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Preanesthetic effect of orphenadrine on the ketamine/xylazine mixture in a chick model

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Abstract

Preanesthetic drugs play an essential role in general anesthesia for smooth induction and recovery and have multiple pharmacodynamic properties; however, they are considered blockers of histamine receptor type 1. The fundamental goal was to determine the properties of orphenadrine as a pre-anesthetic in a chick model**.** Healthy, unsexed chicks were used. Up-and-down methods determined the safety profile of orphenadrine for the average lethal dose and the average analgesic dose. We administered orphenadrine at different doses and times. We then calculated the onset, duration, and recovery of anesthesia using xylazine and ketamine, as well as the body temperature and breathing rate of the chicks that had undergone general anesthesia**.** The median lethal dose was 121.10±8.49 mg/kg, intraperitoneal (IP), and the median analgesic dose was 2.49±0.21 mg/kg IP. Orphenadrine at 2.5, 5, and 10 mg/kg produced analgesia in a dose-dependent manner. Administration of orphenadrine at 5 mg/kg and IP at different times significantly prolonged the duration of anesthesia for xylazine and ketamine in a time-dependent manner, and body temperature and breathing rate were significantly decreased in the lateral recumbency situation in comparison with pre-lateral recumbency and post-lateral recumbency (recovery). Orphenadrine at 5,10, and 20 mg/kg, IP followed by 30 minutes produced a significant decrease in the onset of anesthesia, prolonged duration, and shortened recovery time compared with ketamine and xylazine alone. Orphenadrine also made a significant decrease in body temperature before lateral recumbency compared with xylazine and ketamine. Body temperature and breathing rate were significantly lower in lateral recumbency than in pre- and post-lateral recumbency. Conclusion: Orphenadrine is a safe drug because of the wide range between the average lethal and analgesic doses. It is also a good preanesthetic drug that prolongs the duration of anesthesia and shortens the recovery time in a Chick's model. However, because it has a hypothermic property, it must be used with caution when used as a preanesthetic.

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Introduction

General anesthesia is essential in birds and pets such as cats and dogs (1). When birds are exposed to injury, surgical operations depend on the efficiency of anesthesia to save their lives (2). Poultry is less acceptable to the hospital environment than other animals, and birds often need anesthesia for diagnostic or therapeutic purposes (2-4). Injectable anesthetics are more effective than inhaled anesthetics in birds (5,6). Preanesthetic drugs, known as medication, are taken before general anesthesia, which makes it safer and more pleasant (7,8). The main goals of the use of anesthetic drugs were the decrement of stress with the preservation of hemodynamic values, ease of induction of

anesthesia, and undergo amnesia (9,10). Preanesthetic drugs are also defined as medications that have been used before anesthesia to prepare the patient and reduce anxiety before the surgical operation, which takes about half an hour to the night of the operation (11). Pre-anesthetic medications are typically administered to patients to avoid the negative effects of general anesthesia, make surgery more accessible, and lower the risk of postoperative complications (11,12). Common concerns during surgical procedures include patient anxiety, postoperative pain, nausea and vomiting, and aspiration pneumonitis (13). Preanesthetic medicine is correlated with several outcomes, including the patient's clinical condition, the kind and length of the operation, the length of the postoperative recovery period, the need for postoperative analgesia, and the length of stay in the hospital (14,15). Orphenadrine has antagonistic activity against many receptors like H1 (histaminic), muscarinic, and N-methyl D-Aspartate (NMDA) receptors and is considered a norepinephrine-dopamine reuptake inhibitor. Lastly, the physiological and pharmacological findings verified that orphenadrine has a blocking activity for voltage-gated sodium channels in many types of chronic pain conditions (16,17). It is clinically used for Parkinson's disease and musculoskeletal syndromes like muscle spasms; furthermore, it is used as a painkiller (18-20). Xylazine is an α2-agonist that causes dose-related sedation and analgesia by its effect in the brain by acting on the G protein type (i) receptor, which inhibits adenylate cyclase and decreases calcium levels in the preganglionic neuron and thereby diminishes the release of the noradrenaline (21,22). Ketamine is frequently used in animals, birds, and people, making it a popular medication (23,24). Many studies have proposed it as an acceptable anesthetic for birds, the cardio-pulmonary depression impact is missing, but due to inadequate muscular relaxation, opisthotonus, persistent pain reflex responses, muscle tremors, and complicated recoveries, it is seldom employed alone (25). Various medications, including the xylazine (α2-agonist) molecule, have been used in combination with ketamine to counteract these unwanted side effects (26-28).

