Effect of Isoflurane Anesthesia on Hemodynamics Following the Administration of an Angiotensin-Converting Enzyme Inhibitor in Cats

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ABSTRACT. The objective of this study was to evaluate the hemodynamics of the anesthetic isoflurane in healthy cats given angiotensin-converting enzyme inhibitor (ACEI). The 7 healthy young cats and 3 old cats were received placebo or enalapril 0.5 mg/kg orally. The change in systolic arterial pressure from the baseline to 30 min postanesthesia in the ACEI group was significantly higher than in the placebo group (mean ± SD: –39 ± 13% vs. –17 ± 12%, respectively). The present study indicated that general anesthesia may induce hypotension after the administration of an ACEI.

KEY WORDS: feline, hemodynamics, hypotension.

NOTE. Internal Medicine

Angiotensin-converting enzyme (ACE) inhibitor is used as a standard therapeutic drug for heart and kidney disease [6, 7, 10, 11]. General anesthetics can lower blood pressure in patients receiving ACE inhibitor which is an antihypertensive medication, or angiotensin II receptor antagonist [1, 2, 5, 12, 13]. Therefore, severe hypotension may occur during anesthesia in cats when ACE inhibitor is required for the diagnosis or treatment procedure. The objective of this study was to evaluate the hemodynamics of the anesthetic isoflurane in healthy cats given ACE inhibitor.

Seven young mature cats (2–4 years old, 3.3–4.0 kg each) and three cats of advanced age (17–19 years old, 2.7–4.0 kg each) recognized as clinically healthy by ultrasonography and a blood test were used in this study. The cats were kept individually in cages and fed commercial cat food with free access to water. This study was performed in accordance with the guideline for the care and use of laboratory animals by College of Bioresource Sciences, Nihon University.

The cats were orally administered a placebo or 0.5 mg/kg enalapril maleate 3 hr before the induction of general anesthesia. Each drug was given at randomly, and each administration interval was for 7 days. Prior to the induction of anesthesia, the cats rested quietly in a dark room and their blood pressures and heart rates (HR) were measured. Blood pressure was determined indirectly using a cuff on the antebrachium region with a blood pressure measuring instrument (Colin Medical Japan), and the average value was calculated from three measurements. Atropine sulfate (0.025 mg/kg) was administered intramuscularly as a premedication, and anesthesia was induced by 6 mg/kg propofol and maintained by isoflurane after endotracheal intubation. An anesthetic density of 1.9% isoflurane provided the necessary anesthetic depth. The respiration rate was controlled at 9–10/min, and the body temperature was maintained around 38°C by thermal insulation. Before, during, and after anesthesia, the following measurements and procedures were performed: systolic arterial pressure (SAP), mean blood pressure (MAP), diastolic blood pressure (DAP), HR, body temperature, respiratory rate, exhalation carbon dioxide density, SpO₂, exhalation inspiration end isoflurane level, and echocardiography. Left ventricular fractional shortening (FS) was measured by transthoracic echocardiography in the two-dimensional short-axis view at the level of the chordae tendineae before and 30 min after induction.

A blood sample was collected 30 min after ACE inhibitor was administered and the level of ACE activity was measured by the Cushman method.

Data were described as mean ± standard deviation (SD). Hemodynamics data were analyzed by one factor repeated measures ANOVA followed by post hoc testing (Tukey test). ACE activity and percentage from baseline of HR and SAP were analyzed by paired T-test. A value of P<0.05 was considered statistically significant.

The level of ACE activity in the placebo group after 30 min of anesthesia was 17.0 ± 2.8 pg/ml for the young cats and 15.4 ± 0.8 pg/ml for the aged cats. In contrast, the level of ACE activity measured in the ACE inhibitor-administered group was 4.1 ± 1.1 pg/ml for the young cats and 3.1 ± 1.8 pg/ml for the aged cats.

In terms of the heart rate prior to anesthetic induction, no difference was observed between the placebo group and the ACE inhibitor group among young cats, and no significant change was detected after anesthesia (Fig. 1). Among the cats of advanced age, a decreased HR was observed in the placebo group (Fig. 2).

SAP fell significantly in the placebo group 20–60 min postanesthesia, but in the young cats, the values recovered upon awakening. The baseline SAP of the ACE inhibitor
group did not differ from that of the placebo group. A significant decrease in SAP was observed 5 min after induction and continued until 10 min after awakening. The change in SAP from the baseline to 30 min postanesthesia in the ACE inhibitor group was significantly higher than in the placebo group (mean ± SD: –39 ± 13% vs. –17 ± 12%, respectively).

