The use of methylphenidate for emergence from propofol and ketamine anesthesia in dogs

Imani Rastabi, H.*, Avizeh, R., Kavosi, N., Sabiza, S.

Department of Clinical Sciences, Faculty of Veterinary Medicine, Shahid Chamran University of Ahvaz, Ahvaz, Iran

Keywords:
Anesthesia, emergence, ketamine, methylphenidate, propofol

Correspondence
Imani Rastabi, H.
Department of Clinical Sciences, Faculty of Veterinary Medicine, Shahid Chamran University of Ahvaz, Ahvaz, Iran
Tel: +98(21) 33329763
Fax: +98(21) 33360807
Email: h.imani@scu.ac.ir

Received: 18 December 2017
Accepted: 17 March 2018

Abstract:

BACKGROUND: Methylphenidate (MPH) has been used to induce emergence from general anesthesia. **OBJECTIVES:** The objective of the present study was to evaluate the effect of MPH on recovery from propofol and ketamine anesthesia in dogs. **METHODS:** Six healthy male mix-breed dogs weighing 21.9 ± 3.9 kg were used in a randomized crossover design. Thirty minutes after premedication with acepromazine (0.1 mg/kg; IM), anesthesia was induced with either IV propofol or ketamine (8 and 15 mg/kg, respectively). Dogs, six minutes after induction, received either IV normal saline or methylphenidate (1 mg/kg) (propofol-saline; propofol-methylphenidate; ketamine-saline; ketamine-methylphenidate). Each dog was anesthetized four times randomly with at least one week interval. **RESULTS:** No significant differences were observed between propofol-saline and propofol-methylphenidate as well as between ketamine-saline and ketamine-methylphenidate in the times needed for various chronological sequences of recovery ($p>0.05$). Recovery in the dogs that received methylphenidate was eventful and associated with some adverse effects. Heart rate showed a decrease in propofol-methylphenidate group compared to the base ($p<0.05$). Respiratory rate after administration of methylphenidate was more stable than that of saline. **CONCLUSIONS:** It was concluded that methylphenidate at 1 mg/kg could not shorten recovery time in the dogs premedicated with acepromazine and anesthetized with either propofol or ketamine. Testing lower doses of methylphenidate and using a different premedication agent are recommended for future studies.

Introduction

Recovery from general anesthesia is generally considered as a passive procedure which directly relates to the metabolism and clearance of the pharmacologic agents from the brain (Kushikata and Hirota, 2014). Shortening the recovery time or inducing emergence from general anesthesia results in reducing the hospitalization as well as better management of patient that received overdoses of anesthetics or are at high risk. At present, no specific agent, same as with other drugs like opioids and benzodiazepines, has been introduced which is able to antagonize or actively induce emergence

from general anesthesia (Chemali et al., 2012).

It has been shown that emergence from anesthesia might be a different procedure from induction of anesthesia (Kushikata and Hirota, 2014). Emergence from anesthesia can be induced by activating specific pathways in the brain. Ascending arousal pathway as well as cholinergic, orexinergic, histaminergic and GABAergic arousal pathways have been shown that contribute to emergence from general anesthesia (Kushikata and Hirota, 2014; Solt et al., 2011). Several pharmacologic agents such as norepinephrine (Pillay et al., 2011), physostigmine (Plourde et al., 2003), caffeine (Wang et al., 2014), doxapram (Evers et al., 1965) and orexin (Shirasaka et al., 2011; Tose et al., 2009) have shortened recovery time with different general anesthetic agents.

Methylphenidate (Ritalin®; MPH) is an inhibitor of dopamine and norepinephrine reuptake transporters (Heal et al., 2009). It has also been shown that this drug increases prefrontal cortex histamine levels in rats (Horner et al., 2007). MPH has shortened recovery time in humans and dogs anesthetized with different anesthetic agents (Dobkin, 1960; Dodson and Fryer, 1980; Evers et al., 1965; Gale, 1959). Recently, MPH actively induced emergence from isoflurane and propofol anesthesia in rats by increasing arousal and/or respiratory drive (Chemali et al., 2012; Solt et al., 2011).

Propofol and ketamine are widely used as general anesthetic/analgesic agents in humans and animals. Propofol exerts its anesthetic effects through interaction with $GABA_A$ receptors (Ying and Goldstein, 2005). It provides rapid and smooth induction and maintenance of anesthesia (Kennedy and Smith, 2014). Ketamine, a non-competitive antagonist at NMDA receptors, can also be used for induction and maintenance of anesthesia (Berry, 2015).

To the best of the authors` knowledge, no study has reported the effect of MPH on recovery from propofol or ketamine anesthesia in dogs. Since emergence from anesthesia may follow distinct pathways from induction, it was hypothesized that MPH could accelerate recovery from propofol and/or ketamine anesthesia in dogs.

