General Anesthesia, Utilizing Etorphine Hydrochloride and Azaperone with Supplementary Isoflurane Inhalation Anesthesia, for Gastro-esophageal Endoscopy in a Domesticated Asian Elephant (*Elephas maximus*): A case report

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Abstract

A 30-year-old female domestic Asian elephant (*Elephas maximus*) was referred to Kasetsart University Veterinary Teaching Hospital for investigation of an esophageal obstruction. “Vomiting” had been noted for several days before admission. Initial sedation was achieved by azaperone (80 mg), delivered intramuscularly (IM). Once sedated supporting straps and a sling were fitted, and weight-bearing support was provided by a crane. General anesthesia was induced using 2 mg etorphine hydrochloride (0.00066 mg/kg) by intravenous (IV) injection. Using the crane, she was lowered onto a thickly bedded area on the floor and placed in right lateral recumbency. Oxygen was initially provided via the trunk. Blind endotracheal intubation was unsuccessful until further two incremental doses of etorphine hydrochloride (0.5 and 1.5 mg) had been administered. Even though subsequently maintained on 5% isoflurane, a third increment of etorphine hydrochloride (1 mg) was required to fully abolish jaw tone. Following successful endoscopy for gastro-esophageal evaluation anesthesia was reversed through cessation of isoflurane and administration of naltrexone (500 mg by IM injection). Some reflexes including ear twitching and leg moving were noticed within 1 min and endotracheal extubation was carried out after 2 min, when jaw tone returned. First attempts at standing took place after 3 min, the elephant could stand with support after 8 min and was ambulatory at 11 min after reversal. The total time from sedation to independent walking was 1.16 hr.

**Keywords:** elephant, esophageal obstruction, general anesthesia

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**Introduction**

Due to their large body mass and perceived anesthetic risk, general anesthesia is not frequently performed in Asian elephants (*Elephas maximus*). For standing sedation, xylazine is a drug of choice for Asian elephants. Azaperone has also been used to tranquilize and translocate Asian elephant in India (Cheeran et al., 2002). For major surgery or complex diagnostic procedures maintenance of general anesthesia, potentially for long periods, is required. Historically, etorphine hydrochloride alone or in combination with acepromazine (Immobilon®, C-Veterinary Products, Leyland, Lancs, PR5 3QN) has been used in both African (*Loxodonta africana*) and Asian elephants worldwide (Jainudeen et al., 1971; Bongso et al., 1978; Schmidt, 1986; Kock et al., 1993; Sujit et al., 2005). General anesthesia using an etorphine hydrochloride and azaperone combination has been reported in African elephants (Dunlop et al., 1994; Still, 1993; Still et al., 1996; Stegmann, 1999).

However, there is limited information about the use of etorphine hydrochloride and azaperone in combination in Asian elephants. The use of sequential etorphine hydrochloride injections with isoflurane inhalation has been reported in Asian elephants for extensive foot treatments and surgery (Fowler et al., 2000). In Thailand, general anesthesia using the combination of etorphine hydrochloride and acepromazine (Immobilon®) with subsequent inhalation halothane anesthesia for gastro-esophageal endoscopy of esophageal obstruction has been reported (Sujit et al., 2005). Opioid narcotics usually increase blood pressure. It is believed that this can lead to the potentially fatal “pink foam syndrome” in elephants (Honeyman et al., 1992; Raath, 1993; Fowler and Mikota, 2006; Horne and Loomis, 2007). “Pink foam syndrome” externally manifest as a pink froth from the trunk and is caused by pulmonary edema and capillary bleeding. Several reports recommend that azaperone can be combined with opioid narcotics in order to counteract the hypertensive effects that lead to this clinical syndrome (Hattingh et al., 1994). However, despite its potential attraction in eliminating anesthetic complications, the combination of sedation with azaperone by injection, induction with etorphine injection and maintenance with isoflurane has not yet been reported in Asian elephants. This case report describes the use of azaperone followed by etorphine hydrochloride by injection, and subsequent isoflurane by inhalation to maintain anesthesia, which successfully allowed gastro-esophageal endoscopy in an Asian elephant.

