REMIFENTANIL INFUSION FOR ADULT BURN DRESSING CHANGES

SUMMARY

Remifentanil, a derivative of fentanyl, is an ultra-short-acting μ-opioid receptor agonist with a rapid onset of action (~1 minute) and peak effect, and a rapid offset of action following discontinuation of infusion (~3-10 minutes). The use of remifentanil as an analgesic agent for dressing changes in adult burn patients is not well described; however, the unique pharmacokinetic profile of this agent allows rapid, titratable analgesia without residual sedation regardless of the duration of infusion, making this a valuable opioid analgesic option for use during dressing changes.

RECOMMENDATIONS

- **Level 1**
  - **None**
- **Level 2**
  - **None**
- **Level 3**
  - **Remifentanil infusion is an analgesic option for burn dressing changes due to its rapid onset and short duration of action**
  - **Recommended procedure:**
    - **Initiate remifentanil infusion at 0.15 mcg/kg/min and titrate by 0.025 mcg/kg/min every 5 minutes as needed for desired analgesia/sedation**
    - **Alternative analgesics should be administered prior to discontinuation of infusion as no residual analgesic activity will be present within 5-10 minutes of discontinuation**
    - **Resuscitative and intubation equipment, oxygen, and an opioid antagonist should be readily available during dressing change**

INTRODUCTION

Burn patients must frequently undergo painful dressing changes that require analgesia to maintain an adequate level of sedation throughout the procedure. Large doses of opioids are often required to achieve patient comfort during dressing changes of severe burns; however, these large doses often result in residual somnolence associated with delayed awakening and recovery from procedures. As a result, burn patients may remain ventilator-dependent for an extended period of time.

Remifentanil, a derivative of fentanyl, is an ultra-short-acting μ-opioid receptor agonist with a rapid onset of action (~1 minute) and peak effect, and a rapid offset of action following discontinuation of infusion (~3-10 minutes) (1,2). The unique pharmacokinetic profile of this agent allows rapid, titratable analgesia without residual sedation regardless of the duration of infusion (1,3). Due to its predictable termination of

EVIDENCE DEFINITIONS

- **Class I:** Prospective randomized controlled trial.
- **Class II:** Prospective clinical study or retrospective analysis of reliable data. Includes observational, cohort, prevalence, or case control studies.
- **Class III:** Retrospective study. Includes database or registry reviews, large series of case reports, expert opinion.
- **Technology assessment:** A technology study which does not lend itself to classification in the above-mentioned format. Devices are evaluated in terms of their accuracy, reliability, therapeutic potential, or cost effectiveness.

LEVEL OF RECOMMENDATION DEFINITIONS

- **Level 1:** Convincingly justifiable based on available scientific information alone. Usually based on Class I data or strong Class II evidence if randomized testing is inappropriate. Conversely, low quality or contradictory Class I data may be insufficient to support a Level I recommendation.
- **Level 2:** Reasonably justifiable based on available scientific evidence and strongly supported by expert opinion. Usually supported by Class II data or a preponderance of Class III evidence.
- **Level 3:** Supported by available data, but scientific evidence is lacking. Generally supported by Class III data. Useful for educational purposes and in guiding future clinical research.

effect, remifentanil allows rapid awakening after discontinuation of infusion. Furthermore, because remifentanil is rapidly metabolized by nonspecific blood and tissue esterases to an essentially inactive metabolite, the pharmacokinetics of remifentanil are not altered to a clinically significant extent in patients with renal or hepatic impairment (1,3).

Remifentanil is similar to other opioids with regard to its adverse effect profile. The most significant adverse effects are dose-dependent and include hypotension, bradycardia, and respiratory depression. Peak hemodynamic effects occur within 3 to 5 minutes of an infusion rate increase. While respiratory rate is minimally decreased at infusions of 0.05 to 0.1 mcg/kg/min, incremental increases in rate >0.05 mcg/kg/min and infusions of >0.2 mcg/kg/min have been associated with transient and reversible respiratory depression, apnea, and muscle rigidity. Respiratory depression can be managed by decreasing the rate of infusion by 50% or by temporarily discontinuing the infusion. Bradycardia and hypotension can be reversed by decreasing the rate of infusion or by administering fluids or vasopressors. Anticholinergic agents, such as atropine or glycopyrrolate, may also be used for bradycardia and/or hypotension. Bolus doses or rapid infusions of remifentanil should be avoided as this may result in chest wall rigidity, or the inability to ventilate. Chest wall rigidity can be treated by decreasing the rate or discontinuing the infusion or by administering a neuromuscular blocker. Due to these potential adverse effects, respiratory status, blood pressure, and heart rate must be monitored at all times. These adverse effects dissipate within minutes of discontinuing or decreasing the infusion rate of remifentanil (3).

