The Study of Clinical Pharmacist Participating in the Pain Management of Outpatients with Cancer in A Prescription Period

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Research Article

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Abstract

**Purpose.** The management of outpatients with cancer pain is very important for medication safety. Medical interviews by CP is conducive to pain management. Our objective was to describe the contribution of the clinical pharmacist (CP) to outpatients in pain-relief clinic.

**Methods.** This was a prospective, case-by-case self-control study. One clinical pharmacist conducted three questionnaire surveys. The first happened in the clinic face to face, the second by telephone one week later after the visit and the third by telephone two weeks later. The interventions by CP and comprehensive pain assessment (scored by NRS, sleep, mood and general activities) were both recorded. Analgesic-related knowledge were delivered by CP and were measured both before and after therapy.

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**Results.** 51 patients were enrolled. The top 5 interventions in the first telephone interview (second survey) was suggestions for treating adverse drug reactions (47%), correcting the wrong usage (35%), medication education (26%), recommendations for dosage adjustment (18%) and suggestions for further treatment (15%). While in the second telephone interview (third survey), the rankings were totally inverted. Comprehensive pain assessment showed better in the first interview and then worse in the second. Analgesic-related knowledge increased significantly after the education by CP.

**Conclusions.** CP made a totally different interventions at the different stages of medication in the outpatients with cancer pain, which may be related to the pain control. Patients’ knowledge regarding analgesics significantly increased after education by CP.

Introduction

Pain is defined as an unpleasant feeling and emotional experience related to actual or potential tissue damage by the International Association for the Study of Pain, and is one of the most common symptoms of cancer patients. 64% of patients with advanced cancer pained, 59% of patients receiving cancer treatment had pain, and 33% of patients suffered pain after treatment. The World Health Organization (WHO) advocated the three-step analgesic ladder of cancer pain relief guideline in 1986. To promote the standardized treatment in clinical, 150 “Good Pain Management (GPM) Wards” had been established between 2011 and 2014 in China, which sponsored by the Health Ministry of China and required a clinical pharmacist (CP) providing professional service in the ward, who played an important role in patient education and drug monitoring.
Five steps are crucial for optimal pain management: assessment, planning, implementation of actions, evaluation of these actions, and adaptations if pain management is inadequate. Medical interviews by CP can be regarded as the last two steps, evaluation and adaptations. However, as a relatively new professional in China, Most CPs lack the evidence of medical problems patients may face in the pain management at home and the experience of interviews for outpatients with cancer pain. Long-acting opioids can be prescribed for 15 days for patients with cancer pain in the clinic once in China. How to accomplish the interviews by CP in these 15 days is a great challenge.

The aim of the present study was to conduct a prospective, case-by-case self-control study to describe the interventions by CP and pain control in the outpatients with cancer pain in a prescription period, and evaluate the analgesics-related knowledge after the education by CP.

Patients And Methods

Study population

Patients were recruited in the Pain-relief clinic in the biggest cancer hospital in China between Sep 2020 and April 2021. Eligible patients: i. were diagnosed with cancer by cytological, imaging or pathology tests; ii. had cancer-related pain; iii. visit the pain-relief clinic for the first; iv. used analgesics orally or externally; v. took the medicine prescribed after the visit; vi. no other analgesic treatment was given; vii. were able to communicate verbally. viii. willing to be telephone-interviewed by CP. Patients were excluded: i. Routine patients with continuous treatment with satisfied pain control; ii. had received medication education by CP in the past; iii. had good knowledge of analgesic drugs. The study was approved by Hospital Ethics Committees, and all eligible patients agreed to participate in the study and signed an informed consent.

Method

This was a prospective, case-by-case self-control study. One clinical pharmacist was involved, who participated in the training of clinical pharmacists for pain and was engaged as a full-time clinical pharmacist in GPM ward for three years. The clinical pharmacist joined the pain-relief clinic with a doctor, once a week, for four hours. She was responsible for patient education, pharmaceutical consultation, drug-drug interactions, adverse drug reactions, dose titration and patient interview.

