

Original Article

Evaluation of Pain Assessment and Management in Critically Ill Intubated Patients in a Referral University Hospital in Iran

Babak Alikiaie¹, Sarah Mousavi², Ali Ebrahimi³, Zahra Foroughi⁴

¹Department of Anesthesiology and Intensive Care, Alzahra Hospital, Isfahan University of Medical Sciences, Isfahan, Iran

²Department of Clinical Pharmacy and Pharmacy Practice, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, Iran

³School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, Iran

⁴Intensive Care Unit, Alzahra Hospital, Isfahan University of Medical Sciences, Isfahan, Iran

Received: 14-10-2018.

Accepted: 28-01-2019.

Published: 16-10-2019.

ABSTRACT **Objective:** This study aims to evaluate current pain assessment and management in critically ill patients and to describe (1) pain management episode, according to the behavioral pain scale (BPS), and (2) the effectiveness of analgesics, according to the recommendation of guidelines. **Methods:** In this cross-sectional study, a sample of 60 intubated critically ill patients was selected from the intensive care units (ICUs). A researcher evaluated the patient's pain severity using the BPS tool in patients receiving analgesics according to nurses' note. At each time of analgesic administration, the BPS score was recorded, and this process was repeated 72 h later. The appropriateness of pharmacological interventions was assessed according to the American College of Critical Care Medicine guideline. **Findings:** The most prescribed analgesic was morphine sulfate (48.3%) followed by fentanyl (23.3%). 55% of analgesics on day 1 and 25% on day 3 were prescribed appropriately according to the guideline recommendation and BPS score. Morphine was the most effective drug (17 patients out of 29). Even though a BPS score was <5, 26 patients received analgesics. **Conclusion:** Quality of pain assessment and management in our setting is inappropriate and inadequate, which leads to over- or under-use of analgesics. The lack of an established pain protocol may contribute to this situation.

KEYWORDS: Critically ill, pain, pain assessment, pain management

INTRODUCTION

The International Association for the Study of Pain defines pain as an unpleasant sensory and emotional experience associated with actual or potential tissue damage.^[1] Different studies have indicated that between 10% and 50% of adult hospitalized patients experience moderate-to-severe pain, and this has a negative impact on different levels.^[2-4] In critically ill patients, pain is a significant problem. About 30%–50% of patients in the intensive care units (ICUs) experienced moderate-to-severe pain.^[5] Multiple sources such as underlying health disease, trauma, and routine care procedures contributed to pain development in the ICUs.^[6] Untreated pain can result in negative consequences, including multisystem complications and development of chronic disabling pain.^[7] Since pain is multidimensional and subjective,^[8] the patient's self-report is the gold standard for assessment; however,

in ICU, some factors and patient's condition, including endotracheal intubation, reduced level of consciousness, sedation, and administration of paralyzing drugs can alter verbal communication and make pain assessment difficult.^[9] Appropriate pain management has been shown to reduce the length of hospitalization and cost of care. Appropriate assessment is the first step in managing pain. For this purpose, many objective pain measurements have been developed to assess pain in nonverbal adult patients in ICUs. Some of such pain assessment tools include facial expression (FE), Critical-Care Pain Observation Tool (CPOT), nonverbal pain scale, faces, legs, activity, cry, and scale, behavioral pain scale (BPS), and pain assessment in advanced dementia.^[9,10]

Address for correspondence:

Dr. Sarah Mousavi, E-mail: s.mousavi@pharm.mui.ac.ir

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

How to cite this article: Alikiaie B, Mousavi S, Ebrahimi A, Foroughi Z. Evaluation of pain assessment and management in critically ill intubated patients in a referral university hospital in Iran. *J Res Pharm Pract* 2019;8:137-42.

Access this article online	
Quick Response Code: 	Website: www.jrpp.net
	DOI: 10.4103/jrpp.JRPP_18_81

In 2013, the American College of Critical Care Medicine recommended using these two tools, BPS and CPOT, for evaluating pain in tracheal intubated and unconscious patients.^[11] This guideline recommended against the use of vital signs (or observational pain scales that include vital signs) in pain assessment in adult ICU patients. Further, the guideline recommended the intravenous (IV) opioids as the first-line drug class of choice to treat nonneuropathic pain in critically ill patients. Alongside, the use of nonopioid analgesics to reduce the amount of opioid administration and side effects is recommended too.