Materials and Methods

Six healthy male mix-breed dogs weighing 21.9 ± 3.9 kg and aged 1.5 to 2.5 years were used in a randomized crossover design. The dogs were transferred to the Veterinary Hospital from two weeks before the beginning of the study to four weeks after the completion of the anesthesia sessions. Health condition of the dogs was established on the basis of a thorough physical examination, complete blood count (CBC) and total protein (TP). Health status was evaluated again after two anesthesia sessions as previously mentioned. Prior to each trial food and water were withheld 12 and two hours, respectively. The Institutional Animal Care and Research Committee approved all the procedures in this study.

The current study was performed in two phases. In phase I, dogs received propofol (Anesia 10 mg/mL, Alleman, Germany; 8 mg/kg) and in phase II, dogs received ketamine (Ketamine 100 mg/mL, Alfasan, Holland; 15 mg/kg) as the anesthetic agent. In each phase, dogs were anesthetized two times randomly and received either normal saline or MPH (methylphenidate hydrochloride, Mehr Darou, Iran; 1 mg/kg) (propofol-saline: PS; propofol-MPH: PM;

Table 1. Median (range) of Behavior, sedation, induction and recovery scores. **MPH: methylphenidate, [a] Significantly different from Saline values ($p<0.05$).

	Behavior	Sedation	Induction	Recovery
Propofol-saline	1 (1-1)	3 (2-3)	1 (1-1)	2 (2-3)
Propofol-MPH*	1 (1-1)	3 (2-4)	1 (1-1)	4 (2-6) [a]
Ketamine-saline	1 (1-1)	3 (2-3)	1 (1-2)	2 (2-3)
Ketamine-MPH*	1 (1-2)	3 (2-3)	1 (1-2)	5 (3-6) [a]

ketamine-saline: KS; ketamine-MPH: KM). At least one week interval was allowed between each anesthesia session.

On the day of the experiment, the dogs were premedicated with acepromazine (Neurotranq, 10 mg/mL, Alfasan, Holland; 0.1 mg/kg; ACP) intramuscularly (IM). After 30 min, a 20G intravenous (IV) catheter was introduced into the left cephalic vein. The assigned anesthetic agent was administered IV within 30 sec. After induction of anesthesia, the animals were intubated; positioned in right lateral recumbency and allowed to breathe room air spontaneously. Placement of the tracheal tube was done when tongue movement and swallowing were interrupted. All intubations were performed by the same two investigators. Six min after induction of anesthesia, the dogs received one of the two treatments of MPH or normal saline. Preparation of MPH was done based on the study of Chemali et al. (2012). In brief, methylphenidate (powder) was weighed, dissolved in 2 mL normal saline, and filtered sterile before injection. After administration of treatments, 2 mL normal saline was flushed into the catheter to ensure the drugs` delivery.

In the present study, the times from induction to tracheal extubation, head upraising, sternal recumbency and standing were recorded. Extubation was performed when the animal started to chew and no longer tolerated tracheal tube. When the animals did not show any chewing till 45 min after induction, the tracheal tube was removed. Heart rate (HR), respiratory rate (f_R), and rectal temperature (RT) was obtained at base (before any medication), after sedation (30 min after premedication), and at 5, 10, 15, 20, and 25 min after induction, and then at recovery (when the dog was able to stand without ataxia). After induction of anesthesia, the animal was connected to a multiparameter monitoring system (Burtons, Guardian Industrial Estate, UK) and hemoglobin oxygen saturation (SPO_2), non-invasive systolic, diastolic and mean arterial blood pressure (SAP, DAP, MAP), and end-tidal carbon dioxide tension ($ETCO_2$) were recorded at 5, 10, 15 min after induction. In the current study, behavior (1- calm, in rest 2- happy, tail wagging 3- nervous, agitated) of the animal before any medication as well as sedation (1- no sedation 2-mild sedation, able to stand and walk 3- moderate sedation, reluctant to walk 4- deep sedation, unable to walk), induction (1- rapid induction with no excitement 2- some excitement during induction 3- hyperkinesia, obvious sign of excitement), and recovery (1- early extubation and rapid transition to alertness 2- early extubation, fair transition to alertness 3- some incoordination, generally quiet 4- startles, some paddling 5- startles, vocalization, paddling 6- emergence delirium, trashing) were scored using modification of scoring systems described elsewhere (Jiménez et al., 2012; Muir et al., 2008). All scores were given by the same investigator who was not aware of the treatments.

Statistical analysis was performed using SPSS software version 22 for windows

Table 2. Time (min) needed for various chronological sequences of recovery events. *MPH: methylphenidate; † when data of a dog with prolonged recovery were removed.

