Comparison of the Efficacy of Dexmedetomidine plus Fentanyl Patient-controlled Analgesia with Fentanyl Patient-controlled Analgesia for Pain Control in Uterine Artery Embolization for Symptomatic Fibroid Tumors or Adenomyosis: A Prospective, Randomized Study

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ABSTRACT

Purpose: To investigate whether dexmedetomidine infusion could reduce opioid consumption and opioid-related side effects after uterine artery embolization (UAE).

Materials and Methods: Fifty patients undergoing UAE for symptomatic leiomyomas or adenomyosis were randomized into two groups. In 25 patients, dexmedetomidine infusion was started at 0.2 μg/kg/h at 30 minutes before the procedure, followed by 0.4 μg/kg/h for 6 hours after the procedure. In another 25 patients (control group), volume-matched normal saline solution was administered. Both groups received fentanyl-based intravenous patient-controlled analgesia (PCA; fentanyl 10 μg/h with a bolus dose of 20 μg) during the 24 hours after the procedure. Nonspherical polyvinyl alcohol particles were used. Pain scores, fentanyl consumption, need for additional analgesics, and side effects were assessed for 24 hours after UAE.

Results: Compared with the control group, patients in the dexmedetomidine group required 28% less PCA fentanyl during the 24 hours after UAE ($P = .006$). Numeric rating scale scores for pain (5.0 ± 2.4 vs 7.0 ± 2.2; $P = .026$) and the need for additional analgesics (two of 25 vs 17 of 25; $P < .001$) were lower in the dexmedetomidine group than in the control group during the first 1 hour after UAE. The incidence and severity of nausea and vomiting during the 24 hours after UAE were lower in the dexmedetomidine group than in the control group ($P < .05$).

Conclusions: The addition of dexmedetomidine infusion to fentanyl PCA provides better analgesia, fentanyl-sparing effect, and less nausea and vomiting, without significant hemodynamic instability.

ABBREVIATIONS

BP = blood pressure, HR = heart rate, IV = intravenous, NRS = numeric rating scale, NSAID = nonsteroidal antiinflammatory drug, PCA = patient-controlled analgesia, PVA = polyvinyl alcohol, UAE = uterine artery embolization

Uterine artery embolization (UAE) has gained popularity for symptomatic leiomyomas (fibroid tumors) because it is a minimally invasive treatment alternative to hysterectomy and has a good long-term success rate (1,2). However, severe postprocedural pain can develop after UAE as a result of tumor and possible myometrial ischemia (3–5).

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According to previous reports, more than 92% of patients experienced postprocedural pain and 99% of patients required intravenous (IV) patient-controlled analgesia (PCA) with opioids (5,6). Several modalities with opioid-based IV PCA have been suggested for acute pain control after UAE (5,7–11).

Dexmedetomidine is a selective α2-receptor agonist and has sympatholytic, analgesic, and sedative properties, with a lack of respiratory depression (12). Dexmedetomidine has been approved for use for sedation/analgesia in the intensive care unit and for sedation during surgery or other procedures. Dexmedetomidine also showed superior analgesia and opioid-sparing effects when it was infused as an adjuvant agent to opioid-based IV PCA during the postoperative period (13–15). Therefore, additional administration of dexmedetomidine to opioid-based IV PCA may be useful for patients undergoing UAE who are prone to severe postprocedural pain. The aims of the present randomized study were (i) to investigate the efficacy of dexmedetomidine in the reduction of fentanyl consumption and (ii) to evaluate the effect of dexmedetomidine on the reduction of opioid-related side effects during the first 24 hours after UAE in patients undergoing UAE with uterine fibroid tumors or adenomyosis.