Dosing and Administration

Initiate remifentanil at 0.15 mcg/kg/min starting five minutes prior to dressing change. Starting doses of remifentanil should be based on ideal body weight (IBW) in obese patients (actual body weight [ABW] > 130% IBW) (3). Due to the risk of respiratory depression and muscle rigidity, bolus injections of remifentanil are not recommended in the ICU setting, especially in non-intubated patients. Titrate the infusion rate in increments of 0.025 mcg/kg/min at intervals of ≥5 minutes to achieve the desired level of analgesia/sedation. If sedation is not adequate at an infusion rate of 0.2 mcg/kg/min, initiation of an appropriate sedative agent (e.g. propofol or midazolam) may be recommended, as infusion rates >0.2 mcg/kg/min are associated with respiratory depression. Respiratory and cardiovascular status, blood pressure, and heart rate must be continually monitored. Alternative analgesics should be administered prior to the discontinuation of remifentanil infusion as no residual analgesic activity will be present within 5-10 minutes of discontinuation (e.g. IV morphine or fentanyl 30 minutes prior to end of procedure). In addition, IV tubing should be cleared at time of infusion discontinuation to prevent inadvertent administration of residual remifentanil at a later point in time (3).

Initial IV Infusion Rates & Titration Increments of Remifentanil (mL/hr) for a 50 mcg/mL Solution

Patient Weight (kg)	Starting Infusion Rate (0.15 mcg/kg/min) in mL/hr	Titration Increments (0.025 mcg/kg/min) in mL/hr
40	7.2	1.2
50	9.0	1.5
60	10.8	1.8
70	12.6	2.1
80	14.4	2.4
90	16.2	2.7

Ideal Body Weight = (Height in inches >5 feet) x 2.3 + 50kg (male) or 45.5kg (female)

LITERATURE REVIEW

While the use of remifentanil for conscious sedation during short, painful procedures has been described, there is limited information available specifically on the use of remifentanil as an analgesic agent for burn dressing changes (4-6).

[Class III] Le Floch et al. evaluated the use of remifentanil as the sole analgesic agent during 60 dressing changes in 27 spontaneously breathing non-intubated burn patients over a five-month period. Remifentanil infusion was initiated at a dose of 0.1 mg/kg/min after patients received at least 5 minutes of oxygen to obtain a FiO_2 of 40%. Dressing changes were initiated 5 minutes after the start of the infusion. If the patient expressed pain of >4 on a verbal rating scale (VRS) from 0-10, the procedure was stopped and the dose was increased by 0.025 mg/kg/min. The procedure was continued 3 minutes later and this process was repeated if the VRS remained >4. If drowsiness or reduced pulse oxygen concentration occurred, the dose was decreased in increments of 0.025 or 0.05 mg/kg/min, respectively, every 3 minutes as necessary. Thirty minutes prior to the end of the procedure, patients received IV morphine. If a patient was in pain after the dressing change, an additional 3 mg of morphine was given every 5 minutes until the VRS was <4. No other hypnotic, anxiolytic, or analgesic drug, other than the morphine, was given. Monitoring continued for one hour after the last dose of morphine. The average dose of remifentanil that resulted in a VRS <4 was 0.42 ± 0.22 mg/kg/min. VRS during the procedure ranged from 1.07 ± 1.51 to 5.92 ± 2.38 and no patient had a VRS continuously >4. Even patients with high levels of pain at some point were very satisfied with the analgesia provided. There were no statistically significant variations in vital signs (HR, MAP, SpO_2) during the procedure compared with before, as compared using the Z test. Thirty-eight adverse effects occurred in 19 procedures: 14 episodes of drowsiness, 18 desaturations to <95%, and 3 episodes of decreases in MAP (65-70), all of which were rapidly reversed with reduction or brief interruption of infusion (7). *Note: dosages in this article were written as mg/kg/min; however, mcg/kg/min is more consistent with product information and drug references.*

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