**Elephant signals and supportive treatments:** A 30-year-old female domestic Asian elephant (*Elephas maximus*) was referred to Kasetsart University Veterinary Teaching Hospital (KUVTI) for full diagnostic work up due to a suspected esophageal obstruction. The history obtained indicated that previously, for several days, she had shown passive reflux of non-swallowed food and saliva. She had initially presented at and was then admitted to an animal hospital in Kanjanaburi. After one day, she was referred to KUVTI. On initial presentation at KUVTI she was inappetent and appeared depressed. Saliva was drooling from the mouth. This was gauged to be of normal quantity, rather than hyper-salivation; however, it was not being swallowed. Based on experience, her bodyweight was estimated to be 3,000 kg. The elephant's body temperature was 36.1 °C. The pulse and respiratory rates were 35 beats and 8 breaths per minute, respectively. Her mucous membrane was pale pink. Her dry and withered skin was consistent with severe dehydration. Blood was collected from her ear vein. The hematology and blood chemistry profiles were shown on table 2. The elephant blood results revealed increase of PCV, Hb and creatinine, which correlated with severe dehydration. The elephant was also given 10 liters of fluid therapy (R-Acetate-5, Dextrose 5% in Acetated Ringer's Injection, General Hospital Products Public Co., Ltd., Pathum Thani, Thailand) via ear vein. The elephant was injected with long acting amoxycillin (Longamox®, Vetquino, Lure, France) at a total dose of 7,500 mg/day intramuscularly. Fifty ml of an injectable supplement containing butaphosphan and cyanocobalamin (Catosal®, Bayer Health Care, Kansas, USA) was given by IM injection.

**Elephant anesthesia and gastro-esophageal endoscopy:** After one day of physical examination, work-up and preparation, diagnostic anesthesia was performed. Reported doses for etorphine hydrochloride in Asian elephants are ranged between 0.001-0.004 mg/kg (Fowler, 1995; Kreeger et al., 2002, Nayar et al., 2002, Sujit et al., 2005). We have previously reported using a dose of 0.002 mg/kg (Sujit et al., 2005). This dose was used in an elephant without premedication. In this case, azaperone was used as a sedative. We considered the lowest reported rate of 0.001 mg/kg etorphine hydrochloride to be the most appropriate dosage. Furthermore, as the elephant was deemed to be compromised and weak, a decision was made to further lower the induction dose of etorphine hydrochloride to 0.00066 mg/kg; (a total dose of 2mg).

