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Outcomes/Prediction

Implementation of a protocol for integrated management of pain, agitation, and delirium can improve clinical outcomes in the intensive care unit: A randomized clinical trial

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ABSTRACT

Background: Inappropriate diagnosis and treatment of pain, agitation, and delirium (PAD) in intensive care settings results in poor patient outcomes. We designed and used a protocol for systematic assessment and management of PAD by the nurses to improve clinical intensive care unit (ICU) outcomes.
Materials and Methods: A total of 201 patients admitted to 2 mixed medical-surgical ICUs were randomly allocated to protocol and control groups. A multidisciplinary team approved the protocol. Pain was assessed by Numerical Rating Scale and Behavioural Pain Scale, agitation by Richmond Agitation Sedation Scale, and delirium by Confusion Assessment Method in ICU. The Persian version of the scales was prepared and tested for validity, reliability, and feasibility in a preliminary study. The patients in the protocol group were managed pharmacologically according to the protocol, whereas those in the control group were managed according to the ICU routine.
Results: The median (interquartile range) for the duration of mechanical ventilation in the protocol and control groups was 19 (9.3-67.8) and 40 (0-217) hours, respectively ($P = .038$). The median (interquartile range) length of ICU stay was 97 (54.5-189) hours in the protocol group vs 170 (80-408) hours in the control group ($P < .001$). The mortality rate in the protocol group was significantly reduced from 23.8% to 12.5% ($P = .046$).
Conclusion: The current randomized trial provided evidence for a substantial reduction in the duration of need to ventilatory support, length of ICU stay, and mortality rates in ICU-admitted patients through protocol-directed management of PAD.

1. Introduction

Pain is considered a dominant stressor and a main concern to critically ill patients admitted in the intensive care unit (ICU) with a quite high prevalence of 50% in medical and surgical patients [1,2], yet it is a poorly defined entity particularly because of its subjective nature, which can only be truly reported by the individual who is experiencing it. Most ICU-admitted patients are incapable of reporting their pain because of low level of consciousness, mechanical ventilation, neuromuscular blockage, or deep sedation [3]. Meanwhile, there is always concern over the development of drug dependency to pain-controlling medications, which creates great stress for the patients, their families, and health care staff [4].

Uncontrolled pain can have harmful effects on the function of different body systems, most notable of which are cardiovascular, respiratory, musculoskeletal, and, above all, mental function [5]. Several studies have demonstrated sleep deprivation, fatigue, anxiety, agitation, delirium, and increase in undesirable incidents such as self-extubation as the mental consequences of inadequate pain treatment [6,7]. The ultimate goal for pain management is producing pain-free calm patients [8] and therefore reducing pain-mediated agitation or delirious episodes. Poor pain control also results in severe agitation and further complicates the patient's condition. There are substantial consequences to inadequate control of pain and agitation such as aggressive behavior, self-removal of important tubes and catheters, and patient-ventilator asynchrony [9].

Agitation is usually treated by administration of sedatives to reduce patient's awareness to a sufficient level and induce amnesia. An inherent risk of agitation treatment is prolonged or excessive sedation, which significantly compromises caregivers' control over patient's level of consciousness and increases the duration of ICU stay [10]. Therefore, the optimal goal in agitation treatment would be

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creating manageable short episodes of tranquility, which would improve the quality of sedation and provide easier control over the patient's level of consciousness [11].

Delirium is defined as a syndrome characterized by acute change or fluctuation in an individual's mental status accompanied by disorganized thinking, inattention, or altered level of consciousness [12]. The prevalence of delirium has been reported from 20% to 80% in medical and surgical ICUs. However, delirious state is usually underdiagnosed [13], particularly in mechanically ventilated and deeply sedated patients because of a lack of proper patient-staff communication [14,15]. Frequent fluctuations in patient's sedation levels and changes in mental status as well as disproportionate exposure to pain medication are suggested to be linked to a rise in the incidence of delirious state [16]. Delirium is commonly accompanied by ventilation complications, nosocomial pneumonia, and self-extubation [12]. It may also prolong the duration of hospital stay and increase the need for nursing care and mortality rate [14,17,18]. Long-lasting untreated delirium could be quite dangerous by leaving long-term cognitive impairment and major psychological sequels for the patients [1].

Apparently, pain, agitation, and delirium (PAD) are 3 entirely distinct but closely interrelated entities. Existence of a tight link between PAD necessitates proper management of each individual issue because underdiagnosis or mismanagement of any of them would lead to drastic complications in the other 2 and, ultimately, poor patient condition. Satisfactory outcomes can be obtained by detection, quantification, and treatment of PAD in the ICU patients with or without mechanical ventilation by using a reliable and valid policy [1,12,19]. Devising efficient and self-reliant protocols is a key to effective management strategies.

In the literature, there are a number of protocols for management of PAD, individually. The American Association of Critical Care Medicine and Society of Critical Care Medicine have recently released a multidisciplinary, evidence-based guideline for management of PAD in adult ICU patients [20]. This study started well before the publication of this document; however, the protocol used in our study is largely compatible with the provided recommendations.

