APM ANNALS OF PALLIATIVE MEDICINE
AN OPEN ACCESS JOURNAL FOR HIGH-QUALITY RESEARCH IN PALLIATIVE MEDICINE

Peer Review File

Article information: http://dx.doi.org/10.21037/apm-20-1458

Reviewer A

***General Comments*:**

First, I would like to appreciate the researchers' commitment in measuring the role of pharmacists in cancer pain patients.

Saying this, pharmacists are parts of MDT team in your setup, so is it the existing service report or research?

The method section should be clear and detailed enough.

Reply:

We thank the Reviewer for the positive comments on our study. We have followed your suggestions and made every possible effort to address the concerns. Detailed responses are below. Indeed, pharmacists are parts of MDT team in our setup, and this is a research according to routine pharmaceutical care: **(kindly see page 8),** "In the group of clinical pharmacists, two junior pharmacists (Y. Y. and W. W.) participated in the assessment of cancer pain and identification of DRPs, one senior pharmacist-in-charge (Y. S.) was responsible for checking DRPs as well as providing intervention and feedback. All the DRPs and subsequent recommendations were provided according to the National Comprehensive Cancer Network Adult Cancer Pain Guidelines (version 1.2018). At the initiation of a cancer pain patient's enrollment, pharmacists provided a comprehensive assessment (including pain characteristics, pain intensity, current analgesic strategy, medication adherence and adverse effects), and offered medication education. Afterwards, reassessments were conducted daily and weekly before and after pain control, respectively. During 28-day follow-up, patients were monitored for analgesic efficacy and safety by face-to-face interview during hospitalization, and were scheduled for receiving reassessment of cancer pain via telephone weekly after discharge. Due to a 48-hour window period for patients hospitalized at weekend, examination of these patients' prescriptions was performed within 48 hours from diagnosis of cancer pain. The clinical pharmacists identified and recorded possible DRPs using PCNE DRP classification V9.0. based on daily ward rounds with MDT, patient-pharmacist interview, as well as medication review. Accordingly, advices to optimize analgesic therapy were offered for physicians."

Specific comments:

APM ANNALS OF PALLIATIVE MEDICINE
AN OPEN ACCESS JOURNAL FOR HIGH-QUALITY RESEARCH IN PALLIATIVE MEDICINE

Comment 1:

Is there an intervention team? If not, how many clinical pharmacist/s are involved in the intervention? Who is/are going to declare the existence of actual or potential DRPs? Please specify in detail in method section.

Reply 1:

We are sorry for unclear statement about this issue. Actually, there is not an intervention team. Three clinical pharmacists were involved in the intervention, and responsible for declaring the existence of actual or potential DRPs. we have improved the statements of method section as follows **(kindly see page 8)**: **"**In the group of clinical pharmacists, two junior pharmacists (Y. Y. and W. W.) participated in the assessment of cancer pain and identification of DRPs, one senior pharmacist-in-charge (Y. S.) was responsible for checking DRPs as well as providing intervention and feedback." **(kindly see page 8)**: **"**A typical case was presented to describe the whole process of interventions by clinical pharmacists."

Comment 2:

What are your references used to identify and correct DRPs? Please specify the references used in the method section?

Reply 2:

We thank the Reviewer for the constructive suggestion about our study. As mentioned above, we have added the reference in the method section. **(kindly see page 8),** "The pharmacist identified DRPs and made suggestions mainly according to the National Comprehensive Cancer Network Adult Cancer Pain Guidelines (version 1.2018) (17)."

Comment 3:

Why you preferred examination of prescription within 48hrs of diagnosis?

Reply 3:

On weekdays, examination of prescription was completed within 24 hours of diagnosis, making it timely for identifying DRPs. But the pharmacist did not work on weekends, so there was a window period of 48 hours. Accordingly, we have added statements as follows **(kindly see page 8),** "Due to a 48-hour window period for patients hospitalized at weekend, examination of these patients' prescriptions was performed within 48 hours from diagnosis of cancer pain."

Comment 4:

You compared the results with other studies done elsewhere, but no justification for

discrepancies from other studies done. So, please justify appropriately the reasons behind.

Reply4:

We thank the Reviewer for the constructive suggestion about our study. As suggested, we have improved the statements as follows **(kindly see page 14)**: "To sum up, the DRP incidence found in our study was similar to that reported in cancer patients, but lower than that reported in cancer pain patients. It is possible that some of potential DRPs have been corrected by the clinical pharmacist during her 10-year pharmacy services in the ward. For instance, physicians in our MDT preferred to choose oral morphine or oxycodone rather than fentanyl patch as initial analgesics for opioid-naïve patients."; " In our study, medication education was carried out frequently for cancer pain patients during patient-pharmacist interview, resulting in a low proportion of "nonadherence or missed doses" in the causes of DRPs."