The BPS is based on the sum of three subscales consisting of behavioral domains: FEs, upper limb movements, and compliance with mechanical ventilation. Each domain contains four descriptors that are rated on a scale of 1–4. The total BPS score can range from 3 (no pain) to 12 (most pain). The guideline recommended that patients with BPS score >5 should be received treatment.^[12]

Pain assessment and management in ICU patients need to be a priority with routine monitoring, assessment, reassessment, and clear documentation done to facilitate treatment and communication among healthcare members. The only regular method in evaluating pain in ICU patients in our hospital was an FE and the only item studied in this method was the patient’s face. There are no pain flow sheets in the patient’s medical records. Physicians prescribe analgesics as a “pro re nata (PRN)” method and nurses administered the drug (mostly opioids) according to the FE of patients and some physiological signs (such as increased heart rate or decrease of oxygen saturation). There is no documentation of pain assessment and management in critically ill intubated patients in our hospital. There is a lack of established protocols in clinical settings for pain assessment and management. Limited studies in Iran showed that using pain control protocol can control pain in patients hospitalized in ICU.^[13] Thus, this study aimed to evaluate current pain assessment and management practice in ICU patients with its goal to describe pain management episode according to BPS and describe the effectiveness of pharmacological interventions according to BPS score and recommendation of the guideline.

METHODS

A cross-sectional study was conducted in a single center from October 2017 to March 2018. The study population consisted of consecutive patients admitted to the ICUs in Alzahra Hospital (Isfahan, Iran), a tertiary-level university-affiliated hospital with 60 ICU beds. The institutional ethical committee approved the study (code number: 396554).

All admitted patients who aged >18 years and were under mechanical ventilation for at least 72 h were included in this study. Exclusion criteria were quadriplegia, receiving neuromuscular blocking agents, and extubation earlier than 72 h.

In this study, the consecutive sampling method was used. Patients who met the inclusion criteria entered the study. In the study period, 60 patients with the inclusion criteria were evaluated using convenient sampling method.^[14]

The data collection tool was organized to collect two types of data: (1) general and medical information and (2) pain assessment and management. In the first section, demographic information including age, gender, medical history, admission diagnosis, type of surgery, type of trauma, history of addiction, and drug abuse was included.

In the second section, the medical file of patients was evaluated by a researcher, and if it contained analgesics and sedatives, the BPS form that included FE, upper limb movements and compliance with mechanical ventilation was scored and completed by the researcher and specific accompanying nurse [Table 1]. Physiologic signs including systolic and diastolic blood pressure, pulse and respiratory rate, and consciousness level (according to Glasgow coma scale) collected by the researcher from medical file of the patients and recorded by the monitoring device were also recorded.

If the patient received analgesics according to the nurse’s note, the researcher and the colleague nurse evaluated patient’s pain severity using BPS tool and recorded the obtained score in the data collection tool. On day 1 of a patient’s evaluation, BPS score was recorded at two

Table 1: Behavioral pain scale used for the study patients^[9,10]

Score	Description	Item
Score 1	Relax	Facial expressions
Score 2	Partially tightened (for example, brow lowering)	
Score 3	Fully tightened (for example, eyelid closing)	
Score 4	Grimacing	Upper limbs
Score 1	No movement	
Score 2	Partially bent	
Score 3	Fully bent with finger flexion	
Score 4	Permanently retracted	Compliance with the ventilator
Score 1	Tolerating ventilator	
Score 2	Coughing but tolerating ventilator in most of the time	
Score 3	Fighting with ventilator	
Score 4	Unable tolerating ventilator	

The lowest score 3 and the highest score 12

times, when patients received analgesics. This process was repeated on day 3 (after 72 h). In addition to BPS score, the dose, interval, and route of administration of analgesics were recorded too.

The levels of agitation and sedation were recorded in a patient medical file using Richmond agitation sedation scale (RASS)^[15] in 4 h interval in nurse's note [Table 2]. At each time of pain episode evaluation, the RASS score and the data on the sedative drug (dose, interval, and route of administration) were also recorded simultaneously by a researcher. The physiologic signs recorded at each time of pain episode evaluation.

The nonpharmacological interventions including positioning and physical patient restraint were recorded as well.

