

## RESEARCH ARTICLE

# Effectiveness of Education Interventions for the Management of Cancer Pain: A Systematic Review

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### Abstract

**Background:** Many cancer patients experience poor pain control due to various factors, including misconceptions regarding the use of opioid analgesics. For management of cancer pain, interventions involving education of both patients and physicians have been attempted. **Objectives:** This review aimed to assess the current evidence of the benefits of education for the management of cancer pain. **Methods:** We searched the Medline, EMBASE, Cochrane library, and major Korean databases to identify relevant studies. We included most study designs, but excluded case series. The primary outcomes were pain intensity and quality of life (QoL). Two reviewers assessed the risk of bias using the Cochrane's tool for RCT and Risk of Bias Assessment tool for Non-randomized Studies (RoBANS) for non-randomized studies, independently. **Results:** After extensive searches, 3,324 publications were screened, and 32 studies were selected. The education interventions used in the included studies included a wide variety of education methods, but the most common method was a booklet produced for patients. Regardless of the education method used, the results of the meta-analysis were as follows. The SMDs of the most severe, average, and current pain in the RCTs were significant. The SMD of worst, average, and current pain were  $-0.34$  ( $-0.55$ ,  $-0.13$ ),  $-0.40$  ( $-0.64$ ,  $-0.15$ ), and  $-0.79$  ( $-1.35$ ,  $-0.23$ ). In the non-randomized studies, the effects on average pain were significant, but those on worst and current pain were not. **Conclusions:** Education intervention reduced the pain of cancer patients. Therefore, patient education could be considered to be an effective method of cancer pain management. However, our data should be interpreted with caution, and studies using standardized protocols are needed to confirm these observations.

**Keywords:** Pain - analgesics - management - patient education

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### Introduction

Pain is one of the most common symptoms of cancer patients. To control cancer-related pain, it is necessary to add analgesics to the treatment regimen depending on the intensity of the pain, referring to the World Health Organization (WHO)-recommended three-step analgesic ladder (WHO, 1996). However, pain management following the World Health Organization ladder results in only 75% adequate pain control (Zech et al., 1995). Recently, a total of 45% of patients reported inadequate pain control in a survey of Korean patients carried out between 2001 and 2006 (Hong et al., 2011). Narcotic analgesics commonly have to be prescribed for the proper management of severe cancer pain. However, many patients with cancer have poor pain control for several barriers, including misconceptions concerning opioids (Brant 2010). Therefore, educating both patients and practitioners assists provision of accurate information.

Allard et al. (2001) published a systematic review of the effects of educational intervention on the control

of cancer pain in 2001. In addition, Bennett et al. (2009) assessed the effects of patient-based educational intervention on cancer pain in 2009. However, these studies are not recent, and so an analysis of more recent trials is needed. Therefore, this study evaluated the current evidence of the effectiveness of education intervention in the management of cancer pain by conducting an extensive systematic review and meta-analysis. Unlike previous meta-analyses, we included observational studies and non-randomized trials that assessed intervention and patient outcome.

### Materials and Methods

#### Literature searches

We developed a protocol for the systematic review of the effectiveness of educational intervention for the management of cancer pain. Specifically, the population, method of intervention, method of data comparison, patient outcome, study design and time (PICOST), search methods, data extraction, quality assessment, and

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meta-analysis from published studies were all reviewed. The following parameters and limitations were used: 1) Participants: cancer patients with pain; 2) Interventions: educating cancer patients about the use of analgesics to manage pain; 3) Controls: no limitations; 4) Outcomes: primary outcomes were pain intensity and quality of life (QoL). Secondary outcomes were all other patient outcomes (excluding information from caregivers); 5) Study design: all studies included a control group (for example RCT, non-randomized controlled trials, or cohort studies).

