Post-operative Analgesia in Opioid Dependent Patients: Comparison of Intravenous Morphine and Sublingual Buprenorphine

Shaabanali Alizadeh MD[1], Ghafar Ali Mahmoudi MD[2], Hassan Solhi MD[3], Bahman Sadeghi-Sedeh MD[4], Reza Behzadi MD[5], Amir Mohammad Kazemifar MD[6]

Original Article

Abstract

Background: Acute and chronic pain is prevalent in patients with opioid dependence. Lack of knowledge concerning the complex relationship between pain, opioid use, and withdrawal syndrome can account for the barriers encountered for pain management. This study was designed to evaluate the efficacy of sublingual (SL) buprenorphine for post-operative analgesia, compared with intravenous (IV) morphine.

Methods: A total of 68 patients, aged 20-60 years were randomly selected from whom had been underwent laparotomy due to acute abdomen in a University Teaching Hospital in Arak, Iran, and were also opioid (opium or heroin) abuser according to their history. After end of the surgery and patients' arousal, the patients were evaluated for abdominal pain and withdrawal syndrome by visual analog scale (VAS) and clinical opioid withdrawal score (COWS), respectively 1, 6, and 24 h after the surgery. They received either morphine 5 mg IV or buprenorphine 2 mg SL, 1 h after end of the surgery, and then every 6 h for 24 h.

Findings: VAS was 4.47 ± 0.73 and 2.67 ± 0.53 at h 6 and 24 in buprenorphine group, respectively. The corresponding score was 5.88 ± 0.69 and 4.59 ± 0.74 in morphine group. At the same time, patients in buprenorphine experienced less severe withdrawal syndrome.

Conclusion: The present study confirmed the efficacy of SL buprenorphine as a non-invasive, but effective method for management of post-operative pain in opioid dependent patients. Result of this study showed that physicians can rely on SL buprenorphine for post-operative analgesia.

Keywords: Buprenorphine, Morphine, Post-operative pain, Opioid dependence, Withdrawal syndrome

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1- Assistant Professor, General Surgeon, Department of Surgery, School of Medicine, Arak University of Medical Sciences, Arak, Iran
2- Assistant Professor, Legal Medicine and Clinical Toxicologist, Department of Internal Medicine, School of Medicine, Lorestan University of Medical Sciences, Khorramabad, Iran
3- Associate Professor, Clinical Toxicologist, Department of Emergency Medicine, School of Medicine, Arak University of Medical Sciences, Arak, Iran
4- Assistant Professor, Epidemiologist, Department of Public Health, School of Medicine, Arak University of Medical Sciences, Arak, Iran
5- Researcher, Department of Emergency Medicine, School of Medicine, Arak University of Medical Sciences, Arak, Iran
6- Associate Professor, Clinical Toxicologist, Department of Internal Medicine, School of Medicine, Qazvin University of Medical Sciences, Qazvin, Iran
Correspondence to: Ghafar Ali Mahmoudi MD, Email: mahmoudi.gh@lums.ac.ir

Introduction

Pain management in the perioperative setting refers to actions before, during, and after a procedure that are intended to reduce or eliminate post-operative pain before discharge.[1] Post-operative pain continues to be a challenge and is often inadequately treated, leading to patient anxiety, stress, and dissatisfaction. Inadequately treated pain can lead to detrimental physiological effects and may also have psychological, economic and social adverse effects.[2]

Perioperative techniques for post-operative pain management include, but are not limited to central regional (i.e., neuraxial) opioid analgesia, patient controlled analgesia with systemic opioids, and peripheral regional analgesic techniques.[1] The choice mainly depends on the strategy favored by the physician and the availability of drugs and equipment.[2]

Opioids are typically used for the management of moderate to severe acute pain, but opioid use is limited by the occurrence of a range of side effects. Opioids exert their analgesic effects primarily through agonistic interactions with μ-opioid receptors in neurons in the pain pathway, which lead to a reduction in neurotransmitter release and associated pain.[3] The underuse of opioid analgesics by health care providers to relieve acute pain may be related to attempts to balance analgesia against concerns about opioid-induced side effects and subsequent deleterious repercussions for patient outcome.[3] Clinicians must prescribe and monitor currently available opioids based on the best available evidence that takes into account the uniqueness of each patient's pain management issues.[4]