The researcher-recorded analgesic data were used during patient hospitalization until death or discharge. The type of medicine, dose, and transition between analgesics were recorded.

The appropriateness of analgesic administration was interpreted according to the American College of Critical Care Medicine^[11] guideline and obtained BPS score. According to the guideline, the patient is in significant pain if the BPS >5 and IV opioid analgesics are the first lines of therapy. In the case of BPS <5, if the patient received analgesic, it is considered as inappropriate. If the RASS score is between -2 and 0, the target sedation is achieved. In case of RASS >0, the patient is undersedated, and if the RASS < -2, the patient is oversedated.

The analysis was performed using SPSS 23.0 for Windows Statistical Software (SPSS Inc., Chicago, Illinois, USA). To describe data, the mean and standard deviation for continuous variables and number (percentage) for categorical variables were used.

RESULTS

Sixty participants were included in this study. Most of the patients were male (70%), with a mean age of 53.9 ± 19.7. The majority of the patients (78.3%) were intubated via an endotracheal tube, and the rest of them were intubated via tracheostomy. The most common admission diagnosis was intracerebral hemorrhage (21.7%). 25% of our patients had a history of addiction [Table 3].

As shown in Table 4, the most prescribed analgesic was morphine sulfate (*N* = 29, 48.3%) followed by fentanyl (*N* = 14, 23.3%). 66.7% of our patients received midazolam as a sedative agent. Most of the analgesics were administered intravenously (81.7%)

Table 2: Richmond agitation sedation scale^[15]

Score	Definition	Description
+4	Aggressive and irritable	The patient is very nervous and aggressive and can be dangerous for the nurse
+3	Very agitated	The patient pulls and takes out tubes and catheters and has violent behavior
+2	Agitated	The patient has purposeless and repetitive movements. Patient's ventilation is not on the synchronizing system
+1	Restless	The patient is anxious and restless but he/she does not show aggressive and violent movements
0	Awake and relax	The patient is completely awake and relaxed
-1	Sleepy (lethargic)	The patient is not completely conscious, but can awaken more than 10 s and can open his/her eyes with verbal request

Table 3: Characteristics of the patients (n=60)

Variables	Results
Age (years), mean±SD (range)	53.9±19.7 (18-89)
Sex, male/female	42/18
Admission diagnosis, <i>n</i> (%)	
ICH	13 (21.7)
Multiple trauma	8 (13.3)
SDH	6 (10)
SAH	4 (6.7)
CVA	3 (5)
Gastrointestinal bleeding	3 (5)
Pulmonary thromboembolism	2 (3.3)
Others	21 (35)
Surgical intervention, <i>n</i> (%)	42 (70)
Craniotomy	31 (73.8)
Laparotomy	5 (11.9)
Others	6 (14.3)
Airway situation, <i>n</i> (%)	
Intubation	47 (78.3)
Tracheostomy	13 (21.7)
History of Addiction, <i>n</i> (%)	
Addicted to opioids	10 (16.7)
Addicted to alcohol	1 (1.7)
Not clear	4 (6.6)
Length of stay (days), mean±SD (range)	45.6±41.8 (3-185)
Survival, death, <i>n</i> (%)	28 (46.7)

CVA=Cerebrovascular accident, ICH=Intracerebral hemorrhage, SAH=Subarachnoid hemorrhage, SDH=Subdural hematoma, SD=Standard deviation

and every 6 h (35%). The mean dose of administered analgesics was 3.1 ± 2.3 mg/day. A small percentage of patients (10%) received analgesic medications by continuous infusion.

Two hundred and forty pain episodes were evaluated in this study. According to the American College of Critical Care Medicine guideline and BPS score [Table 5],

Table 4: Characteristics of analgesics and sedatives which were used during patients' hospitalization (n=60)

Parameters	n (%)
Type of analgesics	
Morphine	29 (48.3)
Fentanyl	14 (23.3)
Methadone	12 (20)
Morphine + fentanyl	4 (6.7)
Morphine + methadone	1 (1.7)
Type of sedatives	
Midazolame	40 (66.7)
Midazolame + diazepam	6 (10)
Midazolame + quetiapine	3 (5)
No sedation	11 (18.3)
The dose of analgesics, mean±SD (range)	3.1±2.3 (0.05-10 mg)
Route of administration	
Intravenous	49 (81.7)
Intramuscular	8 (13.3)
Subcutaneous	3 (5)
Interval of administration	
Every 6 h	21 (35)
Every 8 h	14 (23.3)
Every 4 h	9 (15)
Every 3 h	6 (10)
Every 12 h	4 (6.7)
Continuous infusion	6 (10)

