Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/burns

Prediction of effect-site concentration of sufentanil by dose–response target controlled infusion of sufentanil and propofol for analgesic and sedation maintenance in burn dressing changes

Lingyang Chen [a], *Mingcang Wang* [a,*], *Haifei Xiang* [a], *Xianju Lin* [a], *Donghang Cao* [a], *Liyue Ye* [b]

[a] *Department of Anesthesiology, Affiliated Taizhou Hospital of Wenzhou Medical College, Linhai, Zhejiang 317000, China*

[b] *Department of Burn, Affiliated Taizhou Hospital of Wenzhou Medical College, Linhai, Zhejiang 317000, China*

ARTICLE INFO

Article history:
Accepted 4 August 2013

Keywords:
Sufentanil
Target controlled infusion
Effective concentration
Dressing change
Burn

ABSTRACT

This study was to investigate the feasibility and efficiency of by target-controlled infusion (TCI) for analgesia and sedation during burn dressing change, and to predict the effect-site concentration of sufentanil. Eighty burn patients were randomly and evenly divided into four groups according to target sufentanil effect-site concentration (0.2, 0.3, 0.4 and 0.5 ng/ml). The sufentanil–propofol TCI was carried out during dressing changes. The effect-site concentration of propofol was maintained at 1.2 μg/ml. The dose–response relationships of sufentanil for providing adequate analgesia were evaluated by visual analog scales and Ramsay sedation scores. The effect-site concentration of sufentanil was calculated by Probit regression analysis. Incidence of respiratory depression, doctors and patients' satisfaction and adverse events were assessed. The EC_{50} and EC_{95} of sufentanil to maintain anesthesia for uncovering the inner layer dressings during TCI were 0.278 ng/ml (95% CI 0.231–0.318 ng/ml) and 0.394 ng/ml (95% CI 0.366–0.530 ng/ml), respectively, while the EC_{50} and EC_{95} of sufentanil to maintain anesthesia for wound management were 0.349 ng/ml (95% CI 0.299–0.366 ng/ml) and 0.465 ng/ml (95% CI 0.430–0.563 ng/ml), respectively. Doctors and patients' satisfaction were significantly higher in the 0.4 and 0.5 ng/ml groups than the 0.2 ng/ml group. One and three patients had respiratory depression in the 0.4 and 0.5 ng/ml groups, respectively. No adverse events occurred after operations. In conclusion, low dose sufentanil–propofol TCI for anesthesia and sedation maintenance in burn dressing changes is feasible and effective, and wound management requires higher effect-site concentrations of sufentanil than disclosing inner layer dressings.

1. Introduction

Burns are one of the most devastating and intensely painful traumas with long-term physical and psychosocial effects [1,2]. The patients will experience pain varied in severity not only at rest but also during therapeutic procedures [3]. They may further suffer from consequent psychiatric problems [4]. Though the adverse sequalae of inadequate pain control have been long recognized, relieving burn-related pain is still a major unmet medical need [5,6].

* *Corresponding author*. Tel.: +86 0576 85120120.
E-mail address: mingcang_wang@hotmail.com (M. Wang).

0305-4179/$36.00
http://dx.doi.org/10.1016/j.burns.2013.08.002

The use of opioids has been one of the common pharmacologic methods of pain management [7]. Repeated intravenous injection of opioids has been a standard regimens, and intramuscular administration is also used, but very often the analgesic outcomes are inadequate. Patients with repeated administration or increase in dose may also risk opioid-induced respiratory depression, nausea and vomiting, thus prolonging their treatment. However, adjuvant use of intravenous lidocaine for pain relief is also of poor clinical benefit in terms of overall pain control and opioid consumption [8]. Patient-controlled analgesia (PCA) with fentanyl and morphine has showed certain analgesic efficacy, but it is not remarkable during therapeutic procedures [9,10]. Sufentanil is a powerful synthetic opioid analgesic drug, approximately 10 times more potent than its analog fentanyl, with minimal cardiovascular effects. Several studies have shown target controlled infusion (TCI) [11] of sufentanil provides stable and improved quality of anesthesia, better hemodynamic control, as well as anticipated recovery without causing postoperative respiratory depression [12–15].

