The Evidence

Management and Improvement in Cancer Pain: Focusing on Narcotic Analgesics

Introduction

Pain is one of the most common and painful symptoms in the cancer patients. Approximately 30~50% of patients with early-stage cancer or patients who received aggressive anticancer treatment suffer from cancer pain[1]. Also about 60~70% of patients with progressive stage of cancer and 80~90% of patients with end-stage cancer are suffering from cancer pain. In order to control such cancer pain, it is necessary to select or add analgesics depending on the intensity of cancer pain, referring to the World Health Organization(WHO)-recommended 3 step analgesic ladder[2].

For example, use non-narcotic analgesics for mild pain, weak narcotic analgesics for persistent pain and then, potent narcotic analgesics such as Morphine until a patient's pain disappears. Also regardless of pain intensity, adjuvant analgesics should be used in combination by pain type to potentiate the analgesic effects.

In addition, to cope with suddenly occurring breakthrough pain, short-acting analgesics should be prescribed in advance to be used in case of breakthrough pain[2]. Additionally, patients should be provided with knowledge on pain control methods and analgesics use, and education and instruction on pain assessment and expression methods to ensure effective cancer pain control. If pain of cancer patients can be appropriately controlled according to the guideline, unnecessary hospitalization and ER visits will be reduced, resulting in improved quality of life of patients and efficient use of medical expenses; however, a number of obstacles exist for cancer pain control in real practice[3].
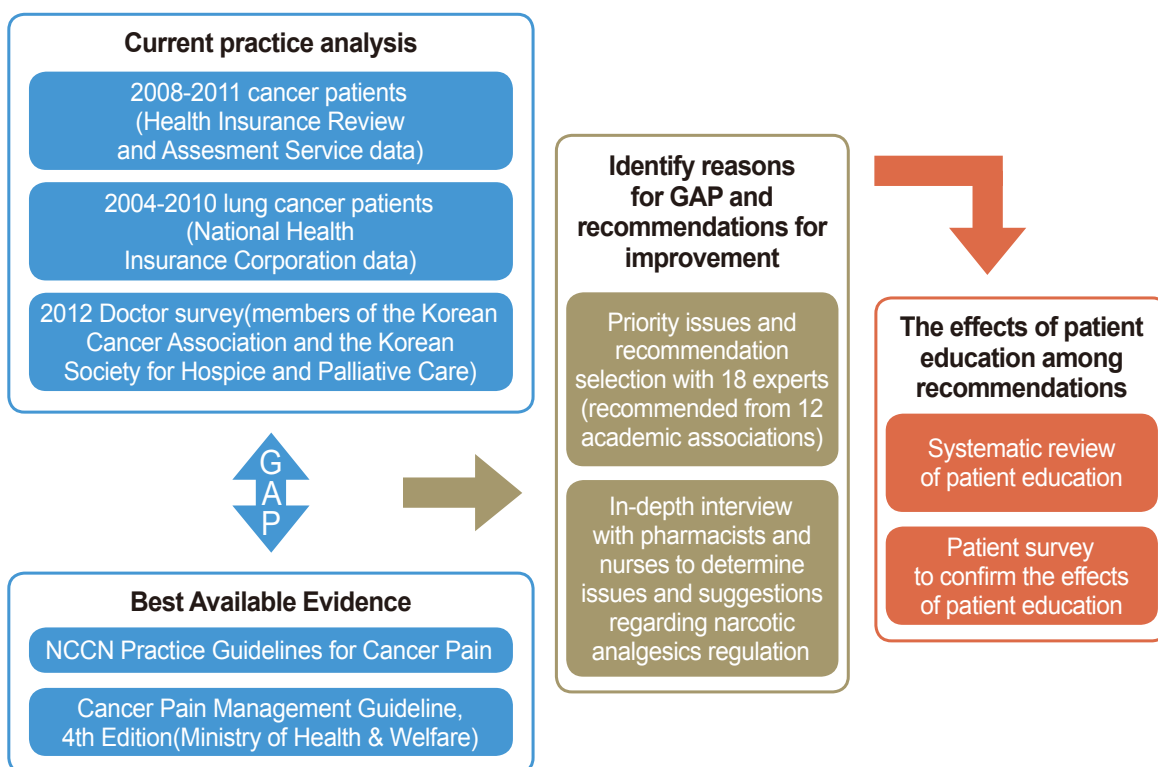
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1) Kim, Yeol; Kim, Daehyun; Park, Sohee; Kong, Kyungae; Choi, Jinyoung(A); Park, Jonghyuk; Ko, Sujin; Cho, Hyunjung; Hwang, Gwanok; Nam, Eunjung; Choi, Jinyoung(B); Park, Eunjung. Research on Developing the Monitoring System for Pain Control among Cancer Patients. National CancerCenter / Ministry of Health and Welfare 2011.
2) Ko, Sujin; Kwon, Ingak; Kim, Doyeon; Kim, Siyoung; Kim, Yeonhee; Kim, Yeol; Park, Jinno; Shin, Sangwon; Oh, Doyeon; Yoo, Eunsun; Yoon, Deokmi; Yoon, Youngho; Lee, Keunsuk; Lee, Changgul; Heo, Daeseok. Recommendation on Guideline for Controlling Cancer Pains(4th Ed.). Ministry of Health and Welfare 2011.
3) Heo, Daeseok. Presentation on Symposium for Effective Management of Cancer Pains. NationalCancerCenter 2002.