For patients who met the criteria for admission, CP conducted three questionnaire surveys. The first happened in the clinic face-to-face, when the doctor had finished the visit and the patient got back to the clinic again taking with the drug prescribed, which included general information, disease condition, comprehensive pain assessment (scored by NRS, sleep, mood and general activities), analgesic-related knowledge(Table 1). After the survey, CP conducted the medication education to patients. The contents of the education are as follows: 1). Three-step treatment principle of cancer pain. 2). The ladder the medicine prescribed belonged to and its pharmacological action. 3). Long-acting analgesic drugs should be taken on time and short-acting drugs should be taken when break-through pain occurred. 4). the dosage of drug. 5). drug precautions: such as daily limit of nonsteroidal drugs and acetaminophen and
avoiding fasting, fentanyl patch should not be cut and be away from heat. 6). Adverse drug reactions (ADR): nausea, vomiting and dizziness are common adverse reactions of opioids in early stage. Constipation is the most common and lasting adverse reaction, taking laxatives if necessary. Central symptoms such as drowsiness, sedation and hallucination should be treated in time, especially for elderly patients and patients with high-dose opioids. Respiratory depression is the most serious adverse reaction of opioids.

The second survey (first telephone interview) happened one week after the visit, including comprehensive pain assessment and analgesic-related knowledge, both the same as the first. CP would make medication education again if the patients had poor analgesic-related knowledge. Besides, CP would ask them whether any ADR occurred and provide guidance, such as taking laxatives for constipation. For some patients who take the medicine according to doctor's advice but have poor effect, CP would advise them to increase the dosage, as expected and informed by doctor in advance.

The third survey (second telephone interview) happened two weeks after the visit, including comprehensive pain assessment (the same as the first). CP would verify the usage, dosage and ADR and educate again if necessary. For some patients with poor pain control, they were recommended to see a doctor again. Both interventions by CP were records.

**Data extraction**

1. Interventions by CP

It was classified into five categories: suggestions for treating adverse drug reactions, correcting the wrong usage, medication education, recommendations for dosage adjustment and suggestions for further treatment.

2. Pain assessment:

i. Pain severity was classified as painless (0), mild (1 ~ 3), moderate (4 ~ 6), and severe (7 ~ 10); ii. The impact of the pain on the sleep: scored by 0 ~ 10 points, contrary to the pain score, 0 for worst sleep while 10 for best sleep; iii. The impact of the pain on the mental status, scored the same as the sleep, 0 for worst and 10 for best. iv. The impact of the pain on the daily activities: 0 ~ 10 points, 0 for worst and 10 for best.

3. Patient's mastery of analgesic-related knowledge

We set up three questions to reflect patient's mastery of analgesic-related knowledge. The higher the score, the more knowledge the patients had. See Table 1 for details.
Table 1
Analgesic-knowledge questionnaire and scoring criteria

| Questions                                                                 | Answers          | Score, points |
|---------------------------------------------------------------------------|------------------|---------------|
| 1. Do you know the name of the analgesic you are using?                   | Yes              | 2             |
|                                                                           | No               | 1             |
| 2. Do you know the usage of the analgesic you are using?                  | Yes              | 3             |
|                                                                           | A Little         | 2             |
|                                                                           | No               | 1             |
| 3. Do you know the side-effects of analgesics?                            | Yes              | 3             |
|                                                                           | A Little         | 2             |
|                                                                           | No               | 1             |

Statistical Analyses

All of the data were analyzed by the statistical software SPSS (version 22.0). One-way repeated Anova test was used to analyze pain, sleep, mood, general activity score in three surveys. A paired student’s \( t \)-test was used to compare the changes of analgesic-related knowledge before and after intervention by CP. The test level was as follows: \( \alpha = 0.05 \), with 95% confidence interval.