Pain control is of high priority for treatment. Effective anesthesia can greatly reduce physical and psychosocial suffering. Pharmacologic methods such as morphine, diazepam, or propofol administration, as well as psychosocial approaches like hypnosis or stress reducing strategies have been successfully used for pain management in burn dressing changes [5,16]. However, exploration for adequate anesthesia is still required. The propofol and sufentanil TCI has been used for anesthesia and sedation [15]. But its application in burn dressing changes has not been reported yet. Besides, the appropriate doses also wait investigation as specific pharmacokinetics and pharmacodynamics may be different in burn patients. We herein investigated the safety and efficiency of sufentanil–propofol by TCI for analgesia and sedation, and predicted the effect-site concentration of sufentanil for analgesia.

2. Materials and methods

The study protocol was approved by Ethics Committee of Affiliated Taizhou Hospital of Wenzhou Medical College. Informed written consent was obtained from all patients.

2.1. Patients

Eighty patients, 49 males and 31 females, with 20–50% total burn surface area (TBSA) were studied in Affiliated Taizhou Hospital of Wenzhou Medical College from August 2009 to October 2011. All patients were between 23 and 50 years of age and ASA 1–2 physical statuses. The exclusion criteria, previously described by Prakash et al. [9] and Gallagher et al. [17], briefly were body weight <45 or >100 kg, pregnancy, age <18 or >70 years, an ASA physical status of IV–V, a history of opioid abuse, an allergy to opioids, or pulse oxygen saturation (SpO_2) <90%. Our preliminary study indicated sufentanil TCI at 0.3–0.4 ng/ml can provide effective anesthesia. Therefore all patients were randomly divided into four groups according to the target effect-site concentration (C_e) of sufentanil for the maintenance of anesthesia as follows: 0.2, 0.3, 0.4 and 0.5 ng/ml. Each group contained twenty patients. Though observed, the differences in burn wound deepness were not yet concerned in this study.

2.2. Study design

Primary endpoints: number of cases without dose adjustment. Secondary endpoint: respiratory depression event, patient and doctor satisfaction. Hypothesis: the ideal effect-site concentration will result in the maximum number of cases without dose adjustment, with less incidence of adverse events but better patient and doctor satisfaction.

2.3. Analgesic treatment and dressing change

Fasting and no premedication were administered to all patients. No oral analgesics was given. Nasal catheter oxygen inhalation was used (3 L/min). Standard monitoring included automatic noninvasive blood pressure (BP), heart rate (HR), respiratory rate (RR), and SpO_2. All patients received TCI with 1.2 μg/ml propofol using the Marsh pharmacokinetic model [18] and sufentanil at each target C_e using Bovill pharmacokinetic model [19] 5 min before dressing changes. Both drugs were controlled by microcomputer-controlled pumps (Orchestra). The 1.2 μg/ml propofol was chosen as patients can keep consciousness and orientation at this concentration according to *Miller's Anesthesia* [20]. Burn dressing change was carried out till target C_e was reached. The target C_e of sufentanil was maintained unchanged throughout the operation when a visual analog (VAS) 0–10 pain scale was 2–4 points, a Ramsay sedation scale (RSC) score was 2 or 3 points, and SpO_2 >90%. Or the target C_e would be adjusted according to VAS and RSC scores. The target C_e was increased by 0.05 ng/ml at regular 5-min intervals if the patient experienced pain or anxiety. In contrast, the target C_e was decreased by 0.05 ng/ml at regular

Table 1 – Clinical and demographic characteristics.

	Target effect-site concentration of sufentanyl (ng/ml)			
	0.2	0.3	0.4	0.5
Number of patients	20	20	20	20
Age (years)	32 ± 6	35 ± 6	33 ± 7	31 ± 6
Male/female ratio	13/7	11/9	14/6	11/9
Body weight (kg)	63 ± 11	59 ± 8	65 ± 10	62 ± 9
Total burn surface area (%)	37 ± 8	39 ± 9	36 ± 12	35 ± 7
Duration of dressing change (min)	32 ± 9	32 ± 8	30 ± 10	35 ± 10

All data are expressed as the mean ± SD or number of patients