

Vital signs of *Cavia porcellus* (Guinea pig) diagnosed with malignant hyperthermia using sevoflurane gas

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Abstract

Malignant hyperthermia (MH) is a life-threatening clinical syndrome of hypermetabolism involving the skeletal muscle. It is triggered in susceptible individuals primarily by volatile inhalational anesthetic agents and the muscle relaxant succinylcholine. MH affects humans, certain pig breeds, dogs, horses, and probably other animals. The classic signs of MH include A dramatic rise in body temperature, rigid or painful muscles, especially in the jaw, flushed skin, sweating, an abnormally rapid or irregular heartbeat, rapid breathing or uncomfortable breathing, brown or cola-colored urine, very low blood pressure (shock), confusion and muscle weakness or swelling after the event. The syndrome is likely to be fatal if untreated. This study therefore assessed the effects of sevoflurane gas on the vital signs of *Cavia porcellus* with malignant hyperthermia. For the determination of malignant hyperthermia, 50, 15 day-old weaned kits of Peru breed were placed in an anesthesia chamber for 5 minutes and subjected to a mixture of air with 3% sevoflurane gas. Only 6% of them reacted positively, while most of them, 94%, were negative. The average body temperature of the positive kits was 38.9°C, oscillating between 38.7 and 39.1 °C, while the negative ones averaged 37.9 °C. The positive kits had an average of 142.3 breaths per minute compared to the negative ones, which was determined to be 83.7. The number of heart beats per minute in the kits with a positive reaction to sevoflurane averaged 205 and the negative ones 119.5. Muscle tremors were observed throughout the body during exposure of the positive kits to sevoflurane gas. It is concluded that for every 16 guinea pigs, 1 will react to the sevoflurane gas exposure positive due to the result obtained from the vital sign. Only the positive ones presented muscle tremors.

Keywords: Malignant hyperthermia, sevoflurane gas, vital signs, *Cavia porcellus*

Signes vitaux de *Cavia porcellus* (cobaye) diagnostiqué avec une hyperthermie maligne à l'aide de gaz sévoflurane



Résumé

L'hyperthermie maligne (HM) est un syndrome clinique d'hypermétabolisme mettant en jeu le pronostic vital impliquant le muscle squelettique. Elle est déclenchée chez les individus sensibles principalement par des agents anesthésiques volatils par inhalation et le relaxant musculaire succinylcholine. MH affecte les humains, certaines races de porcs, les chiens, les chevaux et probablement d'autres animaux. Les signes classiques de MH comprennent une augmentation spectaculaire de la température corporelle, des muscles rigides ou douloureux, en particulier dans la mâchoire, une peau rougeoyante, une transpiration, un rythme cardiaque anormalement rapide ou irrégulier, une respiration rapide ou une respiration inconfortable, une urine brune ou de couleur cola, très faible tension artérielle (choc), confusion et faiblesse ou gonflement musculaire après l'événement. Le syndrome est

Vital signs of Cavia porcellus (Guinea pig)

susceptible d'être fatal s'il n'est pas traité. Cette étude a donc évalué les effets du gaz sévoflurane sur les signes vitaux de Cavia porcellus avec hyperthermie maligne. Pour la détermination de l'hyperthermie maligne, 50 chatons sevrés de 15 jours de race Pérou ont été placés dans une chambre d'anesthésie pendant 5 minutes et soumis à un mélange d'air avec 3% de sévoflurane. Seuls 6 % d'entre eux ont réagi positivement, alors que la plupart d'entre eux, 94 %, ont été négatifs. La température corporelle moyenne des kits positifs était de 38,9 ° C, oscillant entre 38,7 et 39,1 ° C, tandis que les kits négatifs étaient en moyenne de 37,9 ° C. Les kits positifs avaient une moyenne de 142,3 respirations par minute par rapport aux négatifs, ce qui a été déterminé à être 83,7. Le nombre de battements cardiaques par minute dans les kits avec une réaction positive au sévoflurane était en moyenne de 205 et ceux négatifs de 119,5. Des tremblements musculaires ont été observés dans tout le corps pendant l'exposition des kits positifs au sévoflurane. Il est conclu que pour 16 cobayes, 1 réagira positivement à l'exposition au gaz sévoflurane en raison du résultat obtenu à partir du signe vital. Seuls les positifs présentaient des tremblements musculaires.