	Extubation	Head upraising	Sternal recumbency	Standing
Propofol-saline	14.8 ± 2.5 (n = 6)	16.4 ± 2.6 (n = 6)	23.6 ± 2.3 (n = 6)	29.8 ± 5.5 (n = 6)
Propofol-MPH*	23.8 ± 14.3 (n = 6)	24.6 ± 14.9 (n = 6)	29.4 ± 19.6 (n = 6)	48.6 ± 11.4 (n = 6)
	18.5 ± 9.32 (n = 5) †	16.6 ± 2.9 (n = 5)†	25.0 ± 19.5 (n = 5) †	37.3 ± 12.7 (n = 5) †
Ketamine-saline	16.8 ± 6.7 (n = 6)	21.0 ± 14.7 (n = 6)	31.2 ± 14.8 (n = 6)	64.2 ± 35.7 (n = 6)
Ketamine-MPH*	26.6 ± 11.19 (n = 6)	21.4 ± 13.8 (n = 6)	44.2 ± 34.9 (n = 6)	57.4 ± 37.1 (n = 6)
	22.0 ± 4.7 (n = 5) †	15.5 ± 4.8 (n = 5) †	28.75 ± 5.3 (n = 5) †	47.8 ± 38.9 (n = 5) †

Table 3. Mean ± SD of SPO_2, SAP, DAP, MAP, and $ETCO_2$. * MPH: methylphenidate; [a] Significantly different from T5 ($p<0.05$).

	Time (min)		
	5	10	15
SPO_2			
Propofol- saline	93 ± 2	90 ± 2 [a]	94 ± 1
Propofol- MPH*	90 ± 2	91 ± 3	90 ± 1
Ketamine- saline	90 ± 3	90 ± 1	92 ± 2 [a]
Ketamine- MPH*	90 ± 4	90 ± 2	90 ± 1
SAP			
Propofol-saline	148 ± 25	122 ± 9	124 ± 6
Propofol-MPH*	121 ± 10	124 ± 3	119 ± 10
Ketamine-saline	142 ± 29	141 ± 26	137 ± 24
Ketamine-MPH*	158 ± 32	147 ± 29	156 ± 23
DAP			
Propofol-saline	89 ± 8	78 ± 5	80 ± 7
Propofol-MPH*	72 ± 19	80 ± 23	81 ± 5
Ketamine-saline	93 ± 21	91 ± 11	92 ± 14
Ketamine-MPH*	114 ± 30	114 ± 14	104 ± 15
MAP			
Propofol-saline	119 ± 24	91 ± 8	105 ± 19
Propofol-MPH*	79 ± 11	89 ± 10	88 ± 6
Ketamine-saline	106 ± 18	107 ± 14	104 ± 13
Ketamine-MPH*	123 ± 34	127 ± 14	116 ± 16
ETCO2			
Propofol-saline	35 ± 4	30 ± 4	32 ± 3
Propofol-MPH*	35 ± 5	35 ± 2	34 ± 4
Ketamine-saline	36 ± 2	33 ± 4	32 ± 1 [a]
Ketamine-MPH*	30 ± 3	33 ± 4	31 ± 6

(IBM SPSS statistic, IBM Corporation, NY, USA). All normally distributed data were expressed as mean ± standard deviation (SD) and nonparametric data were reported as median (range). The times to the recovery sequences, HR, $f_{R,}$ and RT were compared by ANOVA for repeated measure followed by LSD test. The comparison of behavior, sedation, induction, and recovery scores was done by Friedman test. $p<0.05$ was considered statistically significant.

Results

Body weights were not significantly different among groups at each anesthesia session ($p>0.05$, data not shown). All the animals tolerated anesthesia well and recovered eventually. The animals' behavior was evaluated as normal and no significant differences were observed before any medication in all the groups ($p>0.05$; Table 1); however, dogs No.2 and 3 showed some happy behavior after the last anesthesia session which lasted four weeks after the completion of the trials. Sedation after premedication with ACP was mild to moderate with no significant differences among groups ($p>0.05$; Table 1). Tracheal intubation was performed rapidly and smoothly in all the groups. Although higher induction scores were given to the propofol groups as compared to the ketamine groups, the differences were not significant ($p>0.05$; Table 1).