Some patient groups are at special risk for inadequate pain control and require additional analgesic considerations, including patients with drug abuse.[1] The global epidemic of opiate use continues to spread, especially in developing countries.[5] Iran has one of the highest rates of opioids abuse in the world.[6,7] It is not surprising that some patients with acute abdomen also have an opioid dependency. They need perioperative analgesia too. However, their management may complicate with insufficient analgesia, superfluous opioid overdose, and withdrawal syndrome.

Intravenous (IV) or intramuscular (IM) administration is more commonly the route of choice in critically ill patients with acute pain who need opioid analgesia. However, any other route with less pain of IM injections and safer than direct IV injection is encouraged.

The present study was designed to evaluate the efficacy of sublingual (SL) buprenorphine for post-operative analgesia, compared to IV morphine.

Methods

In this single-blinded randomized clinical trial, 68 patients, aged 20-60 years were randomly selected from whom had been underwent laparotomy due to acute abdomen in a university teaching hospital in Arak, Iran and were also opioid (opium or heroin) abuser according to their history. Their induction of anesthesia was similar (fentanyl 2-5 μg/kg, midazolam 0.03 mg/kg, atracurium 0.5 mg/kg, and nesdonal 3-5 mg/kg).

After end of the surgery and patients' arousal, the patients were evaluated for abdominal pain and withdrawal syndrome by visual analog scale (VAS) and clinical opioid withdrawal score (COWS), respectively by one of the authors 1, 6, and 24 h after the surgery. The patients were randomly divided into two groups. The first group received morphine 5 mg IV 1 h after the end of the surgery, and then every 6 h for 24 h. The second group received buprenorphine 2 mg SL with the same schedule. Moreover, if any patient had VAS score more than 4, or complained from pain at any time, he received meperidine 25 mg IV.

The exclusion criteria were the use of any other analgesic, sedative, or narcotic before or after the surgery, history of head trauma, shock, diabetes mellitus, and neurologic diseases. The study had been approved by Local Ethical Committee of Arak University of Medical Sciences. All the studied patients provided informed consent for participation to the study.

The results were analyzed by SPSS software (version 16, SPSS Inc., Chicago, IL, USA). Differences between the groups were determined by two-way repeated measure or chi-square test, whatever relevant. Statistical significance was set at $P < 0.050$.

Results

68 patients in two equal groups were participated in the study. All of them completed the study. All

of them except two in the first group, and four in the second group were male. Their age was 30.06 ± 7.95 and 30.68 ± 8.45 years in the first and second groups, respectively. The difference was not statistically significant (P = 0.757). The patients had no significant difference in reason for surgery, too.

The groups had comparable pain severity at the start of the study. However, severity of pain reduced more prominently in group 2 during the study, compared to group 1. Meanwhile, the patients in group 2 experienced less severe withdrawal syndrome, too. COWS score and VAS score of the studied groups was demonstrated in table 1.

Discussion

The present study was performed to evaluate the efficacy of SL buprenorphine as a non-invasive, but effective method for management of post-operative pain in opioid-dependent patients. The result of this study showed that physicians can rely on SL buprenorphine for post-operative analgesia.

Buprenorphine, synthesized in the late 1960s was used as a parenteral analgesic since 1978. Buprenorphine is also available in the forms of SL tablets or transdermal (TD) patches. It is a partial agonist at μ-opioid receptors, an antagonist at kappa opioid receptors.[8,9] Buprenorphine partial mu agonist activity may induce a milder withdrawal syndrome than most opioids; thus, discontinuing buprenorphine may be easier. Buprenorphine is also a κ-receptor antagonist and, therefore, less apt to generate dysphoria.[10] Moreover, buprenorphine exhibits ceiling effects on respiratory depression due to its intrinsic agonist/antagonist effects. This exceptional pharmacology offers an enhanced safety profile compared other opioids, when used for analgesia.[10] After SL administration, there is a rapid onset of effect (30-60 min) with a peak effect at about 90-100 min.[11]

