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Analgesic effect of dexmedetomidine in a patient with herpetic stomatitis after living-donor lung transplantation

Yoshifumi Ohashi[1], Noriyuki Ohta[1], Osamu Hirao[1], Akinori Uchiyama[1], Takashi Mashimo[2], and Yuji Fujino[1]

[1] Intensive Care Unit, Osaka University Hospital, 2-15 Yamadaoka, Suita, Osaka 565-0871, Japan
[2] Department of Anesthesiology and Intensive Care Medicine, Osaka University Medical School, Osaka, Japan

Abstract
A 31-year-old woman suffering from bronchiolitis obliterans received bilateral living-donor lung transplantation to treat end-stage respiratory failure. After 5 days' mechanical ventilation, the patient was successfully extubated. During mechanical ventilation, the patient was sedated with a continuous intravenous infusion of propofol and dexmedetomidine (DEX). To assuage postoperative pain, morphine was infused, first intravenously, then epidurally. The administration of DEX was continued after extubation to prevent agitation. After the administration of epidural morphine was discontinued on day 10 in the intensive care unit (ICU), the patient complained of pain in the oral cavity. Greater pain was reported after the discontinuation of DEX, and symptoms of tachycardia and dyspnea appeared. A dermatologist diagnosed the oral symptoms as herpetic stomatitis, and a course of treatment with aciclovir was begun. A continuous infusion of DEX was again started on the same day, and was continued until ICU day 13. During the administration of DEX, the oral cavity pain was bearable. The patient was successfully discharged from the ICU on ICU day 13. We conclude that DEX could be used to provide analgesia for herpetic stomatitis after living-donor lung transplantation, at a dosage that achieves appropriate sedation.

Key words Lung transplantation · Analgesia · Alpha-2 adrenoreceptor · Herpetic stomatitis

Introduction

Dexmedetomidine (DEX) is a unique agent that produces a sedative effect by activating α_2 adrenergic receptors in the locus coeruleus [1,2]. DEX also produces an analgesic effect by activating α_2 receptors in the spinal cord [3,4]. Since it was first used clinically in Japan, DEX has rapidly become popular for use as a sedative drug during the postoperative period [5,6]. Many investigators have also reported the postoperative usefulness and safety of DEX after organ transplantation, especially after liver transplantation [7,8]. Here we report a case in which a sedative dose of DEX provided good pain relief in a patient with herpetic sotmatitis pain after living-donor lung transplantation.

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Case report

A 31-year-old woman suffering from bronchiolitis obliterans received bilateral living-donor lung transplantation to treat end-stage respiratory failure. Lower lung lobes were donated by her elder siblings, a brother and a sister. The patient was admitted to the intensive care unit (ICU) after the operation. She was mechanically ventilated for 5 days and successfully extubated. During mechanical ventilation, the patient was initially sedated with a continuous intravenous infusion of propofol 2 $mg \cdot kg^{-1} \cdot h^{-1}$ and morphine 2 $mg \cdot h^{-1}$. On ICU day 3, the continuous morphine adminstration was switched from intravenous to epidural infusion. At the same time, to achieve a satisfactory level of sedation (Ramsay score II to III), a continuous infusion of DEX was added, at a rate of 0.7 $\mu g \cdot kg^{-1} \cdot h^{-1}$ and this was continued after extubation to prevent agitation. After the cessation of the epidural morphine and DEX on ICU day 10, the patient complained of pain in the oral cavity, and herpetic stomatitis was diagnosed by a dermatologist. A course of aciclovir was begun. The pain in the oral cavity became intractable, and tachycardia and dyspnea developed. To counter these complaints, DEX infusion was started again on the same day. The pain in the oral cavity remained bearable during the administration of DEX. When DEX was discontinued on ICU day 13, the pain in the oral cavity had resolved, and the patient was successfully discharged from the ICU.

Discussion

For intubated patients in our ICU, we use DEX as an adjunctive sedative when, as in the patient reported here, appropriate sedation cannot be achieved by a continuous infusion of propofol or midazolam. Because DEX causes such a small amount of respiratory depression [9], administration can be continued after extubation when necessary. In our experience, the analgesic effects of DEX are not usually sufficient for complete postoperative analgesia. In the patient reported here, continuous morphine infusion, initially intravenous, then epidural, was also applied. For this patient, nonsteroidal anti-inflammatory drugs (NSAIDs) were not appropriate analgesic drugs because of the high risk of nephrotoxicity when these agents are given in conjunction with immunodepressants.

Abnormalities in the oral cavity of our patient were noticed for the first time after the discontinuation of epidural morphine. The pain then worsened after the discontinuation of DEX.

The antinociceptive effects of α_2 adrenoreceptor agonists have been largely attributed to stimulation of the α_2 adrenoreceptor in the substantia gelatinosa of the dorsal horn of the spinal cord [10–13]. In addition, the expression of α_2 adrenoreceptor in rat trigeminal root ganglion neurons has been reported, by Takeda et al. [14], and this phenomenon may explain the antinociceptive effect of DEX in our patient. There are some lines of evidence to suggest that the analgesic mechanism of α_2 agonists is not due to their action upon α_2 adrenoreceptors in the locus coeruleus, although this supraspinal mechanism of analgesic action has not been completely excluded [10,15,16]. In the treatment of postoperative pain, there are a number of reports that the administration of α_2 agonists can reduce the use of opioids, local anesthetics, and other analgesics [17–20]. Furthermore, there have been reports that the systemic administration of α_2 agonists has an analgesic action by dulling the unpleasantness of pain, which may be related to their sedative properties [10,21].

On the other hand, α_2 receptor agonists may block pain in other ways. Several studies have reported the effective application of clonidine hydrochloride to treat the acute pain caused by Herpes zoster infection or post-herpetic neuralgia [22–26]. In these studies, other analgesics such as opioids and NSAIDs were ineffective: only clonidine effectively assuaged the pain. In these studies clonidine was applied topically, directly to the mucosal surface, or it was administered through the neuroaxial route with local anesthetics. In a mouse model of acute herpetic pain, α_2 adrenoreceptor agonists were also effective [26]. These clinical and experimental results suggest that α_2 adrenoreceptors are probably involved in the pain associated with herpetic infection. The analgesia provided by DEX for herpetic stomatitis could be anticipated; however, the analgesic effect of DEX at a clinical dosage that achieves appropriate postoperative sedation has not been reported before.

In Japan, DEX has been officially approved for use for up to 24 h. However, some investigators have reported that DEX can be used safely for more than 24 h. In North America, clinical trials to test the safety of long-term administration of DEX are ongoing. Potential side-effects of the long-term use of DEX are post-cessation rebound hypertension and tachycardia. In the patient reported here, DEX was administered until the oral herpes sores had been almost completely healed by treatment with an antiviral drug. Despite this longer period of administration, no post-cessation side-effects were observed after the patient's discharge from the ICU.

In conclusion, DEX can provide analgesia for herpetic stomatitis after living-donor lung transplantation, at a dosage that achieves appropriate sedation.

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