No significant differences between PS and PM as well as between KS and KM were observed in the times needed for various chronological sequences of recovery ($p>0.05$; Table 2). The insignificant differ-

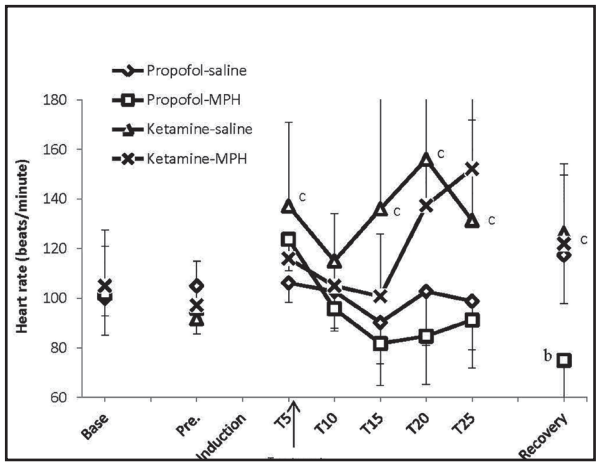

Figure 1. Mean ± SD HR (beats/min) for six dogs anesthetized with either propfol (8 mg/kg IV) or ketamine (15 mg/kg IV) and received either saline or methylphenidate (MPH) (1 mg/kg IV). (b) Significantly different from base value in PM ($p<0.05$). (c) Significantly different from base value in KS ($p<0.05$).

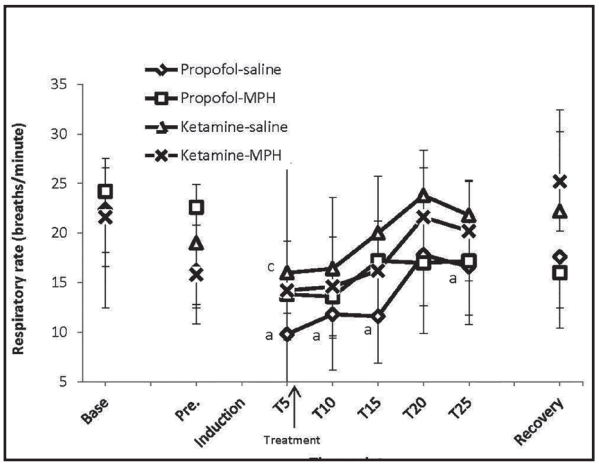

Figure 2. Mean ± SD f_R (breaths/min) for six dogs anesthetized with either propfol (8 mg/kg IV) or ketamine (15 mg/kg IV) and received either saline or methylphenidate (MPH) (1 mg/kg IV). (a) Significantly different from base value in PS ($p< 0.05$). (c) Significantly different from base value in KS ($p< 0.05$).

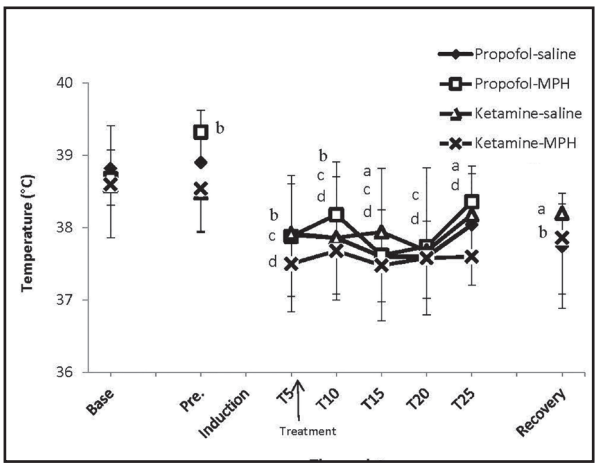

Figure 3. Mean ± SD RT (°C) for six dogs anesthetized with either propfol (8 mg/kg IV) or ketamine (15 mg/kg IV) and received either saline or methylphenidate (MPH) (1 mg/kg IV). (a) Significantly different from base value in PS ($p< 0.05$). (b) Significantly different from base value in PM ($p< 0.05$). (c) Significantly different from base value in KS ($p< 0.05$). (d) Significantly different from base value in KM ($p< 0.05$).

ence remained even when data related to the dogs No.5 in PM group and No.6 in KM group, due to unusual prolonged recovery, was removed (Table 2). Although recovery in saline groups was acceptable, recovery in the animals that received MPH was eventful. In PM group, dog No.1 showed severe nystagmus after the administration of MPH. Dog No.2 after the administration of MPH was recovered immediately. This dog raised its head and tried to eject the tracheal tube. The animal was very sensitive to the environment, responded inordinately to visual or vocal stimuli. This state remained for approximately five hours after the induction; however, the severity of responses decreased with time. Dog No.6 was also sensitive to the environment and stimuli after extubation which remained for about two hours. Since dog No.5 did not show swallowing reflex until 45 min after induction, extubation was performed at this time. During this period, it seemed that the animal was in a deep sedation or sleep-like state and was reluctant to move or to make any effort to eject the tracheal tube. Swallowing reflex was absent but the eyes of the animal were open and the animal was responsive to noxious and visual stimuli. Dog No.6 was also sensitive to the environment but to a lesser degree. In KM group, dog No.1 showed imbalance and wangling after standing. Dogs No.2 and 5 were sensitive to the environment after extubation. Dogs

No.3 and 6 showed periodic involuntary paddling during recovery period. Dog No.6 showed the same signs with the dog No.5 in PM group. Recovery quality was significantly superior in the animals that received saline as compared to those that received MPH ($p< 0.05$; Table 1).

