



Original Article

Investigating the effect of the CPOT-based pain management program on the pain intensity and dose adjustment of analgesics in mechanically ventilated patients: A randomized clinical trial

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ARTICLE INFO

Received 08 April 2023

Accepted 07 June 2023

Available online at:
<http://npt.tums.ac.ir>

Keywords:

critical care pain observation tool;
pain management;
analgesics

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ABSTRACT

Background & Aim: This research was conducted to determine the effect of a pain management program based on the Critical Care Pain Observation Tool (CPOT) on the pain intensity and adjusting the dosage of analgesics in mechanically ventilated patients hospitalized in intensive care units.

Methods & Materials: This randomized controlled clinical trial was conducted during 2019-2022 on 70 mechanically ventilated patients admitted to ICUs of the Imam Reza Hospital, Mashhad, Iran. In the intervention group, patients' pain intensity was measured during endotracheal suctioning using CPOT. Then the dosage of analgesics was adjusted based on the assessed pain level. The pain level was evaluated in the control group according to the department's routine. Data were analyzed using two-way repeated measures analysis of variance (RMANOVA).

Results: CPOT and BPS showed a strong correlation ($r>0.9$, $Pvalue<0.001$) between the two pain intensity instruments. Based on the results of RMANOVA, a significant trend of pain intensity measures was observed during all three suctionings (measurement effect $P<0.05$), which was different between the two groups (interaction effect $P<0.05$). The Sidak post hoc test results showed a significant difference in pain intensity measures between the intervention and control groups during all three suctionings and 5 and 15 minutes after suctionings (all P -values <0.05). Also, significant intervention effects were observed regarding the amount of analgesics prescribed in terms of total fentanyl blouse, total infused Fentanyl, and total Fentanyl (all P -values <0.05).

Conclusion: Using CPOT is a positive step in the evaluation and control of dosage adjustment of analgesic medications for patients with mechanical ventilation.

Introduction

Accurate assessment and management of pain in critically ill and ventilated patients is very challenging for physicians and nurses (1). More than 75% of patients who are admitted to intensive care units (ICUs) have pain during admission, and approximately 50-74% of ICU patients experience moderate to severe pain (2, 3, 4).

Improper pain management of mechanically ventilated patients can induce adverse side effects such as extubation by the

patient, changes in vital signs, release of neuro-endocrine hormones, hypotension, reduction of tissue perfusion, suppression of the immune system, anxiety, agitation, increase in mortality, increase in the duration of connection to the ventilator and unsuccessful separation of the patient from the ventilator (5, 6).

Although there are standard pain management guidelines, pain remains a major problem in the ICU and needs to be evaluated and improved (2, 4, 7). In previous studies, it

Please cite this article as: Kouhi F, Froutan R, Bagheri Moghaddam A. Investigating the effect of the CPOT-based pain management program on the pain intensity and dose adjustment of analgesics in mechanically ventilated patients: A randomized clinical trial. *Nursing Practice Today*. 2023; 10(3):208-218



has been shown that the pain in patients hospitalized in the ICU is not well controlled during the procedures, and more than 50% of critically ill patients in the ICUs experience pain (8), which is due to several factors such as endotracheal tube suctioning, changing the position, wound and chest tube management, and inserting or removing catheters and drains (9, 10).

Prescribing analgesics medications requires correct estimation of pain intensity by nurses. Patients connected to ventilators are not able to verbally communicate and express their pain due to various reasons such as intubation, reduced levels of consciousness, and receiving sedative drugs (9, 11). According to the results of a systematic review, in 70% of the studies, it is stated that pain is either not diagnosed or not treated adequately (4). Therefore, for the management and control of pain, multiple evaluations of pain and individual treatment based on the observation of the patient's condition are needed (8), and this depends on the systematic and correct examination of pain for guidance and the use of analgesics (9).

Pain identification is a fundamental, professional, and legal responsibility of physicians and nurses. Failure in pain diagnosis and management may induce legal and professional problems. Studies showed that nurses often do not estimate patients' pain and do not use analgesics based on the patients' needs (5).

Approximately 35-55 percent of nurses estimate the patients' pain is less than its actual intensity (11). Therefore, the proper management of pain depends on the measurement, evaluation, systematic, and correct examination of pain to choose the correct type of analgesics and adjust their required dosage (12).

