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Process Management of Analgesia and Sedation Can Reduce the Incidence of Delirium

Hao Wang[1], Shaolong Yi[1], Hu Wang[1], Minying Chen[2*]

[1]Department of the Second Intensive Care Unit, The First People's Hospital of Kashi District, Kashi, China
[2]Department of Surgical Intensive Care Unit, The First Affiliated Hospital of Sun Yat-sen University, Guangzhou, China
Email: *chmy1969@hotmail.com

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Abstract

Background: Critical patients in ICU have to experience pain, anxiety, and sleep deprivation which always cause delirium, which will prolong the hospital stay and come up with higher mortality. Analgesia based sedation can reduce the accumulation of sedative effects, and shorten ventilator time and ICU length of stay. Process management of analgesia and sedation can reduce the incidence of delirium. **Objectives:** To explore the clinical benefits of procedural analgesia and sedation for critical ill patients. **Methods:** This is a prospective, two-phase study that focuses on patients who required mechanical ventilation after surgery. Comparing patients' pain and agitation scores, the species and dosage of sedative and analgesic, the incidence of delirium in the observation period and intervention period, data in two groups were collected and analyzed. **Results:** During the observational and interventional periods, we enrolled 213 patients before protocol implantation and 196 patients after protocol implantation. We found that there existed impropriate pain and sedation assessment in patients involved, and after training for procedural protocol, the average dosage of sedatives was decreased ($p > 0.05$). The percentage of reaching standard COPT score was 73.7% vs 84.1% ($p > 0.05$) and RASS score was 70.9% vs 79.6% ($p > 0.05$) in the observation period and intervention period, and the incidence of delirium was significantly reduced (31.9% vs 23.5%, $p < 0.05$). **Conclusion:** We concluded that protocol implantation of analgesia and sedation can reduce the incidence of delirium.

Keywords

Procedural, Analgesia, Sedation, Intensive Care Unit, Delirium

1. Introduction

Critical patients in ICU have to experience pain, anxiety, and sleep deprivation

which always cause mental disorder, namely delirium. Delirium is defined as an acute disturbance in attention and awareness with additional disturbances in cognition, with the exception of a pre-existing neurocognitive disorder [1], and is the most common mental complication in critically ill patients and associated with increased length of stay and long-term cognitive impairment. Chronic pain, sleep deprivation, and long hospital stay in ICU always put patients into high risk of delirium. Thus, the alleviation of pain and anxiety is an important component of ICU treatment strategies. The goals of analgesia and sedation are to minimize physical discomfort and pain, control anxiety, thus reducing the stress response and catabolism and reducing delirium [2]. The ideal state of patient under analgesia and sedation is comfortable, cooperative and calm. Insufficient analgesia and sedation can cause unexpected complications such as unplanned extubations [3] and exceeded analgesia and sedation can cause prolonged ventilation [4]. Delirium is also related to inappropriate analgesia and sedation. Currently accepted protocol of analgesic and sedation is analgesia first, with minimized sedation to avoid unexpected deep sedation [5]. Due to the close connection between delirium, agitation and pain, finding the best strategy of analgesia and sedation is urgent.

In this study, we first investigated the implementation of analgesia and sedation in ICU patient without intervention, and then compare the incidence of delirium after training medical staff for a standard analgesia and sedation procedure, aiming to find an appropriate strategy for analgesia and sedation in ICU patient and reduce the appearance of delirium.

2. Data and Methods

2.1. Patients

The inclusion criteria including the following: older than 18 years, need mechanical ventilation and agree to participate in this study. Exclusion criteria included the following: neurologic diseases, with liver or renal failure, drug abuse, pregnant, any situation not suitable for analgesia and/or sedation, patients who need deep sedation, and short-term expected mortality.

