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Short Communication

EFFECTS OF SHUMIANNING ON ANESTHESIA, RESPIRATION AND CIRCULATION IN DOGS

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ABSTRACT

The present experiment was conducted to study the effects of Shumianning, a compound anesthetic, on the effects of anesthesia as well as respiration and circulation in dogs. Ten adult healthy mongrel dogs were selected, with an equal number of male and female dogs, weighing about 8~10 kg. No. 24 indwelling intravenous catheter was put into the left forelimb (cephalic vein) to create venous tunnel. Shumianning at a dosage of 0.05 mL/kg was intravenously injected at first, and then continuous intravenous infusion was conducted by micropump for 1 hour with the speed of 0.1 mL/kg/hr. 10 min after the injection, heart rate (HR), respiratory rate (RR), mean systolic arterial pressure (SAP), diastolic arterial pressure (DAP), partial pressure of oxygen (PO_2) and arterial oxygen saturation (SpO_2) were measured to evaluate the effects of sedation and recovery. Anesthesia mean onset time was (26.8 ±10.5) min, mean maintenance time was (89.6±17.5) min and mean recovery time was (15.6±5.8) min. There were no differences in the scores of sedation, analgesia and muscle relaxation as well as anesthetic effects at 20, 30 and 60 minutes (p>0.05). Finally, there were 7 dogs (70.0%) with excellent recovery, 2 (20.0%) with good recovery and 1 (10.0%) with an average quality of recovery. Shumianning exerts high effect upon the induction, maintenance and recovery of dog models receiving intravenous general anesthesia.

Key words: Shuumianning; intravenous general anesthesia; micropump; induction period; maintenance period; recovery period.

INTRODUCTION

Intravenous general anesthesia often requires a variety of drugs combined to complete the induction and maintenance of anesthesia. The injection, dose and speed of anesthetics should be repeatedly adjusted according to types of operations, basic conditions of patients, monitoring of vital signs and other indexes to maintain a more stable hemodynamics and meet the needs on operation and recovery after the operation (Thomas, 2011; Grint , Murison, 2008). As a new compound anesthetic, Shumianning is made of an optimal combination of Ketamine, Serazine and Midazolam in a scientific formula (Mair *et al*., 2009), available for intramuscular injection (Belda *et al*., 2009), intravenous injection (Morissette *et al*., 2016) and continuous intravenous injection through pump (Koehn *et al*., 2015). It has been confirmed that single-dose anesthesia takes effect rapidly, and the maintenance and recovery of anesthesia run smoothly with few side effects and good control, so it can be used via intravenous route safely for anesthetizing dogs, cats and other small animals in regular small operations (Waschkies *et al*., 2015). The aim of this study was to analyze whether continuous intravenous injection of Shumianning through micropumps could meet the operational requirements for a long time so as to provide a reference for the development of clinical anesthesia.

MATERIALS AND METHODS

Source of animals: Ten adult healthy mongrel dogs were selected, with an equal number of male and female dogs, weighing about 8~10 kg. They were purchased from the Animal Center of Nanjing Agricultural University. The experiment was carried out after the dogs had adapted to the environment for 1 week.

Research methods and observation indexes: Shumianning injections were purchased from the Animal Disease Center of Nanjing Agricultural University. The specification is 1 mL per one Shumianning injection. Datex-Ohmeda S/5^{TM} anesthesia monitor was purchased from General Electric Medical Group (Finland), and WZS-50F6 micro-injection pumps were purchased from Beijing Liuyi Biotechnology Co., Ltd.