To our knowledge, there are no studies dealing with the use of orphenadrine as a pre-anesthetic drug with a mixture of xylazine and ketamine in birds in general and chickens in particular. Therefore, this study is designed to assess the pharmacological effects of orphenadrine as pre- anesthetic in a chick's model.

Materials and methods

Ethical approval

Members of the Ethical Research Committee of the College of Veterinary Medicine/University of Mosul reviewed the experimental design and unanimously approved the study, which was conducted on 22/1/2023 and has code UM.VET.2023.010.

Animals

Chicken chicks (Ross) were used. They were brought in at one day old and raised in plastic cages under standard conditions at a constant temperature of 33-35°C with 23 hours of light and one hour of dark. The litter consisted of Sawdust. They were fed crushed fodder for newly hatched chicks. Drinking water was prepared from a 1-liter plastic manual dispenser.

Drugs

Orphenadrine (30 mg/mL) Teva® is accessible as an ampule, while ketamine (10% INJ, Dutch Farm, Germany) and xylazine (2%, Xyla, Holland) are available in vials. The suggested dose was acquired by diluting it with normal saline solution and preparing each dose separately in proportion to the chick's weight. The recommended dosage volume for chicks is 5 ml/kg intraperitoneal.

Determination of the median lethal dose of orphenadrine in chicks by Dixon methods

Firstly, the LD_{50} of orphenadrine was determined by Dixon method (29). We chose an initial dose after the pilot study, which was an injection of a single bird with a dose of orphenadrine. We monitored for one day to see if the bird died or survived; if the bird was still alive, we increased the dose at a constant rate, or if it died, we decreased the dose at a constant rate. After the change in condition, death, or life, we repeat the administration to three animals, increasing or decreasing the dose. The Dixon table was used to calculate the average lethal dose. To give the dose reliability, we repeated the experiment three times to obtain the mean and standard error. The LD_{50} was obtained as follows; LD_{50} = xf + Kd. xf = last dose that has been used. K = A value obtained from the table (29). d = The value of increase and decrease in dose.

Determination of the median effective analgesic dose of orphenadrine in chicks by Dixon methods

Several chicks were used to determine the average analgesic dose of orphenadrine, which is defined as the dose that gives 50% of the full effect of the drug. An electrical stimulator device was used to find the pain threshold after injecting the chick with a dose of orphenadrine after 15 minutes, and in the event of a change in the pain threshold, i.e., We reduced the dose at a constant rate and repeated the experiment. If there is no change in the pain threshold, we increase the dose at a constant rate (30-35). After the change in the pain threshold, we used three animals going up and down the dose to calculate the average analgesic dose. We repeated the experiment three times to determine dosage reliability and computed the mean and standard error.

Analgesic effect of orphenadrine in chicks after 30 minutes

Twenty-four chicks were allocated into four groups and treated with orphenadrine at 0 (distilled water), 2.5, 5, and

10 mg/kg body weight intraperitoneally. The voltage required to flap the wing or call was measured in the electrostimulation test after 30 minutes of administration for each chick in all groups.