Articles published before July 27<sup>th</sup> 2012 were searched in six electronic databases, comprising three international and three Korean databases: Ovid-Medline, Ovid-Embase, Cochrane Library, KISS (<http://kiss.kstudy.com>), KMBASE (<http://kmbase.medic.or.kr>), and KoreaMed (<http://www.koreamed.org>). Various combinations of Mesh headings and keywords were used, including “neoplasms”, “analgesics”, “opioid”, “morphine”, “fentanyl”, “oxycodone”, “hydromorphone”, “patient education as topic”, “health education”, “health knowledge, attitudes, practice”, and “pain management”. For more extensive searches, we also manually searched the citations within existing systematic reviews for publications reporting the effectiveness of patient-based educational interventions for the management of cancer pain.

**Study selection**

The inclusion criteria were trials that investigated the effects of educational intervention on the use of analgesics in cancer patients. All included studies were published in the English or Korean language. The exclusion criteria were duplicate publications, studies that were not peer reviewed, and those that used only the assessment of the caregiver as the outcome. All studies were reviewed and selected independently by two researchers (each study was assigned to two of MK Hyun, YJ Jung, JI Shin, and MJ Kang). The titles and abstracts were reviewed, and duplicate studies or those that did not meet PICO requirements were excluded. If the title or abstract appeared to meet the PICO of this review or we could not determine its eligibility, the full text of the article was obtained and eligibility was confirmed. Discrepancies between the reviewers were resolved after discussion.

**Data extraction**

Two independent reviewers extracted data using a standardized data extraction form (each article was assigned to two of MK Hyun, YJ Lee, YJ Jung, and MJ Kang). Any discrepancies were resolved by consensus or consultation with a third reviewer. The characteristics of the studies (study design, and country of origin) and general information (inclusion/exclusion criteria of participants, intervention tools, methods of education, the individual responsible for educating, outcomes, and patient age) were extracted. The study design was classified using DAMI (study design algorithm for medical literature of intervention) developed by Kim et al. (2011).

**Quality assessment**

Four authors evaluated the quality of the studies independently. The risk of bias was assessed using RoBANS [Risk of Bias Assessment Tool for Nonrandomized Studies, Kim et al. (2013)], and the tool from the Cochrane group for RCTs. In the case of disagreement between reviewers, consensus was reached after discussions between the parties. If a consensus could not be reached between the two investigators, a third party joined the discussion and agreement was reached by majority rule.

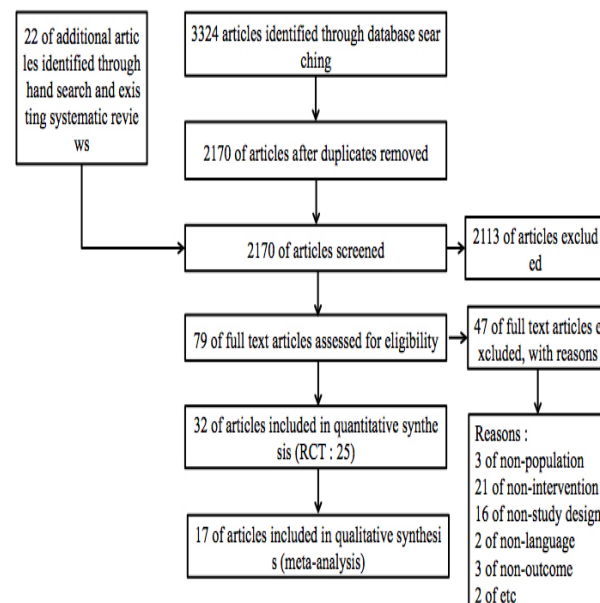
**Meta-analysis**

The outcome of the effectiveness of education was continuous, and was analyzed statistically by calculating the standardized mean difference (SMD). Randomized controlled and non-randomized trials were analyzed separately. Inverse variance methods and the random-effects model were also used. To control for factors such as small sample size and different interventions, outcomes were synthesized as random-effects models. Results are presented as SMDs and CIs. The Review Manager (ver. 5.1; Copenhagen: The Nordic Cochrane Center, the Cochrane Collaboration, 2011) software was used for data analysis.

