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Evaluation of Food Withholding time on Propofol Total Intravenous Anesthesia in Sheep

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Abstract

Objective- Evaluation of the effect of different fasting times on the quality of propofol total intravenous anesthesia (TIVA) and recovery features.
Design- Experimental prospective design.
Animals- Fifteen lambs.
Procedures- Fifteen lambs that anesthetized for carotid translocation surgery were included in this current study and allocated in to three groups randomly. In Group 1, food was withheld for 24 hours, with free access to the water. In Group 2 and 3 the food withhold time was 48 and 72 hours. In all animals the anaesthesia were induced by propofol (5 mg/kg) and maintained by continuous propofol infusion 0.41-0.45 mg/kg/hr for 60 minutes. Heart rate (HR) and respiratory rate (RR), rectal temperature (Temp) and invasive systolic (SAP), diastolic (DAP) and mean arterial pressure (MAP) were measured during anaesthesia. Time to first swallowing attempt, time to lift the head and time to standing were recorded by videoing the animals.
Results- Although the longest recovery times were recorded in group 3 but no significant difference were recorded between groups under study in all measured parameters. The only significant finding was the number of animals that were regurgitated during anaesthesia that was significantly higher in group 3.
Conclusion and Clinical Relevance- Long food withdrawal could not alter different recovery times but regarding to higher regurgitation in group three and lower quality of anaesthesia in this group it seems that the best results were in group one.
Key Words- Food withdrawal, Propofol, Sheep, Regurgitation, Recovery.

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Introduction

Bloat and regurgitation are two major complications of ruminant anesthesia that are due to the anatomy and physiology of the digestive tract in these species.[1] Food withdrawal is a main part of anesthetic preparation in order to prevent regurgitation, bloat and consecutive respiratory disorders.[2] Distention of the rumen in sheep and larger ruminants followed by lower volatile fatty acid (with special concern to propionate as the main source of glucose) production has been shown to impair ventilation, with consequent hypoxemia and hypercapnia.[3]

Duration of food withdrawal is still a matter of research in different species, as in some reports a free intake of clear fluids up to 2 hours before anesthesia is recommended,[4,5] However national guidelines for preoperative fasting still worth to explore in some areas.[6]

Long fasting may reduce glucose and glycogen sources resulted in lowering detoxification potential of the liver and extending recovery from anesthesia that is especially important in liver metabolized anesthetics.[7]

Propofol is one of the intravenous anesthetics that its rapid induction, distribution, metabolism and elimination that makes it a good choice for induction and maintenance of anesthesia by repeated bolus or continuous infusion. No accumulative effect after induction and maintenance with propofol has been reported.[8] Although the main part of metabolism of the drug was is being done in the liver, extrahepatic pathways especially in lungs and kidneys has been reported.[9,10] Propofol conjugates with glucoronide and sulphate by L-glucoronyl transferase, a glucose related enzyme, in liver that result in water soluble products excreted by kidneys.[11]

Since different food withdrawal duration may affect serum glucose levels and detoxification potential of the liver followed by accumulation of the drug in the blood that can lead to cardiopulmonary disturbances and extension of recovery time. In this current study effect of different fasting times on the quality of anesthesia and recovery features after different food withdrawal times were evaluated.

Materials and Methods

Animals

Fifteen healthy lambs (local breeds), aged 5-7 month and weighing between 27 and 36 kg (mean ± SD, 30.56 ± 2.5 kg) were used. They were anesthetized for carotid translocation surgery. The sheep treated for possible parasitic diseases by Albendazole (7.5 mg/kg, Dieverm, Damloran, Iran) and Ivermectin (0.2 mg/kg, Ivectin, razak, Iran) before study. All animals were housed indoors at ambient temperature, bedded with straw and fed hay and straw.