SD=Standard deviation

Table 5: Mean levels of behavioral pain scale and Richmond agitation sedation scale scores during the study

	Mean±SD (range)			
	Pre-BPS	Post-BPS	Pre-RASS	Post-RASS
Day 1	4.8±1.5 (3-9)	4.3±1.4 (3-10)	-2.1±2.3 (-5-2)	-2.4±2.2 (-5-2)
Day 3	4.5±1.5 (3-9)	4.2±1.3 (2-7)	-2.1±2.3 (-5-3)	-2.2±2.2 (-5-2)

BPS=Behavioral pain scale, RASS=Richmond agitation sedation scale, SD=Standard deviation

55% of analgesics on day 1 and 25% on day 3 were prescribed appropriately. The appropriate prescribing was 26.7% and 20% on day 1 and 3 for sedatives.

According to analgesic efficacy (BPS <5 after analgesic administration), the prescribed analgesics were efficient at 50% of pain episodes in total. Morphine was the most efficient drug (17 patients) followed by methadone ($N = 4$) and fentanyl ($N = 6$). Despite a BPS <5, 26 patients received analgesics. Further, regarding the sedative efficacy (RASS score between -2 and 0), the prescribed sedatives were efficient at four patients. Thirty-one patients had RASS<-2 which means oversedation. Despite an RASS >0, four patients received sedative drugs.

Among the 15 addicted patients (mostly opioid), four patients received morphine, three patients received methadone, and three patients combination of analgesics during the period of pain evaluation.

The most common observed physiologic parameter was tachypnea in patients with pain, and the least was hypotension.

Physical restraint ($N = 24$) has been the most often used nonpharmacological intervention to relieve pain. Positioning and use of endotracheal suctioning were other interventions to mostly sedate agitated patients.

DISCUSSION

The results of this study show inappropriate pain management in critically ill intubated patients. This is consistent with the findings of previous research in the same area. As we mentioned, our hospital settings have not established a protocol for both pain assessment and management. Therefore, the analgesics use is very high in our settings as the lack of routine and correct pain assessment. Nurses do not use pain assessment tools for pain evaluation; this often leads to under or over the treatment of pain. Our physicians prescribed analgesics as "PRN" without any condition or definition of pain severity. Therefore, we observed many patients with severe pain who do not receive analgesics and vice versa many patients without pain who received analgesics.

As the pain assessment tools were not used within our setting, it mostly occurs that for the agitated patients, the analgesic was administered and nurses related the agitation as a pain episode. Furthermore, physiologic parameters such as changes in heart rate or blood pressure interpreted as a pain episode and patients receive analgesics.

Although we have not established pain protocols, studies show that even in setting with protocols, pain assessment and management are inadequate. In a prospective study in Jordan, Ayasrah *et al.*^[16] evaluated 301 medical records of critically ill intubated patients regarding pain assessment and management by both nurses and physicians. Results show that only 105 (35%) of total reviewed medical records contained pain assessment data. Observable indicators documented 98% of the 115 pain episodes. Between 87% and 46% of 115 pain episodes, pharmacological and nonpharmacological interventions for pain management were documented. Only 37% of the pain episodes were reassessed with self-report (1%) and observable indicators (36%) to determine the effectiveness of the interventions. In a similar retrospective study by Gélinas *et al.*,^[17] a total of 183 pain episodes in 52 intubated patients were

analyzed. Observable indicators were recorded 97% of the time; pharmacological interventions were used 89% of the time that nonpharmacological intervention (<25%) for managing pain. Pain reassessment was done in 60% of the time, and observable indicators were recorded 66% of the time. Patients' self-report was recorded only 8% of the time.