**Results**

**Included studies**

The authors reviewed the titles and abstracts of 3324 identified studies (including 1437 international and 1887 Korean studies) independently, and 2113 were excluded. The full-text publications of the remaining 79 potentially eligible studies were reviewed in detail. Of these, 47 were excluded based on the inclusion and exclusion criteria (Figure 1), and 32 were included. Twenty-five studies were RCTs, and only seventeen of these were included in the meta-analyses due to varying outcomes. Seven studies were non-randomized trials: four of these were non-randomized controlled trials, and three studies were



**Figure 1. Flow Diagram of Article Selection**

“before and after” studies. The most frequently used educational tool was a booklet. Education commonly comprised multiple interventions, combined with DVDs and audiotapes. Although the educational content was diverse, the most common content was a description of pain management using analgesics, and misconceptions regarding opioids. Additional content included discussions of self-control, relaxation, and individual therapy. The control groups included in the RCTs ranged from no treatment to usual program.

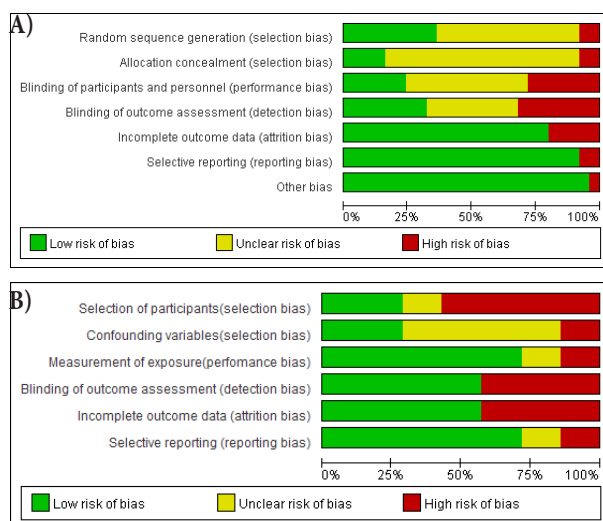
**Risk of bias of the included studies**

Most studies were assessed as having an unclear risk of bias in the domains of random sequence generation, allocation concealment, and blinding. The methods used for random sequencing were either not reported, or were inadequate. In particular, most studies did not consider allocation concealment for appropriate performance. Therefore, the results of these studies must be interpreted with caution (Figure 2).

**Meta-analysis**

Effects on cancer pain (Figure 3), Effects on the most severe pain (Fig. 3A). Most studies used the Brief Pain Inventory (BPI) pain scale. Other tools used to assess pain were 0–10 rating scales, and these results were combined into a meta-analysis of BPI. Ten studies included a meta-analysis of severe pain, including seven RCTs. The SMD of the RCTs was  $-0.34$  (95% CI,  $-0.55, -0.13$ ,  $p=0.001$ ). However, in the non-randomized studies, SMD was not significant due to high levels of heterogeneity (SMD,  $-0.84$ ; 95% CI,  $-2.05, 0.37$ ,  $p=0.17$ ).

Effects on average pain (Figure 3B). The data from 10 studies were available for a meta-analysis of average pain. The effects of educational intervention on average pain were presented in both RCTs and non-randomized studies. The SMD of average pain was  $-0.40$  [95% CI  $-0.64, -0.15$ ,  $p=0.002$ ] and  $-0.73$  [95% CI  $-1.40, -0.05$ ,  $p=0.03$ ] in the RCTs and non-randomized studies, respectively. However, both RCTs and non-randomized studies exhibited high levels of heterogeneity.



