

Thiopental Sodium Anesthesia Following Premedication of Rabbits with Vitamin C

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Abstract

Rabbits are widely used as laboratory animals for experimental surgery. Anesthesia of rabbits may present complications unless the method is easy to apply and safe to use. In present study, effects of different dosages of vitamin C on thiopental sodium induced anesthesia in 25 male New Zealand white rabbits were studied. In the animals that had not received vitamin C treatment before thiopental sodium induced general anesthesia, return mean time of front limb pedal, corneal and ear pinch reflexes were 6.40 ± 1.67 , 6.60 ± 2.96 and 8.00 ± 2.58 minutes, respectively. Pre-treatment of rabbits with 30 and 240 mg kg⁻¹ (IV) of vitamin C followed by thiopental sodium 20 mg kg⁻¹ (IV) resulted in significant ($P < 0.05$) increase in front limb pedal reflex return mean time to 13.00 ± 2.24 and ear pinch to 11.60 ± 4.16 minutes, respectively. There was also significant ($P < 0.05$) decrease in the heart rate following induction of anesthesia in the animals pre-treated with 30 and 90 mg kg⁻¹ (IV) vitamin C and no change in the animals pre-treated with 240 mg kg⁻¹ (IV) vitamin C. Serum analysis indicated a significant ($P < 0.05$) increase in blood glucose. These results suggest that premedication of rabbits with vitamin C despite potentiating of thiopental sodium anesthesia in rabbits is not dose dependent.

Key words: Vitamin C, Thiopental Sodium, General anesthesia, Glucose effect, Rabbit

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Introduction

Rabbit has gained an increased popularity among urban families as a domestic pet. A safe anesthetic method is therefore needed both for surgeons undertaking research and for practicing veterinarians. Especially in veterinary practice anesthesia of the rabbit may present problems unless the method is easy to use and efficient and safe to use. Vitamin C possesses properties of modulating the central nervous system either physiologically and pharmacologically. There are some reports of insomnia and anxiety implicating vitamin C is an important regulator of mood and behavior.^{1,2} Vitamin C appears to be similar in structure to glucose and many animals convert the intermediate gluconic acid to vitamin C. Hence, premedication with vitamin C in thiopental sodium anesthesia may promote a phenomenon called *glucose effect* which prolongs recovery from anesthesia.³ This study was designed to determine the effects of different dosages of vitamin C on thiopental sodium anesthesia in rabbits. High doses of vitamin C has been reported to induce sleep disturbances, headache and gastrointestinal disturbances.^{4,5} Combined effects of stress and anesthesia can result in cardiopulmonary arrests. Rabbits are prone to be easily stressed by improper preoperative handling and/or induction of anesthesia.⁶ Recovery from anesthesia is often slow particularly following use of barbiturates in rabbits.⁷ This study was designed to determine the effects of vitamin C on thiopental sodium anesthesia in rabbits

Materials and Methods

Twenty-five adult (8 to 10 months old) male New Zealand white rabbits weighing 2.00 ± 0.25 kg were included in this study. They were divided into five groups (A, B, C, D and E) of five rabbits each, randomly.

They were kept in a controlled environment (room temperature, 18-21 °C; humidity, 55-65%) and were fed a standard commercial pellet diet (Niro Sahand Co., Tabriz, Iran) to meet all necessary minerals and vitamins requirements (including Vitamin C) and green hay and housed in animal house of Veterinary Teaching Hospital of Faculty of Veterinary Medicine, Urmia, Iran. Tap water was provided *ad libitum*. The rabbits underwent daily standard clinical examination to monitor their health. They were acclimatized for two weeks before the experiment started. The procedures were carried out based on the guidelines of the Ethics Committee of the International Association for the Study of Pain.⁸ The experimental procedures were approved by the clinical sciences committee of Faculty of Veterinary Medicine, Urmia University, with reference number 923.