The dogs were kept 12-hour food fasting and 6-hour liquid fasting before anesthesia. No. 24 indwelling intravenous catheter was put into the left forelimb (cephalic vein) to create venous tunnel. At first, 0.05 mL/kg Shumianning was intravenously injected to the dogs over a period of 20 sec. As soon as the animals were sedated and attained a lateral recumbent position on the operation table, continuous intravenous injections of Shumianning through micropump were administered for 1 hr at the speed of 0.1 mL/kg/hr to maintain the anesthesia. 10 min after the injections, heart rate (HR), respiratory rate (RR), mean systolic arterial pressure (SAP) and diastolic arterial pressure (DAP), partial pressure of oxygen (PO_2) and arterial oxygen saturation (SpO_2) were measured. SpO_2 probe was clamped on the tongue to make the infrared surface in alignment with the sublingual artery, and the breathing machine probe was placed close to the nostrils. The right femoral artery was exposed by dissection and isolated, and the medical T-junction extension tube was connected to the invasive blood pressure measuring device. Finally, the pressure sensor was adjusted to be in the same horizontal line as the heart.

Evaluation criteria of anesthetic effects: The onset time, maintenance time and recovery time of anesthesia were recorded. For Sedative effects: 3 points were given to no response to sound stimulation; 2 points were given to ears moving and eyes opening; 1 point was given to ears moving, eyes opening and instantaneous limbs twitching; and 0 point was given to head raising and struggling. Analgesic effects: 3 points were given to the complete disappearance of the sense of pain after the body surface skin underwent acupuncture, and ears, claws, tails and other parts were clamped; 2 points were given to hypalgesia; 1 point was given to the appearance of obvious sense of pain; and 0 point was given to having the same sense of pain as that before anesthesia. Muscle relaxation effects: 3 points were given to no contraction after abdominal muscle, tongue and tail were pulled; 2 points were given to slight contraction or resistance; 1 point was given to obvious contraction or resistance; and 0 point was given to back looking back and free tail wiggling when being pulled. The total score ≥ 7 indicated good anesthetic effects; 5-6 points indicated average anesthetic effects and the total score ≤ 4 indicated poor anesthetic effects.

Recovery quality assessment is divided into five levels according to Lozano *et al.* (2009), the situation where animals appear no excitement, chirping, tremor or vomiting and disturbance stands for excellent recovery quality; animals becoming slightly excited with no body movement, chirping, tremor or vomiting and no disturbance stands for good recovery quality; animals becoming excited with some body movement, vocalization, tremor or vomiting and no disturbance stands for average recovery quality; animals becoming excitement with body movement, vocalization, tremor or vomiting and no disturbance stands for poor recovery quality; and animals becoming extremely excited and aggressive with chirping, fierce body movement or disturbance, and needing to take sedative or antiepileptic drugs stands for very poor recovery quality, as illustrated in **Table 2**.

Statistical methods: SPSS 20.0 software was used for statistical analysis. Measurement data were expressed as mean ± standard deviation. Variance analysis needing repeated measurement was used to compare the data at different time points; comparisons among multiple groups were conducted by using one-way ANOVA while comparisons between two groups were conducted by using LSD-t test. Count data was expressed as case or (%) and comparisons among groups were conducted by using χ^2 test; $p<0.05$ indicated that the differences were statistically significant.

Analysis of recovery quality: There were 7 dogs (70.0%) with excellent recovery quality, 2 (20.0%) with good recovery quality and 1 (10.0%) with average recovery quality.

Table 1. Analysis of anesthetic effects.

	case	Sedation score	Analgesia score	Muscle relaxation score	Anesthetic effect: excellent	Anesthetic effect: average	Anesthetic effect: poor	Rate of good anesthetic effects
20 min	10	2.5±0.6	2.6±0.5	2.8±0.7	8	1	1	8 (80.0)
30 min	10	2.6±0.5	2.5±0.6	2.7±0.6	7	2	1	7 (70.0)
60min	10	2.6±0.7	2.6±0.7	2.9±0.8	9	1	0	9 (90.0)
F/χ^2		0.096	0.085	0.122				0.000
p		0.932	0.968	0.896				1.000