To achieve general anesthesia, an intramuscular (IM) injection of azaperone (Azaperone, 100mg/mL; Kyron Prescriptions cc, South Africa) using a 18 Gx1.5 inch needle in the triceps of the left foreleg at a dose rate of 0.0266 mg/kg; a total of 80 mg (Cheeran et al., 2002) was performed. For record purposes, this injection was designated as time zero. In 18 min, sedation was deemed to have been achieved when the elephant showed no response to vigorous manual stimulation of the lateral thigh and when the trunk rested on the floor. At this point a combination of webbing straps and a sling were put in place and was supported by using a crane. General anesthesia was induced using etorphine hydrochloride (2 mg) injection intravenously (IV). 3 min post-injection the elephant was noticeably more subdued, with her weight being supported by the sling arrangement as she tried resting on the floor. Using the crane she was lowered onto a thickly-bedded area on the floor and placed on right lateral recumbency (Fig 1). Intravenous fluid (R-Acetate, Dextrose 5% in Acetated Ringer's Injection, General Hospital Products Public Co., Ltd., Pathum Thani, Thailand) was given via ear vein with IV catheter No.18 Gx1.5 inch. The flow rate was maximum. The eyes were lubricated...
with chloramphenicol ointment (Cogetin®, General Drug House). A pulse oximeter (Nellcor N-180™, Williamson Court, Louisville, KY) was attached to the ear. If the oxygen saturation was below 95%, oxygen was delivered using a tube via the trunk, with intermittent manual positive pressure ventilation. An attempt was made to manually insert a 30 mm endotracheal tube by blind technique (Fig 2). However, this failed as there was still jaw tone and the hand insertion initiated chewing reflex. The elephant was given two more doses (0.5 and 1.5 mg) of etorphine hydrochloride IV for jaw relaxation. Sufficient relaxation was achieved to facilitate endotracheal intubation. The endotracheal tube cuff was inflated and the tube was connected to an anesthetic machine delivering 5% isoflurane (Terrell™, Isoflurane, USP, MINRAD INC., Bethlehem, PA, USA) with 10 L/min of oxygen for maintenance. It was noted that, even with successful endotracheal intubation and isoflurane being delivered at 5%, there still remained a small component of reflex chewing. Thus, an additional 1 mg increment of etorphine hydrochloride was administered intravenously. This was sufficient to allow endoscopy for gastro-esophageal evaluation. Gastro-esophageal endoscopy was undertaken, per os, using a 1.7 m long, 1 cm diameter flexible fiber optic video endoscope utilizing a light-source with the images being recorded with a video-processing circuit (PENTAX (EPM3300 and EC3830 fz). A 20 mm rubber tube was inserted and used to guide the endoscope through the pharynx into the esophagus. Good visualization was achieved for the whole of the esophagus. No obstruction was found. The stomach was too voluminous to be fully visualized, but was noted to contain large amounts of fluid and partially digested food. Based on these findings esophageal blockage and gastric impaction were ruled out. Treatment for gastritis was initiated and the medical condition resolved over the following month.
On retraction of the endoscope no further isoflurane was delivered and an opioid antagonist, 500 mg naltrexone (Naltrexone, 50mg/mL; Kyron Prescription cc, South Africa), was administered intramuscularly. One minute after injection of the reversal agent, the elephant became progressively aroused and reflexes returned incrementally. Chewing reflex was detected within 2 min of reversal, prompting extubation of the endotracheal tube. The elephant tried to stand in 3 min and by 8 min the elephant could stand, relying the straps and crane (Fig 3). It was able to walk without support 11 min after reversal. The total time from sedation to independent walking was 1.16 hr (Table 1).

**Discussion**

General anesthesia, using etorphine hydrochloride and azaperone by injection for induction with follow-up isoflurane by inhalation, permitted us to carry out gastro-esophageal endoscopy in an adult female domesticated Asian elephant. She became ataxic within 3 min of the first IV dose of etorphine hydrochloride and, with crane support, was in lateral recumbency in 5 min. This was in accordance to our previous report (Sujit et al., 2005). However, due to the persistence of jaw tone and a chewing reflex blind technique intubation was unsuccessful. A relative under-dose of etorphine hydrochloride at induction due to under-estimating body weight may be the cause. We had deliberately gone below the lowest dosage for etorphine hydrochloride in correspondence to the use of azaperone and the animal’s generally comprised physiology. Further, incremental, etorphine hydrochloride abolished the chewing reflex to the extent that it facilitated endotracheal intubation. However, even when isoflurane was being delivered at 5% via the endotracheal tube a further increment of etorphine hydrochloride was required to abolish completely the chewing reflex in order that we could undertake the endoscopic procedure. Our experience in using “full dose” of etorphine hydrochloride at induction worked well and permitted endotracheal intubation without additional increments of etorphine hydrochloride. In addition, we had previously used halothane rather than isoflurane. This may have aided our management of previous cases. The combination of etorphine hydrochloride and halothane had been successfully used by other practitioners (Fowler et al, 2000). In hindsight, we may have considered a larger induction dose of etorphine hydrochloride, but we had concerns for the elephant’s general health and had erred on the side of caution. However, our objective was accomplished. We achieved using azaperone as a sedative and reactive management for this elephant under anesthesia. Having dedicated anesthetists for this procedure makes for a safer intervention for all parties. This case demonstrates safe and efficacious use of azaperone followed by etorphine hydrochloride and maintenance of general anesthesia by isoflurane in an compromised adult domesticated Asian elephant.
Table 1  Anesthetic summary record during general anesthesia for gastro-esophageal endoscopy

<table>
<thead>
<tr>
<th>Time (min.)</th>
<th>Drugs</th>
<th>Monitor</th>
<th>Notes</th>
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<td></td>
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<td>Pulse rate (beats/min)</td>
<td>Respiration rate (breaths/min)</td>
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<td>Azaperone (80 mg, IM)</td>
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<td>Etorphine (1 mg, IV)</td>
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NA = Not available