Anaesthesia

Animals were transported from their pens to the anaesthetic room by a trolley; the jugular vein was catheterised using an 18G catheter (SUPA, Tehran, Iran.). Anaesthesia induced by propofol (5 mg/kg, Pofol, Dangkook, Korea), Half of the calculated dose was injected rapidly and other half injected slowly in a minute. Immediately following induction of anaesthesia any possible respiratory apnoea was recorded and the trachea was intubated using a 9 mm internal diameter endotracheal tube and the cuff inflated (Blue line, Portex). An oesophageal tube was inserted into the rumen. The sheep were transported to the operating room, positioned on right lateral recumbency. Anaesthesia was maintained using propofol 0.4

mg/kg/min as a continuous infusion in a saline solution. The infusion was performed by an infusion pump (Flo-gard ™ 6200, Travenol) and the animals breathe spontaneously from room air. The preferred depth of anaesthesia determined by lack of reflexes to surgical stimulation and staying in right lateral recumbency. In case of any possible movement or positive reflexes rate of infusion was increased to achieve preferred depth of anaesthesia. The animals were allocated to one of three groups, 5 sheep were allocated to each group randomly. In Group 1, food was withheld for 24 hours, as 24 hours before induction of anaesthesia the animals moved to a new pen without any bedding and without any access to the food. The sheep had accessed to the water. In Group 2 and 3 just the food withhold time was 48 and 72 hours and other specifications of the groups were like group 1. In all animals the anaesthesia were continued to 60 minutes and by the end of infusion the amount of infused propofol were calculated.

Measurements

During the course of anaesthesia the following parameters were measured and recorded. Heart rate (HR) and respiratory rate (RR) by hand held stethoscope, rectal temperature (Temp) and invasive arterial blood pressures systolic (SAP), diastolic (DAP) and mean (MAP) were measured using a Biosys (Biosys, Korea) bedside monitoring system. Measurement of the invasive blood pressures was done by inserting a 23 G catheter in femoral artery and fixing with the suture in place after induction of anaesthesia.

Recovery

At the end of anaesthesia the animals were placed in sternal recumbency and time to first swallowing attempt, after which the endotracheal tube was removed, was recorded. Sheep were then returned to their pen and positioned in sternal recumbency supported by hay bales on each side. All sheep were videoed till complete standing. Recovery from anaesthesia to the point at which the sheep could lift the head and stand spontaneously and therefore no longer required continual observation was taken (the time at which it could lift its head and stand for a continuous period of five minutes).

Data analysis

The cardiopulmonary data at the times 15, 30, 45 and 60 minute 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 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 $\pm$ standard deviation (SD) or standard error of means (SEM). Analyses were carried out using the Statistical software Sigmastat 2.0 (Jandel Scientific).

Results

Demographic data

Table 1 gives the mean of body weight before and after food withdrawal that did not show any significant difference between times and groups ($P<0.05$).

Table1. Body weight (Kg) before and after food withdrawal

Groups	Before food withdrawal (Mean ± SEM)	After food withdrawal (Mean ± SEM)
Group1	30.1±0.71	27.75±0.62
Group2	29.3±0.66	27.2±0.64
Group3	32.3±1.49	27.7±1.15

Total time of anesthesia in different groups recorded as 70.75 ± 4.26 and total infusion time recorded as 64.64 ± 2.95 minutes in all animals that did not show significant difference between groups under study. The apnea was a constant finding in all animals but no significant difference was recorded between groups under study, however the longest apnea was recorded in group 3. (Fig. 1)

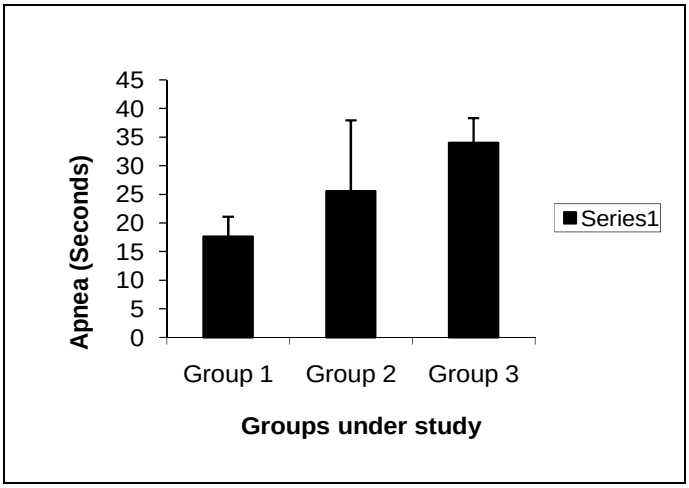

Figure 1. Duration of apnea (Sec) in deferent groups under study.

