The Effect of Combined Epidural and Light General Anesthesia on Stress Hormones in Open Heart Surgery Patients

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Abstract: This study was designed to evaluate the potential advantages of combined epidural and light general anesthesia over the commonly employed general anesthesia during open heart surgery. Twenty-four patients undergoing mitral valve replacement were thus studied. General anesthesia was maintained with an isoflurane–nitrous oxide–oxygen gas mixture and morphine sulfate (0.4 mg/kg i.v. initially) followed by postoperative pain control with morphine in 12 patients (group GA). The remaining 12 patients (group EAA) received continuous epidural bupivacaine (0.125%)–morphine (50 µg/ml) supplemented with the same gas mixture as group GA. Epidural infusion was continued until the third postoperative day. Changes in the serum cortisol and β-endorphin levels together with postoperative pain relief defined as good (scale 0–2), fair (3–4), or poor (5–10) were observed serially. Lower cortisol levels were observed in group EAA than in group GA (P < 0.05) just before skin closure, on the second and the third postoperative day. The β-endorphin levels were substantially lower in group EAA than in group GA throughout the observation. The pain scores were good in 2 patients (17%), fair in 6 (50%), and poor in 4 (33%) for group GA, and good in 8 (67%), fair in 3 (25%), and poor in 1 (8%) for group EAA. We thus conclude that a combined epidural and light general anesthesia is considered to attenuate the stress response and thereby provides a better quality of postoperative pain control.

Key Words: epidural anesthesia, open heart surgery, postoperative pain relief, stress hormones

Introduction

Recently, several investigations comparing general anesthesia with combined epidural and light general anesthesia (EAA) have been reported.¹² The merits of regional anesthesia include a reduced intraoperative blood loss,³ a decrease in postoperative catabolism,⁴ improved postoperative pulmonary function,⁵ and a reduction in the stress response.⁶,⁷ Combined epidural and light general anesthesia has also been associated with less sedation,⁸ earlier ambulation,⁹ better pulmonary function,¹⁰ improved oxygenation,⁸ and better pain control.¹¹ Although the advantages of a combined technique over general anesthesia alone may be controversial, postoperative pain control with epidural analgesia has been shown to be advantageous over the routine administration of intermittent intravenous opiates.¹¹,¹² The most commonly employed method of pain control for open heart surgery is the systemic injection of opioids, which thus include disadvantages such as unpredictable pain relief, a delay in recovery, and the need for large amounts of opioids.¹³,¹⁴ The purpose of this study was to determine whether the use of combined epidural and general anesthesia for open heart surgery may improve the quality of perioperative analgesia and attenuate the endocrine response to surgical stress.

Patients and Methods

This study was approved by the Korea University Hospital Ethics Committee, and informed consent was obtained from each patient prior to surgery. Twenty-four patients scheduled for mitral valve replacement were randomly divided into two groups of equal number. Group GA (n = 12) was designated as the general anesthesia group, and received the routine intraoperative anesthesia with an oxygen–nitrous oxide–isoflurane gas mixture and morphine. Postoperative pain was controlled with the intermittent intravenous injection of morphine (2–3 mg) as needed. The group EAA patients (n = 12) received combined epidural and light general anesthesia, and postoperative pain control with a continuous epidural infusion. Premedication con-
sisted of morphine (0.1–0.2 mg/kg) and glycopyrrolate (0.03–0.04 mg/kg) 1 h before anesthesia. In all patients, anesthesia was induced with intravenous thiopental (3–4 mg/kg) followed by vecuronium (0.1 mg/kg) to facilitate both intubation and mechanical ventilation. In group GA, anesthesia was maintained with a nitrous oxide (2 l/min)–oxygen (2 l/min)–isoflurane (1.0–2.0 vol%) gas mixture and morphine, initially 0.4 mg/kg i.v., was given followed by supplements as needed. In group EAA, an epidural puncture was performed with an 18-gauge Tuohy needle in the T3–4 intervertebral space in a left lateral decubitus position. After the epidural space was identified, a test dose of 2% lidocaine (3–4 ml) was administered before the induction of anesthesia. Five minutes later, 20 ml of a combination of 0.125% bupivacaine and 6 mg of morphine was given slowly as a bolus dose. The level of the neural block was tested 15 min later, and infusion using an infusion pump (Terumo syringe pump, model stc-523, Tokyo, Japan) was started at a rate of 3–5 ml/h (mixture of 0.125% bupivacaine with 50 µg/ml of morphine). The continuous epidural infusion was then continued until the third postoperative day. An electrocardiogram was made while the arterial blood pressure was monitored by means of radial artery cannulation. In addition, a pulmonary artery catheter (Swan-Ganz) was inserted before the start of surgery to measure the hemodynamic profile with a cardiac output computer (Arrow International, model AI-07350, Reading, PA, USA). Blood samples for stress hormones, including cortisol and β-endorphin, were obtained before induction, 30 min after skin incision, 60 min after induction or before cardiopulmonary bypass (CPB), 30 min after CPB, before skin closure, on the first, second, and third postoperative day (POD). Cortisol was determined by a time-resolved fluoroimmunoassay using a Delphia kit (Wallac, Turku, Finland) while β-endorphin was determined using high pressure lipid chromatography. The blood sample was placed in a cold tube within 5 min after withdrawal and was then centrifuged. The plasma was stored at −20°C until analyzed. After the completion of the operation, each patient was carried to the surgical intensive care unit for postoperative care including mechanical ventilation. The severity of pain was scored according to the visual analog pain scale (VAS) (Table 1) as suggested by Jorgensen et al.15 The VAS evaluation was performed at 8 A.M. on the first POD and every 12 h after that until the third POD. The quality of pain relief was then evaluated as good, fair, and poor (Table 2). Epidural catheters were removed in all patients at the end of the study. The unpaired Student’s t-test was used for a statistical analysis. Data comparisons involving the ratios or proportions were performed using the chi-square test. A value of $P < 0.05$ was considered to be statistically significant.

### Results

#### Patient Profile

There was no significant difference between the two groups regarding age (30 ± 5 years for group GA vs 35 ± 14 for group EAA), weight (51 ± 8 vs 50 ± 13 kg), height (159 ± 6 vs 156 ± 10 cm), body surface area (1.57 ± 0.13 vs 1.55 ± 0.10 m²), duration of surgery (332 ± 37 vs 366 ± 84 min), or cardiopulmonary bypass (72 ± 16 vs 83 ± 18 min).

#### Plasma Concentration of Cortisol and β-Endorphin

Plasma cortisol levels were significantly lower in group EAA than in group GA before skin closure, on the second POD and third POD ($P < 0.05$). In the plasma β-endorphin levels, no statistically significant differences were observed between the two groups (Fig. 1).

#### Postoperative Pain

Postoperative pain relief showed a higher percentage of good pain relief in group EAA than in group GA (67% vs 17%, $P < 0.001$) (Table 3).

<table>
<thead>
<tr>
<th>Quality of pain relief</th>
<th>Group GA</th>
<th>Group EEA</th>
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<tbody>
<tr>
<td>Good (0–2)*</td>
<td>2 (17%)</td>
<td>8 (67%)</td>
</tr>
<tr>
<td>Fair (3–4)</td>
<td>6 (50%)</td>
<td>3 (25%)</td>
</tr>
<tr>
<td>Poor (5–10)</td>
<td>4 (33%)</td>
<td>1 (8%)</td>
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* $P < 0.001$, group GA vs group EAA