were reviewed in the first 48 hours of palliative care consultation. The factors associated with challenging pain management were analyzed using logistic regression.

Results: Of 997 palliative patients, 11.03% experienced difficult pain control. Difficult pain control was associated with age, dysphagia, severe symptoms of nausea, depression, anxiety, drowsiness, worse appetite, and worse well-being. Age, dysphagia, and severe depression were significantly related factors (OR 0.98, 95% CI 0.97-0.99, p-value 0.007, OR 1.83, 95% CI 1.03-3.27, p = 0.040, and OR 1.73, 95% CI 1.04-2.89, p = 0.035, respectively).

Conclusion: Age, dysphagia, and severe depression were the main factors for challenging pain management in palliative patients on initial palliative care consultation. Appropriate management of depression should be done to improve the outcomes.

Keywords: factor, difficult pain, palliative, terminally ill patient

Introduction

Pain is one of the most common symptoms in terminally ill patients that increases the patients' discomfort. Up to 70% of patients with end-stage cancer, heart failure, COPD, and renal disease experience pain^{1,2}, and around 10% do not achieve adequate pain control from initial management strategies.³ This suffering affects the quality of life.^{2,4} The prolongation of moderate to severe pain modulates peripheral and central nervous system sensitization,⁵ highlighting early pain management's importance. However, palliative patients usually develop multiple comorbidities and deteriorate in performance status, which may increase the complexity of pain management. The palliative care team, experts in providing care for patients with terminal illnesses and managing symptoms, are the primary healthcare providers equipped to address this challenge. Previous studies⁶ showed the palliative care team is superior to the primary care team in relieving pain, dyspnea, and depression in the first 48 hours of hospitalization. Despite the success rate of early pain control of the palliative care team, some patients do not achieve 50% pain relief within the first 48 hours. Cancer patients with young age, gastrointestinal cancer, lung cancer, neuropathic pain, incidental pain, sleep problems, or anxiety have poor opioid responses and need more time to achieve pain control.⁷ However, no study specific to the palliative care population included terminally ill non-cancer patients. This study aimed to identify the factors associated with challenging pain management of palliative patients within 48 hours of palliative care consultation.

Methods

This retrospective cohort study was conducted at Karunruk Palliative Care Center (KPC), Srinagarind Hospital, Khon Kaen University, Thailand, from 1 October 2021 to 31 July 2023. The study was reviewed and approved by the Institutional Review Board of Khon Kaen University (HE661384). All palliative care patients who reported pain scores of at least 4/10 (moderate) at the first palliative care team assessment were recruited to this study and excluded patients who could not report pain scores at the first palliative assessment and 48 hours later. Patient characteristics, types of pain, morphine equivalent daily dose (MEDD), and pain score within 48 hours

after the first assessment were collected. MEDD was a conversion of daily opioid doses to oral morphine equivalent doses (mg/day). The scores from a validated Thai version of the Palliative Performance Score (PPSV2)⁸ and a Thai version of the Edmonton symptom assessment system (ESAS-Thai)⁹ were obtained at the first palliative care assessment. The Edmonton Symptom Assessment System (ESAS) assessed nine symptoms: pain, tiredness, drowsiness, nausea, lack of appetite, shortness of breath, depression, anxiety, and lack of well-being. This tool contains scores 0 to 10 for each symptom, and classified the severity of symptoms into none (score 0), mild (score 1-3), moderate (score 4-6), and severe (7-10).¹⁰ Additional symptoms identified during the systemic review, which were not included in the ESAS, were also gathered. Effective pain control 6,11 was defined as pain relief of more or equal to 50%, while difficult pain control was less than 50% in the first 48 hours.

Demographic data were presented as frequency, percentage, mean (Standard Deviation, SD), or median (Inter Quartile Range, IQR). The characteristics of both patients' groups, type of pain, pain mechanism, and factors associated with difficult pain control in 48 hours were analyzed using Pearson's chi-square test/Fisher's exact test. To identify the factors related to difficult pain control, all variables of ESAS, systemic review symptoms, and age were analyzed using a univariate logistic regression model. Significant factors (p-value of less than 0.05) were further analyzed in a multivariate logistic regression model. The reduced model was conducted using the backward elimination method. A 95% confidence interval (CI) and p-value were presented in this study. A P-value of less than 0.05 was considered statistically significant. The data was analyzed by the program STATA version 10.0.