Anesthetic protocol. The vital parameters such as body temperature, heart and respiratory rates were recorded before each anesthetic protocol. Marginal vein of rabbit ear was catheterized using local anesthesia. Blood samples were obtained before and after each anesthesia, centrifugated 5000 rpm for ten min and taken to laboratory for serum glucose, calcium and phosphorus assay. Animals in group A (control) received normal saline the same volume as thiopental sodium, and group B received no treatment before thiopental sodium induced general anesthesia. Rabbits of groups C, D and E received 30, 90 and 240 mg kg⁻¹, IV of vitamin C (Vitamin C 500 mg, Osveh Pharmaceutical Co. Tehran, Iran), respectively. Five minutes after the premedication animals underwent general anesthesia using 2.5% thiopental sodium (Specia Rhone-Poulenc Rorer, Paris, France), (20 mg kg⁻¹, IV). Immediately after induction front limb pedal, corneal, palpebral and ear pinch reflexes return mean time were assessed and a baseline recording of vital parameters obtained for

a two minute period. The time animal showing ability to sit unaided on its sternum was recorded.

Statistical analysis. Mean and standard error were used in analyzing the data. Changes in control and experimental values were compared for statistical significance using ANOVA. Values of $P < 0.05$ were considered significant.

Results

In rabbits of group B front limb pedal, corneal and ear pinch reflexes' return mean time were 6.40 ± 1.67 , 6.60 ± 2.96 and 8.00 ± 2.58 minutes, respectively. Pre-treatment of rabbits with 30 and 240 mg kg^{-1} IV of vitamin C followed by thiopental sodium resulted in significant ($P < 0.05$) increase in front limb pedal and ear pinch reflexes return mean time in

animals of groups C and E, respectively (Table 1).Administration of vitamin C prior to thiopental sodium treatment also significantly decreased heart rate in animals of groups C and D, $P = 0.0002$ and $P = 0.004$, respectively. Changes in those of group E were not significant ($P = 0.49$). There was no significant difference in temperature and respiratory rate of any groups ($P > 0.05$). Duration of anesthesia increased in animals of groups C and E, and decreased in group D. Premedication of rabbits with vitamin C prior to administration of thiopental sodium (groups C, D and E) gave rise to significant ($P < 0.05$) increase of serum glucose when compared to the control and thiopental sodium group only (groups A and B). However, serum levels of calcium and phosphorus didn't change significantly ($P > 0.05$) (Table 2).

Table 1. Changes in reflexes return mean time (Mean \pm SD)

Group	Reflexes		
	front limb pedal (min)	Corneal reflex (min)	Ear pinch reflex (min)
B	$6.40 \pm 1.67^{\dagger}$	$6.60 \pm 2.96^{\dagger}$	$8.00 \pm 2.58^{\dagger}$
C	$13.00 \pm 2.24^{\ddagger}$	$3.03 \pm 3.00^{\dagger\ddagger}$	N/A
D	$10.40 \pm 1.67^{\ddagger}$	$3.00 \pm 1.41^{\dagger\ddagger}$	N/A
E	$10.60 \pm 4.50^{\ddagger}$	$2.20 \pm 1.95^{\ddagger}$	$11.60 \pm 4.16^{\ddagger}$

Values with different symbols (\dagger and \ddagger) indicating significant difference at $P < 0.05$.

N/A: Not available

Table2. Changes in blood level of glucose, calcium and phosphorus in study groups (Mean \pm SD)

Group	Glucose (mg dl ⁻¹)	Calcium (mg dl ⁻¹)	Phosphorus (mg dl ⁻¹)
A	121.03 \pm 5.68 [†]	5.66 \pm 0.60	3.89 \pm 0.47
B	77.59 \pm 6.74 [‡]	4.89 \pm 0.79	3.02 \pm 0.65
C	112.01 \pm 6.39 [†]	5.10 \pm 0.57	4.65 \pm 0.49
D	117.07 \pm 6.33 [†]	5.43 \pm 0.55	3.51 \pm 0.51
E	110.54 \pm 6.01 [†]	4.04 \pm 0.56	3.01 \pm 0.44

