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RESEARCH ARTICLE

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Use of Vitamin C for Premedication Prior to Medetomidine–Ketamine Anesthesia in New Zealand White Rabbits

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ABSTRACT

This study aimed to investigate the effects of premedication with ascorbic acid (vitamin C) on physiologic parameters before medetomidine–ketamine anesthesia in New Zealand white rabbits. A total of 14 rabbits of both sexes, 1-4 months of age and 2-4 kg in body weight, were used in this study. The rabbits were randomly assigned one of two groups: medetomidine–ketamine (MK) or ascorbic acid–medetomidine–ketamine (AAMK). The rabbits in the MK group were given 0.25 mg/kg of medetomidine and 15 mg/kg of ketamine intramuscularly. The rabbits in the AAMK group were given 60 mg/kg of vitamin C intramuscularly 20 min prior to the same dose of medetomidine–ketamine anesthesia. The onset of anesthesia, time of surgical anesthesia, and total anesthesia time in the two groups was recorded. Heart rate, respiratory rate, and body temperature were also recorded at 0, 5, 10, 15, 20, 25, 30, 45 and 60 minutes during anesthesia. Physiologic parameters were not statistically different between the two groups. Pretreatment with vitamin C prior to medetomidine–ketamine anesthesia decreased the duration of onset of anesthesia. As a result, it was concluded that vitamin C can be used prior to anesthesia to accelerate the effect of medetomidine–ketamine in rabbits.

Keywords: anesthesia, rabbit, vitamin C, medetomidine, ketamine

Yeni Zelanda Beyaz Tavşanlarında Medetomidin – Ketamin Anestezisi Öncesi Preanestezik Olarak Vitamin C Kullanılması

ÖZ

Bu çalışmada, beyaz Yeni Zelanda tavşanlarında medetomidin – ketamin anestezisi öncesi preanestezik olarak uygulanan askorbik asitin (vitamin C=vit) fizyolojik parametreler üzerine etkisinin araştırılması amaçlanmıştır. Her iki cinsiyette 1-4 aylık ve 2-4 kg vücut ağırlığında sahip toplam 14 tavşan bu çalışma için kullanıldı. Tavşanlar rastgele iki gruba ayrıldı; medetomidin – ketamin (MK) ya da askorbik asit – medetomidin – ketamin (AAMK). MK grubundaki tavşanlara 0.25 mg/kg medetomidin ve 15 mg/kg ketamin intramuscular olarak uygulandı. AAMK grubundaki tavşanlara aynı dozdaki medetomidin-ketamin anestezisinden 20 dk önce 60 mg/kg oranında kas içi C vitamini verildi. İki grupta anestezi başlangıç zamanı, cerrahi anestezi süresi ve total anestezi zamanı kaydedildi. Anestezi sırasında kalp oranı, solunum oranı ve vücut sıcaklığı 0, 5, 10, 15, 20, 25, 30, 45 ve 60 dakikalarda kaydedildi. Fizyolojik parametreler açısından her iki grupta istatiksel olarak fark belirlenemedi. Sonuç olarak, tavşanlarda medetomidin – ketamin anestezisi öncesi C vitaminin kullanılması anestezi giriş süresini kısalttığı görülmüştür.

Anahtar Kelimeler: Anestezi, tavşan, vitamin C, medetomidin, ketamin

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INTRODUCTION

Rabbits are commonly used as a laboratory animals for experimental surgery. Preanesthetic medication is included as part of the anesthetic protocol because it reduces aggression, fear and pain, provides pre-emptive analgesia, and reduces the amount of medication needed to attain the desired level of anesthesia (Flecknell 1997). Medetomidine is an α_2-adrenoceptor agonist used in veterinary practice to induces sedation, analgesia and muscle relaxation (Nevalainen et al. 1989; Blum et al. 1992; Cullen 1996). Ketamine is a dissociative anesthetic drug routinely used for induction and maintenance of anesthesia. Because the sole use of ketamine is not sufficient for anesthesia, it is commonly combined with a preanesthetic drug such as medetomidine (Kılıç 2004; Henke 2005; Grint 2008). A combination of medetomidine and ketamine has been reported to provide effective anesthesia in rabbits and is now commonly used with a wide margin of safety in this species. Vitamin C is a water-soluble vitamin that is abundant in many plants and meat (Egwu et al. 2011). Known to be highly concentrated in the brain, the actual physiologic role of vitamin C in the normal functioning of the central nervous system (CNS) remains unclear. Vitamin C influences the CNS physiologically and/or pharmacologically (Laurence et al. 1997; Sauberich 1994). High amounts of vitamin C may produce effects similar to amphetamines in terms of CNS depression (Egwu et al. 2011; Najafpour and Nadeghi-Hashjin 2007).