HR in PM showed a trend to decrease from T10 in comparison with the base in which significant decrease was observed at the recovery point ($p<0.05$). In KS group, HR showed increase at several time points (T5, T15, T20, T25 and recovery) in comparison with the base ($p<0.05$) (Figure 1). f_R in PS was significantly lower at T5, T10, T15, and T25 than at the base ($p>0.05$). f_R in KS showed a significant decrease at T5 in comparison with the base ($p<0.05$) (Figure 2). RT in all groups showed significant decreases compared to the base at several time points ($p< 0.05$) (Figure 3).

SPO_2 in PS was significantly lower at T10 compared to T5 ($p< 0.05$). A significant higher SPO_2 value was also detected at T15 compared to T5 in KS ($p< 0.05$). $ETCO_2$ was significantly lower at T15 compared to T5 in KS ($p< 0.05$). No other significant differences at each time points in SPO_2, SAP, DAP, MAP, and $ETCO_2$ were seen in the treatments ($p>0.05$) (Table 3).

Discussion

MPH is widely used for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in children and adults (Solt et al., 2011). It has also been used to promote arousal in patients who received overdoses of antipsychotic agents and to facilitate psychiatric interviewing (Ferguson et al., 1956; Kerenyi et al., 1959). Recently, MPH has been suggested for management of neurobehavioral alteration such as obsessive compulsive disorder (OCD) in dogs (Giorgi et al., 2010). MPH has been used to shorten recovery from different anesthetic agents in humans and dogs (Dobkin, 1960; Dodson and Fryer, 1980; Evers et al., 1965; Gale, 1959; Roberts, 1961). Recently, MPH has induced emergence from isoflurane and propofol anesthesia in rats (Chemali et al., 2012; Solt et al., 2011).

The results of the present study demonstrated that MPH did not shorten recovery time from propofol or ketamine anesthesia in dogs. Different recovery times from immediate to prolonged recovery were observed. Even when the results of the two dogs with longer recovery were omitted, no significant differences in recovery times were seen. This is in accordance with the results of Roberts (1961) in human patients who received thiopental combined with nitrous oxide as the anesthetic agents. Roberts (1961) attributed his results to insufficient depression provided by the anesthetic agent. Inability of MPH to shorten the recovery of the dogs used in the current study may be due to four reasons:

First, the dosage of MPH might be inappropriate. MPH was used at 1 mg/kg which is one fifth (5 mg/kg) of the dosage used for emergence from propofol and isoflurane anesthesia in rats (Chemali et al., 2012; Solt et al., 2011). The dosage of 1 mg/kg MPH is the same as that of Dobkin (1960) who recorded a significant reduction in recovery time when MPH was added to thiopentone (25 mg/kg) in anesthetized dogs. Nevertheless, Gale (1959) noted that doses of about 0.045 - 0.09 mg/kg IM are effective in shortening recovery time and larger doses of MPH were less effective in human patients. The second reason is the depth and

duration of anesthesia. It has been noted that effectiveness of MPH is related to the depth of depression. Insufficient depth of anesthesia can mask differences in awaking time (Roberts, 1961). In the current study, propofol and ketamine used at the dose of 8 and 15 mg/kg, respectively, are in the ranges of the highest recommended dose of these anesthetic agents in dogs (Berry, 2015). These dosages were used to produce a deeper anesthesia; however, the remaining the dogs in an identical depth at the time of administration of MPH is unknown. On the other hand, short duration of anesthesia produced by a single dose of propofol and ketamine and subsequently short recovery period might have been concealed the role of MPH on accelerating the recovery. Third, this finding may be related to ACP used as premedication. ACP, a phenothiazine sedative, generally produces long-lasting, mild to moderate sedation in dogs (Zapata and Hofmeister, 2013). The sedative effect of ACP is primarily due to blockade of dopamine receptors (Rankin, 2015). Since both ACP and MPH act at dopamine receptors, it is likely that interaction between ACP and MPH masked the arousal effects of MPH in the anesthetized dogs. Fourth, which is also a limitation of the current study, is the occurrence of hypoxemia in dogs. As hypoxemia might potentially affect recovery time in anesthetized patients, preoxygenation is strongly recommended to prevent hypoxemia in future studies.