Nurses can conveniently use vital signs to evaluate the changes in the patient's status and a significant measure for pain assessment. According to a previous study, over 70% of ICU nurses utilized vital signs

for pain evaluation (13). But some researchers believe that vital signs are unreliable indicators for pain assessment (14).

Therefore, using pain tools to find out the intensity of pain in the patients and reduce it has special importance (15, 16, 17, 18). In clinical guidelines, the Behavior Pain Scale (BPS) and Critical Care Pain Observation Tool (CPOT) are recommended by experts, so they are valid for critically ill patients (19). The CPOT scale evaluates four parameters: facial expression, body movements, mechanical ventilation, and muscle tone. The parameter is assigned a score of zero, one, or two based on the severity of the occurrence. Then the total score of each patient is calculated from 8 points, the highest pain intensity, which helps reduce the need for analgesics (20). BPS consists of three components: facial expression, upper limbs, and compliance with ventilation. This scale includes three main sections, rating from one to four. The minimum score is 3, while the maximum is 12 (21).

Considering the importance of pain management in mechanically ventilated patients who are hospitalized in the ICUs and the need to prescribe analgesics, the present study was conducted to answer the question of whether the use of CPOT can affect the amount of analgesics consumption and pain relief/intensity in patients with a reduced level of consciousness.

Methods

Study design

Randomized controlled clinical trial

Participants

The study was carried out on 70 patients who were admitted to two ICUs (ICUs C and D) of Imam Reza Hospital in Mashhad.

Inclusion criteria

Age 18 to 65 years, intubated (for at least 24 hours), mechanically ventilated with $1 \leq \text{RASS} \leq 3$, absence of neuromuscular disease history, lack of muscle relaxants medications, no history of epilepsy, no history of alcohol consumption or psychotropic drugs, $\text{MAP} > 65$ who receives an infusion of analgesics medications, and homogeneity of Apache-II and SOFA scores for patients.

Exclusion criteria

Obtaining a score greater than/equal to 1- according to RASS criteria, extubation during the study, changing the analgesics prescribed by a physician, discontinuation of prescribed analgesics, significant reduction in the level of consciousness, transfer to another department or hospital, and death of patients.

Randomization

Eligible patients were randomly assigned into two groups of intervention ($n=35$) and control ($n=35$) using www.randomizer.org.

Blinding

This study was conducted in a double-blind manner. The statistical consultant who is responsible for the random allocation of patients, the patients, and the study outcome assessor is unaware of the group allocation.

Control group

In the control group, pain intensity was assessed based on the BPS tool and physiological indicators (heart rate, breathing, systolic and diastolic blood pressure, SPO₂) before, during, 5, 15, and 30 minutes after the procedure tracheal suction. Incensement of 20% of each vital sign, such as systolic blood pressure and heart rate, showed the need for fentanyl administration that was adjusted in the range determined by the physician.

Intervention group

Before the intervention, the ICU nurses who consented to participate in this study were trained in using the CPOT and the pain management protocol based on the CPOT during a one-hour session.

Then, they were asked to measure the patient's pain level with CPOT, before and during painful procedures, 5, 15, and 30 minutes after tracheal suction. Based on the pain assessment, the nurses adjusted the dosage of prescribed analgesics in the range determined by the doctor. If $\text{CPOT} = 3-5$, 25 mcg of Fentanyl and $\text{CPOT} = 6-8$, 50 mcg of Fentanyl were administered as a bolus. This process was done for 6 hours in the morning shift. Along with each pain assessment, the patient's vital signs, including blood pressure, pulse, and percentage of oxygen saturation of arterial blood, were recorded.

The basic level of patients' restlessness was measured using Richmond Agitation Sedation Scale (RASS) for all patients in both groups.

Outcome measurement

The dosage of analgesics received in the form of infusion and bolus.

The pain intensity of the patients was evaluated with the CPOT scale.