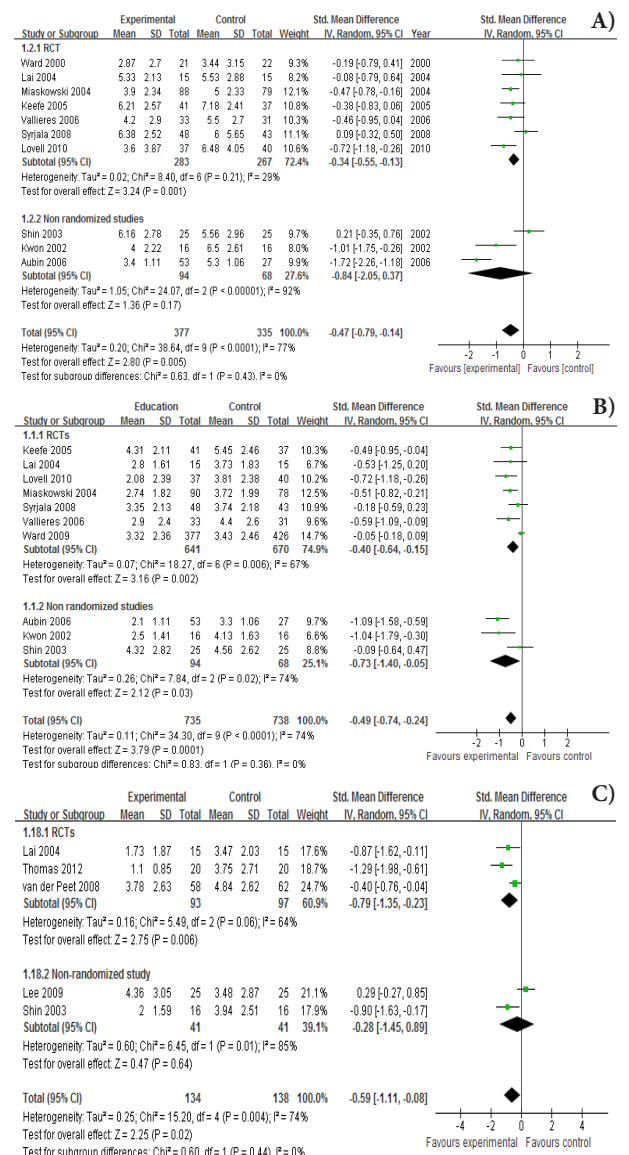
**Figure 2. Risk of Bias of the Included Studies.** A) Risk of Bias Graph of Included RCTs (25 trials); B) Risk of Bias Graph of Included Non-randomized Studies (7 studies)

Effects on current pain (Figure 3C). Data from only six studies were available for use in a meta-analysis of current pain. The SMD effect of education on current pain in RCTs was  $-0.66$  [95% CI  $-1.09, -0.23$ ,  $p=0.002$ ]. In contrast, there was no SMD in the non-randomized studies due to high levels of heterogeneity.

**Effects on quality of life**

**Effects on overall quality of life:** only two studies were included in the meta-analysis of QoL, which were by the same author and reported using EORTC QLQ\_C30 (European Organization for Research and Treatment of Cancer Quality of Life Questionnaire). The SMD of quality of life was  $0.07$  (95% CI  $-0.15, -0.29$ ,  $p=0.82$ ) (data not shown). Educational intervention did not result in improved QoL of cancer patients, although these results are limited by the inclusion of data from only two small studies.

**Effects on pain:** the SMD of pain based on the EORTC questionnaire was  $-0.07$  (95% CI  $-0.55, -0.41$ ,  $p=0.78$ ). Patient education did not result in significant differences



**Figure 3. The Results of Meta-analysis of Cancer Pain (forest plot).** A) Most Severe Pain; B) Average pain; C) Current pain