Mots clés : Hyperthermie maligne, gaz sévoflurane, signes vitaux, Caviaporcellus

Introduction

The guinea pig is a domestic species whose meat is used in most Andean countries in Latin America. This species of animal is prone to malignant hyperthermia (MH), which is a pharmacogenetic disorder of skeletal muscle. It presents itself as a hypermetabolic response to potent volatile anesthetic gases such as halothane, sevoflurane, desflurane and depolarizing muscle relaxant succinylcholine, and rarely, in humans, to stresses such as vigorous exercise and heat. Animals sensitive to general anesthetics as well as humans include pigs, horses, cows, deer, chickens, rabbits, European wild boar, cats, and dogs (Blood, 1988). The first domestic species in which this sickness was detected was coincidentally in the pig, which was called Porcine Stress Syndrome (SSP) or commonly known as the halothane gene (HAL), currently it bears the name of the ryanodine gene "Ryr1", it is an autosomal recessive monogenic disease occurs in the mutation of the DNA chain of pigs, generating neuromuscular disorder (Shen, 1992). A patient will suffer from Malignant Hyperthermia when there is genetic sensitivity to the disease while receiving sudden stimulation. The halogenated inhalation anesthetics that produce Malignant Hyperthermia are: halothane,

enflurane, isoflurane, desflurane, sevoflurane, and succinylcholine as a depolarizing muscle relaxant (Rosenberg, *et al.* 2007). This stress produces the death of the animal as its inadequate meat for the industry. It is also due to small stress situations such as inappropriate transfer of the animal and increase in temperature (Roeslet *al.*, 2014). The guinea pig is sensitive to stress since it has a nervous system. Malignant Hyperthermia is also caused by factors such as changes in temperature and prostration (the state of being extremely weak or subservient) due to heat. Knowing the physiological constants of the guinea pig allows us to know when there are alterations that indicate general metabolism problems (Calderón and Cazares, 2008). The European Medicines Agency (2007), which mentions that adverse effects of sevoflurane can affect more than 1 in 10 in pets (dogs or cats). The tendency to suffer from Malignant Hyperthermia in humans is 1 in 2,000 cases in terms of its genetic frequency (Bandschapp and Girard, 2012). This present study will try to document the vital sign exhibited by guinea pigs who had the Malignant Hyperthermia. Therefore, this study seeks to determine the frequency in the guinea pig population and the vital signs of *Cavia porcellus* with malignant

hyperthermia by using sevoflurane gas.

Materials and methods

Experimental site

The research was carried out in a commercial farm, located in the La Libertad region – Peru.

Experimental animal

Fifty healthy, 15-day-old weaned kits, *Cavia porcellus* of the Peru breed, with a weight of 250 ± 10 g, were randomly selected from all the kits weaned weekly. All the animals were housed in a deep litter floor of 1 m long x 1 m wide with 10 animals per pool. They had the same feed, handling, management and sanitation system. The animals were fed husk and concentrate and had water in the suckers *ad libitum*.

Exposure of animals to sevoflurane gas

All the kits vital signs were checked before and after exposed to sevoflurane gas within an anesthesia chamber of dimensions (40 cm x 35 cm x 30 cm). Three animals are exposed at a time to the mixture of air and sevoflurane at a concentration of 3% for a period of 5 minutes. The behavior of the kits was observed in this chamber and after treatment their vital signs were determined.

Determination of malignant hyperthermia of *Cavia porcellus*

The presence of malignant hyperthermia was established through their body

temperature, respiratory rate, heart rate, and muscle tremors, after exposure of the animals to sevoflurane gas. Hyperthermic animals were considered those that had high body temperature, high respiratory and heart rates, and muscle tremors. Non-hyperthermic animals were classified as those animals whose body temperature were normal and their vital signs were not affected by exposure to sevoflurane gas.

Statistical analysis

The data analysis was carried out through a statistical design of normal distribution Z, using the mean, minimum, and maximum values, and the standard deviation as measures of central tendency to interpret the results obtained. Bar graphs and percentage measurements were made for a better expression and support of the final results. Excel and SPSS version 25 software were used.

Results

Number of cases of positive and negative kits exposed to sevoflurane gas

Of the 50 *Cavia porcellus* monitored, only 3 kits (6%) of them reacted positively to sevoflurane gas exposure, while most of them, 47 kits (94%), were negative (Table 1 and Figure 1). The prism graph pad shows significant difference between the kits that react positive and negative to sevoflurane gas.