Statistical analyses

Statistical analysis was conducted by IBM SPSS Statistics software [ver.28] (IBM SPSS Statistics, Armonk, NY, USA). The normality of the numeric variables was checked by Kolmogorov-Smirnov test. Data were presented using mean (SD) for the Numeric Normal variables and frequency (percent) for categorical variables. The between-group comparisons of baseline measures and demographic variables were carried out by independent t-tests, Mann-Whitney tests, and Fisher-Freeman-Halton Exact tests where appropriate. For pain intensity outcomes, as the

primary outcome, we carried out the two-way analysis of variance with repeated measures (two-way RMANOVA) to assess the main effects of measurement and intervention and their interaction effect. For two-way RMANOVA, the Mauchly test assessed the sphericity assumption, and then multivariate Wilks lambda was used to correct the deviation from the assumption. To assess the effect of the intervention on the number of analgesics prescribed as the secondary outcome, the analysis of covariance (ANCOVA) was used after controlling for background characteristics as covariates (baseline adjusted). All analyses used a per-protocol approach, and P-values less than 0.05 were considered significant.

Ethical consideration

This trial was registered at the Iranian Registry of Clinical Trials (IRCT code: IRCT20201222049801N1). Also, The

approval of the Research Ethics Committee of Mashhad University of Medical Sciences was obtained under the code IR.MUMS.NURSE.REC.1399.101. The principles of confidentiality and informed consent were observed carefully.

Results

Patients' flow

Patient flow in this study involved the recruitment of 135 patients. Initially, 65 patients were excluded, with 40 not meeting the inclusion criteria and 25 declining participation. Subsequently, 70 patients were assigned to either the intervention group (n=35) or the control group (n=35). No participants discontinued the intervention in either group (intervention group: n=0, control group: n=0). Finally, 60 patients (intervention group: n=35, control group: n=35) were included for analysis (Diagram 1).