This study aimed to provide the rationale for policy setting by conducting the following studies, referring to the framework in the Evidence-Practice gaps report by the Australian National Institute of Clinical Studies(NICS).

First, the status of cancer pain management was reviewed by claims data analysis and a survey of physicians, the gap between status and rationale was identified, causes of the gap was investigated with the focus group interview of representative experts, and then the recommendations for improvement were presented. Among the recommendations for improvement, the effect of patient education was also confirmed by a systematic review and patient survey(Figure 1).

Current practice analysis

2008-2011 cancer patients
(Health Insurance Review
and Assesment Service data)

2004-2010 lung cancer patients
(National Health
Insurance Corporation data)

2012 Doctor survey(members of the Korean
Cancer Association and the Korean
Society for Hospice and Palliative Care)

GAP

Best Available Evidence

NCCN Practice Guidelines for Cancer Pain

Cancer Pain Management Guideline,
4th Edition(Ministry of Health & Welfare)

**Identify reasons
for GAP and
recommendations for
improvement**

Priority issues and
recommendation
selection with 18 experts
(recommended from 12
academic associations)

In-depth interview
with pharmacists and
nurses to determine
issues and suggestions
regarding narcotic
analgesics regulation

**The effects of patient
education among
recommendations**

Systematic review
of patient education

Patient survey
to confirm the effects
of patient education

<Figure 1> Framework of the Study

Pethidine which is not a recommended
narcotic analgesic for cancer pain patients was prescribed
for 38.5% of the entire narcotic analgesic users.

Analysis of using narcotic analgesics: claims data analysis

Ⅰ. Method

To define terminal cancer and severely ill patients close to death who are assumed to be suffering severe pain, 0~120 year old cancer patients who received at least one prescription of a 'C00-C99'code within top 6 ranks of main disease code and subordinate disease code over 4 years between 2008 and 2011 have been examined. Among those patients, 203,493 patients who confirmed as 'Death' in the clinical endpoint and had the date of death were defined as cancer deaths. The status of their narcotic analgesics use was analyzed at 1 month(30 days) prior to death, 2 months(30~60 days) before death, and 3 months(60~90 days) before death.

Ⅱ. Results

The use rate of narcotic analgesics in cancer deaths at 1 month prior to death was 82.6%(168,002 patients). Compare with the rate of 52.7% at 2 month before death and 44.3% at 3 month before death, the use rate of narcotic analgesics in cancer deaths at 1 month before death was higher. Of the entire claims statements of cancer deaths at 1 month prior to death, narcotic analgesics claims statements accounted for 41.2% and the distribution was 65% of inpatient statements and 21.7% of outpatient statements, suggesting more prescription of narcotic analgesics for inpatient claims.