Application of the anesthetic significantly decreased the DAP and MAP of the ACE inhibitor group (Fig. 1).

Among the cats of advanced age, no change in SAP was observed in the placebo group. In contrast, in the ACE inhibitor group, the SAP decreased from the baseline by 4 ± 11% in the placebo group and by –35 ± 10% in the ACE inhibitor group.
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inhibitor group 30 min postanesthesia. The DAP and MAP significantly decreased in the ACE inhibitor group after anesthesia (Fig. 2).

The respiration rate was maintained at 9–10/min. No difference in saturation O₂ was observed between the young cats and the cats of advanced age (i.e., 95–100% in both groups). Similarly, the exhalation carbon dioxide density was roughly the same between the two groups (13–20 mmHg in both groups). The body temperature of the animals was 38°C before anesthesia, and decreased to 36°C postanesthesia.

No differences in left ventricular FS were observed by echocardiography before or after anesthesia between the placebo (n=5, baseline: 34 ± 6%, 30 min postanesthesia: 29 ± 14%) and ACE inhibitor groups (n=5, baseline: 33 ± 5%, 30 min postanesthesia: 28 ± 15%) in young cats. Similarly, no difference was detected before or after anesthesia between the placebo (n = 3, baseline: 36 ± 7%, 30 min postanesthesia: 35 ± 4%) and ACE inhibitor groups (n=3, baseline: 33 ± 3%, 30 min postanesthesia: 33 ± 4%) in old cats.

In general, the decision to withhold drugs with cardiovascular effects before surgery depends on the risk balance between the anticipated deleterious interaction of the drug with the anesthesia versus possible morbidity resulting from hemodynamic effects that may occur in the absence of the drug. For example, continuation of perioperative β-adrenergic blockers and α-agonists is widely accepted because of their protective role against myocardial morbidity [8, 17]. In contrast, it has been suggested that because intraoperative hypotension occurs with ACE inhibitors and ARB, these drugs should be withdrawn prior to surgery [4]. The vasodilative effects of ACE inhibitor and ARB decrease 10 hr after administration [3]. In this study, anesthesia was induced 3 hr after the administration of enalapril. Because the effect of ACE inhibitor was at its maximum, the anesthesia was delivered more than 3 hr after ACE inhibitor [15]. In this study, no difference in blood pressure was detected between the placebo group and the ACE inhibitor group preanesthesia. Because ACE activity was inhibited in both groups, we initially believed that this was caused by excitation of the cats during the measurement of blood pressure prior to the induction of anesthesia; however, the remarkable decrease in blood pressure following application of the anesthetic clearly indicated inhibition of ACE activity. The anesthetic isoflurane decreases aortic systolic blood pressure, cardiac output, and vascular resistance in a dose-dependent manner [14]. Isoflurane is known to cause hypotension during anesthesia because hypotension can be ameliorated by terminating delivery of the anesthetic. Our findings indicate that ACE inhibitor influences hypotension during anesthesia. Three hemal vasopressor systems contribute to the regulation of blood pressure during anesthesia: the sympathetic nervous system, the renin-angiotensin system (RAS), and vasopressin [16]. Blood pressure regulation during anesthesia and surgery is RAS-dependent in rats and humans [9, 11]. Since RAS activation leads to angiotensin-induced vasoconstriction, it has been suggested that the inhibition of RAS during general anesthesia can cause serious hypotension. Nephric protection by ACE inhibitor has been reported in cats with chronic renal failure. Previous reports have detailed the effects of ACE inhibitor in cats with chronic renal failure (4–19-year-old cats [6], 1–19-year-old cats [10]) and hypertrophic cardiomyopathy (0.8–11.6-year-old cats [7]). Some kind of intravitam anesthesia is expected in cats that are prescribed ACE inhibitor less than 1–3 years after birth. Particularly old cats may develop renal failure and hyperthyroidism; however, organs besides the kidney may also develop hypotension during anesthesia.

These results show the importance of monitoring the blood pressure and heart rate of cats receiving ACE inhibitor during anesthesia. Moreover, withdrawal of ACE inhibitor the day before surgery or the administration of vasopressor drugs such as noradrenaline or angiotensin II agonist may be indicated when anesthetization is required. This study focused on healthy young and (three) old cats; therefore, additional clinical studies are needed to evaluate the relevance of these results for cats with heart failure, renal failure, metabolic disease, and old age.

REFERENCES