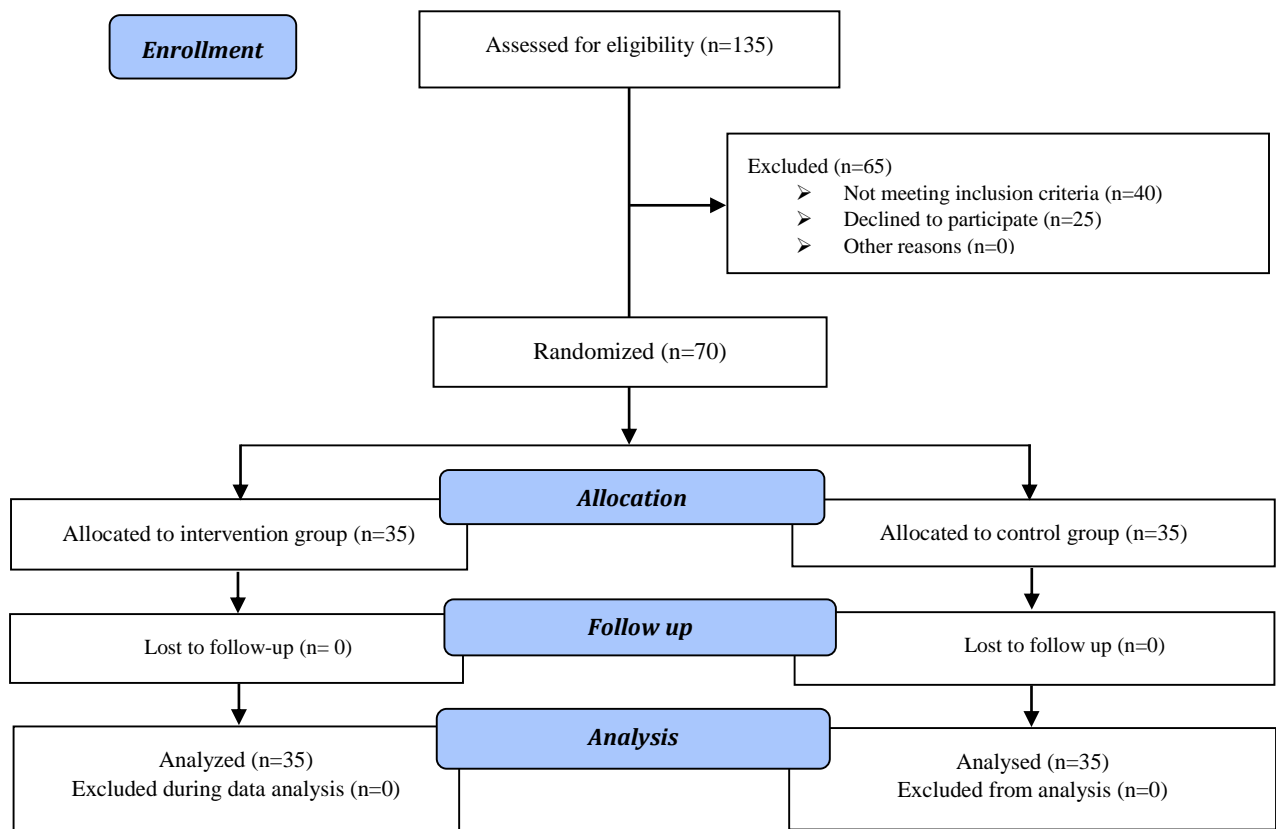


Diagram 1. CONSORT flow diagram

Effect of the pain management program on pain

Patients characteristics in intervention and control groups

Table 1 presents the profile of the patients in this study. The findings indicated no significant differences between the intervention and control groups regarding the background variables (all $P > 0.05$).

Regarding the baseline measurements of vital signs, including heart rate (HR),

respiratory rate (RR), systolic blood pressure (SBP), diastolic blood pressure (DBP), oxygen saturation (SPO₂), and mean arterial pressure (MAP) during all three rounds of suction, no significant differences were found between the intervention and control groups (all $P > 0.05$) (Table 1).

In addition, CPOT and BPS showed a strong correlation ($r > 0.9$, $P < 0.001$) between the two pain intensity instruments.

Table 1. Patients profile and baseline vital signs in intervention and control groups

Variables	Intervention (n=35)		Control (n=35)		P-value
	N/Mean/Median	%/SD/IQR	N/Mean/Median	%/SD/IQR	
Gender					
Male	19	54.29%	17	50.00%	>0.999*
Female	17	48.57%	17	48.57%	
Disease					
Pneumonia	21	60.00%	21	60.00%	0.433*
Chronic obstructive pulmonary disease	9	25.71%	12	34.29%	
Systemic	5	14.29%	2	5.71%	
Disease history					
No history	17	48.57%	4	11.43%	0.060*
Diabetes	22	62.86%	13	37.14%	
Hypertension	7	20.00%	13	37.14%	
Other	7	20.00%	8	22.86%	
RASS					
-3.00	13	37.14%	14	40.00%	0.807*
-2.00	22	62.86%	21	60.00%	
Suction measures					
19.00	3	8.57%	1	2.86%	0.615*
20.00	32	91.43%	33	94.29%	
21.00	0	0.00%	1	2.86%	
Frequency of suction					
2 times	10	28.57%	5	14.29%	0.247*
3 times	25	71.43%	28	80.00%	
Age (years)	56.61	6.37	58.59	4.11	0.130**
Hospital duration (days)	8.778	2.03	8.41	2.56	0.508***
Apache2	13.89	1.98	13.03	1.78	0.061**
GCS	9.889	0.71	9.82	0.72	0.702***
Sofa	6.861	0.59	6.53	0.79	0.053***
HR at baseline	97.14	33.24	91.03	33.25	0.058**
RR at baseline	17.11	1.72	16.62	3.13	0.413**
SBP at baseline (mmg)	112.5	22.78	120.79	22.6	0.131**
DBP at baseline (mmg)	69.5	12.45	71.94	9.02	0.353**
SPO₂ at baseline (percent)	92.64	6.43	94.68	5.85	0.170**
MAP at baseline (mmHg)	83.03	22.1	89.24	19.76	0.220**

*Fisher's exact tests

**Independent t-tests

*** Mann-Whitney tests

The effect of the intervention on pain intensity

Based on the results of the repeated measures analysis of variance (RMANOVA), a significant trend in pain intensity measures was observed during all three suction sessions (all measurement effects $P < 0.05$). Furthermore, this trend differed between the two groups, indicating a significant interaction effect (all interaction effects $P < 0.05$). The results also revealed a significant difference in pain intensity measures between the intervention and control groups for all three sections (all intervention effect P values < 0.05) (Table 2).

