Knowledge of opioid-induced respiratory depression among Chinese health care professionals: A cross-sectional study

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A B S T R A C T

Objective: The purposes of this study were to measure knowledge about opioid-induced respiratory depression (OIRD) among Chinese health care professionals and explore the associated factors that influence Chinese health care professionals’ knowledge.

Methods: A cross-sectional survey was conducted. A convenience sample of 900 Chinese health care professionals from 21 provinces, four municipalities, and four autonomous regions was used. The OIRD knowledge questionnaire, which is a self-designed questionnaire based on evidence, was used to judge the degree of knowledge among Chinese health care professionals according to the accuracy rate. The questionnaire included questions on six dimensions of knowledge. Sociodemographic characteristics were also measured by a multi-item questionnaire.

Results: The overall accuracy rate on the OIRD knowledge questionnaire for all participants were 64.5% ± 10.0% (mean ± SD) with a range from 20% to 100%. According to univariate analysis, Chinese health care professionals’ OIRD knowledge was positively correlated with age, region, profession, hospital level, type of hospitals and departments, education level, years of clinical working, and clinical practice of chronic cancer pain (CP) management. Multiple linear regression analysis showed differences in professions and regions (all P < 0.05).

Conclusions: Most Chinese health care professionals had misconceptions about OIRD and lacked relevant knowledge. We should assign importance to developing targeted training programs and exploring feasible and effective training methods.

Introduction

Pain is one of the most common symptoms among cancer patients and seriously affects their quality of life. According to statistics, the incidence of pain during treatment in cancer patients is approximately 55%. The incidence of pain in patients with advanced cancer is approximately 60%–80%, of which one-third of patients have moderate to severe pain. Chinese researcher Wang et al.2 conducted an investigation on the current status of cancer pain (CP) management in a population of 477 patients in 11 hospitals in Beijing. The results showed that there is still a relatively high proportion of patients with moderate to severe CP (65.82%). As one of the treatment drugs for moderate to severe pain, opioids are widely used in hospitalized patients with CP. While opioids relieve pain, they also cause many adverse drug reactions (ADRs).

Among them, opioid-induced respiratory depression (OIRD) is one of the most serious ADR to opioids. Rosenfeld DM et al.3 reviewed the use of naloxone in a tertiary hospital within 3 years and found that the incidence of OIRD in medical patients and surgical patients was 0.2% and 0.38%, patients with patient-controlled analgesia and epidural opioids infusion were high at risk at 1.2% and 1.31%. Gupta et al.4 reviewed 10 studies and concluded that the total occurrence of OIRD in postoperative patients was 0.5%. Although the incidence is not high, it may be life threatening once it occurs.

Medication safety is one of the goals of patient safety, and it is also the focus of medical institutions. The Joint Commission (TJC)5 and the Chinese Hospital Association6 specifically emphasized “To ensure drug safety, medical institutions should safely and strictly implement the use and management of special drug regulations.” Health care professionals play an important role in ensuring drug safety, including drug use, monitoring, and management. Management guidelines for OIRD have been formulated by many countries and institutions in domestic and foreign recent years. In them, the risk factors, diagnosis, prevention, and
management of OIRD are discussed. For example, the American Society for Pain Management Nursing (ASPMN) developed the “Guidelines on Monitoring for Opioid-induced Sedation and Respiratory Depression,” the American Association of Anesthesiologists developed the “Practice Guidelines for the Prevention, Detection, and Management of Respiratory Depression Associated with Neuropathic Opioids Administration,” and Chinese Medical Association Anesthesiology Branch developed the “Expert Consensus on Pain Management after Surgery in Adults” in 2014. Kamendat et al. implemented the ASPMN’s “Guidelines on Monitoring for Opioid-induced Sedation and Respiratory Depression” in a hospital, and in-hospital online educational resources were used to educate and train 324 nurses. The results showed that after the implementation of the guidelines, the number of occurrences of respiratory depression in the hospital decreased, and the nurses’ knowledge improved. The results suggest that the improvement in knowledge helps nurses identify OIRD early and take measures to prevent the occurrence of OIRD. Although there are many guidelines for OIRD, the correct implementation of health care professionals is closely related to their knowledge of OIRD. A cross-sectional study on opioid-related knowledge and attitudes among 133 nurses in the United States showed that nurses lacked knowledge about the risk of opioid addiction, monitoring, and management of respiratory depression, and disposal and storage of opioids. This situation may affect the ability of nurses to provide effective drug treatment and management to patients. At present, there are a number of studies on the knowledge and attitude of health care professionals on CP and opioids, but the knowledge of OIRD contained in them is very limited, so the results cannot fully represent the current situation of health care professionals on OIRD. In addition, studies have shown that health care professionals’ knowledge of CP and opioids are often influenced by factors such as demographics and experience in pain management.