Results

1. Patient Characteristics

We enrolled 63 subjects. 2 were excluded because of death, and 8 were dropped for lost visit in the second follow-up. 2 were dropped for lost visit in the third. The final enrollment was 51 subjects. Baseline characteristics are presented in Table 2.
Table 2
Baseline Characteristics of Enrolled Patients

| Characteristics          | Subjects n(%) |
|-------------------------|---------------|
| Sex                     |               |
| Male                    | 29 57%        |
| Female                  | 22 43%        |
| Age (y)                 |               |
| < 60                    | 27 54%        |
| >=60                    | 24 46%        |
| Primary disease         |               |
| Lung tumor              | 4  7.8%       |
| Hepatobiliary tumor     | 8  15.7%      |
| Gynecologic tumor       | 10 19.6%      |
| Digestive tract tumor   | 2  3.9%       |
| Breast tumor            | 3  5.9%       |
| Tumor of urinary system | 3  5.9%       |
| Head and neck tumors    | 2  3.9%       |
| Bone tumour             | 2  3.9%       |
| Other                   |               |
| Extent of disease       |               |
| Local or regional       | 43 84%        |
| Metastatic              |               |
| Previous treatment      | 21 41%        |
| One treatment(Surgical/Chemotherapy/Radiotherapy) | 17 33% |
| Two kinds of treatment  | 3  6%         |
| Three kinds of treatment| 10 20%        |
| Untreated               |               |

2. Changes of interventions by clinical pharmacist in the interviews

The top 5 interventions in the first telephone interview was suggestions for treating adverse drug reactions (47%), correcting the wrong usage (35%), medication education (26%), recommendations for
dosage adjustment (18%) and suggestions for further treatment (15%). While in the second interview the rankings were totally inverted. They were 11%, 14%, 16%, 24% and 51% respectively (Fig. 1).

3. Pain control

The pain, sleep, mood and general activity scores in three surveys are shown in Fig. 2. Both items were statistically different. The pain score in three survey was 7.92 ± 1.34, 3.73 ± 1.74, 4.37 ± 2.34 (P < 0.001) respectively (7.92 ± 1.34 vs 3.73 ± 1.74, P < 0.001; 3.73 ± 1.74, 4.37 ± 2.34, P = 0.141). The sleep score was 2.78 ± 1.12, 6.35 ± 2.30, 5.86 ± 2.47 (P < 0.001) respectively (2.78 ± 1.12 vs 6.35 ± 2.30, P < 0.001; 6.35 ± 2.30, 5.86 ± 2.47, P = 0.297). The mood score was 3.06 ± 1.41, 6.08 ± 2.51, 5.41 ± 2.64 (P < 0.001) respectively (3.06 ± 1.41 vs 6.08 ± 2.51, P < 0.001; 6.08 ± 2.51, 5.41 ± 2.64, P = 0.287). The general activity score was 5.20 ± 2.43, 6.94 ± 2.64, 6.39 ± 2.84 (P < 0.001) respectively (5.20 ± 2.43 vs 6.94 ± 2.64, P < 0.001; 6.94 ± 2.64, 6.39 ± 2.84, P = 0.455).

4. Analgesic-related knowledge

Patients’ knowledge regarding analgesics including drug name, usage and side-effect and total score was significantly increased after the education by CP. (P < 0.001, Fig. 3).

Discussion

This study reported the changes of interventions by CP in the pain management of outpatients with cancer in a prescription cycle for the first time. We designed a prospective, case-by-case self-control study and found that CP played totally different roles in different stages of patients' medication in a prescription period.

On the first interview, the highest frequency of interventions was suggestions for adverse drug reactions (47%), corresponding to the pain control improved significantly from 7 to 3 and sleep, mood and daily activities related to pain also showed a similar trend. In the initial stage of medication, the drug worked quickly and the main problem is the adverse drug reactions. In particular, some common adverse reactions of opioids, like nausea, vomiting and dizziness, often occur in the early stage of medication, and then gradually tolerated. Therefore, when CP followed up the patients for the first time on the 7th day of medication, the most frequent of intervention is the guidance of the adverse drug reactions.

Seven days later, we set the second interview. Unexpectedly, the pain, sleep, mood and daily activities related to it changed, which became deteriorated, although statistically significant. It may be due to, first, drug tolerance, which needs increasing the dose to achieve analgesic effect. Second, many patients are in the advanced stage of the disease and the pain aggravated rapidly. Finally, poor medication compliance may be due to adverse drug reactions. Thus CP suggested the patients for a visit for further treatment (51%), prescribing new drug, adjusting the dosage or conducting further examinations.

Pain is a devastating symptom of cancer that affects the quality of life of patients. Despite the development of novel analgesics and updated pain guidelines, cancer pain remains undermanaged.
Inadequate cancer pain management in the outpatient setting can be attributed to barriers on different levels, related to health care professionals, patients, and the health care system \[5-7\]. Particularly in the outpatient setting, health professionals are unable to monitor pain and provide adequate follow-up \[8\].