In the current investigation, recovery events in the animals that received MPH did not have the same characteristics and some adverse effects were seen. Gale (1959) recorded momentary nausea or retching after administration of MPH in the clinical dose range. Roberts (1961) reported continuous head movement in some patients who received MPH. Cognitive dysfunction, delirium, increasing locomotion activity, and compensatory sleep have been reported as potential complications of MPH in anesthetized subjects (Petrenko et al., 2012). In the present study, sensitivity to environment, a deep sedation or sleep-like state and transient muscle twitching were observed in dogs anesthetized with propofol and that had received MPH.

In ketamine groups, dogs which received MPH showed more complications during the recovery period. Ketamine is unique among anesthetic agents. This drug resembles a cataleptic state in CNS (Berry, 2015). Ketamine maintains or increases cardiac output via increasing activity of sympathetic efferent system (Wong and Jenkins, 1974). Emergence delirium may occur during recovery from ketamine (Berry, 2015). It can also be accompanied by muscle rigidity, convulsion, ataxia, hyperreflexia, increased motor activity and violent recoveries (Berry, 2015; Haskins et al., 1986). The complicated recovery in the dogs that received ketamine and MPH can be attributed to the concurrent effects of ketamine and MPH on CNS stimulation; however, the mechanisms of the two drugs for CNS stimulation are different.

Increase in HR has been reported after MPH administration (Bortoluzzi et al., 1963; Dodson and Fryer, 1980). Interestingly, in the current study, the dogs in the PM group had a trend in decreasing HR over time. Although the exact reason remains unknown, it is likely due to inappropriate dose of MPH or interaction between pharmacologic agents. Interaction is more likely because HR in KM group also decreased after administration of MPH at T10 and T15,

but it was not significant and HR increased again. Increase in HR in this group can be attributed to the direct effects of ketamine on cardiac function (Kennedy and Smith, 2014). A slight insignificant increase in MAP was seen five min after administration of MPH in PM and KM groups. Increase in blood pressure has also been reported after MPH administration (Gale, 1959; Martin et al., 1970; Roberts, 1961); nevertheless, blood pressure did not increase in the study of Dodson and Fryer (1980). The latter authors have attributed their results to the α-blocking effect of MPH. It is possible that the insignificant changes in MAP in the present study followed the same mechanism.

It has been reported that f_R increases after MPH administration in both humans and animals (Dodson and Fryer, 1980). MPH has increased minute ventilation in humans and rats anesthetized with thiopental and isoflurane, respectively (Chemali et al., 2012). In addition, one of the mechanisms for MPH that has been reported to play a role in accelerating recovery is the ability of MPH to increase respiratory drive (Chemali et al., 2012; Solt et al., 2011). In the current study, f_R in PS and KS showed significant decrease at several time points; but f_R in PM and KM groups did not show any significant change. Furthermore, SPO_2 and $ETCO_2$ in the MPH groups were relatively more stable than those which received saline. It is possible that increase in respiratory drive after administration of MPH compensated respiratory depression produced by propofol and ketamine.

RT decreased after anesthesia induction in all groups which can be explained by the effect of premedication and anesthesia on cutaneous vessels and thermoregulatory mechanisms (Clarke et al., 2014). It appears that MPH has no effect on temperature of the dogs anesthetized with either propofol or ketamine.

Conclusion: MPH at 1 mg/kg could not induce emergence or shorten recovery from propofol or ketamine anesthesia in dogs premedicated with ACP. Recovery in the dogs that received MPH was eventful and associated with some adverse effects. HR showed decreases in PM group. f_R was more stable in MPH groups. Testing lower doses of MPH and using a different premedication agent is recommended for future studies on accelerating recovery from anesthesia in dogs.

Acknowledgments

This work was supported by the [Research Council of Shahid Chamran University of Ahvaz, Iran] under grant [93/3/02/31579]. The Authors would like to thank Mr. Norouzi and Mr. Tab, the technicians of Department of Clinical Sciences for their precious and technical support.

References

Berry, S.H. (2015) Injectable Anesthetics, In: Veterinary Anesthesia and Analgesia. The Fifth Edition of Lumb and Jones. Grimm, K.A., Lamont, L.A., Tranquilli, W.J., Greene, S.A., Robertson, S.A. (eds.). John Wiley & Sons Inc., Pondicherry, India. p. 277-296.

Bortoluzzi, E., Roella, C., Bortoluzzi, S.L., Montoli, E. (1963) Methylphenidate in the treatment of shivering. Anesth Analg. 42: 325-331.

Chemali, J.J., Van Dort, C.J., Brown, E.N., Solt, K. (2012) Active emergence from propofol general anesthesia is induced by methylphenidate. Anesthesiology. 116: 998.