At present, there is no investigation on the knowledge and influencing factors of OIRD in health care professionals. The purpose of this study was to measure Chinese health care professionals’ knowledge regarding OIRD and related factors and provide a basis for targeted training programs and safety of clinical opioids use.

Methods

Design, setting, and sample

This descriptive cross-sectional study included 900 health care professionals from the medical institution where the member of the Oncology Committee of the Chinese Nursing Society is located. They were selected using convenience sampling methods. The inclusion criteria were individuals aged >18 years who engaged in medical or nursing work, had physician qualifications or nurse qualifications, and volunteered to fill out the questionnaire.

According to the calculation formula for a cross-sectional study, \( n = \left(\frac{m \times S}{\delta^2}\right)^2 \), the study presumes that the standard deviation of the self-designed questionnaire’s accuracy is 12.6%, which is based on the results of 30 pretests, the allowable error is 0.012, which is 0.1 times the standard deviation, \( \alpha = 0.05, t_{0.05,2} = 1.96, \) and the sample size is approximately equal to 361. Considering an efficiency of 80% of the questionnaires, the minimum sample size was 451.

Instruments

Demographic data and OIRD’s knowledge information of the Chinese health care professionals were collected by a general information questionnaire and self-developed questionnaire about OIRD. The general information questionnaire was designed by the researchers based on a literature review, which included gender, age of health care professionals, area of work, grade and type of hospital, department, education level, work experience, CP-related training experience, and the average monthly frequency of managing patients with chronic CP.

The OIRD knowledge of Chinese health care professionals was assessed by a self-developed questionnaire about OIRD, which based on relevant guidelines and literature, such as Practice Guide, the United States Joint Committee developed ‘Sentinel Event Alert,’ and China issued “Expert Consensus on Pain Management in Adults after Surgery.” The questionnaire was reviewed and revised by two rounds of medical, anesthesia, and nursing experts. The members of the expert committee included one medical oncologist, one anesthesiologist, one pain physician, and three nursing experts, all with senior titles. The questionnaire includes 20 questions covering six dimensions, including the incidence of OIRD, judgment criteria, risk factors, preventive measures, close monitoring, and correct administration. The question types are true or false and single choice. The accuracy, ranging from 0 to 100%, represents the number of correct answers/the number of all questions. If the accuracy was more than 80%, this represented adequate knowledge and attitudes regarding OIRD.

Data collection

For preventing possible deviations, all data were submitted anonymously. If there was an omission, the system automatically jumped to the missing items after clicking ‘submit’ to ensure the integrity of the questionnaire. An electronic questionnaire was used to collect data, and before data collection, team members uniformly explained the purpose and significance of the research to the participants.

Data analysis

Database construction, data input, and data analysis were performed using IBM SPSS 25.0. The missing data included in the self-developed questionnaire about OIRD were random and were filled by manual method. According to the Chinese regional economic development and geographic location criteria issued by the State Council, health care professionals who participated in the questionnaire were divided into eastern, central, western, and northeastern regions. Means, standard deviations, frequencies, and percentages were used to describe the sample characteristics. Pearson correlation, independent sample t test, analysis of variance, and least-significant difference, post hoc tests, and multiple linear regressions were used to explore the related factors of OIRD accuracy. The accuracy of OIRD knowledge questionnaire was used as the dependent variable, and the variables with statistical significance in univariate analysis were used as independent variables for multiple linear regression analysis, enter regression analysis was used, \( \alpha_{in} = 0.05, \alpha_{out} = 0.10, \) and \( P < 0.05 \) was taken as the significant difference standard. Ordinal categorical variables were regarded as continuous variables for statistical analysis, and dummy variables were used for the analysis of unordered categorical variables. And final two-sided P-values < 0.05 were considered statistically significant.