According to the Canadian guideline for safe and effective use of opioids for chronic non-cancer pain, buprenorphine can be used for the treatment of opioid addiction in chronic non-cancer pain.[12,13] Furthermore, it can treat opioid-induced hyperalgesia, which occur with chronic opioid therapy.[14]

Though, we did not found any similar studies to compare them with the present study, there are some studies in the literature about the role of buprenorphine in the management of pain. Study of Bounes et al. showed that acute and chronic pain has a negative impact on the persistence of opioid maintenance treatment, particularly in users of buprenorphine.[15] Neumann et al. have showed that SL buprenorphine can be used for the treatment of chronic pain in patients with co-existent opioid addiction.[16] Wang et al. have performed an in-vitro study.[17] They have suggested that the efficacy of morphine, but not buprenorphine for pain control is reduced, when the cancers cells have P-glycoprotein expression.[17]

Hoflich et al. have focused on peripartum pain management in opioid-dependent women.[18] They have concluded that delivering women who are on opioid maintenance treatment need more analgesic drugs compared to control.[18] Study of Przeklasa-Muszynska and Dobrogowski has confirmed high efficacy and good tolerability of TD buprenorphine in the treatment of moderate to severe pain that cannot be effectively treated with non-opioid analgesics.[19] Zoltie and Cust have suggested that buprenorphine can be used in patients with acute abdominal pain without fear of masking the diagnosis.[20]

Study of Finlay et al. has confirmed the superiority of buprenorphine to Pethidine in control of pain in ureteric colic.[21] Bullingham et al. have evaluated the efficacy of buprenorphine and paracetamol for pain after minor orthopedic surgery with favorable results.[22]

Table 1. COWS score and VAS score (mean ± SD) of the groups during the study

Groups	VAS score				COWS score			
	Hour 0	Hour 1	Hour 6	Hour 24	Hour 0	Hour 1	Hour 6	Hour 24
Group 1 (mean ± SD)	8.58 ± 0.74	7.14 ± 0.31	5.88 ± 0.69	4.59 ± 0.74	16.94 ± 2.71	2.91 ± 1.33	7.05 ± 1.93	12.52 ± 3.29
Group 2 (mean ± SD)	8.70 ± 0.93	7.22 ± 0.47	4.47 ± 0.73	2.67 ± 0.53	18.26 ± 3.40	8.47 ± 2.25	3.02 ± 1.16	7.00 ± 1.68
P	0.621	0.550	0.001	< 0.001	0.095	< 0.001	< 0.001	< 0.001

COWS: Clinical opioid withdrawal score; VAS: Visual analogue scale; SD: Standard deviation

Study of Conaghan et al. showed that 7 days buprenorphine patches plus oral paracetamol are non-inferior to co-codamol (codeine plus paracetamol) tablets with respect to analgesic efficacy in older adults with osteoarthritis pain in the hip/knee.[23]

The present study also confirmed that SL buprenorphine is more effective than parenteral morphine in control of post-operative pain in opioid-dependent patients. Additionally, it produces less sever withdrawal syndrome in them.

Conclusion

Patients with opioid addiction who need analgesia for various reasons present a therapeutic challenge. Increased pain sensitivity and the development of opioid tolerance complicate the treatment of pain experienced by opioid-dependent patients. The present study suggests SL buprenorphine for control of pain and withdrawal syndrome in opioid-dependent patients.

Conflict of Interests

The Authors have no conflict of interest.

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درمان درد بیماران وابسته به مواد مخدر اپیوئیدی پس از جراحی: مقایسه بوپرنورفین زیرزبانی با مرفین وریدی

دکتر شعبانعلی علیزاده[۱]، دکتر غفار علی محمودی[۲]، دکتر حسن صلحی[۳]، دکتر بهمن صادقی سده[۴]، دکتر رضا بهزادی[۵]، دکتر امیر محمد کاظمی‌فر[۶]

مقاله پژوهشی

چکیده

مقدمه: درد حاد و مزمن در بیماران وابسته به مواد مخدر اپیوئیدی شایع است. عدم وجود درک کافی از کنش بین درد، مصرف اپیوئید و سندرم محرومیت، منجر به ایجاد مانعی برای مدیریت صحیح درد بیماران می‌گردد. مطالعه حاضر با هدف مقایسه تأثیر بوپرنورفین زیرزبانی با مرفین وریدی در کنترل درد بیماران وابسته به مواد پس از عمل جراحی انجام شد.