**Table 1. The Characteristics of the Included Randomized Controlled Trials**

Country	Inclusion criteria	Exclusion criteria	No. of Patients**	Educational content	Educator	Educational tools	Control Group	Outcomes
USA Keefe et al., 2005	1) Advanced cancer diagnosis; 2) Cancer related worst pain >3; 3) Life expectancy <6 months; 4) No change in treatment plans; 5) Age >18 years	NR	78 (41/27)	Cancer pain management, information of a variety of pain coping strategies, methods of how caregivers can help	Nurse	Booklet, videotape, audiotope	Usual care	BPI, FACT-G, Chronic Pain Self-efficacy scale, caregiver version, CSI
Taiwan Lai et al., 2004	1) Age >18 years; 2) Cancer-related pain during the last 2 weeks; 3) Patient could communicate verbally; 4) Informed patient consent	Surgery during the 2-week study period	30 (15/15)	Information and drugs for cancer pain, misconceptions of using pain medicine, methods to prevent side-effects, non-pharmacological interventions, and ways to communicate problems with pain	Nurse	Booklet	Usual care	BPI, POABS-CA, CSQ-Cat, KPS
Australia Lovell et al., 2010	1) Cancer pain intensity $\geq 2$ in the last week; 2) English proficiency; 3) Life expectancy >1 month	1) Cognitive, visual, or hearing impairment; 2) Previous exposure to education	217 (booklet, 51; video, 51; video and booklet, 61; standard care, 54)	Cancer pain management with evidence-based information	NR	3 groups (booklet, video, and booklet)	Standard care	BQ, BPI, PMI, Uniscale for Global Quality of Life, HADS
U.S.A Muskowski et al., 2004	1) Age >18 years; 2) Oncology outpatients; 3) The use of English language; 4) KPS $\geq 50$ ; 5) Pain intensity $\geq 2.5$ ; 6) Evidence of bone metastasis	No family caregiver that could participate.	174 (93/81)	Improving pain relief by altering the times and frequency of analgesic intake, assessment of pain, prevention of side-effects	Specialty trained oncology nurse	Booklet, visiting, phone calls	Standard care	Pain intensity, intake of opioid analgesics
U.S.A Syrjala et al., 2008	1) Cancer patients with persistent pain and ambulatory status; 2) Life expectancy and an expected cancer treatment duration $\geq 6$ months; 3) Age >18 years; 4) Ability to communicate in English 5) Age >18 years; 2) Receiving analgesics for pain; 3) French-speaking patients;	1) Alcohol or other abuse; 2) Major psychiatric diagnoses	93 (48/45)	Common barriers to pain relief, essential ways to communicate with physicians, prominent pain treatment-related symptoms, 26 common medications and other pain treatments	Nurse	Print material, video	Education of nutrition	BQ, BPI, MSAS, Mean daily opioid use, ECOG performance status, FACT-G (baseline)
Canada Vallieres et al., 2006	1) The ability to communicate in English 2) Receiving analgesics for pain; 3) French-speaking patients; 4) A history of radiation therapy >1 week	Receiving strictly analgesic radiotherapy	64 (33/31)	The principles and philosophy of analgesic treatment including myths and misconceptions	NR	Brochure	Standard pain management	Pain levels validated by the American Pain Society
U.S.A Ward et al., 2009	1) The ability to communicate in English; 2) Age >18 years; 3) Moderate to severe pain	Previous exposure to pain education	1256 (391/434/431)	Education regarding barriers (fatalism, fear of addiction or complaining, worries of potential side effects or tolerance)	Nurse or health educators	Booklet	No intervention and no assessment, or no intervention and assessment only	Pain duration, BPI, BQ-II
U.S.A Ward et al., 2000	1) Metastatic or progressive gynecological cancer; 2) Cancer pain in the last 2 weeks	NR	43 (21/22)	Individualized tailored information regarding pain barriers and the management of side-effects	Nurse	Booklet	Usual care	BQ, PMI, MSEC, BPI, FACT-G
Taiwan Chang et al., 2002	1) Localized cancer; 2) Age >18 years; 3) Not currently receiving surgery, radiotherapy, or chemotherapy; 4) The use of analgesics for cancer pain; 5) Scheduled for discharge	Pain-related treatments	37 (18/19)	Information of barriers to effective pain management	Research assistant	Booklet, Q&A	NR	BQ, BPI, medication adherence, demographic questionnaire
Netherlands Van der Peet et al., 2008	1) Cancer patients; 2) Age >18 years; 3) The ability to understand and complete the questionnaire; 4) Present pain score $\geq 4$ ; 5) Informed patient consent	Curative anticancer treatment before 2000	120 (62/58)	Enhancement of pain knowledge, instructions on how to keep a pain diary, and stimulating help-seeking behavior	Booklet, CD, pain diary	NR	Ferrell's Pain Questionnaire, EORTC-C30, HADS	
U.S.A Thomas et al., 2012	1) The ability to read and understand English; 2) Access to a telephone; 3) Life expectancy >6 months; 4) Pain intensity $\geq 2$	Cognitive or psychiatric condition, or substance abuse	228 (75/coaching 64/control/88)	The use of analgesics and non-pharmacological pain management strategies, and communication of pain management.	Nurse or psychology interns	Telephone	Coaching or usual care	BQ, BPI, SF-36, FACT-G
Turkey Yildirim et al., 2009	1) Cancer diagnosis; 2) Experiencing cancer pain & currently taking at least second-step analgesics; 3) Pain duration $\geq 1$ month; 4) Life expectancy $\geq 3$ months; 5) No brain metastasis; 6) Age >18 years; 7) Able to communicate verbally	History of surgery within 2 weeks	40 (20/20)	Comprehensive information regarding pain and the treatment of cancer-related pain	Nurse	Booklet	Standard care	MPQ, NRS, BQ-r, KPS