The detailed results of pain intensity measures are presented in Figures 1-3. During all three suction sessions, the Sidak post-hoc tests showed no significant difference between the intervention and control groups in terms of baseline pain intensity measure. However, significant differences were observed between the intervention and control groups at the suction time, after 5 minutes, and after 15 minutes (all $P < 0.05$). Specifically, patients in the intervention group reported higher pain intensity at the suction time but experienced lower pain intensity at 5 minutes and 15 minutes after suction. Eventually, both groups reached the same level of pain after 30 minutes of suction (all $P > 0.05$).

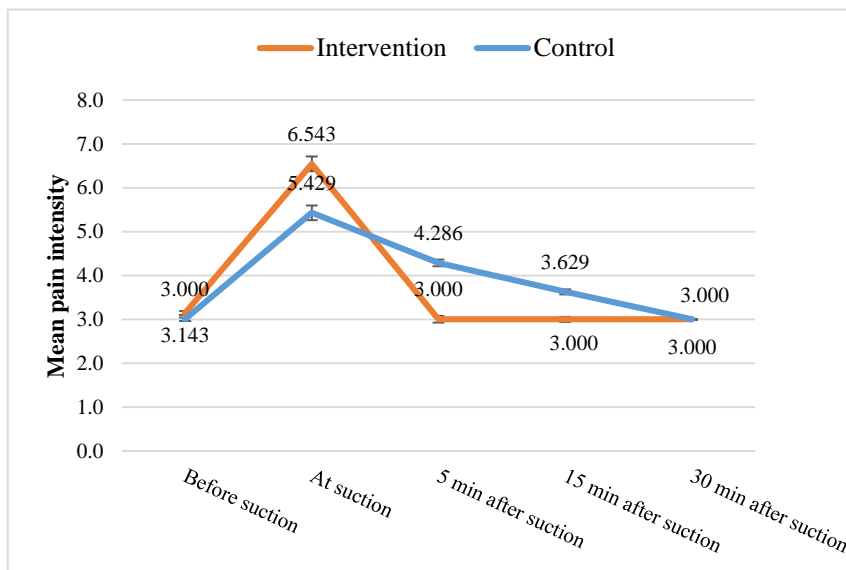


Figure 1. Changes in pain intensity measurements across intervention and control groups (1st suction)

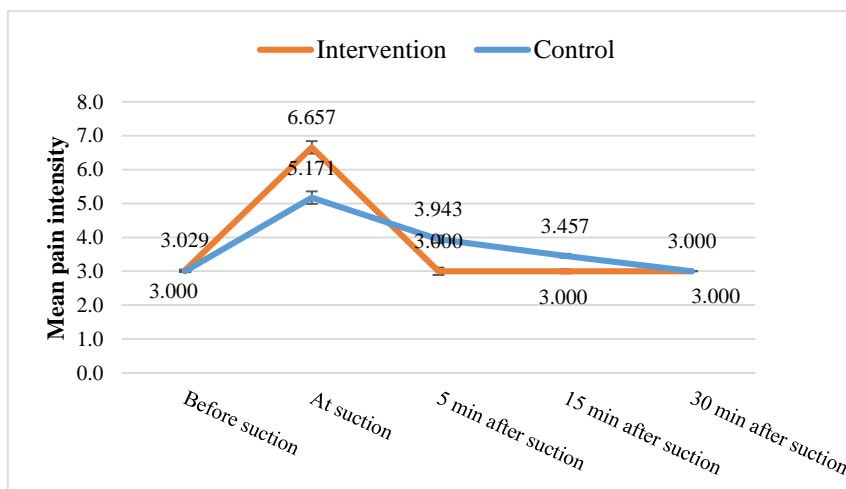


Figure 2. Changes in pain intensity measurements across intervention and control groups (2nd suction)