Clarke, K.W., Trim, C.M., Hall, L.W. (2014) Veterinary Anaesthesia, (11th ed.) Elsevier Ltd., China. p. 71-100.

Dobkin, A.B. (1960) Drugs which stimulate affective behaviour. Anaesthesia. 15: 146-153.

Dodson, M., Fryer, J. (1980) Postoperative effects of methylphenidate. Br J Anaesth. 52: 1265-1270.

Evers, W., Malik, K., Dobkin, A.B. (1965) Influence of doxapram hydrochloride on recovery from Thiopental anaesthesia. Can Anaesth Soc J. 12: 281-287.

Ferguson, J.T., Linn, F.V., Sheets, J.A., Nickels, M.M. (1956) Methylphenidate (Ritalin) hydrochloride parenteral solution: preliminary report. J Am Med Assoc. 162: 1303-1304.

Gale, A. (1959) The clinical use of methylphenidate for central stimulation in oversedated patients. Anesth Analg. 38: 406-413.

Giorgi, M., Prise, U., Soldani, G., Neri, D., Lavy, E. (2010) Pharmacokinetics of methylphenidate following two oral formulations (immediate and sustained release) in the dog. Vet Res Commun. 34: 73-77.

Haskins, S., Farver, T., Patz, J. (1986) Cardiovascular changes in dogs given diazepam and diazepam-ketamine. Am J Vet Res. 47: 795-798.

Heal, D., Cheetham, S., Smith, S. (2009) The neuropharmacology of ADHD drugs in vivo: insights on efficacy and safety. Neuropharmacology. 57: 608-618.

Horner, W.E., Johnson, D.E., Schmidt, A.W., Rollema, H. (2007) Methylphenidate and atomoxetine increase histamine release in rat prefrontal cortex. Eur J Pharmacol. 558: 96-97.

Jiménez, C.P., Mathis, A., Mora, S.S., Brodbelt, D., Alibhai, H. (2012) Evaluation of the quality of the recovery after administration of propofol or alfaxalone for induction of anaesthesia in dogs anaesthetized for magnetic resonance imaging. Vet Anesth Analg. 39: 151-159.

Kennedy, M.J., Smith, L.J. (2014) A comparison of cardiopulmonary function, recovery quality, and total dosages required for induction and total intravenous anesthesia with propofol versus a propofol-ketamine combination in healthy Beagle dogs. Vet Anesth Analg. 42: 350-359.

Kerenyi, A., Koranyi, E., Sarwer-Foner, G. (1959) The use of intravenous methylphenidate (ritalin) in psychiatric interviewing. Can Med Assoc J. 80: 963.

Kushikata, T., Hirota, K. (2014) Mechanisms of Anesthetic Emergence: Evidence for Active Reanimation. Curr Anesthesiol Rep. 4: 49-56.

Martin, W., Sloan, J., Sapira, J., Jasinski, D. (1970) Physiologic, subjective, and behavioral effects of amphetamine, methamphetamine, ephedrine, phenmetrazine, and methylphenidate in man. Clin Pharmacol Ther. 12: 245-258.

Muir, W., Lerche, P., Wiese, A., Nelson, L., Pasloske, K., Whittem, T. (2008) Cardiorespiratory and anesthetic effects of clinical and supraclinical doses of alfaxalone in dogs. Vet Anaesth Analg. 35: 451-462.

Petrenko, A.B., Takamatsu, M., Baba, H. (2012) Should we use psychostimulant drugs to boost the emergence from general anesthesia? Anesthesiology. 117: 1393-1394.

Pillay, S., Vizuete, J.A., McCallum, J.B., Hudetz, A.G. (2011) Norepinephrine Infusion into Nucleus Basalis Elicits Micro-Arousal in Desflurane-anesthetized Rats. Anesthesiology. 115: 733.

Plourde, G., Chartrand, D., Fiset, P., Font, S., Backman, S. (2003) Antagonism of sevoflurane anaesthesia by physostigmine: effects on the auditory steady-state response and bispectral index. Br J Anaesth. 91: 583-586.

Rankin, D.C. (2015) Sedatives and Tranquilizer. In: Veterinary Anesthesia and Analgesia. The Fifth Edition of Lumb and Jones. Grimm, K.A., Lamont, L.A., Tranquilli, W.J., Greene, S.A., Robertson, S.A. (eds.). John Wiley & Sons Inc., Pondicherry, India. p. 196-206.

Roberts, H. (1961) Postoperative administration of methylphenidate. Can Anaesth Soc J. 8: 257-264.

Shirasaka, T., Yonaha, T., Onizuka, S., Tsuneyoshi, I. (2011) Effects of orexin-A on propofol anesthesia in rats. J Anesth. 25: 65-71.