MATERIALS AND METHODS

This study was approved by our institutional review board and was registered at http://clinicaltrials.gov (registry number NCT01578174). Between April 2012 and September 2012, we enrolled 50 consecutive patients, aged 30–50 years, who underwent UAE for uterine fibroid tumors or adenomyosis. Written informed consent was obtained from all patients before randomization. Patients were not admitted to the study if any of the following criteria were present: known or suspected allergy to α2 adrenergic agonists or nonsteroidal antiinflammatory drugs (NSAIDs), history of uncontrolled hypertension (dexmedetomidine can cause transient hypertension), heart block greater than first degree (dexmedetomidine can cause bradycardia), cognitive impairment, chronic use of antipsychotic medications, kidney or liver disease (dexmedetomidine undergoes almost complete hepatic metabolism with very little unchanged excretion in urine and feces), and body mass index of 30 kg/m^2 or greater.

Patients were randomly assigned into two groups by computer-generated random numbers by using SAS software (version 9.2; SAS, Cary, North Carolina). In the dexmedetomidine group (n = 25), dexmedetomidine (Precedex 100 μg/mL; Hospira, Lake Forest, Illinois) infusion was started at 0.2 μg/kg/h at 30 minutes before the procedure, followed by 0.4 μg/kg/h for 6 hours after UAE; the recommended dose for dexmedetomidine infusion is in the range of 0.2–0.7 μg/kg/h (12). In the control group (n = 25), volume-matched normal saline solution infusion was administered as placebo. Dexmedetomidine was diluted with normal saline solution at a concentration of 2 μg/mL in 100 mL. Dexmedetomidine or normal saline solution was prepared and labeled with a particular identification marker, A or B, by an anesthesiologist who did not participate in data collection. Both groups received IV PCA (Accumate 1100; WooYoung Medical, Seoul, Korea) during the 24-hour period after the UAE procedure. The PCA regimen was composed of fentanyl (Hana Pharm, Seoul, Korea) 1,500 μg, ketorolac 90 mg (Keromin; Hana Pharm, Seoul, Korea), and ramosetron 0.3 mg (Nasea, Astellas, Tokyo, Japan), all of which were mixed with normal saline solution to a total volume of 150 mL. The bolus dose was 2 mL at a basal infusion rate of 1 mL/h, with a lockout interval of 10 minutes. Therefore, fentanyl was delivered at a rate of 10 μg/h with a bolus dose of 20 μg.

All patients in both groups received one tablet of Ultracet (Janssen, Seoul, Korea), which is a combination of tramadol 75 mg and acetaminophen 650 mg, every 12 hours for 24 hours. The investigator, radiologists, and nurses, as well as patients, were blinded to group assignment of identification marker A or B. For safety evaluation, patients were monitored for noninvasive blood pressure (BP), pulse oxygen saturation, and heart rate (HR) during dexmedetomidine or normal saline solution infusion.

Embolization Procedure

All patients in both groups received ketorolac 30 mg and ondansetron 4 mg IV (Onseran; Yuhan, Seoul, Korea) just before starting the procedure. Unilateral right femoral artery access was used in all cases. A 5.0-F RHR catheter (Cook, Bloomington, Indiana) was placed in the internal iliac artery, and a coaxial 3-F microcatheter (MicroFerret; Cook) was advanced distally into the uterine artery. Embolization was performed with the catheter tip beyond the origin of the cervicovaginal branch. The embolic agent was nonspherical polyvinyl alcohol (PVA) particles (Contour; Boston Scientific, Natick, Massachusetts) mixed with 60 mL of 1:1 saline solution/contrast agent mixture. PVA particles 250–355 μm or 355–500 μm in size were injected at the beginning of embolization for uterine leiomyomas, and particle size was progressively increased to 355–500 μm or 500–700 μm toward the endpoint. In patients with adenomyosis, 150–250-μm PVA particles were employed initially, and larger particles were progressively used—250–355 μm and then 355–500 μm—until the endpoint (16). Embolization was done until complete cessation of blood flow was achieved in the ascending uterine artery for 10 cardiac beats.

In patients in whom unilateral fibroid disease was present with blood flow from only the ipsilateral uterine artery, the contralateral normal uterine artery was also embolized by using one half or two thirds of a 355–500-μm or 500–700-μm PVA particle, but sluggish blood flow was allowed to persist. The choice of particle size was made during the procedure by an interventional radiologist (M.D.K.) with 10 years of experience in UAE who has