Intra-operative findings

A suitable and stable depth of anaesthesia was achieved easily in all three groups.

Regurgitation was a relatively constant finding in group 3 as 80% of the animals in this group were regurgitated that led to aspiration pneumonia and death in one sheep. This it was less prominent in group 2 as 40% of the animals regurgitated and no regurgitation was recorded in group one. Totally a significant increase in regurgitation recorded in group 3 in comparison to group 1 (Chi-square, $P<0.05$). No acute tympany was recorded in the animals in all groups under study.

Table 3 details the parameters measured during anaesthesia.

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

Table2. Infused propofol in different groups under study

Groups	Dosage (mg/kg/min) (Mean ± SEM)
Group1	0.41±0.035
Group2	0.45±0.025
Group3	0.41±0.019

Table3. Cardiopulmonary and body temperature during anaesthesia (mean ± SD)

Groups	Measurement	15	30	45	60
Group1	HR (Beat/min)	114.5 ± 10.71	104.75 ± 8.80	110.75 ± 5.34	111.5 ± 9.17
	RR (Breath/min)	19 ± 1.08	19.5 ± 2.21	19.75 ± 1.18	19.5 ± 2.21
	SAP (mmHg)	97 ± 15.87	109.5 ± 13.10	114.5 ± 7.75	108.5 ± 11.18
	DAP (mmHg)	76.33 ± 15.6	85 ± 11.35	90 ± 13.33	78.25 ± 11.79
	MAP (mmHg)	84 ± 15.50	94.5 ± 12.07	98.75 ± 11.71	89.25 ± 12.19
	Temp (C)	38.5 ± 0.30	38.5 ± 0.26	38.1 ± 0.25	38.9 ± 0.30
Group2	HR (Beat/min)	118 ± 15.38	123.6 ± 12.92	126.4 ± 12.79	114.4 ± 6.10
	RR (Breath/min)	18.8 ± 2.41	21.8 ± 2.32	18.8 ± 2.57	17.5 ± 2.53
	SAP (mmHg)	99.25 ± 12.31	95.4 ± 11.86	99.2 ± 9.65	105.8 ± 8.66
	DAP (mmHg)	68.25 ± 15.84	67 ± 13.60	70.8 ± 11.46	76.4 ± 11.21
	MAP (mmHg)	85 ± 15.78	78.4 ± 13.28	81 ± 10.49	87.2 ± 9.99
	Temp (C)	38.38 ± 0.48	38.84 ± 0.26	38.72 ± 0.35	39.16 ± 0.14
Group3	HR (Beat/min)	128.2 ± 11.10	135.5 ± 19.51	146.4 ± 12.08	145.6 ± 26.93
	RR (Breath/min)	19.6 ± 4.65	14.25 ± 3.42	16.2 ± 3.62	18 ± 2.44
	SAP (mmHg)	107.66 ±13.97	124.6 ± 6.99	111.4 ± 13.99	116.5 ± 15.32
	DAP (mmHg)	86.2 ± 9.68	87.4 ± 9.17	87.6 ± 15.67	86.5 ± 17.15
	MAP (mmHg)	83.33 ± 14.04	102.2 ± 7.57	98.6 ± 13.88	97.5 ± 16.76
	Temp (C)	38.2 ± 0.29	37.96 ± 0.21	37.88 ± 0.23	38.66 ± 0.40

Figure 2 gives recovery times, as measured by extubation time, ability to maintain a head lift and then standing for 5 minutes. Despite of longer recovery times in group three, there were no significant differences between the Groups. All sheep recovered calm and uneventfully.