The effect of orphenadrine at different times on anesthesia with xylazine and ketamine

Twenty-four chicks were allocated into four groups and treated with orphenadrine at 5 mg/kg body weight intraperitoneally. as follows. Group 1: Orphenadrine 5 mg/kg +xylazine 20, ketamine 5 concomitantly. Group 2: Orphenadrine 5 mg/kg +xylazine 20, ketamine 5 after 15 minutes. Group 3: Orphenadrine 5 mg/kg +xylazine 20, ketamine 5 after 30 minutes. Group 4: Orphenadrine 5 mg/kg +xylazine 20, ketamine 5 after 60 minutes. Then we calculated the onset of anesthesia, duration of anesthesia, and recovery. Furthermore, we calculated the cloacal temperature and respiratory rate at pre-lateral recumbency, during lateral recumbency, and post-lateral recumbency. The cloacal temperature was measured by the insertion of a lubricated digital thermometer 1.5-2 cm into the cloacal opening of the chicks (36), while the respiratory rate was measured by direct observation of the chest (30).

The effect of orphenadrine at different doses on anesthesia with xylazine and ketamine

Twenty-four chicks were allocated into four groups and treated with orphenadrine at different doses and 30 minutes later treated with half of the doses of xylazine and ketamine as follows; group 1: xylazine 10, ketamine 2.5 mg/kg. Group 2: Orphenadrine 2.5 mg/kg +xylazine 10, ketamine 2.5 mg/kg. Group 3: Orphenadrine 5 mg/kg +xylazine 10, ketamine 2.5 mg/kg. Group 4: Orphenadrine 10 mg/kg +xylazine 10, ketamine 2.5 mg/kg. then we calculated the onset of anesthesia, duration of anesthesia, and recovery. Furthermore, we calculated the cloacal temperature and respiratory rate at pre-lateral recumbency, during lateral recumbency, and post-lateral recumbency.

Statistical analysis

The statistical program SPSS was used to analyze the results obtained, and the one- and two-way analysis of variance test was used with the LDS test. The probability was used at a value of $P<0.05$.

Results

Determination of the median lethal dose of orphenadrine in chicks by Dixon methods

The median lethal dose of orphenadrine was 121.10±8.49 mg/kg when the median lethal dose was repeated three times: 134.82, 106.1, and 125.98. Signs of poisoning appeared on the chicks before death, which were trembling, lying on the sternum, and convulsions that ended in the death of the chick (Table 1).

Determination of the median effective analgesic dose of orphenadrine in chicks by Dixon methods

The median effective analgesic dose of orphenadrine was 2.49±0.21mg/kg when the median lethal dose was repeated three times: 2.259, 2.299, and 2.916 (Table 2).

Table 1: The median lethal dose of orphenadrine in chicks by the Dixon method

Repetition	First	Second	Third
LD_{50} (mg/kg) (ip)	134.82	106.1	122.44
Doses range	140-80=60	120-80=40	140-100=40
Early dose	80	100	100
Latest dose	120	100	140
+ or - in dose	20	20	20
Total of chicks used	7 oooxoxo	5 xooxo	5 oxoox
Equation application	LD_{50}=120+(0.741)20=134.8	LD_{50}=100+(0.305)20=106.1	LD_{50}=140+(- 0.878)20=122.44

X- death; O- alive.

Table 2: The median effective dose of orphenadrine in chicks by the Dixon method after 30 minutes

Repetition	First	Second	Third
LD_{50} (mg/kg) (ip)	2.259	2.299	2.916
Doses range	5-3=2	3-2=1	3-2=1
Early dose	5	3	3
Latest dose	3	3	3
+ or - in dose	1	1	1
Total of chicks used	7 xxxoxox	5 xoxox	5 xoxoo
Equation application	ED_{50}=3+(-0.741)1=2.259	ED_{50}=3+(-0.701)1=2.299	ED_{50}=3+(-0.084)1=2.916

X- analgesia; O- No.

Analgesic effect of orphenadrine in chicks after 30 minutes

Orphenadrine at 2.5, 5, and 10 mg/kg IP produced a dose-dependent analgesic impact in the electrostimulator test compared to the control group; the analgesic efficacy was 27,81 and 148% (Table 3).