2.2. Methods

2.2.1. Study Design

The study was a prospective, two-phase (before-after), non-randomized and involved in patients who required mechanical ventilation after surgery. The first phase of this study was a two-month observational phase followed by data analysis in which none standard analgesia and sedation protocol was designed, and the level of pain and agitation, and whether needs to adjust medication was evaluated according to the experiences of the nurses. And then a two-month of interventional phase was applied after nurse and medical training for a fixed process of medication adjustment and pain and agitation assessment. Data in two groups were collected and analyzed.

2.2.2. Procedural Analgesia and Sedation

The second phase of analgesia and sedation protocol was as following: the basic analgesia and sedation score was proceeded immediately on patients' admission to ICU, and then started medication with minimum dose. Analgesia and sedation score were played every 30 min for the first hour, and adjusted medication according to the score to achieve the target score, then do the assessment every 30 min after medication adjustment. If target score was achieved continuously twice, then do the assessment every 2 h, and if target score was achieved continuously twice after, do the assessment every 4 h, and do the assessment every 6 h if target score was achieved continuously twice until the study was over.

2.2.3. Data Collection and Assessment Tools

The following data in the two groups were collected: patient baseline, the type and dosage of analgesics and sedatives administered, analgesia and sedation score, the occurrence of delirium. The analgesic score used was Critical care pain Observation tool (CPOT score), and the sedative score used was Richmond Agitation-Sedation Scale (RASS score). The target analgesia score was CPOT < 3, and target sedation score was −2 - 1. CAM-ICU score was used for delirium assessment every day.

2.2.4. Outcome Measures

The primary outcome was the incidence of delirium. The second outcome were the percentage of reaching analgesic and sedative target score, the species and dosage of sedative and analgesic in different periods.

2.2.5. Statistical Analysis

All numerical data are expressed as the mean ± standard deviation. Student's t test was used to compare the mean between the two groups, and chi-square test was used to compare the incidence between the two groups. $p < 0.05$ was considered to indicate a statistically significant difference. SPSS 22.0 software (IBM SPSS, Armonk, NY, USA) was used to do statistical analysis.

3. Results

3.1. Characteristics

During the observational and interventional periods, we enrolled 213 patients in the observational group and 196 patients in the interventional group. The baseline characters of patients in two groups had no statistical difference (Table 1).

3.2. Different Types of Analgesic and Sedatives between the Two Periods

Fentanyl and Sufentanil were the most frequently used drugs for analgesia and sedation. Other medication included propofol, midazolam, Remifentanil, morphine. The type of drugs used in two phases had no statistical difference (Table 2).

Table 1. Baseline characters of patients.

Variables	Before intervention	After intervention	*p* value
Male	119	113	>0.05
Age	66 ± 21	64 ± 19	>0.05
APACHE II	17 ± 5	19 ± 3	>0.05
Operation type			
Trauma	132	126	>0.05
Vascular surgery	13	8	>0.05
Abdominal surgery	27	23	>0.05
Other surgery	41	39	>0.05

Table 2. Type of medications in different periods.

Variables	Before intervention	After intervention	*p* value
Analgesic			
Fentanyl	132	118	>0.05
Sufentanil	56	54	>0.05
Remifentanil	25	24	>0.05
Sedatives			
Dexmedetomidine	104	116	>0.05
Propofol	50	39	>0.05
Midazolam	59	41	>0.05

3.3. Different Doses of Analgesic and Sedatives between the Two Periods

The assessment of pain and sedation were proceeded 2.9 ± 3.3 times per day in observational patients and 7.6 ± 2.1 times per day in intervention patients. We compared the average rate and average daily dose of dexmedetomidine and remifentanil, and even though no statistical significantly, trend of less dose of dexmedetomidine was observed in the intervention group ($p > 0.05$) (Table 3).

3.4. Rate of Reaching Analgesic and Sedative Target and Incident of Delirium

Before intervention, the percentage of achieved COPT score was 73.7% (157/213) and RASS score was 70.9% (151/213). After the procedural implantation, the percentage of achieved COPT score was 84.1% (165/196) and RASS score was 79.6% (156/196), $p > 0.05$. Meanwhile, 68 patients (31.9%) presented delirium before intervention, as 46 patients (23.5%) presented delirium after intervention ($p < 0.05$), significantly (Table 4).