Prescription was analyzed separately for inpatient and outpatient cases by ingredients of narcotic analgesics. For inpatient prescription at 1 month prior to death, Morphine represented 33.9%, followed by Fentanyl 18.3%, and Oxycodone 14.8%. But in case of outpatient prescription, Oxycodone represented 30.9%, followed by Fentanyl 23.2%, and Tramadol 18.5%. It represents different inpatient and outpatient prescription patterns.

In addition, by level of a healthcare facility, prescription frequency was the highest for Morphine, followed by Fentanyl, and Oxycodone for hospital or higher levels at 1 month prior to death. However, Tramadol was most frequently prescribed in nursing hospitals and clinics. It could be speculated that managing Tramadol is more convenient among narcotic analgesics in nursing hospital or lower levels.

In terms of the combination prescription status of short-acting drugs, the short-acting drug prescription rate for outpatient visits at 1 month prior to death was as low as 22.2%. And the combination prescription rate was lower in lower levels of medical facilities compared to general hospital or higher levels.

Additionally, although combination prescription of an internal medicine(Oxycodone) and patch(Fentanyl) is not recommended for cancer pain patients, this study found that 28.8% of patients received combination prescription at 1 month before death. And Pethidine which is not a recommended narcotic analgesic for cancer pain patients was prescribed for 38.5% of the entire narcotic analgesic users.

The daily amount of narcotic analgesics used by cancer deaths was transformed to Morphine 10mg-equivalent; the per-patient daily average was 193.7mg at one month prior to death, 134.2mg at two months before death, and 111.3mg at three months before death. It shows that the daily amount of narcotic analgesics at 1 month before death is about 1.7-times more than at 3 months before death. It also shows that the daily used amount of narcotic analgesics decreases with age. The total amount of the reviewed and decided insurance coverage expenses for cancer deaths at prior to death was KRW 6,414,582/person. Among those expenses, the cost of narcotic analgesics use was KRW 209,729/person at 1 month prior to death, representing only 3.3% of the total amount of insurance coverage.

By contrast, examination fees cost KRW 1,035,651/person, accounting for 16.1% of the total amount of insurance coverage, treatment and surgery fees were 12.8%, and radiographic diagnosis and treatment represented 4.5%, suggesting that aggressive treatment was ongoing at 1 month prior to death.

By ingredient of narcotic analgesics, in case of Morphine, the cost of narcotic analgesics per-capita were the highest for Morphine Sulfate with KRW 190,277/person compared to KRW 13,729 for Morphine HCl, followed by Fentanyl, Oxycodone, and Hydromorphone. The combination prescription rate for non-narcotic analgesics and adjuvant analgesics was 66.2% for narcotic analgesics uses for 1 month prior to death, and the adjuvant analgesics use rate was 68.3%.

Analysis of using narcotic analgesics: questionnaire survey of physicians

Ⅰ. Method

An online survey and face-to-face survey had been made to review the status of experts in cancer pain management, cancer pain education, and using narcotic analgesics. The survey was conducted by physicians who were members of the Korean Society for Hospice and Palliative Care and Korean Cancer Association from October to November 2012.

Ⅱ. Study results

Physicians evaluated the pain assessment for cancer patient as highly important by scoring as 9.44 out of 10 points. And the accuracy of patient self-reports about pain was rated 7.13 out of 10 points. Efforts of cancer specialists in relieving pain for cancer patients was rated 6.65/10 points.

And the satisfaction in establishing multidisciplinary system with experts such as organizing a pain management team was relatively poorly assessed, as 5.36/10 points. When they asked about why physicians are not cooperating with other pain experts(anesthesiology and pain medicine department, radiation oncology department, dedicated pain nurse, pharmacist, etc.) for cancer pain management, absence of the compensatory medical fee for multidisciplinary system among experts was highly rated with 7.34 points.

The major issue was the lack of systemic education
and interests in cancer pain management
by the medical professionals and pharmacists.

In addition, for the adequacy of education on cancer pain management, a training process was rated 4.03/10 points. And the adequacy of their residency training and medical school training in cancer pain management was rated only 4.00 points and 3.14 points respectively.