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References


บทคัดย่อ

การวางยาสลบด้วย etorphine hydrochloride ร่วมกับ azaperone และคงการสลบด้วย isoflurane inhalation เพื่อส่องกล้อง endoscope ตรวจหลอดอาหารและกระเพาะช้างเอเชีย (Elephas maximus): รายงานสัตว์ป่วย

นิกร ทองทิพย์¹,² อุมาพร ใหม่แก้ว³ วัลยา ทิพย์กันทา³ ประชา ธีริyo ยิมติ¹ นิชารีย์ อินค้า⁶ เบญจพล หล่อสัญลักษณ์¹ เพชร ศิริอรุณรัตน์³ สุเมธ กมลนรนารถ³ ช้างเอเชียเพศเมียอายุ 30 ปี ถูกนำส่งเข้ารับการตรวจวินิจฉัยภาวะหลอดอาหารอุดตันที่โรงพยาบาลสัตว์มหาวิทยาลัยเกษตรศาสตร์ ก้าแพงแสน ช้างแสดงอาการคล้ายการสูญเสียอาหารประมาณสองสามวันก่อนส่งมารักษา กระบวนการวินิจฉัยเริ่มต้นด้วยการให้ยา azaperone ขนาด 80 มก. ฉีดเข้าลิ้น เมื่อช้างแสดงอาการซึม ทำการใส่ชุดพยุงช้างที่ขาทั้งสี่ข้างและแขวนยึดกับสลิง และผูกสลิงยึดไว้กับตะขอของรถครนขนาดใหญ่เพื่อพยุงน้ำหนักตัวของช้าง จากนั้นทำการให้ยา etorphine hydrochloride ขนาด 2 มก. (0.00066 มก.ต่อกก.) ซึ่งช้างดื้อต่อการตั้งเหงื่อ เมื่อช้างเริ่มแสดงอาการสลบโดยที่น้ำหนักตัวช้างจ่อหยุดออกจากรถ มีการสอดกล้องเข้าตรวจการอุดตันหลอดอาหารและกระเพาะ ทำให้การสอดอุดตันอย่างลึกลับไป แต่เนื่องจากช้างยังไม่สลบลึกพอที่จะสอดท่อช่วยหายใจได้ ช้างยังคงแสดงอาการเคี้ยวปากอยู่จึงฉีดยาสลบ etorphine hydrochloride เข้าเส้นเลือดดาเพิ่มอีกครั้ง (0.5 มก. และ 1 มก.) จนสามารถสอดท่อช่วยหายใจได้สำเร็จ จากนั้นทำการสอดท่อช่วยหายใจเข้ากระเพาะท้อง โดยใช้ยาสลบ isoflurane ขนาด 5% แต่อย่างไรก็ตามช้างยังคงแสดงอาการเคี้ยวปาก ทำให้การสอดท่อช่วยหายใจล้มเหลว จึงทำการให้ยาสลบ etorphine hydrochloride (1 มก.) เข้าเส้นเลือดดาเพิ่มอีกครั้งคือ ใช้ยาสลบ isoflurane ขนาด 2.5% แต่อย่างไรก็ตามช้างยังคงแสดงอาการเคี้ยวปาก ทำให้การสอดท่อช่วยหายใจล้มเหลว จึงทำการให้ยาสลบ etorphine hydrochloride (1 มก.) และค่อยๆปล่อยเครนจากนั้น ทำการสอดกล้อง endoscope เพื่อตรวจการอุดตันของหลอดอาหารและกระเพาะช้างได้ ช้างลุกขึ้นยืนได้ในเวลาสามนาที สามารถยืนได้ด้วยตัวเองในเวลาแปดนาที รวมเวลาทั้งหมดในการทำงานดังกล่าวช้างเจ้าข้างได้เดินไปได้เมื่อสัมผัสหรือสัมผัสด้วยสัมผัสที่ดี

ค่าสำคัญ: การวางยาสลบ, ช้าง, หลอดอาหารอุดตัน

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