Values with different symbols ([†] and [‡]) indicating significant difference at $P < 0.05$

Discussion

The results of this study indicated potentiating effects of premedication with vitamin C in generally anesthetized rabbits with thiopental sodium. Increase in the duration of anesthesia in animals of groups C and E, and the decrease in those of group D showed the potentiating effect was not dose dependent. Thiopental sodium and vitamin C combination caused significant ($P < 0.05$) decrease in heart rate of the rabbits. This is an important finding since thiopental sodium solely did not reduce the heart rate significantly ($P > 0.05$) in this study. This decrease may have resulted from vitamin C induced central nervous system depressant activity. Body temperature decreases following the administration of barbiturates through reduction of muscular activity and depression of thermoregulatory center and also decreasing the cellular metabolism activity.^{9,10} In present study premedication with vitamin C prior to administration of thiopental sodium did not influence body temperature. Recovery from pentobarbital is always slow but the duration varies according to the species of animal. The drug is metabolized more rapidly in horses, sheep and goats than in pigs, dogs and cats.³ Convulsive movements, paddling and vocalization may occur in the

recovery period but such excitatory phenomena can usually be suppressed with analgesics or tranquilizers although these will further delay complete recovery. The *glucose effect* – a reanaesthetizing effect due to a glucose induced decreased microsomal activity – exhibits a marked species variability and is of no significance in dogs, cats, mice or rats although it has been demonstrated to prolong recovery in rabbits.³ Glucose causes a decrease in activity of components of the microsomal electron chain resulting in decreased microsomal metabolism.¹¹ In this study premedication of rabbits with vitamin C prior to administration of thiopental sodium resulted in significant ($P < 0.05$) increase in serum level of glucose and subsequent increase in duration of anesthesia. These results suggest that thiopental sodium anesthesia preceded by vitamin C administration is potentiated and could be used to increase the duration of anesthesia. However, it is not dose-dependent. This combination may be useful in hypoglycemic animals subjected to surgery.

References

1. Pitt B, Pollit N. Ascorbic acid and chronic schizophrenia. Br J Psychiatry 1971; 118: 227-228.

2. Sauberich HE. Pharmacology of vitamin C. *Annu Reev Nutr* 1994; 14: 371-391.
3. Thurmen JC, Tranquilli WJ, Benson GJ. *Lumb & Jones' Veterinary Anesthesia* (3 Ed). .Williams & Wilkins, Baltimore, 1996; pp 217
4. Gregg DA, Olson LD. The use of ketamine hydrochloride as an anaesthetic for raccoon. *J Wildl Dis* 1975; 11: 335-337.
5. Laurence DR, Bennett PN, Brown MJ. *Clinical Pharmacology*, 8th ed. Churchill Livingstone, London, 1997; 383-384,
6. Flecknell P. *Laboratory animal anesthesia*. Academic Press, London, 1992; 88-889
7. Elsa A, Ubandawaki S. Ketamine anesthesia following premedication of rabbits with vitamin C. *J. Vet. Sci.* 2005; 6: 239-241.
8. Zimmermann M. Ethical guidelines for investigations of experimental pain in conscious animals. *Pain* 1983;24:109-110.
9. Gurnani A, Sharma PK, Rautela RS, et al. Analgesia for acute musculoskeletal trauma; Low- dose subcutaneous infusion of ketamine. *Anaesth Intensive Care* 1996; 24: 32-36.
10. Hemila H. Vitamin C and common cold. *Br J Nutr* 1992; 67: 3-6.
11. Peters M, Strother A. A study of some possible mechanisms by which glucose inhibits ground metabolism in vivo and in vitro. *J Pharmacol Exp Ther* 1972; 180: pp 151.