Results

Description of the sample

Of the 900 health care professionals recruited from 21 provinces, four municipalities, and four autonomous regions in this study. Nine hundred questionnaires were used for the ultimate data analysis. The number of males was 60, and the number of females was 840. The average age was 33.15 ± 8.05 years old (mean ± SD), with a range from 20 to 80. Furthermore, 81.4% of health care professionals had a bachelor’s degree or above; 77.1% of health care professionals had worked for more than 5 years. Table 1 summarizes the health care professionals’ sociodemographic characteristics.

Self-reported knowledge regarding OIRD

The overall percentage of accuracy was 64.5% ± 10.0% (mean ± SD), with a range from 20% to 100%. Only 74 (8.1%) health care
professionals had an accuracy of more than 80%. The items of accuracy from high to low are listed in Table 2.

Factors associated with knowledge regarding OIRD

Health care professionals’ age was significantly and positively related to the OIRD knowledge questionnaire accuracy ($r = 0.94, P < 0.05$). The OIRD’s accuracy of health care professionals in the eastern, western, and central regions was higher. Moreover, the accuracy varied by grade and type of hospital, department, education level, work experience, and the average monthly frequency of managing patients with chronic CP. Among them, the higher the education level and grade of and hospitals, the higher the accuracy of the OIRD knowledge questionnaire. The more often that health care professionals take care of patients with chronic CP, the better knowledge they have (Table 2).

Professions and regions were independent of accuracy on the OIRD knowledge questionnaire and could jointly explain 12.1% of the Chinese health care professionals’ knowledge about OIRD when adjusted for region, education level, and work experience (Table 3).

Discussion

Although respiratory depression is one of the serious ADR to opioids, it is often overlooked because of its low incidence. Based on available evidence, this study designed an OIRD’s knowledge questionnaire to evaluate Chinese health care professionals’ knowledge, which included six dimensions: incidence of OIRD, judgment criteria, risk factors, preventive measures, close monitoring, and correct administration. The average accuracy was 63.62% ($\pm 8.2\%$). This finding shows that Chinese health care professionals have a poor grasp about the safe use of opioids and needs to be improved. Among them, knowledge of the OIRD was caused by opioid overdose. Some disease factors can increase the risk of OIRD, including lung diseases such as chronic obstructive pulmonary disease (COPD) or obstructive sleep apnea (OSA), diabetes, heart disease, and kidney or liver dysfunction. The results for this survey item 3 (correct rate 95.9%) and item 7 (correct rate 93.8%) show that health care professionals have a good grasp of this information.
The accuracy of items in the opioid-induced respiratory depression knowledge questionnaire.