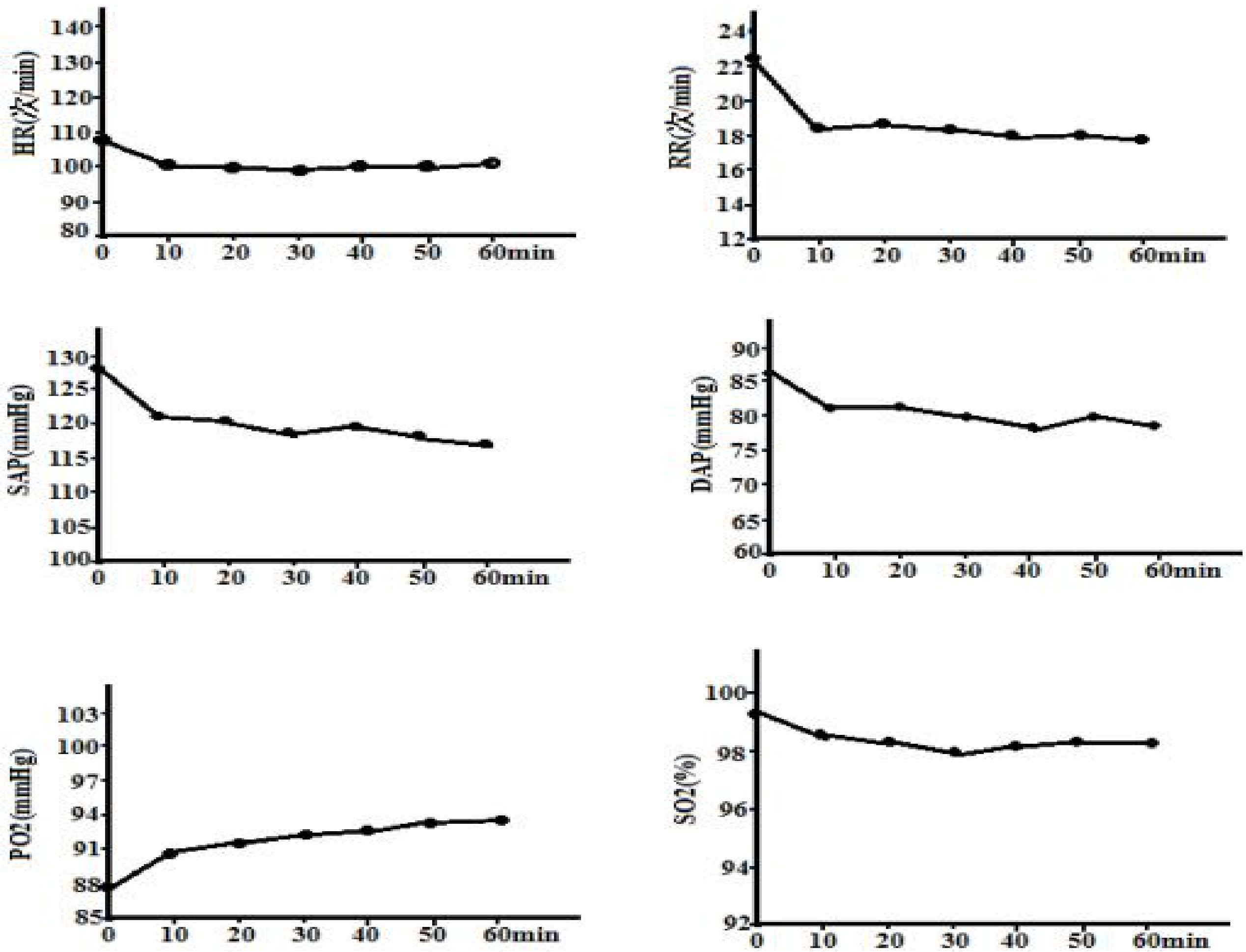

Figure 1 Comparisons of HR, RR, SAP, DAP, PO_2 and SpO_2 at different time points

Table 2. Recovery Quality Assessment.