Solt, K., Cotten, J.F., Cimenser, A., Wong, K.F., Chemali, J.J., Brown, E.N. (2011) Methylphenidate actively induces emergence from general anesthesia. Anesthesiology. 115: 791.

Tose, R., Kushikata, T., Yoshida, H., Kudo, M., Furukawa, K., Ueno, S., Hirota, K., Orexin, A. (2009) Orexin A decreases ketamine-induced anesthesia time in the rat: the relevance to brain noradrenergic neuronal activity. Anesth Analg. 108: 491-495.

Wang, Q., Fong, R., Mason, P., Fox, A.P., Xie, Z. (2014) Caffeine accelerates recovery from general anesthesia. J Neurophysiol. 111: 1331-1340.

Wong, D.H., Jenkins, L.C. (1974) An experimental study of the mechanism of action of ketamine on the central nervous system. Can Anaesth Soc J. 21: 57-67.

Ying, S.-W., Goldstein, P.A. (2005) Propofol suppresses synaptic responsiveness of somatosensory relay neurons to excitatory input by potentiating GABA. Mol pain. 1: 2.

Zapata, M., Hofmeister, E. (2013) Refinement of the dose of doxapram to counteract the sedative effects of acepromazine in dogs. J Small Anim Pract. 54: 405-408.

مجله طب دامی ایران، ۱۳۹۷، دوره ۱۲، شماره ۲، ۱۳۴-۱۲۵

استفاده از متیل فنیدات به منظور خارج‌سازی از بیهوشی با پروپوفول و کتامین در سگ

هادی ایمانی‌راستابی رضا آویزه نرگس کاووسی سروش سابیزا

گروه علوم درمانگاهی، دانشکده دامپزشکی دانشگاه شهید چمران اهواز، اهواز، ایران

(دریافت مقاله: ۲۷ آذر ماه ۱۳۹۶، پذیرش نهایی: ۱۵ اسفند ماه ۱۳۹۶)

چکیده

زمینه مطالعه: نشان داده شده است که متیل فنیدات (MPH) می‌تواند موجب خارج‌شدن از بیهوشی عمومی گردد. **هدف:** هدف از مطالعه حاضر ارزیابی اثر MPH بر ریکاوری از بیهوشی با پروپوفول و کتامین در سگ است. **روش کار:** شش قلاده سگ سالم نر بالغ نژاد مخلوط (با میانگین وزنی ۳/۹ kg±۲۱/۹) به صورت مطالعه متقاطع تصادفی مورد استفاده قرار گرفتند. سی دقیقه پس از پیش‌بیهوشی با آسپرومازین (۰/۱mg/kg)، بیهوشی با یکی از دو داروی پروپوفول یا کتامین (به ترتیب۸ mg/kg و ۱۵) داخل وریدی القا شد. شش دقیقه پس از القای بیهوشی، سگ‌ها یکی از دو درمان داخل وریدی نرمال سالین یا متیل‌فنیدات (۱ mg/kg) را دریافت نمودند (پروپوفول-سالین: PS، پروپوفول-MPH: PM، کتامین-سالین: KS، کتامین-MPH: KM). هر یک از سگ‌ها چهار مرتبه و به فاصله حداقل یک هفته بیهوش شدند. **نتایج:** تفاوت معنی‌داری در زمان رخدادهای متوالی دوره ریکاوری بین گروه PS و PM و همچنین KS و KM مشاهده نشد ($p>۰/۰۵$). ریکاوری در سگ‌های دریافت‌کننده MPH پرحادثه و همراه با عوارض بود. ضربان قلب در گروه PM نسبت به زمان پایه کاهش معنی‌داری را نشان داد ($p<۰/۰۵$). تعداد تنفس در حیوانات دریافت‌کننده MPH نسبت به دریافت‌کننده نرمال سالین، ثبات بیشتری را نشان داد. **نتیجه‌گیری نهایی:** در پایان نتیجه‌گیری شد که MPH با دوز ۱ mg/kg نمی‌تواند زمان ریکاوری را در حیواناتی که داروی آسپرومازین را به عنوان پیش‌بیهوشی دریافت نمودند و با یکی از دو داروی پروپوفول یا کتامین بیهوش شدند، کاهش دهد. استفاده از دوزهای پایین‌تر MPH و یک داروی پیش‌بیهوشی دیگر در مطالعات آینده توصیه می‌شود.

واژه‌های کلیدی: بیهوشی، خارج‌سازی، کتامین، متیل فنیدات، پروپوفول

---

*) نویسنده مسؤول: تلفن: ۳۳۳۲۹۷۶۳ (۶۱)۹۸+ نمابر: ۳۳۳۶۰۸۰۷ (۶۱)۹۸+ Email: h.imani@scu.ac.ir