\*NR, Not reported; BQ, Barriers Questionnaire; BPI, Brief Pain Inventory; MSAS, Memorial Symptom Severity; FACT-G, Functional Assessment of Cancer Therapy-General; MPQ, McGill Pain Questionnaire; NRS, Numeric Rating Scale; BQ-r, Barriers Questionnaire-Revised; KPS, Karnofsky Performance Status; CSI, Caregiver Strain Index; POMS-B, Profile of Mood States; B, PMI, Pain Management Index; HADS, Hospital Anxiety and Depression Scale; MSEC, Medication Side Effect Checklist; \*\*Intervention group/Control group



Table 2. The Characteristics of the Included Studies (non-randomized trials)

Country	Inclusion criteria	Exclusion criteria	No. of patients**	Educational content	Educator	Educational tools	Control Group	Outcomes
Shin et al., 2003	Korea 1) Patients with cancer pain; 2) Able to communicate in Korean; 3) No other physical or psychological diseases; 4) Patient informed consent; 5) Age >20 years; 6) The use of analgesics for cancer pain management	NR	50 (25/25)	Cause of pain, methods of pain management, and analgesics	Nurse	Booklet and audio tape	No intervention	Pain intensity, Barriers Questionnaire
Kwon et al., 2002	Korea 1) Cancer patients ages >18 years; 2) Cancer pain duration >2 weeks; 3) The ability to read and understand	NR	32 (16/16)	Information on cancer pain	Nurse	Booklet and audio tape	No intervention	Satisfaction, Patient Outcome Questionnaire, Pain intensity, BPI, FPQ
Aubin et al., 2006	Canada 1) Life expectancy >6 weeks; 2) No cognitive impairment	NR	80 (53/27)	Didactic material on pain management, a pain diary, and specific instructions on how to react to pain	Nurse	Video tape	Usual home care service	MPG, EORTC QLQ-C30, Pain intensity, Average pain intensity
De Wit et al., 1997	Netherlands 1) Pain related to cancer, cancer therapy, or illness; 2) Cancer pain duration $\geq$ 1 month; 3) Life expectancy $\geq$ 3 months; 4) The ability to read and speak Dutch; 5) Access to a telephone	NR	209 (106/103)	Information and instructions regarding pain and pain management, the self-recording of pain in a pain diary, and seeking help for pain and pain management	Trained nurse	Booklet, audio cassette	Usual care	MPG, EORTC QLQ-C30, Pain intensity, Average pain intensity
De Wit et al., 2001	Netherlands 1) Pain duration $\geq$ 1 month; 2) Cancer related pain; 3) Life expectancy >3 months; 4) The ability to read and speak Dutch; 5) Access to a telephone 6) Not residing in a nursing home or retirement home	NR	104 (53/51)	Information and instructions to improve the knowledge of pain, enhanced motivation to adhere to treatment, pain monitoring, and stimulating help-seeking behavior	Nurse	Audio tape, booklet	Usual care	EORTC QLQ-C30

\*NR, Not reported; BPI, Brief Pain Inventory; FPQ, Family Pain Questionnaire; MPQ, McGill Pain Questionnaire; \*\*Intervention group/Control group

in physical functioning, role functioning, cognition functioning, fatigue, nausea and vomiting, or sleep disturbance (data not shown).