The purpose of the present study was to investigate the effect with premedication vitamin C on New Zealand White rabbits anesthetized with a medetomidine–ketamine combination.

MATERIALS and METHODS

Animals

Ethical approval (file number: 2017/113) from the university's Institutional Animal Care and Use Committee was obtained prior to the study. A total of 14 rabbits of both sexes, 1-4 months of age and 2–4 kg in body weight, were evaluated in this study. The rabbits were maintained at a room temperature of 18–21°C and 55–65% humidity. The rabbits were allowed to acclimatize for 14 days prior to the study, provided water ad libitum and fed commercial pellet food. Food and water were not withdrawn prior to anesthesia.

Anesthetic protocols

The rabbits were separated randomly into two groups: medetomidine–ketamine (MK group) and ascorbic acid–medetomidine–ketamine (AAMK group) groups. The rabbits in the MK group were given 0.25 mg/kg medetomidine (Domitor®)[1] and 10 min later 15 mg/kg ketamine (Alfamine®)[2] intramuscularly. Those in the AAMK group were given 60 mg/kg vitamine C (Injacom C®)[3] intramuscularly 20 min before medetomidine-ketamine anesthesia. All anesthetic drugs were injected into the quadriceps femoris muscle. The body temperature (°C), heart rate (beats/per min), and respiratory rate (respiration/min) of the rabbits were recorded before anesthesia, immediately after induction, and at 5, 10, 15, 20, 25, 30, 45, and 60 min of anesthesia. The respiratory rate and heart rate were measured with a stethoscope. The body temperature was measured with a digital thermometer. The onset of anesthesia was evaluated in terms of recumbency, diminished respiratory rate, loss of pedal reflexes and loss of pinprick sensation on the skin. Surgical anesthesia time was evaluated in terms of loss of withdrawal and ear-pinch reflexes. The time between the administration of anesthesia and the recovery of all reflexes was referred to as total anesthesia time (Henke et al., 2005).

Statistical analysis

All statistical comparison was performed using SPSS software. Study data were assessed by calculating mean and standard error of the mean (mean ± SE). Differences were considered statistically significant if P value was < 0.05. Generated data were analyzed by analysis of variance. Differences among mean values were evaluated with the paired-samples t test for normally distributed data.

RESULTS

The onset of anesthesia, time of surgical anesthesia, and total anesthesia time are shown in Figures 1, 2, and 3, respectively. The MK group showed a longer onset surgical time of anesthesia, and total anesthesia time compared to the AAMK group but there were no significant differences ($P > 0.05$). The changes in heart rate, body temperature, and respiratory rate are shown in Table 1. No difference between groups was determined in terms of heart rate, respiratory rate, and body temperature. There were statistically significant differences within groups over time.

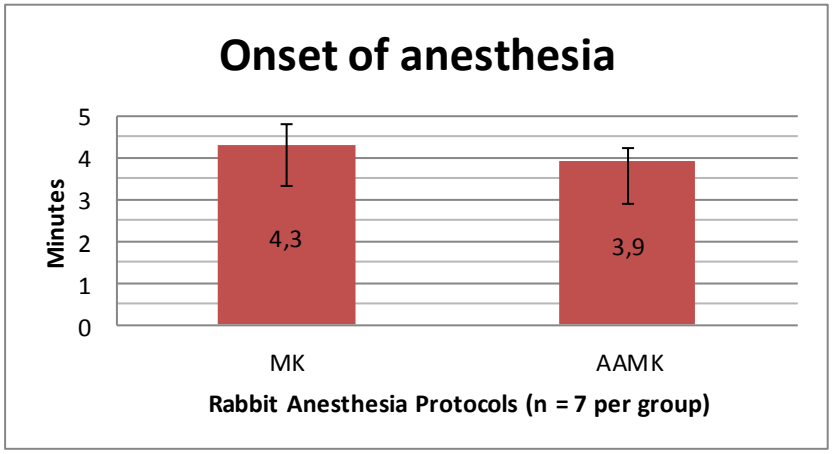

Figure 1. Onset of anesthesia, evaluated in terms of recumbency, diminished respiratory rate, loss of pedal reflexes, and loss of pinprick sensation on the skin MK = medetomidine–ketamine; AAMK= ascorbic acid–medetomidine–ketamine

