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Clinical Evaluation of Repeated Propofol Total Intravenous Anesthesia in Dog

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Abstract: This current study designed to evaluate any possible changes in required doses and other cardiopulmonary findings after repeated propofol total intravenous anesthesia (TIVA) in dog. The study was conducted in 6 healthy sheepdogs, weight between 16.5 and 28 kg. Anaesthesia induced by 8 mg kg^{-1} of propofol and maintained by continuous propofol (0.3 mg/kg/min) infusion in saline solution. All dogs received three times of propofol anaesthesia with the same protocol in a cross over design. As the animals in first, second and third time of anaesthesia allocated into groups 1, 2 and 3, respectively. Heart Rate (HR), rectal temperature (Temp), blood oxygen saturation (SpO_2) by pulse oximetry and non invasive arterial blood pressures were measured. Times to the first swallowing attempt, ability to lift the head and standing were measured during recovery. The apnea was recorded in all animals but no significant difference was recorded between groups under study. Calculated doses of induction were sufficient for intubation of the animals. The average doses foe maintenance of anesthesia did not show any significant difference between groups under study. There were no significant differences found between groups in any comparable parameter. Despite of longer recovery time in group three, there were no significant differences between the Groups in different recovery times. Repeated propofol anesthesia did not improve resistance and respiratory changes in this species. However, some effects on blood pressure may happen without any effect on heart rate.

Key words: Propofol, anesthesia, TIVA, dog, recovery

INTRODUCTION

Propofol has been used in total intravenous anesthesia of dog (Andress *et al*., 1995; Hall and Chambers, 1987), as a sole agent or combined anesthesia with remifentanil, ketamin, medetomidine and pentazocin (Nonaka *et al*., 2006; Umar *et al*., 2007; Gozdemir *et al*., 2007). Repeated anesthesia may be done in different animal species regarding to complete a procedure (Cortínez *et al*., 2001) that may result in improvement of a kind of tolerance after repeated anesthesia (Buehrer *et al*., 2007; Tobias, 2007; Scheiber *et al*., 1996) that is the subject of some studies (Calderon *et al*., 2002; Cortínez *et al*., 2001; Chandran and Sluka, 2003).

In humane anesthesia no signs of tolerance has been reported (Setlock *et al*., 1996; Mayhew and Abouleish, 1996) in adult and children (Keidan *et al*., 2004; Calderon *et al*., 2002; Buehrer *et al*., 2007). A case of a minor tolerance has was reported in humane (Deer and Rich, 1992), also improvement of tolerance was reported several days after anesthesia (Albrecht *et al*., 1999; Buckley, 1997). It is obvious that most of these cases reported from hospital cases that may complicate with other medications as well (Ihmsen *et al*., 2005). Repeated administration of the CNS depressant medications may result in tolerance and make some difficulties in determination of the drug doses (Buehrer *et al*., 2007; Tobias, 2000; Scheiber *et al*., 1996). Improving tolerance resulted in reducing the potency of the drug and increasing the doses for producing a suitable anesthesia (Calderon *et al*., 2002). Immoos and Buehrer didn't confirm any changes in doses of the propofol after repetitive administration in children (Buehrer *et al*., 2007).

Cockshott and colleagues reported a tolerance after 4-6 h anesthesia in dog (Cockshott *et al*., 1992). Repetitive propofol administration in cat resulted in significantly longer recovery time (Andress *et al*., 1995) that was not confirmed in dog (Nora *et al*., 2004). Fassoulaki *et al*.

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(1994) show a metabolic tolerance to bolus administration of propofol in cats that was criticized by further studies because of type of administration, bolus instead of infusion (Fassoulaki *et al*., 1994; Larsson and Wahlstrom, 1996). Ihmsen *et al.* (2005) didn't observe any clinical tolerance but they showed that a pharmacodynamic tolerance has been improved in their study. In a clinical repetitive model for comparing dogs and cats no adverse effects of repeated propofol administration has been reported (Nora *et al*., 2004).

Regards to presence of laboratory indices of possible tolerance after repeated propofol administration, this current study was designed to evaluate any possible changes in required doses and other cardiopulmonary findings after repeated propofol total intravenous anesthesia in dog.

