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 or Adenomyosis: A Prospective, Randomized Study

Poster No.: C-0777
Congress: ECR 2013
Type: Scientific Exhibit
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Keywords: Sedation, Embolisation, Catheter arteriography, Interventional vascular, Genital / Reproductive system female
DOI: 10.1594/ecr2013/C-0777

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Purpose

Uterine artery embolization (UAE) has gained popularity for symptomatic uterine fibroids and adenomyosis because it is a minimally invasive treatment. However, significant post-procedural pain is a main limitation of UAE. More than 92% of patients experienced post-procedural pain and 99% of patients required intravenous (IV) patient-controlled analgesia (PCA) with opioid. Dexmedetomidine is a selective #2-receptor agonist and has sympatholytic, analgesic and sedative properties without respiratory depression. Post-operative dexmedetomidine infusion as an adjuvant to opioid-based IV PCA produced superior analgesia and opioid-sparing effect. This study aimed to investigate the efficacy of dexmedetomidine in the reduction of fentanyl consumption and opioid-related side effects during the first 24 h in patients undergoing UAE with uterine fibroids or adenomyosis.
Methods and Materials

Between April 2012 and September 2012, we enrolled 50 consecutive patients, aged 30-50 years, who underwent UAE with uterine fibroids or adenomyosis. Patients were randomly assigned into two groups. In the dexmedetomidine group (Group D, n = 25), dexmedetomidine (Precedex® 100 µg/mL, Hospira Inc, Rocky Mount, USA) infusion was started by 0.2 µg/kg/h at 30 min before procedure, followed by 0.4 µg/kg/h for 6 h after UAE. In the control group (Group C, n = 25), volume-matched normal saline infusion was administered as placebo. Dexmedetomidine was diluted with normal saline to a concentration of 2 µg/mL in 100mL. Both group received IV PCA (Accumate 1100®, WooYoung Medical, Seoul, Korea) during post-procedure 24 h. The PCA regimen was composed of fentanyl 1500 µg, ketorolac (Keromin®, Ha Na Pharm, Seoul, Korea) 90 mg, and ramosetron (Nasea®, Astellas, Tokyo, Japan) 0.3 mg and mixed with normal saline in a total volume of 150 mL. The basal infusion rate was 1 mL/h, and a bolus dose was 2 mL with a lockout interval of 10 min.

Patients characteristics including age, height, weight, history of postoperative nausea and vomiting or motion sickness, current smoking, diagnosis, presence of exclusive unilateral uterine artery supply and duration of UAE procedure were recorded. Administered fentanyl doses at post-procedural 6, 12, 18, and 24 h. The assessment of pain, sedation, and side effects such as nausea and vomiting, dizziness, headache, pruritus, hypotension, bradycardia, desaturation were made at the end of procedure and post-procedural 1, 2, 4, 6, 8, 12, and 24 h. Pain was evaluated using an 11-point numerical rating scale (NRS). Nausea and vomiting was graded on a four-point scale (0 = no nausea; 1 = mild nausea; 2 = severe nausea requiring antiemetics; and 3 = retching and/or vomiting). Sedation scores were recorded on a four-point scale (0 = fully awake; 1 = drowsy, closed eyes; 2 = asleppy, easily aroused with light tactile stimulation or a simple verbal command; 3 = asleep, arousable only by strong physical stimulation; and 4 = unarousable).
Results

50 patients received dexmedetomidine or saline after randomization and all patients completed the study (Fig. 1). Patients characteristics were similar between the two groups (Table 1). Doses of fentanyl consumption via PCA are shown in Figure 2. Patients in Group D required less fentanyl during first 6 h after procedure (Bonferroni corrected $P < 0.001$), but fentanyl consumption was not significantly different between the two groups after 6 h. The cumulative fentanyl consumption at 24 h was 28% less in Group D compared with Group C (729 ± 342 µg vs 1017 ± 363 µg, $P = 0.006$). NRS score for pain (5.0 ± 2.4 vs 7.0 ± 2.2, Bonferroni corrected $P = 0.026$) and the need for additional analgesics (2/25 vs 17/25, $P < 0.001$) were lower in Group D compared with Group C during first 1 h after procedure (Figure 3 and Table 2). Highest NRS score during 24 hours was lower in Group D compared with Group C (7.2 ± 2.1 vs 8.8 ± 1.4, $P = 0.004$). The level of sedation was higher in Group D compared with Group C ($P < 0.001$) and one patient in Group D had a sedation score of 3 during first 6 h for which dexmedetomidine infusion was maintained (Table 3). However, sedation scores were similar between the two groups after dexmedetomidine infusion discontinued. The patients in Group D had less nausea and vomiting and received less antiemetics compared with Group C ($P < 0.05$).

Discussion

Dexmedetomidine infusion provided better analgesia and reduced fentanyl requirement by 28% after UAE. The incidence of nausea and vomiting were reduced in patients who received dexmedetomidine.

