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Clinical outcomes of cardiac arrest patients according to opioid use history

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ABSTRACT

Purpose: Opioid analgesics are potent respiratory depressants. The purpose of this study was to describe the effects of opioids administered within 24 hours before cardiac arrest on clinical outcomes.
Materials and methods: We retrospectively collected the cardiac arrest data of noncancer patients who were admitted to the general ward of Asan Medical Center from January 2008 to August 2012. We investigated the proportion of these patients who received opioids within 24 hours of a cardiac arrest event, as well as the cardiac arrest characteristics, survival rates, and opioid administration patterns.
Results: Of the 193 patients identified, 58 (30%) had been administered opioids within the previous 24 hours (the opioid group), whereas the remaining 135 (70%) had not been administered opioids (the nonopioid group). The survival rate did not differ significantly between these 2 groups. In the opioid group, as-needed opioid administration was associated with a lower 24-hour survival rate than regular opioid administration (9 [33.3%] of 27 patients vs 20 [64.5%] of 31 patients; $P = .030$). In multivariate logistic regression analysis, as-needed opioid administration was negatively associated with 24-hour survival.
Conclusions: Opioid administration within 24 hours before cardiac arrest per se was not associated with adverse outcomes. However, administration of opioid analgesics on an as-needed basis was associated with poorer survival outcomes than regular dosing. Greater attention should be paid to patients who receive as-needed opioid administration in the general ward.

1. Introduction

In-hospital cardiac arrest occurs in 1 to 4 per 1000 patients, with 30% to 50% occurring in the general wards of hospitals [1–4]. One of the major reasons for cardiac arrest is respiratory insufficiency related to various diseases and medications [5]. Among the medications used in hospitals, opioid analgesics, in particular, are known to cause severe adverse effects, including hypoventilation. Although tolerance to the hypoventilation caused by opioid analgesics develops at a relatively early stage [6,7], its impact can be severe in older patients and those with obesity, sleep apnea, organ failure (eg, renal insufficiency, chronic obstructive pulmonary disease, hepatic insufficiency, and congestive heart failure), and with the concomitant use of sedatives [8]. Moreover, the risk of hypoventilation is greater at the beginning of opioid analgesic treatment, especially within the first 24 hours [9,10].

Recent studies have reported that respiratory depression induced by opioid analgesics can lead to cardiac arrest and death [11–14]. The rate of unintentional opioid overdose-related death in the United States is increasing [15,16]. However, only a few studies have examined the relationship between opioid analgesics and cardiac arrest. Therefore, in our study, we examined the effects of these agents on the clinical outcomes of noncancer patients who received cardiopulmonary resuscitation (CPR) in the general ward of our hospital. We investigated the proportion of these patients who received opioids within 24 hours of cardiac arrest, as well as the cardiac arrest characteristics, survival rates, and opioid administration patterns. We also attempted to identify any relationship between these outcomes and the opioid administration pattern.

2. Materials and methods

2.1. Study design and patient population

The patients included in our study were all adults (>18 years old) who received CPR due to a cardiac arrest in the general ward of Asan

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Medical Center between January 2008 and August 2012. Asan Medical Center is a tertiary referral hospital in Seoul, Korea, with approximately 2700 beds and approximately 900 000 admissions per year. Our study was a retrospective investigation of the electronic medical records and the in-hospital cardiac arrest registry created from Utstein-style reports [17]. For patients who experienced more than 1 cardiac arrest, we included only the first event. We excluded cardiac arrest cases for which resuscitation was initiated outside the hospital before the patient's arrival at the emergency department. We also excluded all cardiac arrests that occurred in any hospital area except for the general ward, that is, the intensive care unit, emergency department, operating room, and a diagnostic or treatment unit such as a computed tomography room or endoscopic examination room. Patients who had signed a "do not resuscitate" form or who had made a verbal do not resuscitate agreement with the medical staff were excluded. Patients with cancer were also excluded because they frequently require administration of opioids for pain control [18] (Fig. 1). This study was approved by the Ethics Committee of Asan Medical Center (no. 2013-383). The requirement for informed consent was waived because of the retrospective nature of the analysis.

2.2. Data collection

Opiates are found naturally in the opium poppy, whereas opioids are all drugs with opium-like effects. These compounds bind to μ-, δ-, and κ-opioid receptors of various organs, and opioid-induced respiratory depression is mediated largely by μ-opioid receptors in the medulla [19]. Tramadol has unknown mechanisms of action but does act on opioid receptors [20]. It is also reported to cause similarly adverse effects to opioids, including respiratory depression [21]. Therefore, tramadol was considered an opioid analgesic in our study. Considering the effective half-lives of the opioid analgesics used in our hospital, our opioid study group was confined to patients who were administered opioid analgesics within 24 hours before their cardiac arrest event.