MATERIALS AND METHODS

Animals: The study was conducted in 6 healthy sheepdogs, weight between 16.5 and 28 kg (mean±SD, 22.16±5.7 kg) between August to October 2007. The dogs were housed indoors at ambient temperature and fed with a fixed amount of the chicken. All animals treated for possible parasitic disease by Praziquantel (5 mg kg^{-1}) (Lorencite, D amloran, Borujerd, Iran) and Mebendazol (20 mg kg^{-1}) (MD Mebendazol, Mehrdaru, Iran). Prior to anaesthesia, food was withheld for 24 h but the animals had free access to water.

Anaesthesia: Dogs were transferred to the theater, the cephalic or saphenous vein was catheterised using an 18 G Angiocath (SUPA, Tehran, Iran), then anaesthesia induced by 8 mg kg^{-1} of propofol (Pofol 1%, Dangkook Pharm. Co. Ltd., Korea) Immediately following induction of anaesthesia, the trachea was intubated using a 9 mm internal diameter endotracheal tube (Blue line, 279. IT, Portex) and the cuff inflated. Dogs were positioned in left lateral recumbency. Anaesthesia was maintained using continuous propofol (0.3 mg/kg/min) infusion in saline solution by an infusion pump (FLO-GARD™6270, TRAVENOL).

All dogs received three times of propofol anaesthesia with the same protocol in a cross over design. As the animals in first time of anaesthesia allocated into group 1, the animals in second time of anaesthesia allocated in group 2 and the animals in third time of anaesthesia allocated in group 3.

Measurements: During the course of anaesthesia the following parameters were measured and recorded. Heart Rate (HR), rectal temperature (Temp), blood oxygen saturation (SpO_2) by pulse oximetry and non invasive arterial blood pressures (systolic (SAP), diastolic (DAP) and mean (MAP)) were measured using a Biosis monitoring machine (Biosys Co. Ltd., Korea). Measurement of the non-invasive blood pressures used an inflatable cuff on the metacarpal region, with zero taken as the level of the right atrium. The pulse oximeter probe was placed on the tongue. Respiratory rate also was measured using direct watching of the chest movements.

After induction duration of possible apnoea was recorded. The preferred depth of anaesthesia determined by lack of palpebral, pedal and haemostatic pinch forceps reflex and no movement from lateral recumbency. In case of any possible movement or positive reflexes rate of infusion were increased to achieve preferred depth of anaesthesia.

Recovery: On the end of anaesthesia animals were placed in sternal recumbency in surgery theater. Times were recorded of the first swallowing attempt, after which the endotracheal tube was removed. Dogs were then returned to their kennel and positioned in sternal recumbency. Further recovery was recorded by close watching. Recovery from anaesthesia to the point at which the dogs could lift the head and stand spontaneously was watched.

Data analysis: The cardiopulmonary and SpO_2 data at the times 10, 30, 60 and 90 min after induction of anaesthesia were selected for analysis. The hypothesis that mean time to extubation and adequate recovery following discontinuation of anaesthesia differed significantly between treatments was assessed using a one-way ANOVA.

A repeated measures ANOVA was used to determine whether the two main effects, time and treatment, were significant for the variables SpO_2 and diastolic, systolic and mean blood pressure, temperature, heart rate and respiratory rate.

A p-value of 0.05 or less was considered significant. Results are presented as mean±standard deviation unless stated otherwise. Analyses were carried out using the Statistical software Sigmastat 2.0 (Jandel Scientific).

RESULTS

Demographic data: The apnea were recorded in all animals but no significant difference was recorded between groups under study (Table 1).