Pain score (5 vs 7), dose of PCA fentanyl consumption (47 µg vs 83 µg) and need for additional analgesics (2 vs 17) were significantly lower in Group D compared with Group C during first 1 h, respectively. Lesser requirement of fentanyl in Group D might account for not only analgesic action of dexmedetomidine, but sedative effect since sedation score was higher in Group D during 6 h, compared to Group C.

Dexmedetomidine infusion reduced the incidence of vomiting by 56% and antiemetics usage by 37%. It is not determined whether dexmedetomidine has its own property of reduction of nausea and vomiting, but probably opioid-sparing effect of dexmedetomidine could reduce nausea and vomiting.

We administered dexmedetomidine at a low dose (0.2 µg/kg/h) for minimizing hypotension and bradycardia before and during the procedure. But we doubled the dose at the end of procedure when pain is developed by ischemic changes. Although there were no statistical differences of the episodes of hypotension and bradycardia between
the two groups, four patients had hypotension and one patient experienced bradycardia in Group D, whereas no hypotension or bradycardia developed in Group C. Our finding suggest that dexmedetomidine might potentiate the fentanyl-induced bradycardia and hypotension in patients receiving IV PCA. Close observation may be necessary for patients receiving fentanyl PCA with dexmedetomidine although those symptoms were transient and easily manageable. Although sedation score was significantly high in Group D compared with Group C during dexmedetomidine infusion, incidence of desaturation was similar between the two groups.
Fig. 1: Patient assignment to study group (randomized) and treatment protocols.

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Fig. 2: Doses of fentanyl consumption via patient-controlled analgesia during 24 hours after procedure. Values are mean ± SD. *P < 0.001 compared with Group C (Bonferroni-corrected). †P = 0.006 compared with Group C.

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**Fig. 3:** Numerical rating scale for pain during 24 h after procedure. Values are mean ± SD. \( *P = 0.026 \) compared with Group C (Bonferroni-corrected).

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Table 1. Patient characteristics

<table>
<thead>
<tr>
<th></th>
<th>Group C (n = 25)</th>
<th>Group D (n = 25)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>40 ± 6</td>
<td>40 ± 4</td>
<td>0.692</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>161 ± 5</td>
<td>160 ± 5</td>
<td>0.454</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>58 ± 9</td>
<td>59 ± 6</td>
<td>0.741</td>
</tr>
<tr>
<td>History of motion sickness or PONV</td>
<td>9</td>
<td>5</td>
<td>0.208</td>
</tr>
<tr>
<td>Smoking</td>
<td>4</td>
<td>3</td>
<td>0.684</td>
</tr>
<tr>
<td>Diagnosis</td>
<td></td>
<td></td>
<td>0.945</td>
</tr>
<tr>
<td>Single myoma</td>
<td>7</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Multiple myoma</td>
<td>13</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Adenomyosis with or without myoma</td>
<td>5</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Exclusive unilateral uterine artery supply</td>
<td>5</td>
<td>3</td>
<td>0.440</td>
</tr>
<tr>
<td>Duration of UAE procedure (min)</td>
<td>42 ± 8</td>
<td>43 ± 8</td>
<td>0.440</td>
</tr>
</tbody>
</table>

Values are mean ± SD or number. C, control with normal saline; D, dexmedetomidine; PONV, postoperative nausea and vomiting; UAE, uterine artery embolization.

Table 1: Patients characteristics

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Table 2: Number of patients who required additional analgesics during 24 hours after procedure

<table>
<thead>
<tr>
<th>Additional analgesics</th>
<th>Group C (n = 25)</th>
<th>Group D (n = 25)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-1 h</td>
<td>17</td>
<td>2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>1-6 h</td>
<td>9</td>
<td>7</td>
<td>0.544</td>
</tr>
<tr>
<td>6-12 h</td>
<td>5</td>
<td>8</td>
<td>0.333</td>
</tr>
<tr>
<td>12-24 h</td>
<td>2</td>
<td>1</td>
<td>1.000</td>
</tr>
</tbody>
</table>

Table 3: Highest sedation score during 24 hours after procedure

<table>
<thead>
<tr>
<th>Highest sedation score</th>
<th>Group C (n = 25)</th>
<th>Group D (n = 25)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-6 h</td>
<td>0 (0-1)</td>
<td>1 (0-3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>6-12 h</td>
<td>0 (0-1)</td>
<td>0 (0-1)</td>
<td>0.190</td>
</tr>
<tr>
<td>12-24 h</td>
<td>0 (0-1)</td>
<td>0 (0-1)</td>
<td>0.556</td>
</tr>
</tbody>
</table>

Values are median (range). C, control with normal saline; D, dexmedetomidine. Sedation scores: 0 = fully awake; 1 = drowsy, closed eyes; 2 = asleep, easily aroused with light tactile stimulation or a simple verbal command; 3 = asleep, arousable only by strong physical stimulation; and 4 = unarousable.

Table 3: Highest sedation score during 24 hours after procedure

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Conclusion

In conclusion, the addition of dexmedetomidine infusion to fentanyl PCA provides better analgesia and fentanyl sparing effect after UAE. Furthermore, it reduces nausea and vomiting without untoward significant hemodynamic changes.
References


