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Opioid Analgesics and Depressive Symptoms in Burn Patients: What Is the Real Relationship?

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Objective: Major burn injuries are strongly associated with both psychological trauma and severe pain, and opioids are the mainstay analgesics for the treatment of severe burn pain. The objectives of this study are to find the complex relationship between opioid dose, depression, and post-traumatic stress disorder (PTSD) symptoms during the acute management of pain in burn patients.
Methods: The symptoms of depression and PTSD were assessed in 43 burn patients immediately following wound stabilization and 2 weeks after the initial evaluation.
Results: Total opioid doses and Hamilton Depression Scale (HAMD) scores obtained during the second evaluation were positively but weakly correlated after controlling for age and total burn surface area (R=0.33, p=0.03). Moreover, pain management with opioids was significantly more common in burn patients with low Clinician Administered PTSD Scale scores (evaluation 1) and high HAMD scores (evaluation 2) (F=6.66, p=0.001).
Conclusion: High opioid dose following acute burn trauma might have correlation with depressive symptoms. Monitoring of depressive symptoms may be important following acute burn trauma and consequent opioids pain management, particularly when PTSD symptoms appear minimal during the early stabilization of patients.

KEY WORDS: Burns; Depression; Post-traumatic stress disorders; Opioid analgesics.

INTRODUCTION

Opioids are among the oldest and most frequently prescribed analgesic medications for the relief of pain. In addition to their clinical use in pain management, opioids are also attempted to use for the treatment of depression.[1-3] Some studies have shown that burn patients with concomitant depression require significantly higher doses of analgesics for pain control.[4] However, the high risk of psychological and physiological dependence on opioids may forbid clinical use of opioids in patients with depression.[1] Also opioids are well known to have many side effects include drowsiness and mood changes. Future clinical research studies should focus on the clear relationship between depression and opioids.

Opioids are most commonly used in the clinical management of acute and procedural pain following severe burn trauma.[5] And nowadays, opioids are known to be effective for the treatment of post-traumatic stress disorder (PTSD).[6-8] As PTSD symptoms and burn pain are highly comorbid, an increased reliance on opioids often occurs during the clinical treatment of burn patients. Consequently, the pain-management protocol in our burn center was adjusted accordingly to provide sufficient and appropriate analgesia including opioids to patients following severe burn trauma.

Although previous studies have suggested the use of opioids in the treatment of depression,[1-3] many burn patients appear to display an increase in depressive symptoms under our current pain-management protocol.

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Maybe it comes from the sequelae and treatment process of the burn, we have chance to focus on the relationship between opioid dose and depression. Therefore, the present study examined the complex relationship between opioid dose, depression, and PTSD symptoms during the acute management of pain in burn patients.

METHODS

Subjects

All participants were recruited from the Burn Center in Hallym University Hangang Sacred Heart Hospital (Seoul, Korea) following acute burn injuries. Inclusion criteria included the absence of any previous neurological or psychiatric disorder. One aim of the current study was to determine whether opioid use and depressive symptoms have correlation; therefore, four participants were excluded from the study due to the use of antidepressant medication for the treatment of PTSD and depression at the time of the inclusion. Eleven subjects took quetiapine as a sleep aid. No other benzodiazepines or antipsychotics were used by the patients during the course of the study.

The first evaluation was conducted following the initial stabilization of the injury (17.9±17.8 days after the burn injury). The second evaluation was conducted approximately 2 weeks (16.6±3.3 days) later. Injury stabilization was defined at approximately 14 days for patients admitted to the general ward and following a sequential organ failure assessment (SOFA)[9] score of less than 3 and no apparent symptoms of delirium among patients in intensive care unit. Depression and PTSD symptoms were evaluated with Korean versions of the Hamilton Depression Scale (HAMD)[10] and the Clinician-Administered PTSD Scale (CAPS).[11] High validity and reliability have previously been reported for these versions in the Korean population.[10,11] Burn severity was evaluated in terms of the mean total surface area of the burn(s) (TSABs). Pain was scored using a visual analogue scale (VAS).[12]

Written informed consent was obtained from each participant prior to the start of the study. The study was approved by the Institutional Review Board of Hallym University Hangang Sacred Heart Hospital in Korea (IRB #: 2010-068).

Opioid Analgesics

Total cumulative opioid dose (morphine and fentanyl) were determined by chart review. Total opioid dose was calculated as follows: total morphine dose plus total fentanyl dose (i.e., fentanyl doses were first converted to the equivalent doses of morphine).[13] Pethidine was used during burn dressing procedures in some patients; however, it was not included in the total cumulative opioid dose due to its short half-life.

Statistical Analysis

Demographic data were compared using the Mann-Whitney *U*-test. Interactions between PTSD symptoms present during the first evaluation, total opioid dose, and depressive symptoms 2 weeks after patient stabilization were evaluated using one-way analysis of variance (ANOVA). Total opioid dose was compared between groups with two-way ANOVAs. Regression analysis was also performed to determine the correlations between measures. The two-tailed α-level was set at 0.05. Statistical analyses were conducted using IBM SPSS Statistics ver. 19.0 statistical software for Windows (IBM Co., Armonk, NY, USA).

RESULTS

The mean TSAB for the 43 participants was 26.1±19.7%. Participants were divided into high- and low-acute stress disorder (ASD) groups after the first interview based on a CAPS score above or below 25. Demographic data and clinical characteristics between these two groups are shown in Table 1. There was no significant correlation between characteristics of burn, including the duration from burn to initial stabilization and pain, and the initial HAMD scores.