The effect of orphenadrine at different times on anesthesia with xylazine and ketamine

There was no statistically significant difference between the groups regarding the time of onset of anesthesia, while there was a significant increase in the duration of anesthesia based on the time when orphenadrine was administered, and there were no statistically significant differences between the groups concerning the recovery time. The decrease in body temperature of chicks undergoing anesthesia varied, as the decline peaked statistically for the four groups in the recovery time from anesthesia compared to the body temperatures of the chicks' time of lateral recumbency and the body temperatures before lateral recumbency. It is worth noting that the body temperature decreased statistically at the time of lateral recumbency compared to before it. All groups' respiratory rate of anesthesia chicks was statistically reduced at lateral recumbency compared with the respiratory rate of chicks before lateral recumbency and at the time of recovery **(**Table 4). The respiratory rate was statistically increased at the time of recovery compared with the time of lateral recumbency but did not return to the normal range before lateral recumbency **.**When comparing the respiratory rate between groups at the time of lateral recumbency, we noted a statistically significant increase in the respiratory rate in groups 2, 3, and 4 compared to 1 group **(**Table 5).

Table 3: Analgesic effect of orphenadrine in chicks after 30 minute

Groups	Pain threshold (Volt)	Analgesic efficacy
Control	5.57±0.20	-
Orph 2.5	7.10±0.28∗	27%
Orph 5	10.10±0.21∗a	81%
Orph 10	13.80±0.41∗ab	148%

Data expressed as Mean ±SE for six chicks per group. * Referred to significantly dissimilar from the control values. a Referred to significantly dissimilar from the values of orphenadrine 2.5 mg/kg. b Referred to significantly dissimilar from the values of orphenadrine 5 mg/kg.

Table 4: The effect of orphenadrine at different times on anesthesia with xylazine and ketamine

Groups	Onset (sec)	Duration (min)	Recovery (min)
Orph 5+xk 20, 5 concomitantly	22.14±3.14	90.00±2.43	107.4±0.15
Orph 5+xk 20, 5 After 15 min	23.57±2.60	118.56±8.28∗	90±0.11
Orph 5+xk 20, 5 After 30 min	26.42±5.84	174.00±6.38∗a	98.4±0.14
Orph 5+xk 20, 5 After 60 min	21.85±2.62	351.43±21.65∗ab	102.6±0.11

Data expressed as Mean ±SE for six chicks per group. * Referred to significantly dissimilar from the control values. a Referred to significantly dissimilar from the values of the second group. b Referred to significantly dissimilar from the values of the third group.

Table 5: The effect of orphenadrine at different times on body temperature and breathing rate during anesthesia

Groups		A	B	C	D
Pre lateral recumbency	Rectal temperature (ºC)	40.2±0.1	40.0±0.1	40.0±0.2	40.0±0.1
	Respiratory rate (breaths/min)	30.4±1.3	29.5±1.3	30.3±1.6	30.2±4.4
During lateral recumbency	Rectal temperature (ºC)	39.5±0.1*	39.1±0.1*	39.0±0.2*	39±0.1*
	Respiratory rate (breaths/min)	27.5±1.3*	25.2±1.3*	24.5±1.6*	25.1±1.9*
Post lateral recumbency	Rectal temperature (ºC)	38.0±0.1*	38.0±0.1*	37.5±0.2*	38.0±0.1*
	Respiratory rate (breaths/min)	30.1±1.3a	29.1±1.3a	29.2±1.6a	29.4±2.5a

A: Orph 5+xk 20,5 concomitantly. B: Orph 5+xk 20,5 After 15 min. C: Orph 5+xk 20,5 After 30 min. D: Orph 5+xk 20,5 After 60 min. Data expressed as Mean ±SE for six chicks per group. * Referred to significantly dissimilar from the values of Pre lateral recumbency. a Referred to significantly dissimilar from the values of During lateral recumbency.