Priority issues and recommendation selection in cancer pain management

Ⅰ. Study method

Priority issues and recommendation selection were conducted two times with 18 experts who are recommended from 12 academic associations to identify problems and resolution measures for cancer pain and narcotic analgesics management in clinical settings. During the first priority issues and recommendation selection, involved experts completed a questionnaire to provide their brief personal information, and answered open-ended questions on obstacles and recommendations in cancer pain management.

After questionnaires were completed, its obstacles and recommendations were collected, and obstacles with similar characteristics were categorized. Then the top 3 key issues were selected based on their response rate in each category, and its recommendations were provided. In the second priority issues and recommendation selection, the Basic Priority Rating System(BPRS) and PEARL[4], basic priority selection tools, were used to set priority of recommendations and policy practicality was evaluated.

Ⅱ. Study results

The first selected key issue from the first priority issues and recommendation selection in a total of 12 respondents was the lack of systemic education and interests in cancer pain management by the medical professionals and pharmacists. Based only on BPRS scores, 'implementation and obligatory requirement of systemic and continuous cancer pain management education for medical professionals and pharmacists' was highly placed, followed by 'inclusion of cancer pain management in the regular curriculum of colleges nurturing medical professionals and pharmacists', and 'obligatory requirement of pain assessment in cancer patients'.

The second key issue was the lack of understanding of patients and guardians in cancer pain management including narcotic analgesics. The highest ranked recommendation was 'education of patients and guardians on cancer pain management by dedicated personnel for patient education', followed by 'promotion of the guideline on standardized cancer pain management', and 'recommendation of the obligatory requirement of instruction by medical staff and pharmacists to enhance medication compliance of analgesics'.

The third key issue was the necessity of cancer pain management system improvement. For the recommendation

4) P: Propriety, E: Economic feasibility, A: Acceptability, R: Resourse availability, L: Legality

selection, 'establishment of medical payment system for ward- and home-based palliative care' was highly placed, followed by 'establishment of multidisciplinary system with experts by organizing a pain management team', and 'establishment of a new medical payment system for cancer pain management fees'.

Confirmation of the effects of patient education among recommendations: systematic review

Ⅰ. Study method

Systematic review was performed for the established rationale of cancer patient education on the use of narcotic analgesics. Each 3 international and domestic DBs were searched, and the risk of bias assessment of literature was performed using the Cochrane's Risk of Bias(RoB) in case the questionnaire study type was a randomized comparative clinical study, and the Risk of Bias Assessment tool for Non-randomized Studies(RoBANS) for non-randomized comparative clinical studies, cohort studies, case-control studies, and before-after studies.
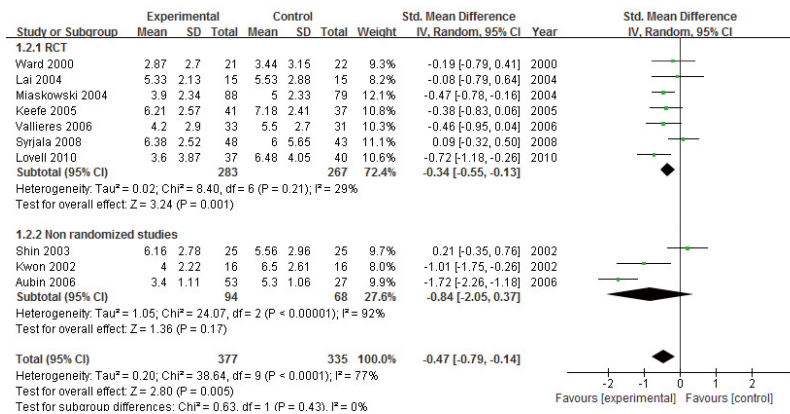
Ⅱ. Study results

A total of 1,437 studies were retrieved from international databases, and 1,887 articles from domestic databases. After removal of redundancy and the first selection, 55 studies were selected. From manual search and review of clinical studies included in the previous systematic review, 25 were added, and after finding out total 80 full texts and conducting the second selection, 32 articles in total were included in the qualitative synthesis, and meta analysis was conducted for 10 investigations in total.