Lack of an established protocol leads to both overuse of analgesics and many transitions between analgesics in our patients. Soltani *et al.*,^[18] in the study in the same hospital of our study, reviewed 1024 medical records and showed that the consumption of parenteral opioids was high with a defined daily dose (DDD) of 730.51. The surgery ward and emergency department had the most amounts of use based on the number of DDDs (445.8 DDDs). This amount was 17.96 DDDs in ICUs of our hospital. In 61% of evaluated profiles, nursing reports were in agreement with physician orders. The reasons of disagreement were as follows: drug administration without any physician order (11%); wrong dosage (9%); wrong dosage interval (8%); no administration of the ordered drug (8%), and administration of morphine instead of meperidine and vice versa (3%). As the authors of this study emphasized, the discrepancy between a physician's order and nursing practice increases the risk of medical errors and treatment failure. Our results confirm this discrepancy. Hence, the development of a local protocol for pain assessment and management or adherence to international guidelines is mandatory in our setting to reduce medical errors and improve the rational use of drugs.

Studies using pain assessment tools and management protocol in ICUs showed improved routine assessment of pain and better use of analgesic agents and sedatives, as well as a decrease in the duration of mechanical ventilation and the number of nosocomial infections.^[9,19]

In a quasi-experimental study, Keykha *et al.*^[13] investigated the effect of applying the instructions of pain control and sedation of the patients hospitalized in ICU. Eighty critically ill patients randomly assigned patients in two control and intervention groups. In the intervention group, patients' pain control and sedation were performed using pain and sedation instruction. In the control group, patients received usual, none protocol pain control and sedation. BPS and RASS were used for data collection. Level of patients' pain in the intervention group was significantly lower in comparison with patients in the control group ($P < 0.000$). In addition, level of patients' sedation in the intervention group was near to ideal sedation of Richmond in comparison with patients in the control group. There was a statistically significant difference in sedation level of patients

between the two groups ($P = 0.005$). The authors recommended that using pain control and sedation can improve pain control and also better sedation remarkably in patients hospitalized in ICU.

Most of our addicted patients received methadone in our study. There is no consensus protocol for pain management in opium-dependent critically ill patients, and the number of these patients is high within our settings. Methadone is a drug of choice in an outpatient setting for pain control in opium-addicted patients, and so, our physicians use it in hospitalized addicted patients. Sabetian *et al.*^[20] used methadone to prevent withdrawal syndrome and pain in 30 opium-addicted critically ill patients and assessed pain by BPS and through a protocol. The results showed that pain and sedation scores within an acceptable limit in 93% and 98% of occasions, respectively. Although methadone was prescribed by our physician for opium-addicted patients, it is not based on a protocol, and the pain was not controlled appropriately in these patients.

According to Van Niekerk and Martin,^[21] some factors such as nurse-patient ratio, lack of nurse-physician cooperation, inadequate perception of analgesic agents, and physician's lack of knowledge concerning pain assessment and management are barriers to optimal pain management. Our results reinforce the importance of using clinical practice guidelines to manage pain in critically ill patients and also the importance of documentation of pain assessment and management by nurses.

Nonpharmacologic interventions for pain management, such as music therapy and relaxation techniques, may be opioid sparing and analgesia enhancing; they are low cost, easy to provide, and safe.^[11] Based on our results, physical restraint has been the most often used nonpharmacological intervention to relieve pain in our patients. The accepted nonpharmacologic methods were not used for our critically ill patients. Although a multimodal approach to pain management in ICU patients has been recommended,^[11] few studies have been published on the effectiveness of nonpharmacologic interventions in these patients. However, as we observed overuse of analgesics at our center, it is possible that with the use of recommended nonpharmacologic interventions, the use of analgesics drugs decreases. More studies are needed to confirm this.

The limitations were the small sample size and not using a randomization method for patients sampling, which could lead to a selection bias. Some of the data were collected retrospectively from patients' medical file, which could affect the precision of data and be a source of bias as well.

Our results indicate that quality of pain assessment and management in our setting is inappropriate and inadequate which leads to over- or under-use of analgesics. Pain is a real problem in critically ill patients. Inadequate pain assessment leads to mismanagement of pain and irrational use of analgesic drugs. Therefore, development of a local protocol, education of physicians and nurses, and implementation of the protocol are necessary for rational use of analgesics, better pain control in patients, and reducing the risks of medical errors and treatment failure.