The effect of orphenadrine at different doses on anesthesia with xylazine and ketamine

In this experiment, the goal was to determine the effect of different doses of orphenadrine 30 min after injection on anesthesia caused by half doses of xylazine and ketamine. Our results showed a significant decrease in the onset of anesthesia in groups of chicks treated with orphenadrine at doses of 2.5,5 and 10 mg/kg compared to the group treated with xylazine and ketamine alone. There was a significant dose-dependent increase in the period of anesthesia for

groups treated with orphenadrine compared to the group treated with xylazine and ketamine alone, and the recovery time of groups treated with orphenadrine showed a notable decline in comparison with the recovery time of group one with ketamine and xylazine alone (Table6). The chicks' temperature decreased when orphenadrine was administered at 2.5, 5, and 10 mg/kg with a mixture of xylazine and ketamine compared to those injected with xylazine and ketamine alone. It was also noted that the body temperature of the chicks decreased significantly when comparing the time of lateral recumbency and the time of recovery to the time before lateral recumbency. The breathing rate of anesthetized chicks in all groups was statistically reduced at lateral recumbency compared to the respiratory rate of chicks before lateral recumbency and at the time of recovery. When comparing the respiratory rates between the groups when lying down, we observed a significant decrease in the respiratory rate for the groups injected with orphenadrine with the xylazine mixture compared to the group injected with the xylazine and ketamine mixture alone **(**Tables 6-7).

Table 6: The effect of orphenadrine at different doses on anesthesia with xylazine and ketamine

Groups	Onset (sec)	Duration (min)	Recovery (min)
kx 2.5+10	132.57±11.58	56.43±4.80	180±0.15
Orph 2.5kx 2.5+10	56.57±3.10*	87.86±3.42*	76.8±0.14*
Orph 5 kx 2.5+10	60.00±4.75*	122.86±7.78*a	81±0.14*
Orph 10kx 2.5+10	55.71±2.02*	175.71±11.77*ab	85.2±0.17*

Ketamine and xylazine injections, and after half an hour, orphenadrine was injected. Data expressed as Mean ±SE for six chicks per group. * Referred to significantly dissimilar from the control values. a Referred to significantly dissimilar from the values of the second group. b Referred to significantly dissimilar from the values of the third group.

Table 7: The effect of orphenadrine at different doses on body temperature and breathing rate during anesthesia

Groups		A	B	C	D
Pre lateral recumbency	Rectal temperature (ºC)	40.3±0.1	39.5±0.1	39.6±0.2	39.0±0.2
	Respiratory rate (breaths/min)	31.4±1.3	30.5±1.5	33.3±1.2	30.9±2.5
During lateral recumbency	Rectal temperature (ºC)	39.2±0.1*	38.6±0.1 *	39.0±0.2*	38.5±0.1*
	Respiratory rate (breaths/min)	26.2±1.1*	23.2±1.3 *ω	23.5±1.8*ω	24.1±2.4* ω
Post lateral recumbency	Rectal temperature (ºC)	37.5± 0.1*a	37.0±0.2*a	37.0±0.2* [a]	36.0±0.1*a
	Respiratory rate (breaths/min)	31.0±1.4	30.1±1.1	30.2±1.6	29.7±2.8

A: Orph 5+xk 20,5 concomitantly. B: Orph 5+xk 20,5 After 15 min. C: Orph 5+xk 20,5 After 30 min. D: Orph 5+xk 20,5 After 60 min. Data expressed as Mean ±SE for six chicks per group. Data expressed as Mean ±SE for six chicks per group. * Referred to significantly dissimilar from the values of Pre lateral recumbency. a Referred to significantly dissimilar from the values of During lateral recumbency. ω Referred to significantly dissimilar from the values of group one.