Recommendations to overcome barriers include a multidisciplinary approach that promotes collaboration between different health professionals and ongoing assessment of pain with regular follow-up appointments \[9\]. Educational interventions for patients may improve the success of pain management. Effective pain control mandates multidisciplinary interventions from interprofessional teams.

Many studies had shown that clinical pharmacists play an active role in the treatment of cancer pain. Gagnon evaluated the contributions of a clinical pharmacist in a palliative radiotherapy clinic, and found CP played a key role in holistic patient assessment and optimization of pharmacologic therapy, with pain improving at week 1 and week 4 \[10\]. Liu evaluated the participation by the pharmacist in the cancer pain management team and found a marked reduction in most of the drug-related problems and a statistically significant change in pain score during the 4 visits, which indicated that pharmacists play an active role \[11\]. The study mainly intervened in prescription and doctor, and the whole period was short, 4 days. John Valgus described a pharmacist-led, interdisciplinary method in a cancer clinic and found that pharmacists participated in 78% of patient consultation and symptom scores including pain improved \[12\]. Chen found a Clinical Pharmacist-Led Guidance Team significantly improved standardization, efficiency, and efficacy of cancer pain therapy in China \[13\]. Wang found clinical pharmacist-led medication education resulted in improved pain control in patients with cancer \[14\]. These studies have proved the necessity of clinical pharmacists participating in the treatment of cancer pain, which can bring benefits to patients. However, they did not show specific interventions in one prescription period for outpatients with cancer pain.

In fact, many outpatients with cancer pain need to be closely monitored, especially for opioid-naïve patients, patients converting from one opioid to another, patients using high dosage of opioids, elderly patients, patients with liver and kidney dysfunction and poor tolerance of adverse reactions, and patients using several kinds of analgesics. There is an urgent to know how to manage these outpatients with cancer pain, educating them, monitoring the outcome, treating analgesic adverse effects, and providing guidance for further treatment. Based on a 15-days prescription cycle, this study described the different interventions of CP at different time for the first time, combined with the changes of pain score, better first and then worse. It is suggested that the interventions by CP were combined with the pain control.

The patient’s knowledge about analgesics greatly improved after treatment, which may be due to the education of CP, who send patients drug cards when prescribing drugs, and introduced the pharmacological characteristics, usage, precautions and adverse reactions of drugs when following-up, which could improve the knowledge of patients. It still reflects the role of pharmacist interventions. Yan Wang found that patients got greater knowledge in pharmacist-education group compared with control group \[15\].
This study has several limitations: 1) the small sample size drawn from a single clinic; a large-scale and multicenter study would be necessary to generalize the study findings; 2) more follow-up should be designed, such as every three days.

**Conclusion**

In summary, despite the limitations, the study confirmed the clinical pharmacists made a totally different interventions at the different stages of medication in the outpatients with cancer pain in one prescription cycle, and patients’ knowledge regarding analgesics significantly increased after education by CP.

**Declarations**

**Funding:** N/A

**Conflicts of interest/Competing interests:** N/A

**Availability of data and material:** The data that support the findings of this study are available upon reasonable request.

**Code availability:** N/A

**Authors' contributions:** All authors participated in the work of this study, such as follow-up and recording, and made contributions.

**Ethics approval:** The study was approved by Hospital Ethics Committees.

**Consent to participate:** All eligible patients agreed to participate in the study. Consent for publication: All authors agree to publish

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**Figures**
1. Suggestions for treating adverse drug reactions
2. Correct the wrong usage
3. Medication education
4. Recommendations for dosage adjustment
5. Suggestions for further treatment

Figure 1. Changes of interventions by CP in the follow-ups

See image above for figure legend.
Figure 2. Changes of pain, sleep, mood and general activity score in three surveys. Data presented as mean±SD, One-way Repeated Measures Anova, *P<0.001

See image above for figure legend.
Figure 3. Changes of analgesic-related knowledge.

Data presented as mean ±SD

Paired Student’s t-test, *P<0.001

Figure 3

See image above for figure legend.