Result

This study obtained 997 palliative care patients with moderate to severe pain. These patients consisted of 923 cancer patients and 74 non-cancer patients. The top three cancers were hepatobiliary, gastrointestinal, and lung. The baseline characteristics of non-cancer patients were not different from those of cancer patients. The median PPS score was 50 (IQR 40, 50). After palliative care consultation and pain management

were performed in the first 48 hours, 11.03% of palliative care patients had difficulty controlling pain. The baseline characteristics between effective and difficult pain control groups were not significantly different (Table 1). Both groups were similar in type of pain. Around 90% of patients had nociceptive pain (Table 2).

The baseline pain score was 6 (IQR 5, 8) in the effective pain control group and 7 (IQR 5, 8) in the difficult pain control group. The dose of opioids before palliative care consultation was 10 (IQR 0, 30) MEDD and increased to 30 (IQR 20, 40) MEDD at 48 hours in both groups.

The result revealed patients with severe nausea (23.64% vs 13.19%, $p = 0.003$), severe depression (30% vs 15.78%, $p < 0.001$), severe anxiety (25.45% vs 16.35%, $p = 0.017$), severe drowsiness (23.64% vs 13.42%, $p = 0.004$), severe lack of appetite (28.18% vs 15.56%, $p = 0.001$), and severe lack of well-being (26.36% vs 16.12%, $p = 0.007$) according to the ESAS score, was significantly associated with difficult pain control. Moreover, the difficult pain control group had dysphagia symptoms more than the effective control group (17% vs 9.9%, $p = 0.029$). In contrast, other symptom problems, such as oral problems,

Table 1. Demographic data of palliative care patients in both effective and difficult pain control groups

Characteristics	Pain control		p-value
	Effective (n=887 (88.97%))	Difficult (n=110 (11.03%))	
Age; median (IQR)	62 (52, 70)	61 (51, 68)	0.177
Gender: Male	492 (55.47)	64 (58.18)	0.539
Ethnicity			> 0.999
Thai	884 (99.66)	110 (100.00)	
Religion			> 0.999
Buddhism	885 (99.77)	110 (100.00)	
Marriage			0.752
Married	649 (73.17)	78 (70.91)	
Widowed	112 (12.63)	16 (14.55)	
Single	75 (8.46)	12 (10.91)	
Divorce	51 (5.75)	4 (3.64)	
Occupation			0.307
Retired	315 (35.51)	40 (36.37)	
Farmer	206 (23.22)	31 (28.18)	
Government officer	130 (14.66)	11 (10)	
Own business	72 (8.12)	8 (7.27)	
Others	164 (18.49)	20 (18.19)	
Cancer group			0.531
Hepatobiliary	325 (39.35)	33 (34.02)	
GI tract	123 (14.89)	14 (14.43)	
Lung	86 (10.41)	12 (12.37)	
Gynecology	80 (9.69)	8 (8.25)	
Head & Neck	67 (8.11)	13 (13.4)	
Others	145 (17.55)	17 (17.52)	
PSS; median (IQR)	50 (40, 50)	40 (40, 50)	0.289

Values are described as n (%) unless specifically stated in the table

Table 2. Type of pain and pain mechanism

Pain mechanism	n (%)	Pain control		p-value
		Effective	Difficult	
Neuropathic	187 (78.76)	160 (18.04)	27 (24.55)	0.099
Nociceptive	879 (88.16)	779 (87.82)	100 (90.91)	0.345
Incident	70 (7.02)	65 (7.33)	5 (4.55)	0.281

Values are described as n (%)

Table 3. Factors associated with difficult pain control within 48 hours

	Univariate logistic regression			Multivariate logistic regression		
	Odds ratio	95%CI	p-value	Odds ratio	95%CI	p-value
Age	0.99	0.97-0.99	0.048*	0.98	0.97-0.99	0.007*
Severe nausea	2.04	1.26-3.30	0.004*			
Severe depression	2.29	1.46-3.57	<0.001*	1.73	1.04-2.89	0.035*
Severe anxiety	1.75	1.10-2.78	0.019*			
Severe drowsiness	2.00	1.24-3.23	0.005*			
Severe poor appetite	2.13	1.35-3.35	0.001*			
Severe poor well-being	1.86	1.18-2.95	0.008*			
Dysphagia	1.86	1.06-3.29	0.031*	1.83	1.03-3.27	0.040*

Values are described as n (%)

constipation, itching, and wounds, were not statistically significant differences.