Discussion

In the current study, we evaluated the simultaneous and preanesthetic administration of orphenadrine with xylazine and ketamine and the administration of different doses at the level of onset, period, and recovery from anesthesia. We also assessed some important physiological parameters of anesthesia, including body temperature and respiratory rate. Preanesthetic drugs are crucial in anesthesia management. They can affect events that occur before, during, and after surgery. As a result, they may also impact the development and intensity of perioperative stress responses.

Our findings reveal that the LD_{50} of orphenadrine was 121.10±8.49 mg/kg, IP, which harmonized with previous findings that referred to the LD_{50} of orphenadrine in mice was 150mg/kg orally. Another study demonstrated that the orphenadrine at 144mg/kg in anesthetized rats causes cardiac arrest (31-37). The newly hatched chicks treated with orphenadrine at 10 mg/kg IP showed shivering and moderate seizures long-lasting for about 25 min. Orphenadrine at 25 mg/kg IP produces strong clonic convulsions, after which the birds collapsed and remained quiet for about 20-35 min. The birds then partially recovered, with slight tremors and convulsions persisting for about 60-90 min (38).

The median effective analgesic dose of orphenadrine was 2.49±0.21 mg/kg IP in chicks, whereas the median effective analgesic dose in mice was 13.5mg/kg IP (39); this variation may be attributed to the species variation between poultry and rodents. We also demonstrated that the duplication of the median analgesic dose of orphenadrine once and twice produced a dose-dependent antinociceptive effect; orphenadrine exhibited a longer duration of sensory antagonism than motor antagonism. Our outcomes supported the experimental data by proving that orphenadrine had a substantial block of Na v1.7, Na v1.8, and Na v1.9 channels, which were critical for experiencing pain sensations (16). In

the present study, the substantial prolonged duration of anesthesia in chicks injected with orphenadrine at different times was similar to the earlier studies in mice (40,41). The decrease in body temperature and reduction of respiratory rate in chicks anesthetized with xylazine and ketamine and treated with orphenadrine is likely due to the anesthetic effect (42,43). It inhibits the respiratory center and reduces the body's vital activities, or it may be due to the action of orphenadrine to block target receptors (44,45). Here, we rule out that the reason for its lowering of temperature is its blocking of histamine receptor, which, when closed, reduces sweating and raises body temperature (46). Preanesthetic administration of orphenadrine at different doses for chicks that underwent anesthesia with a mixture of xylazine and ketamine produced a smooth induction and prolonged duration with short recovery; it should be noted that the decrease in body temperature for the groups continued from the lateral recumbency until the time of recovery, while the decrease in the respiratory rate that occurred at the time of loss of the body reflex was no longer present at the time of recovery. The prolongation of the duration of anesthesia in groups injected with orphenadrine and injected with a mixture of xylazine and ketamine may be attributed to its action in blocking the NMDA receptors, which play an essential role in suppressing the central nervous system, even though the blocking activity of orphenadrine is not as strong as the most specialized drugs in blocking this receptor, like ketamine, synthetic opioids, such as pethidine and phencyclidine (47-50). NMDA is an ionotropic receptor that facilitates the transfer of electrical signals between nerve cells in the central nervous system. The NMDA receptor must be open for electrical signals to flow, and glutamate and glycine must bind to the NMDA receptor (49).

Another hypothesis for the prolonged duration of anesthesia is the blockage of histamine receptors in the central nervous system (16). The nerve cells that produce histamine, histaminergic neurons, are located exclusively in the posterior hypothalamus and transport histamine to almost all brain areas. H1 antagonists or antihistamines, often prescribed to treat allergic disorders, sometimes lead to drowsiness and cognitive deficits (50). The mechanism of these central nervous system side effects is that antihistamines block the H1Rs in the brain. The histamine receptor in the brain is associated with Ach and glutamate, both of which have agonist activity on the histamine receptor and are considered excitatory neurotransmitters potentially responsible for arousal (51,52).