A total of 10 studies could be used for meta analysis of the effects of educational intervention on severe pain intensity as measured by the Brief Pain Inventory(BPI) or equivalent tool; 7 of them were randomized comparative clinical studies and 3 were non-randomized studies. Randomized comparative clinical studies all showed the same direction and low heterogeneity but non-randomized studies exhibited high heterogeneity and no significant results(I2=92%, SMD[5] –0.84(95% CI: –2.05, 0.37)). Effects of the educational intervention as estimated with randomized comparative clinical studies were SMD –0.34(95% CI: –0.55,–0.13)(Figure 2).

There were total 10 studies on the average pain effects as measured by BPI or similar tool. Effects of the educational intervention as estimated with randomized comparative clinical studies were SMD –0.40(95% CI: –0.64,–0.15). Effects of the educational intervention as estimated with non-randomized comparative clinical studies were SMD –0.73(95% CI: –1.40, –0.05), but moderate heterogeneity was shown due to diversity of interventions and study designs(Figure 3).

5) Standarized Mean Difference

<Figure 2> Meta-Analysis Result for Severe Pains
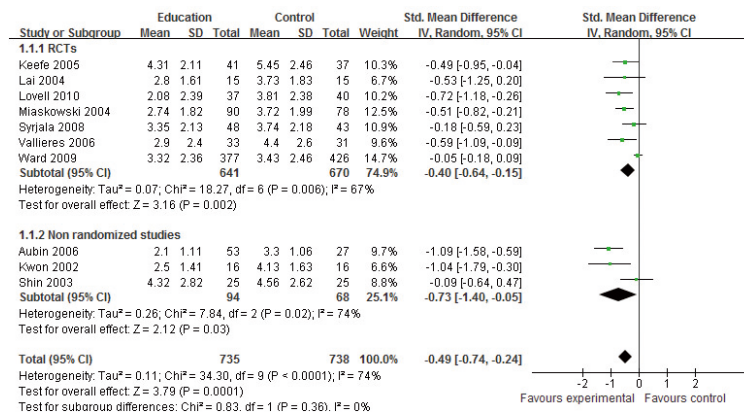
<Figure 3> Meta-Analysis Result for Average Pains

Confirmation of the effects of patient education among recommendations: patient survey

Ⅰ. Study method

To investigate the effects of education by comparing characteristics before and after the pain management program, a survey was conducted among cancer outpatients at 3 local hospitals(hematology-oncology department) and cancer inpatients at 3 hospitals. As education materials for the pain management program, the Ministry of Health and Wel-

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and the influence of pain also declined after the education.

fare-issued 'Guideline on cancer pain management for patients' was commonly used along with an educational booklet in each hospital. Also a review meeting was organized for clinical research nurses(CRNs) who actually conduct the questionnaire survey in order to coordinate the contents and approach of patient education. The education program was conducted by CRNs with a booklet for an individual patient. A separate education space was arranged for education and the average education time was about 30 minutes. All involved patients completed the questionnaire for a total of 3 times; prior to, immediately after, and by 1 week after the education.

Ⅱ. Study results

A total of 176 patients were collected and 163 patients completed the questionnaire up to 1 week after the education. Pain as perceived by patients before/after the education on narcotic analgesics use was evaluated by the NRS scale. Overall, pain intensity decreased after the education, and the influence of pain also declined after the education. For the number of experiencing breakthrough pain episodes, both inpatients and outpatients showed no significant difference before/after the education. In terms of taking short-acting analgesics due to breakthrough pain, inpatients showed no large difference before/after the education in the use of short-acting analgesics.

However, outpatients showed an increase of taking short-acting analgesics from 25.5% before the education to 73.5% after the education, and the difference was statistically significant. Education time on narcotic analgesics use was classified into two groups; 30 minutes or less and over 30 minutes. The change of pain and influence of pain were not significantly different by their education time. The change of perception in 8 items were also examined before and after the education of narcotic analgesics use. All items showed significantly different based on the education, indicating improved perception on narcotic analgesics use after education.

In the change of perception by their education time, different results were shown by its item. The items that showed different perception change by their education time were 'A good patient should endure pain', 'It is better to endure pain if it is not severe because analgesics should be saved to used in case of severe pain', 'People are easily addicted to analgesics', 'It is better to endure pain and avoid using analgesics because analgesics cause adverse effects', and 'It is better to use analgesics whenever you feel pain, but not regularly.'

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