روش‌ها: ۶۸ بیمار با سن ۶۰-۲۰ سال به طور تصادفی از میان بیماران وابسته به مواد مخدر اپیوئیدی که به دلیل شکم درد حاد در یک بیمارستان آموزشی دانشگاهی در شهر اراک تحت لاپاراتومی قرار گرفته بودند، برای مطالعه حاضر انتخاب گردیدند. پس از اتمام جراحی و بیدار شدن بیمار، شدت درد وی و شدت سندرم محرومیت با استفاده از مقیاس سنجش نظری درد (Visual analog scale یا VAS) و مقیاس بالینی سندرم محرومیت (Clinical opioid withdrawal score یا COWS) در فواصل ۱ ، ۶ و ۲۴ ساعت پس از اتمام عمل جراحی سنجیده شد. در همان حال بیماران به دو گروه مساوی تقسیم شدند و با مرفین (۵ میلی‌گرم وریدی) یا بوپرنورفین (۲ میلی‌گرم زیرزبانی) اولین دوز ۱ ساعت پس از عمل و سپس هر ۶ ساعت (در ۲۴ ساعت اول) تحت درمان ضد درد قرار گرفتند. نتایج حاصل شده با استفاده از نرم‌افزار SPSS تجزیه و تحلیل گردید.

یافته‌ها: مقیاس سنجش نظری درد ۶ و ۲۴ ساعت پس از عمل جراحی در گروه بوپرنورفین به ترتیب ۰/۷۳ ± ۴/۴۷ و ۰/۵۳ ± ۲/۶۷ به دست آمد؛ در حالی که این مقادیر در گروه مرفین به ترتیب ۰/۶۹ ± ۵/۸۸ و ۰/۷۴ ± ۴/۶۸ بود. بیماران گروه بوپرنورفین به طور هم‌زمان علایم سندرم محرومیت با شدت کمتر را نیز نشان دادند.

نتیجه‌گیری: مطالعه حاضر نشان داد که بوپرنورفین زیرزبانی یک داروی مؤثر و غیر تهاجمی برای کنترل درد پس از عمل در بیماران وابسته به مواد مخدر اپیوئیدی است. پزشکان می‌توانند با اطمینان خاطر، از این دارو جهت درمان درد پس از عمل بهره ببرند.

واژگان کلیدی: بوپرنورفین، مرفین، درد پس از عمل، وابستگی به مواد مخدر اپیوئیدی، سندرم محرومیت

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۱- استادیار، جراح عمومی، گروه جراحی، دانشکده پزشکی، دانشگاه علوم پزشکی اراک، اراک، ایران
۲- استادیار، سم‌شناس بالینی و متخصص پزشکی قانونی، گروه داخلی، دانشکده پزشکی، دانشگاه علوم پزشکی لرستان، خرم‌آباد، ایران
۳- دانشیار، سم‌شناس بالینی، گروه طب اورژانس، دانشکده پزشکی، دانشگاه علوم پزشکی اراک، اراک، ایران
۴- استادیار، اپیدمیولوژیست، گروه بهداشت عمومی، دانشکده پزشکی، دانشگاه علوم پزشکی اراک، اراک، ایران
۵- پژوهشگر، گروه طب اورژانس، دانشکده پزشکی، دانشگاه علوم پزشکی اراک، اراک، ایران
۶- دانشیار، سم‌شناس بالینی، گروه داخلی، دانشکده پزشکی، دانشگاه علوم پزشکی قزوین، قزوین، ایران
نویسنده مسؤول: دکتر غفار علی محمودی Email: mahmoudi.gh@lums.ac.ir