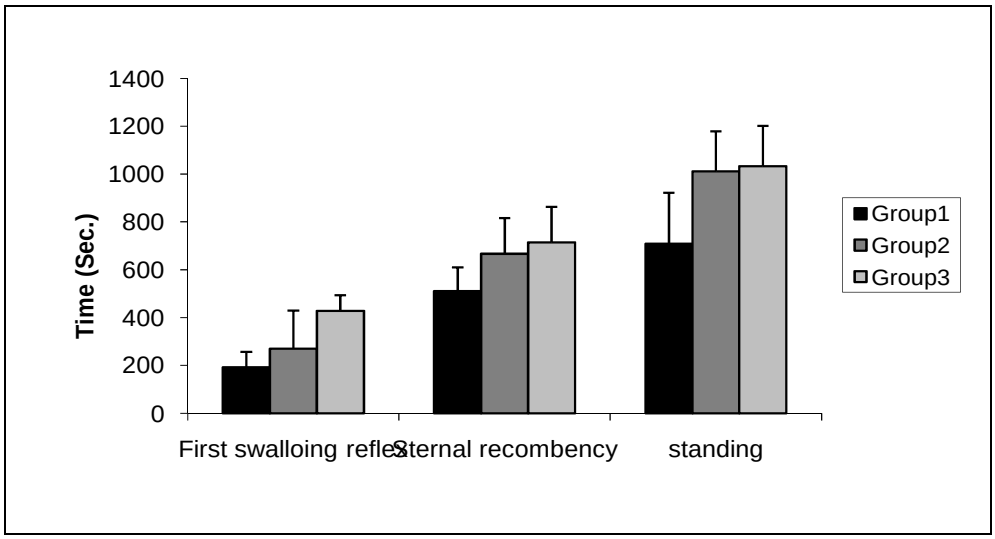

Figure 2. Recovery times (minutes) from cessation of administration of anaesthetic agent.

Discussion

Food withdrawal in ruminants did not affect the amount and volume of the ruminal contents and it seems that it is just to decrease the pressure of the rumen on the diaphragm, to decrease severity of bloat, aid in ventilation and decrease the prevalence and volume of regurgitation.[12] Ruminal contents are one of the main elements of total body weight in ruminants. It has been reported that the mean volume loss after a 4 day food deprivation in sheep were about half the body weight loss[13] regarding to non significant body weight loss in this current study it can be concluded that the capacity of the ruminal contents also didn't change significantly.

The apnea as a consequence of propofol induction were reported previously.[14,15] Duration of apnea up to 72.9 ± 38.3 seconds was reported that was not dose dependent,[15] however apnea was not a constant finding in some other reports.[14] In the this current study mean duration of apnea in all groups were less than 35 seconds, however lowering speed of administration may reduce apnea after induction.[16] Longer duration of apnea in group 3 may be a result of decreased metabolic activity of the liver and increase potential of propofol delivery to the effectors organ that has been reported in long term fasting for other drugs with liver metabolism.[7]

Three to 7 mg/kg Propofol were used as induction agent in small ruminants[17-19] with the possibility of easy endotracheal intubation.[17,20,21] These doses were followed with 0.3-0.6 mg/kg/min for maintenance of anesthesia.[18,19] Induction and maintenance rates were between previously reported doses without any difference among groups under study.

Regurgitation following propofol anesthesia in case of food withholding before anesthesia is not common.[14] However some reports indicate food regurgitation after non premedicated propofol anesthesia,[14,21,22] that was higher in anesthetized non fed cows than fed cows.[23] The amount of regurgitation (massive, acute, chronic) and its physical character may be affected by different anesthetic and food withdrawal protocols.[24] Significant higher occurrence of regurgitation in group 3 and its frequency (80%) that is higher than previous reports[25] can be a consequence of free access to water that result in dilution of ruminal contents that was the case in cows as larger volume of ruminal regurgitation following prolonged fasting reported in this species.[23] however reduction of ruminal fluid after 2-3 days of water deprivation were reported.[13] Although limitation of food does not empty the rumen, the possibility of

regurgitation is perhaps reduced if water is withheld for 12-24 hrs prior to induction[3] by decreasing the volume of fermentable ingesta.[16]

Reduction in diastolic blood pressure and heart rate without any other adverse effects,[19,26,27] an ncrease in MAP and heart rate,[28,29] bradycardia and sinus arrhythmia in cattle deprived of food for 48 hours were reported.[16,25] Muir et al. (1995) reported a dose-dependent decrease in arterial blood pressure caused by decreases in cardiac output and systemic vascular resistance, with minimal change in heart rate that is the case in the current study and reported previously,[30,31] However different food withdrawal times could not affect this finding.