Comment 5:

Do you have data on comorbid medical conditions to include in your table?

Reply5:

We thank the Reviewer for pointing out this issue. This is a constructive suggestion, and comorbid medical conditions will be included in our future studies. This limitation has been added in the limitation part in revised manuscript **(kindly see page 17)**: Fourthly, comorbid medical conditions were not addressed in present study, and will be included in our future studies.

Comment 6:

Did you check an inferential statistics and other robust statistical analysis?

Reply6:

We thank the Reviewer for pointing out this issue. This is an exploratory research with limited sample size. Therefore, inferential statistic may not be meaningful and were not calculated. Further studies included control groups are necessary to be conducted.

Comment 7:

One of the clinical pharmacists' role is measuring the pain level and identifying some clinical diagnosis that is beyond medication reconciliation. Hence, why you excluded patients without confirmed cancer pain diagnosis, who might develop undiagnosed and untreated cancer pain as well.

Reply7:

The aim of present research is to evaluate the characteristics of drug-related problems (DRPs) in cancer pain patients, and to identify the impact of pharmacists' intervention in cancer pain associated DRPs. As the reviewer mentioned, one of the clinical pharmacists' role is assessing the pain level and identifying some clinical diagnosis that is beyond medication reconciliation. To ensure the consistency of the patients in our research and exclude the impact of clinical pharmacist before intervention, only patients with confirmed cancer pain diagnosis were included.

Reviewer B

Comment 1:

background

maintain the consistencies of observation use

it is not clear about the rational of conducting this study in the study setting. please revise and state at the end of the background section

Reply1:

We thank the Reviewer for the suggestive comments about background. As suggested, we have improved the statements as follows: "Of late years, DRPs has been growingly studied by pharmacists. Although patients with cancer pain are at a significant risk of DRPs, no DRP-related studies currently have been specifically addressed in cancer pain patients based on PCNE classification system in China (9,16)."

Comment 2:

Patients and methods

line 103: please correct the English

Reply2:

We have improved the statement as follows. **(kindly see page 7)**: "This is an investigative, single-arm intervention trial that conducted in a teaching hospital (Renji Hospital, School of Medicine, Shanghai Jiaotong University) in China."

Comment 3:

line 108: why diagnosis of cancer pain by the treating physician is considered as a n eligibility criteria?

Reply3:

The aim of present research is to evaluate the characteristics of drug-related problems (DRPs) in cancer pain patients, and to identify the impact of pharmacists' intervention in cancer pain associated DRPs. Indeed, clinical pharmacists also assess the pain level

and identify some clinical diagnosis that is beyond medication reconciliation. However, to ensure the consistency of the patients in our research and exclude impact of clinical pharmacist before intervention, only patients with confirmed cancer pain diagnosis were included.

Comment4:

line 109: why patients with invasive pain treatment (nerve block or patient-controlled analgesia) excluded from the study?

Reply4:

The purpose of this study is to discuss the pharmacological treatment of cancer pain, but the invasive pain treatment (nerve block or patient-controlled analgesia) is beyond the scope of pharmacists' intervention. Accordingly, we have added statements as follows: "As present trial focused on the pharmacological treatment of cancer pain, patients in case of invasive pain treatment (e.g., nerve block or patient-controlled analgesia) were excluded."

Comment5:

line 112: did u take written or oral consent to do the data collection. It was not mentioned in the manuscript

Reply5:

We appreciate the Reviewer for pointing out this issue. We have revised as follows **(kindly see page 7)**: "All patients have provided written informed consent."

Comment6:

the study design is not clear

the type of clinical pharmacist interventions should be stated under the method section

the sample size calculation and study design were not indicated in the method section

Reply6:

We are sorry for unclear statement about this issue. we have improved the statements of method section as follows **(kindly see page 7)**: "This is an investigative, single-arm intervention trial that conducted in a teaching hospital (Renji Hospital, School of Medicine, Shanghai Jiaotong University) in China. Because this is an exploratory research, the sample size was not calculated." **(kindly see page 8) "**A multi-disciplinary team (MDT), including physicians, nurses and clinical pharmacists, was consisted for medical care in the present study. In the group of clinical pharmacists, two junior pharmacists (Y. Y. and W. W.) participated in the assessment of cancer pain

and identification of DRPs, one senior pharmacist-in-charge (Y. S.) was responsible for checking DRPs as well as providing intervention and feedback. All the DRPs and subsequent recommendations were provided according to the National Comprehensive Cancer Network Adult Cancer Pain Guidelines (version 1.2018) (17). At the initiation of a cancer pain patient's enrollment, pharmacists provided a comprehensive assessment (including pain characteristics, pain intensity, current analgesic strategy, medication adherence and adverse effects), and offered medication education. Afterwards, reassessments were conducted daily and weekly before and after pain control, respectively. During 28-day follow-up, patients were monitored for analgesic efficacy and safety in face-to-face interview during hospitalization, and were scheduled for receiving reassessment of cancer pain via telephone weekly after discharge. Due to a 48-hour window period for patients hospitalized at weekend, examination of these patients' prescriptions was performed within 48 hours from diagnosis of cancer pain. The clinical pharmacists identified and recorded possible DRPs using PCNE DRP classification V9.0. based on daily ward rounds with MDT, patient-pharmacist interview, as well as medication review. Accordingly, advices to optimize analgesic therapy were offered for physicians." And **(kindly see page 8)**: **"**A typical case was presented to describe the whole process of interventions by clinical pharmacists."

Comment7:

Results

line 146-167: this way of data presentation is not scientific since it is not a case report. please revise it accordingly. if u want to state the whole process of the intervention, describe under the method section

Reply7:

Thanks for your advice and we have described it in the method section. **(kindly see page 8)**: **"**A typical case was presented to describe the whole process of interventions by clinical pharmacists."

Comment8:

line 170: if the authors enrolled study participants between November 2018 and November 2019, when did they make the intervention? Was it a retrospective study or what?

Reply8:

Actually, this is a prospective study. At the initiation of a cancer pain patient's enrollment, pharmacist's intervention was started and lasted till 28-day follow-up.

Therefore, enrollment and intervention were conducted simultaneously during November 2018 and November 2019. **(kindly see page 8)**: **"**At the initiation of a cancer pain patient's enrollment, pharmacists provided a comprehensive assessment (including pain characteristics, pain intensity, current analgesic strategy, medication adherence and adverse effects), and offered medication education. Afterwards, reassessments were conducted daily and weekly before and after pain control, respectively. During 28-day follow-up, patients were monitored for analgesic efficacy and safety by face-to-face interview during hospitalization, and were scheduled for receiving reassessment of cancer pain via telephone weekly after discharge. Due to a 48-hour window period for patients hospitalized at weekend, examination of these patients' prescriptions was performed within 48 hours from diagnosis of cancer pain."

Comment9:

line 173: The mean age of patients was 59 years old; the percentage of male was 66.7 and average. remove old after 59 years.

Reply9:

We accordingly have revised the statements as follows: "The mean age of patients was 59 years; the percentage of male was 66.7 and average education years were 9.31."

Comment10:

The aspect of English should be given due consideration through out the whole manuscript.

correct the flow of information in this section

Reply10:

We thank the Reviewer for pointing out language issue about our study. As suggested, we have invited a native speaker to make an improvement for our language and hope that the current version can meet the requirement for publication in APM. The revised sentences are presented with red marks.

Comment11:

Discussion

Revise the flow of information through the whole discussion and reason out the plausible explanation for any differences and similarities.

Reply11:

We thank the Reviewer for the suggestive comments about our study. As suggested, we added the statements in discussion section as follows **(kindly see page14): "**To

sum up, the DRP incidence found in our study was similar to that reported in cancer patients, but lower than that reported in cancer pain patients. It is possible that some of potential DRPs have been corrected by the clinical pharmacists during their 10-year pharmacy services in the ward. For instance, physicians in our MDT preferred to choose oral morphine or oxycodone rather than fentanyl patch as initial analgesics for opioid-naïve patients." "In our study, medication education was carried out frequently for cancer pain patients during patient-pharmacist interview, resulting in a low proportion of "nonadherence or missed doses" in the causes of DRPs." "In consistent with previous results, almost all interventions (99.4%) were accepted by prescribers or patients and 93.6% of DRPs were totally solved in our study, indicating the necessity and popularity of pharmaceutical care for physicians and patients."

Comment12:

line 230: Maral S, et al, Remove " s" after the Maral

Reply12:

Accordingly, we have revised the statement as follows **(kindly see page13):** "Maral et al also conducted a retrospective study at an academic medical center in Los Angeles, and indicated that 98.7% of pain clinic patients had one or more DRPs (18)."