Observed signs	Assessment level
No excitement, chirping, tremor or vomiting and disturbance	Excellent recovery quality
Slightly excited with no body movement, chirping, tremor or vomiting and no disturbance	Good recovery quality
Excited with some body movement, vocalization, tremor or vomiting and no disturbance	Average recovery quality
Excitement with body movement, vocalization, tremor or vomiting and no disturbance	Poor recovery quality
Extremely excited and aggressive with chirping, fierce body movement or disturbance	Very poor recovery quality

DISCUSSION

This study showed that in the absence of other anesthetics, the mean onset time of anesthesia of Shumianning was about 26.8 minutes, the mean maintenance time was about 89.6 minutes (60 minutes of continuous use) and the mean recovery time was about 15.6 minutes; this indicates that Shumianning takes effect rapidly with fast metabolic rate, and recovery of animals is quick and smooth, after the injection. Ketamine, an isolated anesthetic in Shumianning, takes effect rapidly with good analgesic effects on the body surface (Valentim *et al*., 2013). As documented by Canfrán *et al.* (2016), the onset time of intravenous anesthesia of propofol (4 mg/ kg) in dogs is about 50 min, and that of Shutai is about 45 min. For operations lasting for a long time, the doses of drugs must be added repeatedly as it is difficult to control the depth of anesthesia. Unlike previous findings, Shumianning alone was administered throughout the procedures in the induction, maintenance and recovery phases of general anesthesia in this experiment. HR, RR, SAP, DAP, PO_2, and SpO_2 parameters were measured 10 minutes after the injection, suggesting that the amplitude of fluctuation was small and stayed within the normal reference range. This suggested that Shuminaning is relatively safe to be used for anesthesia, which is almost consistent with the following reports. A study Savvas, *et al*. (2005) showed that the anesthetic Shutai tends to easily cause significant tachycardia and Sumianxin can lead to significant bradycardia. Xylazine in Shumianning may cause bradycardia as it belongs to α_2-adrenergic agonists. Different doses of Shuminaning can keep animals in quiet, lethargy, anesthesia and other states, as also reported by Kanda *et al.* (2016). Less than 90 % SpO_2 represents hypoxia and 92-94% SpO_2 represents the lack of ventilation. Continuous intravenous infusions through micro-pump can maintain blood plasma concentration at a certain level so as to ensure the appropriate depth of anesthesia, thus achieving the best anesthetic effect (Mezerová *et al.,* 1992; Yamashita *et al.,* 2000). There were no differences in sedation, analgesia and muscle relaxation scores as well as anesthesia effects at 20, 30 and 60 min after comparison, and the recovery quality was good. Common causes of delayed recovery include overdose anesthetic, hypothermia, liver and kidney dysfunction and hypoxemia, leading to slower anesthesia metabolism and excretion, water and electrolyte imbalance, abnormal glucose metabolism and other results, as documented by Valentim *et al.* (2013 Jul; 2013 Jan). Repeated additions of anesthetics can cause accumulation, but the cumulative effect of repeated injections of Shumianning is relatively small (Lee-Jayaram *et al.,* 2010).

Pharmacological studies suggested that the combination of xylazine and ketamine in Shumianning can produce synergistic effect (Svorc *et al.,* 2013), and the combination of ketamine and benzodiazepines such as midazolam can significantly reduce ketamine-induced fast heart rate, high blood pressure, irritability and other side effects (Mellish *et al.*, 2010), and midazolam and ketamine are water-soluble, which is similar in the pharmacokinetic characteristics. Midazolam can strengthen the central inhibitory effect of ketamine and alleviate mental symptoms (MacPherson *et al.*, 2008). There were some studies analyzing it from the body temperature (Valentim *et al.*, 2013), arterial blood gases (Langoi *et al.*, 2009), liver and kidney function (Bahrami *et al.,* 2011), inflammation (Ordek *et al.*, 2013) and oxidative stress (Arango-Gonzalez *et al.*, 2012) and other aspects. These studies showed that intravenous injection of Shumianing and continuous pumping of Shumianing through micropump can produce a stable hemodynamic effect with satisfactory anesthetic effects.

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