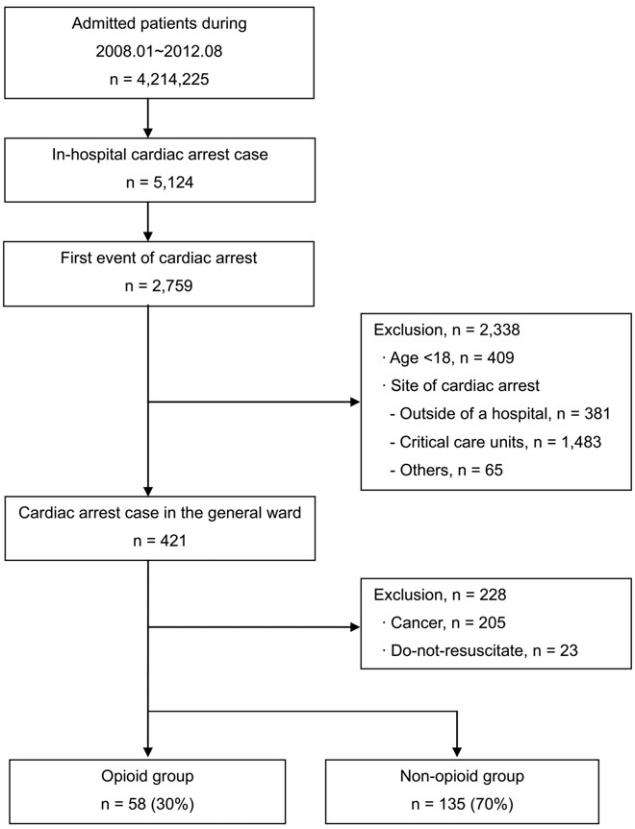

Fig. 1. Flowchart of the enrollment and exclusion of the study patients.

According to the Utstein-style definition, return of spontaneous circulation (ROSC) was defined as medical staff–confirmed sustained (at least 20 minutes) spontaneous circulation after CPR. Survival to discharge was defined as the patient leaving the hospital alive.

To assess the effects of opioids on the changes in patients' conditions, we collected information such as altered mentality, drop in blood pressure, respiratory rate, and oxygen desaturation within 24 hours before the cardiac arrest. The baseline values were obtained at 24 hours before the cardiac arrest. Altered mental status was defined as a decrease in 1 or more levels of consciousness from the baseline. The levels of consciousness of general ward patients at our hospital are assessed as 5 levels: alert, drowsy, stupor, semicoma, and coma. A drop in blood pressure was defined as a systolic pressure less than 90 mm Hg or 20% lower than baseline. A decreased respiratory rate was defined as a respiratory rate of less than 12 breaths per minute or showing a 20% decrease from baseline. Desaturation was defined as an oxygen saturation level less than 90%.

We used the Deyo-Charlson score to standardize the value of underlying disease. The score is calculated by summing the scores of the differential impact on mortality of 17 different chronic diseases [22]. The total scores (obtained by summing individual item scores) range from 0 to 33 points, and higher scores indicate a greater degree of chronic disease. In agreement with the results of Ehlenbach et al [23], who reported a low survival rate after in-hospital cardiac arrest in patients with a Deyo-Charlson score of 3 or higher, our study established a baseline score of 3. The opioid administration pattern was based on nursing medication administration records.

2.3. Outcome measures

To investigate the clinical outcomes of the cardiac arrest patients, general characteristics, cardiac arrest characteristics, and survival rates were compared between the opioid group and the nonopioid group. General characteristic variables included patient age, sex, underlying diseases, Deyo-Charlson score, and changes in their condition within 24 hours before cardiac arrest, such as an altered mental status, drop in blood pressure, decrease in respiratory rate, and oxygen desaturation. Cardiac arrest characteristic variables included cardiac arrest occurrence during the night (11:00 PM to 7:00 AM), a witnessed cardiac arrest, data monitoring during the cardiac arrest (electrocardiogram, pulse rate, or oxygen saturation), the first documented electrocardiogram (ECG) rhythm, cardiac arrest cause, and the CPR duration. Survival variables included the ROSC, survival for 24 hours, and the survival to discharge rate.

To investigate the pattern of opioid analgesic administration, the pain-related diagnosis, opioid dosing schedule, opioid analgesic type, and route of administration were compared between patients who survived for 24 hours and those who did not. Pain-related diagnostic variables included acute pain, chronic pain, and sedation. The opioid dosing schedule variables included regular opioids, as-needed opioids, and regular plus as-needed opioids. Opioid analgesic type variables included only opioids, only tramadol, and both opioids and tramadol. The route of administration variables included only intravenous, only per oral, only intramuscular, and more than 1 route.

To analyze the prognostic factors associated with 24-hour survival, independent variables that showed a significant difference in univariate analysis were included in multivariate logistic regression. The variables used for univariate analysis included general characteristics, cardiac arrest characteristics, and the pattern of opioid analgesic administration.

2.4. Statistical analysis

Statistical analysis was conducted using SPSS version 21.0 for Windows (SPSS, Chicago, Ill). Data are expressed as means ± SD and