Respiratory acidosis, reduction in respiratory rate and increase in CO_2 content might be seemed in propofol anesthesia.[29] In this current study no significant changes were recorded in cardiopulmonary indices that have been reported in other species.[30,31]

Propofol chief advantage lies in its rapid detoxification and elimination resulting in rapid recovery from anesthesia even after multiple supplements.[12] Emergence from propofol extubation, turning to sternal recumbency and standing reported as 2.8, 6.3 and 10.9 minutes in sheep,[20] and 7.3, 9.2, 17.7 after premedication with detomidine and butorphanol in goats.[15] However returning to standing position in unpremedicated sheep took 14.7 minutes.[17] Longer recovery time in group 3 may be a result of accumulation of the drug in the liver with lowering the capacity of detoxification in this organ. Propofol is metabolized mostly in liver by conjugation to glucoronic acid that is a glucose metabolite and in case of glucose fall following prolonged food withdrawal could be a reason to decrease detoxification activity of the liver. However despite of non significant difference between groups under study a longer recovery time is recorded in all groups that could be a result of decrease in available serum energy sources (propionate and glucose).

The hypothesis that long food withdrawal can affect recovery time was rejected in this study. It should be noted that longer food withdrawal time didn't have any advantages for anaesthetic indices and in longer fasting times regurgitation is increased and the quality of the anaesthesia is decreased. According to these results it seems that the best food withdrawal time is 24 hours in this species.

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چکیده

ارزیابی مدت پرهیز غذایی
بر روی بیهوشی کامل داخل وریدی با پروپوفل در گوسفند

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هدف- ارزیابی اثر زمان های گوناگون پرهیز غذایی برروی بیهوشی کامل داخل وریدی (TIVA) و ویژه گی های بازگشت از بیهوشی در این زمان ها.

طرح مطالعه- مطالعه تجربی آینده نگر.

حیوانات- 15 راس بره نر.

روش کار- پانزده بره که برای جراحی سطحی کردن سرخرگ کاروتید بیهوش می شدند در این مطالعه به کار گرفته شدند. بره ها در سه گروه به شکل تصادفی تقسیم شدند. در گروه یک پرهیز غذایی به مدت 24 ساعت اعمال گردید و حیوانات به طور آزاد به آب دسترسی داشتند. در گروه 2 و3 زمان پرهیز غذایی 48 و 72 ساعت در نظر گرفته شد. در تمامی حیوانات بیهوشی با استفاده از پروپوفل القا شده (5 میلی گرم به ازای هر کیلوگرم وزن بدن) و همچنین با استفاده از تجویز مداوم پروپوفل به میزان 0/45 – 0/41 میلی گرم به ازای هر کیلوگرم در ساعت به مدت 60 دقیقه نگهداری شد. ضربان قلب (HR)، تعداد تنفس (RR)، دمای مقعدی (Temp)، و فشارخون مستقیم سیستولیک (SAP)، دیاستولیک (DAP) و میانگین (MAP) در طول بیهوشی اندازه گیری شد. زمان تا اولین تلاش برای بلع، زمان تا بلند کردن سر و همچنین زمان تا ایستادن حیوان با استفاده از فیلم برداری ویدئو پس از قطع داروی بیهوشی اندازه گیری شد.

نتایج- هرچند طولانی ترین زمان بازگشت از بیهوشی در گروه 3 اتفاق افتاد ولیکن هیچ اختلاف معنی داری بین گروه های مورد مطالعه در پارامترهای اندازه گیری شده ثبت نگردید. تنها میزان برگشت غذا در حین بیهوشی به شکل معنی داری در گروه 3 بیشتر از سایر گروه های مورد مطالعه بود.

نتیجه گیری و کاربرد بالینی- زمان های طولانی پرهیز غذایی تاثیری روی زمان های بازگشت از بیهوشی نداردادما با توجه به میزان برگشت غذایی بالاتر در گروه 3 و کیفیت پایین تر بیهوشی در این گروه به نظر می رسد که بهترین زمان پرهیز غذایی در گروه 1 (24 ساعت) باشد.

کلید واژگان- پرهیز غذایی، پروپوفل، گوسفند، برگشت مواد غذایی، بازگشت از بیهوشی.