Table 1: Number and proportion of positive and negative reaction to sevoflurane gas

Positive reaction		Negative reaction	
N	%	N	%
3	6	47	94

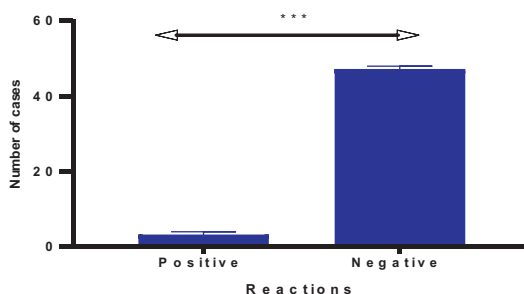


Figure 1. Positive and negative reaction of *Cavia porcellus* to sevoflurane gas

Vital signs of Cavia porcellus (Guinea pig)

Vital signs of positive kits

Body temperature

Table 2 shows the descriptive statistics of the body temperature of the positive kits. The average body temperature of the positive kits was 38.9°C, ranging between 38.7 and 39.1 °C.

Breathing frequency

Breathing frequency is presented in Table 2. The positive kits had an average of 142.3 breaths per minute.

Heart rate

The kits with a positive reaction to sevoflurane had an average of 205 heart

beats per minute (Table 2).

Muscle spasms

During exposure of the positive kits to sevoflurane gas, muscle spasms were observed throughout the body of the animals.

Vital signs of negative kits

Body temperature

Table 3 shows the average body temperature of the negative kits. The average body temperature of the negative kits was 37.9°C, varying between 37.2 and 38.5 °C.

Table 2: Descriptive statistics of the body temperature of the positive kits

Vital sign	Numberof Kits	Minimum	Maximum	Mean	Standard deviation
Temperature °C	3	38.7	39.1	38.9	±0.21
Breathing frequency (Rep / min)	3	132	149	142.3	±9.10
Heart rate (Beat / min)	3	190	215	205	±13.20

Table 3: Descriptive statistics of the body temperature of negative kits

Vital sign	Numberof kits	Minimum	Maximum	Mean	Standard deviation
Body temperature °C	47	37.2	38.5	37.9	±0.46
Breathing frequency (Rep/ min)	47	61	111	83.7	±13.9
Heart rate	47	87	159	119.5	±19.90

Breathing frequency

An average of 83.7 **breathing frequency** was calculated. The range between a minimum value of 61 and a maximum of 111 breaths per minute (Table 63). The coefficient of variation for this characteristic was 16.6%.

Heart rate

The heart rate ranged from 87.00 to 159.00, with an average of 119.50 beats per minute (Table 3). A coefficient of variation of 16.7% was calculated for this characteristic.

Muscle spasms

The kits that reacted negatively to sevoflurane gas exposure did not show muscle movements.

Comparison between the values of the vital signs of positive and negative kits to

exposure to sevoflurane gas

As shown in Table 4, the vital sign values for the malignant hyperthermia positive kits were higher than the negative ones. When calculating the percentage increase based on the mean of the negative kits, values of 2.5% for body temperature, 41.2% for respiratory rate, and 41.7 for heart rate were determined. Regarding muscle spasms, only the kits with positive reaction show muscle spasms. The prism graph pad shows further the significant differences between the kits that react positively and negatively to the sevoflurane gas. It was observed that kits that react positively to the sevoflurane gas had higher body temperature than those that react negatively to the sevoflurane gas. Respiratory rate and heart rate of the kits also showed the positive and negative

reaction of kits to the sevoflurane gas. As well shows significant. Although the values

obtained for the positive reaction was higher than those obtained for the negative reaction.

Table 4: Comparison of the means of the vital signs of the positive and negative kits

	Positive kits (x)	Negative kits (x)	Percentage of superiority of (positive/negative)*100 (%)
Body temperature, ° C	38.90	37.90	2.50
Respiratory rate, resp/min	142.30	83.70	41.20
Heart rate, beats/min	205.00	119.50	41.70
Muscle spasms	Yes	No	100.00