Conclusion

According to the study's findings, orphenadrine combined with xylazine and ketamine administered before anesthesia is a helpful and highly effective anesthetic protocol for ideal induction, sufficient muscle relaxation, satisfactory duration of anesthesia, and smooth recovery in chicks. Prolonged anesthetic induction and abbreviated recovery, along with specific side effects, such as hypothermia and respiratory depression. Neither the anesthetic nor the recovery period caused any chick death. If properly administered, a combination of orphenadrine, xylazine, and ketamine can be safely used during surgery. Further research is necessary to assess the effects of anesthesia efficacy in large animals.

Conflict of interest

Ahmed S. Naser and Yasser M. Albadrany declare no competing interests.

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تأثير ما قبل التخدير للاورفينادرين على التخدير المحدث بمزيج الزايلازين والكيتامين في نموذج أفراخ الدجاج

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الخلاصة

تلعب أدوية ما قبل التخدير دورا أساسيا في التخدير العام من أجل التحريض السلس والتعافي السلس، الأورفينادرين دواء ذو خصائص ديناميكية دوائية متعددة ولكنه يعتبر ضادا لمستقبلات الهيستامين من النوع ١. وكان الهدف الأساسي تحديد خصائص الأورفينادرين كمخدر في أفراخ الدجاج. تم استخدام أفراخ دجاج من كلا الجنسين. تم تحديد ملف أمان الأورفينادرين عن طريق إيجاد الجرعة المميتة الوسطية والجرعة المسكنة الوسطية باستخدام طريقة الصعود والنزول في الجرعة قمنا بإعطاء الأورفينادرين بجرعات مختلفة وأوقات مختلفة ثم قمنا بحساب بداية التخدير ومدته وتعافيه بواسطة الزيلازين والكيتامين، علاوة على ذلك تم حساب درجة حرارة الجسم ومعدل التنفس للأفراخ التي خضعت للتخدير العام. كانت الجرعة المميتة المتوسطة ١٢١,١٠٠±٨,٤٩ ملغم / كغم في الخلب وكانت الجرعة المسكنة المتوسطة ٢,٤٩±٠,٢١ ملغم / كغم في الخلب. أدى الأورفينادرين بجرع ٢,٥، ٥، و١٠ ملغم/كغم، تأثيرا مسكنا للألم يعتمد على الجرعة. أدى إعطاء الأورفينادرين بجرعة ٥ ملغم/كغم، في أوقات مختلفة إلى إطالة مدة تخدير الزيلازين والكيتامين إحصائيا بطريقة تعتمد على الوقت، كما انخفضت درجة حرارة الجسم ومعدل التنفس بشكل ملحوظ في حالة الاستلقاء الجانبي مقارنة بوقت قبل الاستلقاء الجانبي ووقت ما بعد العودة من الاستلقاء الجانبي. أدى الأورفينادرين بجرع ٥,١٠ و٢٠ ملغم/كغم، بعد ٣٠ دقيقة من الحقن، إلى انخفاض كبير في وقت بدء التخدير، وإطالة مدة التخدير وتقصير وقت التعافي مقارنة بالكيتامين والزيلازين فقط، كما أدى الأورفينادرين إلى انخفاض كبير في درجة حرارة الجسم. قبل الاستلقاء الجانبي بالمقارنة مع الزيلازين والكيتامين. انخفضت درجة حرارة الجسم ومعدل التنفس بشكل ملحوظ عند الاستلقاء الجانبي مقارنة بالاستلقاء الجانبي قبل وبعد. الأورفينادرين دواء آمن بسبب النطاق الواسع بين متوسط الجرعة المميتة ومتوسط جرعة المسكن. الأورفينادرين دواء جيد للتخدير. فهو يطيل مدة التخدير ويقصر فترة التعافي في نموذج الأفراخ. الأورفينادرين له خاصية خفض الحرارة لذلك يجب الانتباه عند استخدامه كمخدر.

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