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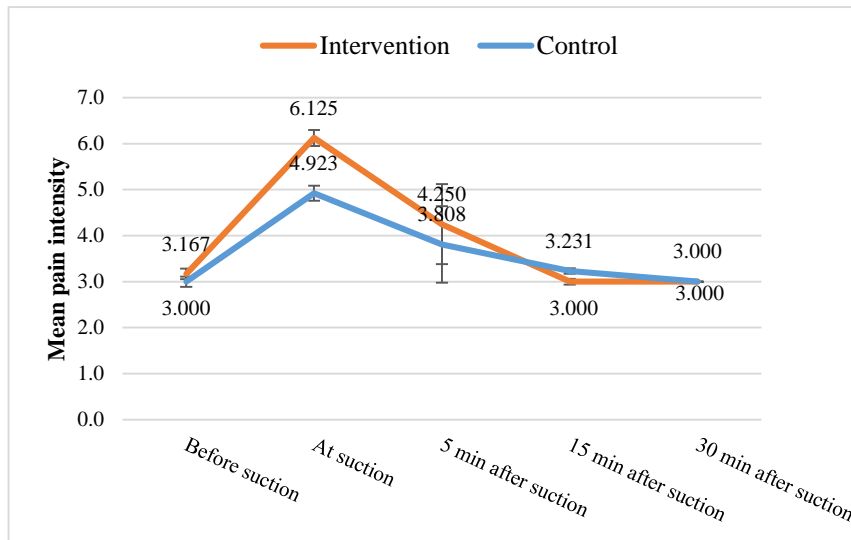


Figure 3. Changes in pain intensity measurements across intervention and control groups (3rd suction)

Table 2. The effect of the intervention on pain intensity measures

Variables	Intervention effect P-value	Measurement effect P-value	Interaction effect P-value
Pain intensity at first suction	0.038	<0.001	<0.001
Pain intensity at the second suction	0.044	<0.001	<0.001
Pain intensity at the third suction	0.047	<0.001	<0.001

Based on two-way analysis of variance with repeated measures (two-way RMANOVA)

The effect of the intervention on the number of analgesics prescribed

The comparison of the amount of prescribed analgesics is provided in Table 3. The results indicated no significant difference between the intervention and control groups regarding the initial prescription of Fentanyl (Pvalue>0.05). Furthermore, after controlling for patients' characteristics in the covariance (ANCOVA) analysis, the results remained unchanged.

However, significant differences were observed between the intervention and control groups regarding the amount of analgesics prescribed in total Fentanyl (blouse), total Fentanyl (infused), and total Fentanyl (all Pvalues<0.05). These significant differences persisted even after controlling for patients' characteristics in ANCOVA. Specifically, patients in the control group received a significantly lower amount of fentanyl blouse but were treated with significantly higher amounts of infused Fentanyl and Fentanyl overall (Table 3).

Table 3. The effect of the intervention on analgesics prescribed

Variables	Intervention (n=35)		Control (n=35)		Mean difference (95% CI)	P-value*	P-value**
	Mean	SD	Mean	SD			
Fentanyl First	52.14	11.13	52.13	7.10	0.01(-4.53 to 4.54)	>0.999	0.659
Total Fentanyl (blouse)	82.85	26.96	0.00	0.00	82.85 (73.76 to 91.95)	<0.001	<0.001
Total Fentanyl (Infusion)	171.42	53.25	312.85	42.60	-141.43 (-164.43 to -118.43)	<0.001	<0.001
Total Fentanyl	254.28	35.08	312.85	42.60	-58.57 (-77.19 to -39.96)	<0.001	<0.001

* Independent t-tests

** Analysis of covariance adjusted for background characteristics

Discussion

Due to the nature of the disease and routine procedures such as endotracheal suctioning, the mechanically ventilated patients are at a higher risk of not being diagnosed and treated their pain. These patients need continuous evaluation, appropriate treatment, and assessment for effective pain management. For adequate pain control, the first step is to diagnose pain intensity, which should be measured with a valid and reliable method. For this reason, the above study was conducted to determine the effect of using CPOT and BPS on the pain management of patients with reduced levels of consciousness hospitalized in intensive care units.

Our results showed that mechanically ventilated patients with depressed levels of consciousness experienced the highest pain level during suctioning. Considering that the fentanyl infusion for patients was based on the measurement of both BPS and CPOT scales, and the patients had no pain before the painful procedures, but during the suction time, even with the fentanyl infusion, the patients experienced pain (from moderate to severe). The study's results by Gomarverdi et al. (2019) also emphasized that without the infusion of analgesics, patients experience pain even while resting and performing any care measures (22).

Regarding the severity of tracheal tube suction pain, a study conducted in 2008 on patients hospitalized in the intensive care unit is in line with the results of the present study because the results indicated that in the study of pain, during the time of performing the procedures Common and uncommon treatments in the intensive care unit (such as suctioning secretions, removing the drain from the wound site or from the femur area, before and after suctioning secretions), moderate to severe pain was reported in the majority of patients (93%). Suctioning

secretions as A painful treatment was reported in the intensive care unit (23).