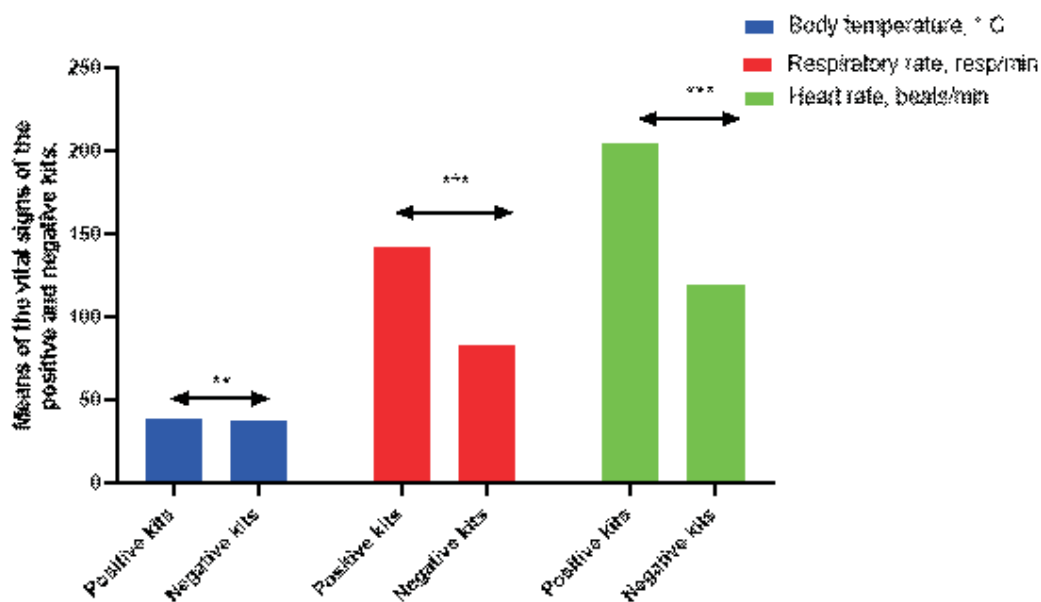


Figure 2. Comparison of the means of the vital signs of the positive and negative kits

*** = Highly significant

Discussion

Number and proportion of positive and negative kits to sevoflurane gas

In this research, it was observed that, out of the 50 guinea pigs monitored, only 6% of them reacted positively to sevoflurane gas exposure, while most of them, 94%, were negative. This result implied that for every 16 guinea pigs, 1 will react to the sevoflurane gas exposure. The average body temperature of the sevoflurane positive kits was 38.9 ° C, ranging between

38.7 and 39.1 ° C and the average body temperature of the negative kits was 37.9, varying between 37.2 and 38.5 ° C. Similar values have been reported by Chancafe (2019) who determined a temperature range; between 37.2 - 39.5 ° C. Likewise, other investigations such as those of Pardo (2016), INIA (2005) indicate as biological data an average of 38.6 ° C, oscillating between 37.2 - 39.5 ° C.

Breathing frequency

The sevoflurane positive kits had an

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average of 142.3 breaths per minute while the negative kits had an average of 83.7; ranging from a minimum value of 61 to a maximum of 111 breaths per minute. Similar values ?? were established by Chancafe (2019) with an average of 90 breaths per minute, varying from 69 to 104 respiratory movements per minute. In the same way, INIA (2005), Pardo (2016) mention that this biological characteristic has values ?? of 40 - 150 breaths per minute.

Heart rate

It was determined that the kits with a positive reaction to sevoflurane had an average of 205 heart beats per minute, while, in the kits with a negative reaction, the heart rate ranged between 87 and 159, with an average of 119.5 beats per minute. These results agree with those established by INIA (2005), which calculated a value of this physiological variable in the Peruvian breed of 130 - 190 beats per minute. But they are much lower than those reported by Chancafe (2019) who points out that the average heart rate is 275 beats per minute with a range of 150-400 beats per minute. In the same way, it does not agree with Pardo (2016) who gives us the value of the heart rate of 190-300 beats per minute.

Muscle tremors

During the exposure of the positive kits to sevoflurane gas, muscle tremors were observed throughout the body of the animals, while the kits that reacted negatively to the exposure of sevoflurane gas did not show muscle movements. European Medicines Agency (2007), mentions that the most frequent adverse effects of sevoflurane, which can affect more than 1 in 10, animals, are low blood pressure, rapid breathing, muscle tension, excitement, momentary inability to breathe, small contractions muscles and vomiting.

Conclusion

Out of the 50 *Cavia porcellus* used in this

study, only 6% reacted positively to sevoflurane gas exposure, while 94% were tested negative. This result implied that for every 16 guinea pigs, 1 will react to the sevoflurane gas exposure due to the average body temperature of the positive kits was 38.9°C, ranging between 38.7 and 39.1 ° C, while the negative ones had an average of 37.9 ° C. The positive kits had an average of 142.3 breaths per minute compared to the negative ones, which was determined to be 83.7. The number of heart beats per minute in the kits with a positive reaction to sevoflurane averaged 205 and the negative ones 119.5. Muscle tremors were observed throughout the body during exposure of the positive kits to sevoflurane gas. It is concluded that positive kits have a slightly higher body temperature and a 41% higher respiratory and heart rate than negative kits. Only the positive ones presented muscle tremors.

Conflict of interest

The authors declare that they have no conflict of interest.

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