**Effects on the functional assessment of cancer therapy - general (FACT-G):** only two studies were included in this meta-analysis, and there were no significant effects on QoL based on FACT-G (data not shown).

## Discussion

To control cancer pain, it is necessary prescribe different analgesics depending on the intensity of the pain, referring to the World Health Organization (WHO)-recommended three-step analgesic ladder (WHO, 1996). To treat suddenly occurring breakthrough pain, short-acting analgesics should be prescribed in advance, so that they can be used when necessary. Belief about analgesics related with patients' opioid adherence, myths and misconception induced poor pain control. Therefore, patients should be educated on the different methods of pain control and the use of analgesics, as well as instructed on pain assessment and methods of expression to ensure effective control of cancer pain. If the pain of patients can be controlled appropriately following guidelines, unnecessary hospitalization and ER visits will be reduced, resulting in improved quality of life for the patients and a more efficient use of medical expenses. However, a number of obstacles exist for the adequate control of cancer pain. To close gap, several interventions including leadership of cancer care providers and education for patients were emphasized (Nevidjon, 2010). Therefore, we performed a comprehensive systematic literature review and meta-analysis to assess the established rationale of cancer patient education on the use of narcotic analgesics. Our results revealed that the SMDs of the most severe, average, and current pain in the RCTs were significant. In the non-randomized studies, the effects on average pain were significant, but those on worst and current pain were not.

Patient-based education reduced the pain of cancer patients, and so could be considered an effective method of cancer pain management. However, these results should be interpreted with caution due to the wide confidence intervals and the heterogeneity of qualitative analysis due to use of different study designs and diverse educational protocols including content, educational tools, measurement tools, and the education time.

In a 2001 review, educational intervention

had little effect on the pain levels of patients (Allard et al., 2001). In contrast, a 2009 review suggested that educational intervention reduced the intensity of the average and worst pain compared with normal care or control (Bennett et al., 2009). In this study, patient-based education was also effective at reducing the intensity of cancer pain. Based on these data, patient-based education for the management of cancer pain is highly recommended.

Patient quality of life was assessed using various tools in the included studies, and so a meta-analysis of QoL included only four trials, with no significant effects. Previous systematic reviews suggested that pain medication improved the QoL of cancer patients, and that tramadol significantly improved QoL compared with placebo [assessed using the Activities of Daily Living (ADL) scale (Quigley, 2008)]. In addition, transdermal fentanyl and sustained-release oral morphine improved the QoL of cancer patients (appetite, sleep, daily activities, mental state, emotion, communication, and interest) in six separate trials (Yang et al., 2010). However, we were unable to find any systematic reviews on the effects of patient-based education for QoL. Therefore, further studies are needed to determine the effects of patient education on QoL and provide practical recommendations. In addition, unified measurement tools are required for accurate analysis.

Our study had some limitations. There was significant heterogeneity in the qualitative analysis, because the methods and tools used to educate patients were highly variable, and the individuals in responsible for the education varied between nurses, researchers, physicians, and students. Therefore, meta-analysis of only specific qualified outcomes was possible in some reports. Nevertheless, our data are important, despite these limitations, because our study included non-randomized trials.

In conclusion, educational intervention reduced the pain of cancer patients. Therefore, patient-based education could be an effective management method, and should be strongly recommended. However, to assure positive effects on QoL and prevent patient misunderstanding, studies using standardized protocols should be performed.

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