AUTHORS' CONTRIBUTION

Sarah Mousavi designed the work, analyzed the data, drafted the manuscript, and approved the final article. Babak Alikiaie interpreted data for the work, revised the manuscript, and approved the final manuscript. Ali Ebrahimi and Zahra Foroughi collected the data, revised, and approved the final manuscript. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

- Treede RD. The International Association for the Study of Pain definition of pain: As valid in 2018 as in 1979, but in need of regularly updated footnotes. *Pain Rep* 2018;3(2):e643.
- Puntillo KA. Pain experiences of intensive care unit patients. *Heart Lung* 1990;19:526-33.
- Pasero C. Pain in the critically ill patient. *J Perianesth Nurs* 2003;18:422-5.
- Sinatra R. Causes and consequences of inadequate management of acute pain. *Pain Med* 2010;11:1859-71.
- Stein-Parbury J, McKinley S. Patients' experiences of being in an intensive care unit: A select literature review. *Am J Crit Care* 2000;9:20-7.
- Alderson S, McKechnie S. Unrecognised, undertreated, pain in ICU: Causes, effects, and how to do better. *Open J Nurs* 2013;3:108.
- Sigakis MJ, Bittner EA. Ten myths and misconceptions regarding pain management in the ICU. *Crit Care Med* 2015;43:2468-78.
- van Boekel RL, Vissers KC, van der Sande R, Bronkhorst E, Lerou JG, Steegers MA, *et al.* Moving beyond pain scores: Multidimensional pain assessment is essential for adequate pain management after surgery. *PLoS One* 2017;12:e0177345.
- Gélinas C. Pain assessment in the critically ill adult: Recent evidence and new trends. *Intensive Crit Care Nurs* 2016;34:1-11.
- Pudas-Tähkä SM, Axelin A, Aantaa R, Lund V, Salanterä S. Pain assessment tools for unconscious or sedated intensive care patients: A systematic review. *J Adv Nurs* 2009;65:946-56.
- Barr J, Fraser GL, Puntillo K, Ely EW, Gélinas C, Dasta JF, *et al.* Clinical practice guidelines for the management of pain, agitation, and delirium in adult patients in the intensive care unit. *Crit Care Med* 2013;41:263-306.
- Young J, Siffleet J, Nikolett S, Shaw T. Use of a behavioural pain scale to assess pain in ventilated, unconscious and/or sedated patients. *Intensive Crit Care Nurs* 2006;22:32-9.
- Keykha AA, Enayati H, Borhani F, Rafiei H, Khodadadi Hoseini BM. Applying the instruction of pain control and sedation of the patients hospitalized in intensive care unit. *Iran J Crit Care Nurs* 2013;6:249-58.
- Martínez-Mesa J, González-Chica DA, Duquia RP, Bonamigo RR, Bastos JL. Sampling: How to select participants in my research study? *An Bras Dermatol* 2016;91:326-30.
- Sessler CN, Gosnell MS, Grap MJ, Brophy GM, O'Neal PV, Keane KA, *et al.* The richmond agitation-sedation scale: Validity and reliability in adult intensive care unit patients. *Am J Respir Crit Care Med* 2002;166:1338-44.
- Ayasrah SM, O'Neill TM, Abdalrahim MS, Sutary MM, Kharabsheh MS. Pain assessment and management in critically ill intubated patients in Jordan: A prospective study. *Int J Health Sci (Qassim)* 2014;8:287-98.
- Gélinas C, Fortier M, Viens C, Fillion L, Puntillo K. Pain assessment and management in critically ill intubated patients: A retrospective study. *Am J Crit Care* 2004;13:126-35.
- Soltani R, Vatanpour H, Shafiee F, Sadeghian N. Evaluation of parenteral opioid analgesics utilization in patients hospitalized in a referral teaching hospital. *J Pharm Care* 2016;3:16-20.
- Georgiou E, Hadjibalassi M, Lambrinou E, Andreou P, Papathanassoglou ED. The impact of pain assessment on critically ill patients' outcomes: A systematic review. *Biomed Res Int* 2015;2015:503830.
- Sabetian G, Farid Z, Khalili F, Afshari R, Masjedi M, Maghsoodi B, *et al.* Implementation of a protocol to control pain, agitation and delirium in the patients admitted to intensive care unit with opioid drug dependency: A feasibility study. *Biomed Res* 2017;28:3666-71.
- Van Niekerk LM, Martin F. The impact of the nurse-physician relationship on barriers encountered by nurses during pain management. *Pain Manag Nurs* 2003;4:3-10.