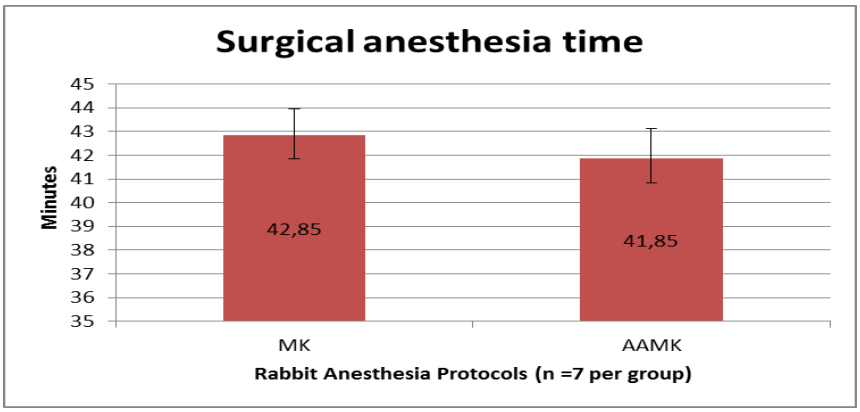

Figure 2. Surgical anesthesia time, evaluated in terms of loss of withdrawal and ear-pinch reflexes MK = medetomidine–ketamine; AAMK= ascorbic acid–medetomidine–ketamine

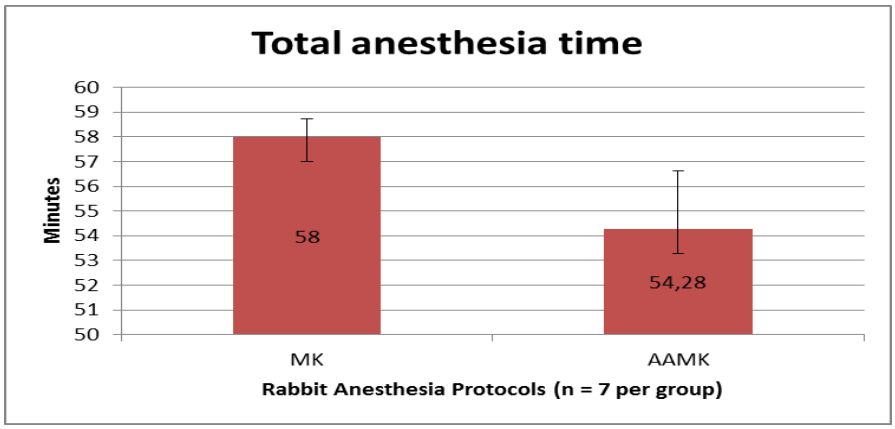

Figure 3. Total anesthesia time, between the administration of anesthesia and recovery of all reflexes MK = medetomidine–ketamine; AAMK= ascorbic acid–medetomidine–ketamine

Table 1. Changes in heart rate, body temperature, and respiratory rate before and during anesthesia