Typically, a CAPS score of >20 has been associated with mild ASD symptoms. However, 25 was used as the

Table 1. Demographic data between high- and low-ASD groups, divided by CAPS scores in the first interview

Characteristic	Low-ASD (n=18)	High-ASD (n=25)	*p* value
Age (yr)	42.5±12.4	50.2±11.2	0.05
Sex, male/female	13/5	19/6	
TSAB (%)	27.1±24.1	25.3±16.4	0.59
First CAPS	11.56±7.3	41.3±11.3	0.00
Second CAPS	7.9±14.8	26.8±22.9	0.00
First HAMD	10.2±6.3	19.2±5.1	0.00
Second HAMD	6.2±5.6	12.4±6.0	0.01
Total opioid dose (mg)	445.6±707.4	666.4±688.2	0.14

Values are presented as mean±standard deviation or number only.
ASD, acute stress disorder; CAPS, Clinician-Administered Posttraumatic Stress Disorder Scale; TSAB, total surface area of the burn; HAMD, Hamilton Depression Scale.
Low-ASD: the group with CAPS scores below 25 at the first interview after stabilization of burn injuries.
High ASD: the group with CAPS scores above 25 at the first interview after stabilization of burn injuries.
p values were calculated using the Mann-Whitney *U*-test.

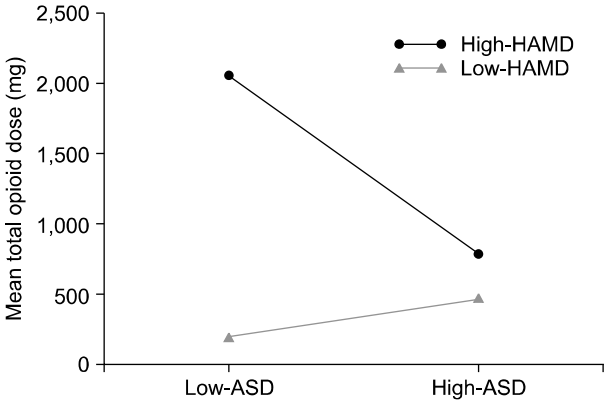

Fig. 1. Total opioid dose according to the first interview CAPS scores (high- and low-ASD groups) and the second interview HAMD scores (high- and low-HAMD groups).
HAMD, Hamilton Depression Scale; ASD, acute stress disorder; CAPS, Clinician- Administered Post-traumatic Stress Disorder Scale.

cut-off point for high- and low-ASD groups based on our dataset because there was nadir in 25. Participants were also separated into two groups based on a HAMD score higher or lower than 10 during the second evaluation. In the present study, groups were divided based on symptom severity and not based on the diagnosis of depression or ASD.

The high-ASD group was significantly older and had higher HAMD scores during the initial evaluation. No significant difference in the TSAB was noted between the low- and high-ASD groups. VAS pain scores also did not differ significantly between the groups (p=0.932).

After controlling for age and TSAB, total opioid doses were weakly correlated with HAMD scores obtained during the second interview (R=0.33, p=0.03) but not with CAPS scores obtained during this interview (R=0.21, p=0.20).

A significant main effect of total opioid dose was determined in relation to CAPS and HAMD scores (F=6.66, p=0.001). Figure 1 presents total opioid doses in relation to first-interview CAPS scores (high- and low-ASD groups) and second-interview HAMD scores (high- and low-HAMD groups). A low CAPS score during the first evaluation and a high HAMD score during the second evaluation were associated with a significantly higher total opioid dose.

DISCUSSION

Depression is an extremely common complication associated with severe burn injuries and frequently interferes with successful rehabilitation.[14] Burn patients who exhibit injury-related depression typically display difficulty returning to daily activities and report a reduced quality of life.[15]

Pain is also a devastating symptom of burn trauma, rendering clinical pain management a principal focus in the treatment of burn patients.[5,16,17] Historically, opioids have been the primary treatment of choice for pain management; however, fears of opioid dependence and side effects held by clinicians make tendency to use lesser dose of opioids for many burn patients.[17] Recent reports on opioids have emphasized the importance of pain management and the effect on PTSD symptoms; therefore, the use of opioids for this population appears to be increasing.

Despite this trend, we found that patients with low CAPS scores during the first interview and high HAMD scores during the second interview received significantly higher doses of opioids. If future studies replicate the association between opioids and depression, it will be critical to consider issues related to adequate analgesia, PTSD, and depression in relation to opioid dosing in clinical settings.

The side effects of morphine, such as drowsiness, may be confused with symptoms of depression. In the current study, the mean opioid dose in the period between the two evaluations (approximately 16 days) was 125.9±162.0 mg. It is our belief that this low dose is unlikely to have resulted in side effects that could be confused with depression. Although pain severity can impact depression, we found no significant differences in the VAS scores of the groups. Furthermore, burn severity (TSAB) did not affect ASD symptoms, as has been previously reported.[18]

The limitations of the current study are the small sample, the restriction of the participants to burn victims, and the large variation in the interval before the first evaluation. However, to ensure reliability to scales, time to wound stabilization was inevitable. And another limitation is that we divided the group based not on the diagnosis but the symptom severity with scale. Future studies with larger number of subjects should try on with diagnosis groups.

Taken together, our findings suggest that opioids may somewhat impact depressive symptoms and should be used with caution for the pain management of burn patients with low levels of PTSD during the early stages of recovery (17.5±17.9 days post-burn). Future studies are warranted to confirm the relationship between excessive opioid use and the development of depression.

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