Other results of this study show that in the intervention group, during suctioning, according to the setting of fentanyl judgment based on pain instruments, the patients had a lot of pain. At the same time, the fentanyl drug, which was adjusted based on the pain intensity based on CPOT, was infused for them as a bolus dose. And 5, 15, and 30 minutes after the drug infusion, the pain intensity decreased, and there was no pain. But in the control group, due to the infusion of a high dose of Fentanyl before suctioning, based on physiological indicators (heart rate, breathing, systolic and diastolic blood pressure, SPO2), their pain intensity during suctioning did not increase significantly compared to the intervention group. Therefore, we conclude that patients have high pain during suction and fentanyl bolus should be injected into patients before suction, as shown by the results of the study by Duzkaya and his colleagues (2015), patients who bolus doses of sedative drugs and had received analgesics before performing endotracheal suction, they had a lower pain score after performing suction (24).

Contrary to this study, the study of Novoa and his colleagues showed that patients who receive narcotic, analgesic, and non-steroidal anti-inflammatory drugs in the form of a bolus dose one hour before endotracheal suction have a higher pain score during endotracheal suction than before (23), which was in contrast with the present study, the reasons for which can be pointed to the time of onset of the drug effect and the maximum effect of narcotic drugs, so the duration of the effect of narcotic drugs such as Fentanyl is between half an hour and after one hour in suction pain is not effective.

Another outcome of our study was the amount of fentanyl drug consumption, which was significantly lower in the

intervention group than in the control group. These findings show that the CPOT tool leads to better pain management, followed by a reduction in the use of sedatives in patients with a reduced level of consciousness.

Another finding of this study is the use of a bolus dose of Fentanyl in the intervention group by identifying episodes of severe pain, which has reduced the basic dose of Fentanyl during its continuous infusion, so with this method, patients have received narcotic drugs according to the protocol. In this regard, the results of the studies of Arbor et al. (2011) (25), Rose et al. (2013) (26), and Wibbenmeyer et al. (27) have similar results in the implementation of CPOT for pain management in ICUs.

Also, the studies of Lucki et al. (2015) (28) and Chanques et al. (2010) (29) showed that the use of the CPOT tool tends to reduce the average daily sedative dose for propofol, lorazepam, midazolam, and dexmedetomidine, which is reported by the study. This finding was consistent with our results, with the difference that Fentanyl was used in the present study for pain management.

Therefore, in general, it can be concluded from the present study and previous studies that the CPOT and BPS scales are suitable indicators for determining the presence and intensity of pain in patients who, for any reason, are unable to communicate or express pain. This index can be of special importance in patients under mechanical ventilation.

Diagnosing the pain and its severity in intubated patients might reduce the pain and prescribe analgesics dosage, which results in improving the patient's condition and speeding up the patient's extubation. Among the limitations of this current study, we can point out the low sample size and not investigate other factors affecting the patients' pain. Although many studies are needed in this field, according to the

discussions, we recommend that the CPOT be used more widely in mechanically ventilated patients.

Conclusion

The present study showed that the CPOT is suitable for determining the presence and intensity of pain and reducing the number of narcotic drugs in patients with a reduced level of consciousness. On the other hand, tracheal tube suction is considered a painful procedure. In order to reduce the pain caused by it, we should assess and examine the pain based on pain measurement scales.

Previous studies evaluated the pain intensity caused by endotracheal tube suctioning mainly after the procedure. The experience of the researchers of the present study indicates that the patient's pain has the most intensity during the procedure. Therefore, it seems that administration of analgesics should be done before suctioning. Therefore, it is suggested that further studies should be conducted to investigate the effect of analgesic administration before endotracheal tube suctioning on the pain intensity of patients.

Acknowledgment

The present study was derived from a thesis in Master of Nursing, Mashhad University of Medical Sciences, School of Nursing and Midwifery. The authors' most profound appreciation goes to all the patients involved in the study, the respected authorities of Imam Reza Hospital, the research deputy of Mashhad University of Medical Sciences, and the School of Nursing and Midwifery.

Conflict of interests

The authors declare no conflict of interest.

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