Table 1: Duration of apnea (sec) in deferent groups under study

Group	Duration of apnea (sec)
1	47.4±10.93
2	46.8±9.06
3	48.0±9.77

Table 2: Cardiopulmonary and body temperature during anesthesia

		Time after induction (min)			
Group	Measurements	10	30	60	90
1	HR (beat min^{-1})	115.17±7.24	97.33±4.22	103.00±7.01	101.17±6.25
	RR (beat min^{-1})	19.67±3.98	20.83±1.90	33.00±11.85	31.67±14.16
	SpO_2 (%)	84.00±1.87	86.00±1.51	89.33±0.61	90.83±1.12
	SAP (mmHg)	123.83±8.71	123.67±6.76	132.33±13.64	137.33±11.44
	DAP (mmHg)*	81.83±7.56	62.50±8.13	79.83±13.47	90.50±9.69
	MAP (mmHg)*	103.00±7.01	85.50±6.88	101.50±14.65	111.17±9.32
	Temp (°C)	38.17±0.25	38.12±0.22	37.56±0.05	37.13±0.14
2	HR (beat min^{-1})	124.83±10.25	92.33±7.88	91.33±6.08	9 8.50±10.59
	RR (beat min^{-1})	16.60±0.00	21.00±6.17	22.50±5.33	24.67±5.88
	SpO_2 (%)	82.80±0.97	89.80±1.50	91.80±0.49	91.60±0.75
	SAP (mmHg)	107.40±2.91	106.60±2.98	108.80±5.10	115.40±4.89
	DAP (mmHg)	56.80±3.93	55.40±3.88	65.60±4.49	65.20±5.07
	MAP (mmHg)	79.20±4.19	77.00±3.96	84.80±5.34	83.80±6.94
	Temp (°C)	38.80±0.19	38.18±0.22	38.03±0.15	38.03±0.19
3	HR (beat min^{-1})	121.00±3.40	98.83±5.56	93.50±3.78	95.00±0.82
	RR(beat min^{-1})	18.83±1.00	34.83±16.26	22.83±2.61	18.67±1.76
	SpO_2 (%)	80.50±2.22	90.00±1.57	91.33±0.88	90.33±1.56
	SAP (mmHg)	118.83±6.89	109.00±6.36	118.83±9.65	122.00±7.99
	DAP (mmHg)	66.83±3.44	61.00±2.37	67.83±3.74	75.00±3.77
	MAP (mmHg)	84.50±3.41	81.50±3.39	87.17±3.73	94.33±5.46
	Temp (°C)	38.47±0.22	38.00±0.21	37.75±0.14	37.72±0.18

*Significantly different from other groups under study

Table 3: Recovery times (min) from cessation of administration of anaesthetic agent

Group	Extubation time (min)	Head lifting time (min)	Standing time (min)
1	13.00±6.56	77.00±4.53	37.60±5.66
2	14.33±4.45	78.17±6.38	41.33±9.73
3	9.33±7.86	76.00±3.83	79.33±4.10

Calculated doses of induction were sufficient for intubation of the animals as all dogs except one were intubated easily without any complication. The average doses foe maintenance of anesthesia 0.33±0.01, 0.28±0.02 and 0.29±0.02 mg/kg/min in groups 1, 2 and 3 did not show any significant difference.

Findings during anesthesia: A suitable and stable depth of anesthesia was achieved easily in all three groups and there were no untoward or unexpected occurrences except one dog that showed tremor and shivering during anesthesia in all groups.

Table 2 details the parameters which were measured during anaesthesia.

There were no significant differences found between groups in any comparable parameter ($p<0.05$).

Recovery: Table 3 shows the times to recovery, as measured by extubation time, ability to maintain a head lift and then standing for 10 min. Despite of longer recovery time in group three, there were no significant differences between the Groups. All sheep recovered calmly and uneventfully.

DISCUSSION

Selection of induction doses was in the range of previous reports (Maddison *et al*., 2002) that resulted in rapid and uneventful induction that was reported previously (Watkins *et al*., 1987). Anesthesia was maintained uneventfully except one dog that shivering was a constant finding during all three anesthesias that may be a result of lack of preanesthesia (Maddison *et al*., 2002).

Propofol anesthesia resulted in reduction of blood pressure (Hall and Chambers, 1987), although blood pressure didn't show any significant difference during study but groups two and three showed lower blood pressure that maybe a result of repeated anesthesia. In a human study similar results following propofol anesthesia were reported that indicates lowering systolic and mean blood pressure without any effect on heart rate (Belo *et al*., 1994).

Apnea is a constant finding in this current study that was reported previously (Bufalari *et al*., 1996; Bufalari *et al*., 1997; Muir and Gadawski, 1998; Murison, 2001) that differs with the type and speed of induction (Maddison *et al*., 2002; Andrews *et al*., 1997). However, in another study that time of one and more than one revealed as apnea, no apnea were reported (Nora *et al*., 2004). In this current study in 6 cases apnea of more than one minute was recorded that may be a result of speed and dose of induction.

SpO_2 decreased in the first time maybe a result of higher propofol concentration in this time; however,

another possible reason is the technical problems of fixing head and transducer on the tongue; however no significant difference found between groups under study. No resistance against the propofol was recorded in this current study that was in contrast to earlier reports (Keidan *et al*., 2004; Buehrer *et al*., 2007).

CONCLUSION

Fast induction and recovery from anesthesia recorded in propofol anesthesia. Repeated propofol anesthesia with interval of 14-19 days did not improve resistance and respiratory changes in this species. However some effects on blood pressure may happen without any effect on heart rate.

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