Groups	Medetomidine–Ketamine (n=7)			Vitamin C–Medetomidine–Ketamine (n=7)		
	Body temperature (°C) $\overline{X} \pm S_{\overline{x}}$	Respiratory rate (respiration per minute) $\overline{X} \pm S_{\overline{x}}$	Heart rate (beats per minute) $\overline{X} \pm S_{\overline{x}}$	Body temperature (°C) $\overline{X} \pm S_{\overline{x}}$	Respiratory rate (respiration per minute) $\overline{X} \pm S_{\overline{x}}$	Heart rate (beats per minute) $\overline{X} \pm S_{\overline{x}}$
Baseline Values Pre-anesthesia	39.75 ± 0.305	142.85 ± 13.65	219.42 ± 7.58	40.00 ± 0.069	130.28 ± 6.10	197.42 ± 5.06
At Induction 0 min	39.31 ± 0.353	65.14 ± 4.75***	170.85 ± 7.28*	39.84 ± 0.71	67.85 ± 3.43***	146.28 ± 8.13***
Anesthesia 5 min	38.97 ± 0.370	101.71 ± 16.27*	167.42 ± 10.56*	39.70 ± 0.123	80.00 ± 6.81***	170.85 ± 5.90**
Anesthesia 10 min	39.07 ± 0.544	73.71 ± 8.80**	168.0 ± 9.02**	39.51 ± 0.96*	63.42 ± 5.55***	163.57 ± 6.71**
Anesthesia 15 min	38.84 ± 0.533	75.42 ± 8.39**	165.71 ± 8.36**	39.12 ± 0.156**	58.28 ± 4.43***	177.14 ± 8.36*
Anesthesia 20 min	38.5 ± 0.402**	71.42 ± 12.44**	161.14 ± 8.49**	39.12 ± 0.156**	64.00 ± 6.17***	164.00 ± 5.92**
Anesthesia 25 min	37.98 ± 0.482**	64.57 ± 11.46**	160.00 ± 8.09**	38.84 ± 0.218**	61.71 ± 11.60***	182.57 ± 3.10
Anesthesia 30 min	37.98 ± 0.571**	56.00 ± 7.14***	159.57 ± 5.29***	38.91 ± 0.118***	59.42 ± 9.61***	182.2.98 ± 2.98
Anesthesia 45 min	37.37 ± 0.589**	66.85 ± 13.02**	161.14 ± 8.31***	38.58 ± 0.138***	59.42 ± 6.95***	152.00 ± 4.0***
Anesthesia 60 min	36.74 ± 0.576***	55.42 ± 5.48***	165.00 ± 7.51***	38.17 ± 0.233***	59.42 ± 6.95***	164.00 ± 8.28**

* Significant difference between anesthesia protocol time points ($P < 0.05$).
** Significant difference between anesthesia protocol time points ($P < 0.01$).
*** Significant difference between anesthesia protocol time points ($P < 0.001$)

DISCUSSION

Vitamin C is a water-soluble micronutrient required for various biological functions. However, the effect of vitamin C on the CNS remains unclear. Its deficiency has been reported to cause impairment of CNS function (Laurence et al. 1997). Previous studies reported that the use of vitamin C for premedication could accelerate the onset of anesthesia and increase the time of surgical anesthesia (Elsa and Ubandawaki 2005; Ito et al. 2014). Elsa and Ubandawaki (2005) administered different doses of vitamin C to rabbits before ketamine anesthesia. They found a statistically significant increase in total anesthesia time with an increasing dose of vitamin C as CNS functions were disrupted. In the present study, the time to onset of anesthesia was slighty longer in the MK group compared to the AAMK group.

Although the duration of total anesthesia was slightly shorter in the AAMK group, no difference was found between the groups most likely due to the low dose of vitamin C used. No complications occurred while anesthetizing the rabbits. Some studies (Elsa and Ubandawaki 2005; Yanmaz et al. 2016) showed that vitamin C had a depressive effect on the CNS and reduced the heart rate. In the present study, although the decrease in heart rate was statistically significant in both groups, the decrease in the MK group was greater than that in the AAMK group however, no significant difference in heart rate was found between the groups ($P > 0.05$).

Egwu et al. (2011) reported a slight increase in the temperature of rabbits after administering vitamin C most likely due to the modulatory effect of vitamin C. In the present study, the body temperature decreased in both the MK and AAMK groups and there was no statistically significant difference between the two groups ($P > 0.05$). Various studies (Henke et al. 2005; Kılıç 2004) reported a decrease in body temperature following medetomidine administration in laboratory animals. This decreased body temperature was attributed to thermoregulatory failure as a result of the inhibition of limbic–hypothalamic centers and

deterioration of homeostasis following reduced metabolic and muscular activities.

Previous studies (Hedengvist et al. 2001; Hellebrekers et. al. 1997) reported that medetomidine–ketamine anesthesia decreased the respiratory rate. In the present study, preinduction respiratory rates (RR) varied between 142.85 ± 13.65 and 130.28 ± 6.10 respirations per minute for the MK and AAMK groups, respectively. RR was significantly below the baseline value during anesthesia in both groups, however, no significant difference in RR was found between the groups ($P > 0.05$). Egwu et al. (2011) reported a decrease in RR after vitamin C administration in rabbits.

In conclusion, the present study showed that while vitamin C administered to rabbits before medetomidine–ketamine anesthesia decreased the duration of anesthesia, physiologic parameters were not statistically different between the two groups. As a result we conclude that vitamin C can safely be used before anesthesia to accelerate the effect of medetomidine–ketamine anesthesia in rabbits.

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