Further analysis by univariate logistic regression found that age (OR 0.99, 95%CI 0.97-0.99, p-value 0.048), dysphagia (OR 1.86, 95%CI 1.06-3.29, p = 0.31), severe nausea (OR 2.04, 95%CI 1.26-2.30, p = 0.004), severe depression (OR 2.29, 95%CI 1.46-3.57, p < 0.001), severe anxiety (OR 1.75, 95%CI 1.10-2.78, p = 0.019), severe drowsiness (OR 2.00, 95%CI 1.24-3.23, p = 0.005), severe lack of appetite (OR 2.13, 95%CI 1.35-3.35, p = 0.001), and severe lack of well-being (OR 1.86, 95%CI 1.18-2.95, p = 0.008) were significantly associated with difficult pain control (Table 3). After identifying variables from our univariate logistic regression and then utilizing a multivariate logistic regression, we put the significant variables from univariate logistic regression analysis in the first round. We found that they were not statistically significant. Then we performed a backward stepwise analysis and found that age (OR 0.98, 95%CI 0.97-0.99, p = 0.007), severe depression (OR 1.73, 95% CI 1.04-2.89, p = 0.035), and dysphasia symptom (OR 1.83, 95%CI 1.03-3.27, p = 0.040) were statistically significant related with difficult pain control (Table 3).

Discussion

Our study showed that the factors associated with difficult pain control in the first 48 hours after palliative consultation were age, severe nausea, severe depression, severe anxiety, severe drowsiness, severe lack of appetite, severe lack of well-being, and dysphagia. Age, severe depression, and dysphagia were strongly related factors.

Age was associated with challenging pain control in our study. Previous studies^{7,12} found similar results that young age was associated

with poor opioid response, high pain score, and prolonged pain control, the components of complex pain management. While older patients had more sensitivity to opioids¹³ and other medications, aging might affect pain control.¹⁴ This study also showed that one year of increasing age was associated with easier pain control (OR 0.98, 95%CI 0.97-0.99, p = 0.007). However, our study was mainly focused on pain relief, not opioid response, as in the previous study. We did not perform subgroup analysis for young and elderly patients.

The psychological distress symptoms, such as depression and anxiety, were quite common in palliative care patients.^{15,16} They also found that psychological distress was associated with pain,¹⁷ perhaps by the coexistence of neurobiological pathways and neurotransmitters, the psychological distress and pain affected each other.^{18,19} Our result of severe depression and severe anxiety was similar to the recent systematic review by Lucenteforte⁷ that revealed depression and anxiety were associated with poor opioid response, the complex pain management condition in advanced cancer patients. Severe depression emerged as a related factor in our study. Effective management of depression is crucial to enhancing psychological well-being and improving pain treatment outcomes.²⁰

Palliative patients who had difficulty treating pain also had other suffering symptoms, not only psychological distress. These symptoms should be regularly evaluated in palliative patients with a specific tool, the ESAS. This study found that severe nausea, severe drowsiness, severe lack of appetite, and severe lack of well-being were associated with difficult pain control. These symptoms were frequent adverse events among

cancer patients treated with strong opioids.²¹ Patients experiencing nausea and vomiting tended to miss doses or discontinue medication due to their symptoms.²² However, no clear evidence of the association between these symptoms and torturous pain existed. It could be the effect of psychological distress from physical symptoms.¹⁶

Dysphagia was associated with difficult pain control in our study, similar to the previous studies.^{23,24} However, our data was collected from inpatients in which intravenous or subcutaneous route would be prescribed for dysphagic patients. Unfortunately, this symptom still impacted physical and psychological distress,²⁴ which may have affected pain control.

This study has some limitations: First, our study was a retrospective study which did not include some factors such as smoking, stage of cancer, current treatment, adjuvant medications, addiction status, or genetics that are associated with high pain scores and delayed opioid response that might affect the result. Second, some data was missing from the review. We excluded patient records that had missing data, as they had less than 10% of the whole data. Third, we focused on severe ESAS symptoms; another degree of ESAS severity may need further exploration. The last limitation was the small number of non-cancer patients included. Thus, we could not do a subgroup analysis to differentiate the result between cancer and non-cancer groups. Further study should consider these patients. The clinical-related factors in our study could be included in the following difficult pain predictive models.

Conclusions

Age, dysphagia symptoms, severe nausea, severe depression, severe anxiety, severe drowsiness, severe lack of appetite, and severe lack of well-being were associated with challenging pain management within 48 hours of palliative care management. The main factors of challenging pain management in palliative care patients include age, dysphagia, and severe depression. The good practice of pain management should not focus only on pain control but on other symptom control, such as depression.

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