| No. | Item content (correct answer) | Correct (n) | Accuracy (%) |
|-----|--------------------------------|-------------|--------------|
| 6   | For avoiding overdose with opioid, the patient's analgesic medication history and adverse reactions should be evaluated before a medical order is issued, and the skin should be thoroughly examined to rule out the use of fentanyl transdermal patches, implantable pumps, etc. (T) | 867 | 96.2 |
| 10  | Because excessive sedation precedes respiratory depression caused by opioids, the degree of sedation should be evaluated during the use of opioids. (T) | 865 | 96.0 |
| 3   | Patients with lung diseases such as COPD or OSA, taking opioids, are at increased risk of respiratory depression. (T) | 864 | 95.9 |
| 12  | The incidence of respiratory depression is highest within 24 hours after opioids analgesia treatment, and monitoring should be strengthened during this period. (T) | 859 | 95.3 |
| 2   | The criteria for determining respiratory depression caused by opioids include decreased respiratory rate (≤ 8 breaths/min), decreased blood oxygen saturation (< 90%), or increased end-tidal carbon dioxide partial pressure (> 50 mmHg). (T) | 856 | 95.0 |
| 7   | Patients who use opioids and have diabetes, heart disease, kidney or liver dysfunction, are at increased risk of respiratory depression. (T) | 845 | 93.8 |
| 11  | For patients who use opioids for the first time or after stopping the drug, use short-acting opioids to start titration from a low dose, and increase the drug dose after no adverse reactions. (T) | 837 | 92.9 |
| 9   | Anticonvulsants such as gabapentin and opioids can increase the risk of respiratory depression. (T) | 757 | 84.0 |
| 16  | To prevent respiratory depression caused by an opioid overdose in analgesia treatment, which of the following measures is wrong? (A) | 744 | 82.6 |
|     | A. Encourage patients to endure pain and minimize the use of opioids. | | |
|     | B. For patients who use opioids for the first time or after stopping the drug, use short-acting opioids to start titration from a low dose, and then increase the drug dose after no adverse reactions. | | |
|     | C. Even for opioid-tolerant patients to quickly and dramatically increase the dose to avoid. | | |
|     | D. When it is necessary to switch to another opioid or change the route of administration, perform an equivalent dose conversion. | | |
| 14  | The clinical manifestations of respiratory depression caused by opioids are not included which of the following options? (C) | 686 | 76.1 |
|     | A. Reduced respiratory rate (≤ 8 breaths/min) and/or reduced tidal volume, tidal breathing. | | |
|     | B. Needle-point pupils, lethargy, coma, cyanosis, skeletal muscle relaxation, clammy skin. | | |
|     | C. Tachycardia and hypertension. | | |
|     | D. In severe cases, apnea, deep coma, circulatory failure, cardiac arrest, death. | | |
| 5   | Sedative drugs, such as benzodiazepines, have analgesic effects and do not increase the risk of respiratory depression. (F) | 613 | 68.0 |
| 4   | The longer the patient uses opioids, the more likely they are to have respiratory depression. (T) | 469 | 52.1 |
| 1   | Patients who continue to use opioids analgesia for more than 1 month rarely develop respiratory depression. (T) | 468 | 51.9 |
| 19  | A 70-year-old patient with gastric cancer and malignant intestinal obstruction was admitted to the hospital with an NRS score of 9-10 for abdominal pain. He was given intravenous morphine treatment and was evaluated 2 hours later. It was found that the patient was frequently drowsy, awakened, and fell asleep during conversation. The following incorrect approach is (C) | 444 | 49.3 |
|     | A. Close monitoring of respiratory status and sedation level. | | |
|     | B. Consider reducing the opioids dose 25%-50%. | | |
|     | C. Stop opioids immediately. | | |
|     | D. If there are no special contraindications, instruct the patient to take a deep breath every 15-30 minutes. | | |
| 20  | A 70-year-old patient with gastric cancer and malignant intestinal obstruction was admitted to the hospital with an NRS score of 9-10 for abdominal pain. He was given continuous morphine injection by PCA. After evaluation 2 hours later, the patient was found to be lethargic, slightly responding to physical stimulation, and breathing less than 8 Times/min, check the pupils with pinpoint. The following approach is incorrect: (B) | 408 | 45.3 |
|     | A. Stop opioids immediately. | | |
|     | B. High concentration oxygen. | | |
|     | C. Rescue with naloxone. | | |
|     | D. Close monitoring of respiratory status and sedation level. | | |
| 8   | For patients with pain while dying, the amount of opioids should be minimized to avoid respiratory depression. (F) | 355 | 39.4 |
| 13  | A patient with persistent cancer pain has been receiving daily opioids analgesics for 2 months. Yesterday the patient was receiving morphine 200 mg/hour intravenously. Today he has been receiving 250 mg/hour intravenously. The likelihood of the patient developing clinically significant respiratory depression in the absence of new comorbidity is: (A) | 228 | 25.3 |
|     | A. < 1% | | |
|     | B. 1%-10% | | |
|     | C. 11%-20% | | |
|     | D. 21%-40% | | |
| 15  | Risk factors that cause opioid-induced respiratory depression do not include: (D) | 223 | 24.8 |
|     | A. Preoperative drunk ASA grade > II or general anesthesia time is relatively long | | |
|     | B. PCA postoperative analgesia | | |
|     | C. Elderly and obese patients | | |
|     | D. Taking opioids for a long time | | |
| 18  | The patient was 65 years old and returned to the ward after lung cancer surgery. He was given oxygen inhalation via a nasal catheter and opioids analgesia via PCA. Which of the following monitoring indicators could not detect opioid-induced respiratory depression early? (C) | 156 | 17.3 |
|     | A. Breathing rate | | |
|     | B. Sedation level | | |
|     | C. Finger tip oxygen saturation | | |
|     | D. End-tidal carbon dioxide partial pressure | | |
| 17  | The most important predictor of respiratory depression in patients receiving opioids therapy is: (C) | 74 | 8.2 |
|     | A. Breathing rate | | |
|     | B. Patients reported pain intensity | | |
|     | C. Sedation level | | |
|     | D. Blood pressure | | |