In summary, after the implantation of standardized analgesia and sedation procedures, the types of drugs used for critical ill patients did not change, and the drug dosage showed a little decreased, but there was no significant difference. The rate to reaching the target of analgesia and sedation had a tendency to

Table 3. Dose of main medication in different periods.

Variables	Before intervention	After intervention	*p* value
Dexmedetomidine (μg/kg/h)	0.65 ± 0.16	0.57 ± 0.17	>0.05
Fentanyl (ug/h)	52 ± 1.4	46 ± 1.7	>0.05

Table 4. The percentage of analgesia and sedation target score and incident of delirium in different periods.

Variables	Before intervention	After intervention	*p* value
CPOT score	73.7% (157/213)	84.1% (165/196)	>0.05
RASS score	70.9% (151/213)	79.6% (156/196)	>0.05
Delirium	31.9% (68/213)	23.5% (46/196)	<0.05

increase, without significant difference. But the incidence of delirium was significantly reduced.

4. Discussion

In this two-phase study we found that procedural analgesia and sedation protocol can reduce delirium and optimize the effect of analgesia and sedative. In the observation phase, there assessment of pain and sedation was done almost every 8 h per day on average, and quite a few patients did not acquire appropriate pain relief or sedation. After training of procedural protocol, the assessment increased to nearly 8 times per day and more than 80% of patients acquire suitable analgesia and sedation. Meanwhile, the incidence of delirium was also decrease significantly following procedural protocol.

Nearly 40% percent of patients aged 65 or more developed into delirium during ICU stay [6]. Patients with delirium will have cognitive dysfunction and prolonged hospital stay, and also come up with higher mortality [7]. Risk factors of delirium including age, infection, length of hospital stay, sleep deprivation, the use of opioids and benzodiazepines [8]. Given these reasons, guidelines have recommended strategies for preventing and treating pain, agitation, and delirium [8].

Analgosedation was defined as analgesia-first sedation to make treatment pain a priority in providing sedatives, aiming to achieve and maintain a mild level of sedation [9]. Primary studies have demonstrated that analgosedation can reduce the accumulation of sedative effects, shortened ventilator time and ICU length of stay [10]. Use of non-benzodiazepine sedatives was approved to be associated with decreased incidence of delirium [11], and proper pain management, through routine assessment and monitoring of pain scale, improves the prognosis of patients treated in the ICU [8].

Present guidelines do not give recommendations about the frequency to do the assessment, and medical staff can only do this according to their experiences. High frequency of assessment may improve the effect of pain relief and the inci-

dence of delirium, but it also brings some problem, such as increase the workload of nurses, and is difficult to achieve especially in the area where there exists shortage of medical staff. In addition to this, the frequency of assessment should base on the characteristics of the medications (*i.e.* long term or short term, the elimination half life). And how to adjust the dosage of the drug according to the present assessment score is also a great challenge.

Even if the negative outcome between classical and novel ant-delirium medications in delirium prevention which were latest published in New England journal of medicine [12], our study proved that procedural analgesia and sedation can reduce the incidence of delirium, and provide a possible protocol for pain and sedation, and recommended that once analgesia and sedation was proceeded on a patient, a protocol for assessment and medication adjustment should be accomplished. The protocol should be individual according to the manpower, the type of drugs and the experiences of clinician and nurses.

5. Conclusion

Delirium has poor effect on the prognosis for critical ill patients. Drug intervention doesn't effectively reduce the incidence of delirium. Our study shows that procedural analgesia and sedation can reduce the incidence of delirium. The protocol for assessment and medication adjustment should be accomplished individually according to the manpower, the type of drugs and the experiences of clinicians and nurses.

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Conflicts of Interest

There are no conflicts of interest.

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