Most of the studies in the field of PAD in ICU patients either focus on one of these issues or are before-after studies, comparing historical outcomes with new ones after the intervention. We aimed to design a prospective parallel-group, randomized, clinical trial after implementing a multidisciplinary generated PAD protocol in 2 mixed medical-surgical ICUs. To the best of our knowledge, this study is among the very few studies carried out in this field, thus far [21,22].

2. Methods

The present randomized controlled clinical trial was aimed to design and implement a collective PAD protocol and to evaluate its effects on the outcome of patients hospitalized in 2 mixed university-affiliated ICUs of Namazi Hospital, Shiraz, Iran. The study was approved by the ethics committee of the Shiraz University of Medical Sciences and registered in the Iranian Registry of Clinical Trials. All patients older than 18 years who were admitted in the 2 ICUs (central and general ICU) were screened for eligibility. Admissions were caused by trauma, surgical (postoperative), neurologic, medical, and cardiovascular problems. Written informed consents were obtained from the families (because of patients' low level of consciousness), and the patients were randomly assigned to the protocol or the control group based on a computer-generated table of random numbers. Patients were excluded if they had ICU stay less than 24 hours, were expected to die in less than 48 hours, had received muscle relaxant, received anticonvulsant drugs for convulsion, had psychological illness, or had upper extremity paralysis or immobilization in cast.

Pain was assessed by Behavioural Pain Scale (BPS) in the patients who were under the support of mechanical ventilation, BPS nonintubated in those who were noncommunicating but not under mechanical ventilation, and Numerical Rating Scale (NRS), when feasible. The level of agitation was evaluated by Richmond Agitation Sedation Scale (RASS), and the patients were assessed by Confusion Assessment Method in ICU (CAM-ICU) to determine whether delirium existed or not. Patients' Acute Physiology and Chronic Health Evaluation IV (APACHE IV) score was recorded within the first 24 hours of arrival to the ICU.

Initially, BPS, RASS, and CAM-ICU were translated to Persian by 1 of the researchers and revised by 8 experts of the field. Then, they were back translated to English by a translator familiar with medical terminology, and the draft was then compared with the original one by the first group, and the final versions were prepared. To determine the validity and reliability of the translated versions, a nurse and the researcher evaluated 30 ICU patients were evaluated using each of the scales. Each patient was simultaneously assessed by 2 investigators. Pearson correlation coefficients obtained were 0.88 and 0.92 for BPS and RASS, respectively. In addition, κ coefficient of CAM-ICU was 0.88. All nurses working in 2 ICUs were trained to check the scores in 3 separate sections, and all questions were addressed during a 1-month period. The nurses were also encouraged to participate in the project by both financial and nonfinancial incentives.

In the next step, the researchers searched the Web for protocols and guidelines for the management of PAD from 1998 up to 2010. A new protocol was designed and developed after discussions in several group meetings including 3 intensivists, a neurologist, a clinical pharmacist, a psychiatrist, and 2 ICU nurses. It is noteworthy to mention that the major part of the final protocol was extracted from ICU sedation guideline from San Diego Patient Safety Council [23]. The protocol was taught to the nurses during 3 educational sections. The knowledge and skill of the nurses on PAD scores and use of the protocol were tested twice (once during the first and another during the fourth month of the study), and appropriate feedbacks were provided.

The patients in the protocol group were evaluated by BPS/NRS and RASS every 1 hour by CAM-ICU every working shift and whenever it deemed to be needed by the nurse's discretion. Then, each patient was treated according to the approved protocol based on the scores obtained by the scales. The protocol was designed to keep BPS less than 5, NRS less than 3, and RASS score between -1 and $+1$ (light sedation). The protocol also followed a first-analgesia policy but did not include any daily sedation interruptions.

The nurses had the authority to adjust the analgesic and sedative drugs according to the protocol to keep the pain and agitation scores within the acceptable range. Also, if the delirium was positive, the patients were treated according to the protocol. All scores and administered medications were recorded. In the control group, pain and sedation were managed as routine according to as-needed physician orders without regular assessment for pain or sedation. No screening for delirium was done in the control group, too. All used medications in the control group were recorded in the designated forms. During the study, adherence to the protocol was monitored by 1 of the researchers and 2 assistants at all the shifts. The targeted outcomes included ICU length of stay in hours, duration of mechanical ventilation in hours, all-cause mortality rate in ICU, the number of self-extubations, the effectiveness of the protocol to control PAD, and dose of the drugs used for treating these complications.

Data were analyzed by SPSS statistical software version (SPSS, Chicago, Ill) [21] using the χ^2 test, t test, and the Mann-Whitney U test. The differences were considered statistically significant when P values were .5 or less. Data were described in mean $\pm$ SD or median and interquartile range (IQR).

3. Results

During the 9-month period of the study, 329 patients were admitted in these wards. One hundred seven patients did not fulfill the inclusion criteria, and 6 patients did not consent. A total of 216