ASA, American Society of Anesthesiologists Physical Status; COPD, chronic obstructive pulmonary disease; NRS, numerical rating scale; OSA, obstructive sleep apnea; PCA, patient-controlled analgesia.

* The item is a judgment question. T stands for right and F stands for wrong.

* The item is a single choice.
In addition, factors related to combined medication cannot be ignored. The guidelines suggest that the simultaneous use of central inhibitory drugs and opioids can increase the risk of OIRD, including anticonvulsants and benzodiazepines. The results for research item 9 (correct rate 84%) and item 5 (correct rate 68%) show that health care professionals do not have a good grasp of this information. In particular, for the item, “The simultaneous use of benzodiazepines and opioids can increase the risk of respiratory depression,” the accuracy was only 68%. Yu et al. conducted a survey of CP knowledge and attitudes among 505 oncology nurses and found that “whether benzodiazepines have analgesic effects and whether they can be used as routine analgesic drugs in combination with analgesics.” The accuracy among health care professionals was 36.3%. There was a general misunderstanding among health care professionals that benzodiazepines can be used in combination with analgesics for analgesia, but they ignore the risk of increased respiratory depression. In pain treatment, although it may be beneficial to use benzodiazepines in CP patients with anxiety, it is not recommended for routine pain treatment.

It is worth noting that items 1 (correct response rate 51.9%), 4 (correct response rate 52.1%), and 15 (correct response rate 24.8%) examined the relationship between opioid use time and respiratory depression. The results show that health care professionals generally believe that the longer the use of an opioid is, the more likely they are to develop respiratory depression. However, this situation was not the case. The TJC pointed out that patients who use opioids for the first time or who restart after stopping are at a higher risk of respiratory depression. In the treatment of chronic CP, the existence of such misunderstandings by health care professionals limits the use of opioids or increases the dose for pain patients, resulting in poor pain management.

OIRD has predictable risk factors and risk groups. It is very important to use correct preventive measures. This study shows that health care professionals comprehensively evaluate the current use of opioids and other drugs before issuing a medical order and have a good grasp of information about cautious titration and dosage. However, what is worrying is that item 1 shows that 17.4% of health care professionals agree that “patients should be encouraged to endure pain and minimize the use of opioids.” In particular, item 8 examines the health care professionals’ consideration of respiratory depression in a patient’s near-death analgesia. The results showed that 60.6% of health care professionals believed “for patients who are dying with pain, the amount of opioid should be minimized to avoid respiratory depression,” and the results are worrying. Bonnie Freeman mentioned in her book “Compassionate Person-Centered Care for the dying” that progressive loss of consciousness is a manifestation of the death process, not an ADR of opioids, especially those who have been tolerant of opioids. It is inhuman for patients in the near-death stage whose death is in distress and unable to die with dignity because of fear of accelerated death.

Items 12 and 18 show that postoperative patients are prone to respiratory depression, which requires health care professionals to monitor the degree of sedation. However, only 8.2% of health care professionals understand that “the most important predictor of respiratory depression in patients who are receiving opioid therapy is the sedation level.” Most health care professionals do not know that the sedation level can be quantitatively assessed and can predict the occurrence of respiratory depression. In addition, the results of item 18 show that only 17.3% of health care professionals understand that for patients inhaling oxygen, fingertip oxygen saturation monitoring cannot detect respiratory depression early. Thompson et al. conducted a prospective study on 211 patients to understand the timing of ADR. The results showed that opioid-induced sedation usually occurs between awareness and respiratory depression before respiratory depression appears. Close monitoring is very important. The “Guidelines on Monitoring for Opioid-Induced Sedation and Respiratory Depression” developed by ASPMN pointed out that the sedation level is a sensitive indicator for predicting respiratory depression, and nurses should monitor and evaluate patients. For patients taking oxygen, fingertip blood oxygen saturation monitoring cannot detect respiratory depression early. Because fingertip blood oxygen saturation is an alternative oxygenation measurement method and cannot measure ventilation, the ability to identify respiratory depression is limited. It also needs to be determined in conjunction with capnography.

Once OIRD occurs, it may be life threatening, and it is very important for health care professionals to master correct administration. Item 19 uses a case to investigate whether health care professionals can take correctly respond with measures based on the sedation level. The results showed that the correct response rate was only 49.3%. Item 20 examines how health care professionals correctly rescue the patient when OIRD occurs. Conventional treatment methods, such as the use of naloxone, are well-mastered, but only 45.3% of health care professionals know “whether to give high-concentration oxygen inhalation.” High-concentration oxygen inhalation will cause a hypoxia reflex to stimulate respiration to disappear, thereby increasing respiratory depression, leading to carbon dioxide retention, and even respiratory arrest. The “Practice Guidelines for the Prevention, Detection, and Management of Respiratory Depression Associated with Neuropsychiatric Opioid Administration” developed by the American Association of Anesthesiologists recommends that patients with altered levels of consciousness, respiratory depression, or hypoxemia should be given routine oxygen at a low flow that continues until the patient is conscious and has no respiratory depression or hypoxemia.

A single factor analysis of the knowledge of Chinese health care professionals shows that health care professionals in different regions have different knowledge of OIRD. The knowledge of health care professionals in the central and western regions is better than that of the northeastern region. Considering the findings, on the one hand, the sample size from the central and western regions included is less than that of the northeastern region, and the smaller sample size cannot fully reflect the overall situation. On the other hand, medical institutions and technology in these areas have advantages. There are many cancer patients and many opportunities for health care professionals to participate in the management and practice of OIRD. The results show that doctors’ knowledge of OIRD is better than that of nurses, which is similar to the survey results from Yu et al. on CP knowledge. This finding may be because domestic CP diagnosis and treatment is dominated by doctors, and the organizational model with nurses as the main body is still in the preliminary exploration and development stage, and there are fewer opportunities for nurses to receive training. The knowledge of oncology health care professionals is better than that of nononcology health care professionals and the knowledge of health care professionals with more clinical experience and experience in managing CP patients is better than that of health care professionals with less experience and a lack of management experience with CP patients. This finding suggests that the experience of health care professionals participating in clinical practice can improve their knowledge of OIRD.

Table 3
Factors associated with the accuracy of the opioid-induced respiratory depression knowledge questionnaire in multivariate analysis (n = 900).

| Factors          | Unstandardized coefficients (B) | Standard error (SE) | Standardized coefficients (β) | t    | P     |
|------------------|---------------------------------|---------------------|-------------------------------|------|-------|
| Constant         | 0.762                           | 0.056               | –                             | 13.541 | 0.001** |
| Profession       | –0.410                          | 0.013               | –0.134                        | –3.132 | 0.002* |
| Northeast region | –0.050                          | 0.011               | –0.212                        | –4.594 | 0.000** |

R² = 0.121; adjusted R² = 0.107; F = 8.644; P < 0.001. *P < 0.05. **P < 0.001.
Further multiple linear regression analysis showed differences in professions and regions, suggesting that in the future, relevant training programs should focus on nurses, especially nurses with insufficient clinical practice experience, to promote their professional role in improving opioids safety. $\Delta R^2 = 0.107$; this result suggested that occupation and region accounted for 10.7% of the OIRD's accuracy in Chinese health care professionals. There are other factors that have not been explored, and this is the direction of future research.

**Limitations**

Convenience sampling was used in this study, and the health care professionals adopted the principle of voluntary participation. The sample distribution across the country and gender are uneven. In the future, a cluster sampling method should be used to make the results more representative.

**Conclusions**

Health care professionals play an important role in the prevention, monitoring, and management of OIRD. The results of this research indicate that Chinese health professionals have insufficient knowledge and need to be improved. Further exploration of effective intervention measures to improve the knowledge of the prevention and management of OIRD in health care professionals and to promote the safety of opioids use is the focus of future research.

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**Declaration of competing interest**

None declared.

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Nil.

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