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## **Anesthetic, Physiologic and Hematologic Effects of Three Pentobarbitone Drug Combinations in Rabbits**

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### **ABSTRACT**

This study investigated the anesthetic, physiologic and hematologic effects of atropine-pentobarbitone, atropine-xylazine-pentobarbitone and atropine-acepromazine-pentobarbitone drug combinations in rabbits. The duration of anesthesia was significantly ( $p < 0.05$ ) longer in the atropine-acepromazine-pentobarbitone anesthetized rabbits. All drug combinations induced severe respiratory depression greater than 45%. The percentage depression of heart rate in atropine-acepromazine-pentobarbitone group was significantly ( $p < 0.05$ ) lower than heart rate depression in atropine-pentobarbitone and atropine-xylazine-pentobarbitone groups. The red blood cell and packed cell volume of the rabbits in all the groups were significantly ( $p < 0.05$ ) lower than their baseline values during anesthesia. The white blood cell counts of atropine-pentobarbitone treated rabbits increased significantly ( $p < 0.05$ ) during anesthesia. This study showed that administration of the drug combinations caused severe respiratory depression, cardiovascular depression and decrease in the erythrocytes count. We concluded that pentobarbitone and its drug combinations are unsuitable for rabbit anesthesia.

**Keywords:** Pentobarbitone, intraperitoneal, respiratory depression, erythrocytes

### **INTRODUCTION**

Anesthesia of rabbits is challenging since it often leads to intra-operative and post-operative mortality (Kramer, 1998; Hedenqvist *et al.*, 2003). The high incidence of mortality during rabbit anesthesia has been attributed to the sensitivity of the rabbit's respiratory center to the depressant effects of anesthetics (Hobbs *et al.*, 1991; Borkowski and Karas, 1999).

Injectable anesthetics are popularly used in rabbits since they are easy to inject, inexpensive and relatively safe. These anesthetics can be given through the intravenous, intramuscular, intraperitoneal or subcutaneous routes. Currently, injectable agents such as propofol, alphaxalone-alphadolone and ketamine are used for anesthesia of this species (Difilipo *et al.*, 2004; Eze and Nweke, 2004). These agents when used alone or in combination with sedatives have been proved by various studies to produce adequate and safe anesthesia in rabbits (Hellebrekers *et al.*, 1997; Difilipo *et al.*, 2004; Eze and Nweke, 2004).

Pentobarbitone a short acting oxybarbiturate is still widely used in laboratory rodents and rabbits for experimental surgery. Sole use of this drug for anesthesia in this species has been associated with cardiopulmonary depression (Flecknell *et al.*, 1983; Peeters *et al.*, 1988). According to Branson (2001), concomitant use of atropine, xylazine and acepromazine with low dose

pentobarbitone for anesthesia might reduce these side effects of pentobarbitone (Branson, 2001). No study has evaluated the effect of the aforementioned drugs on the quality and safety of anesthesia induced by pentobarbitone. We studied the anesthetic, physiologic and hematologic effects of atropine-pentobarbitone, atropine-xylazine-pentobarbitone and atropine-acepromazine-pentobarbitone drug combinations in rabbits.

## **MATERIALS AND METHODS**

**Drugs:** The drugs use in this study were: Xylazine (Xylazin<sup>®</sup>, Kepro Ltd., Holland), atropine sulphate (Atropine<sup>®</sup>, Embassy pharmaceutical, Lagos), acepromazine (Calmivet<sup>®</sup>, Vetoquinol, France) and pentobarbitone Na (Pentobarb<sup>®</sup>, Kyron Laboratories, Benrose).

**Experimental animals:** Fifteen clinically healthy rabbits were used for the study. They weighed between 1.0-1.2 kg. Feed and water were provided free choice during the period of stabilization. They were randomly divided into three groups (n = 5).

**Anesthetic effects:** Group 1 rabbits were anesthetized using atropine (0.05 mg kg<sup>-1</sup>, i.m.) and pentobarbitone (15 mg kg<sup>-1</sup>, i.p.). Groups 2 rabbits were anesthetized using atropine (0.05 mg kg<sup>-1</sup>, i.m.), xylazine (5 mg kg<sup>-1</sup>, i.m.) and pentobarbitone (15 mg kg<sup>-1</sup>, i.p.) while anesthesia of group 3 rabbits was achieved using a combination of atropine (0.05 mg kg<sup>-1</sup>, i.m.), acepromazine (0.5 mg kg<sup>-1</sup>, i.m.) and pentobarbitone (15 mg kg<sup>-1</sup>, i.p.). All pre anesthetic medications were administered 10 min prior to pentobarbitone administration. After induction of anesthesia, the onset of anesthesia and duration of anesthesia were monitored as described by Eze and Nweke (2004).

**Physiologic variables:** The heart rate (Hr), respiratory rate (Rr) and temperature (Rt<sup>°</sup>) of rabbits were measured at 0 min before treatment and later at 20, 40, 60 and 80 during anesthesia. Percentage depression of the Rr and Hr were calculated.

**Hematology:** Blood samples were collected from the jugular vein of all rabbits into heparinized sample bottles. These samples were used to determine the baseline values of Packed Cell Volume (PCV), Red Blood Cell count (RBC) and White Blood Cell (WBC) counts as described by Simpson, (1990). Thirty minutes post induction of anesthesia, blood samples were collected from all rabbits for repeat hematology.

**Data analysis:** The anesthetic, physiologic and hematologic data obtained were summarized as Mean ± standard error. They were compared using one way analysis of variance. The LSD was used to separate variant means. Significant differences were considered at 5% probability levels.

## **RESULTS**

**Anaesthetic effects:** As shown in Table 1, the onset of sleep was significantly (p<0.05) faster in rabbits treated with atropine-acepromazine-pentobarbitone (A-A-P) drug combination. The duration of anesthesia was significantly (p<0.05) longer in the A-A-P anaesthetized rabbits (Table 1).

Table 1: Onset and duration of anesthesia in rabbits

Groups	Onset of anesthesia	Duration of anesthesia
1	13.2±8.1	77.0±18.1 <sup>a</sup>
2	13.0±3.2	80.2±17.0 <sup>a</sup>
3	9.2±6.9	151.0±6.5 <sup>b</sup>

Different letters indicate significant ( $p < 0.05$ ) difference between group means in a column. Group 1: Atropine-pentobarbitone, Group 2: Atropine-xylazine-pentobarbitone, Group 3: Atropine-acepromazine-pentobarbitone

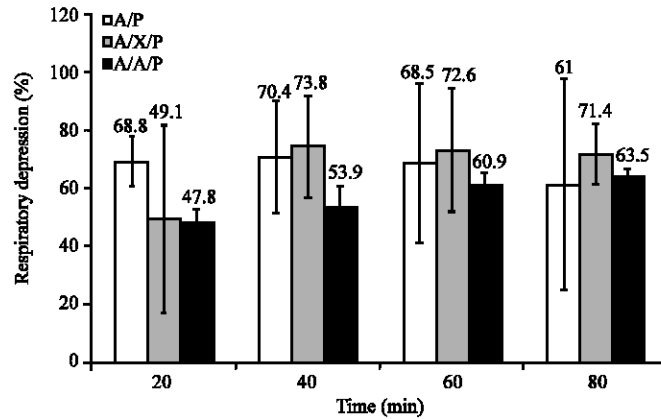


Fig. 1: Percentage respiratory depression in anaesthetized rabbits

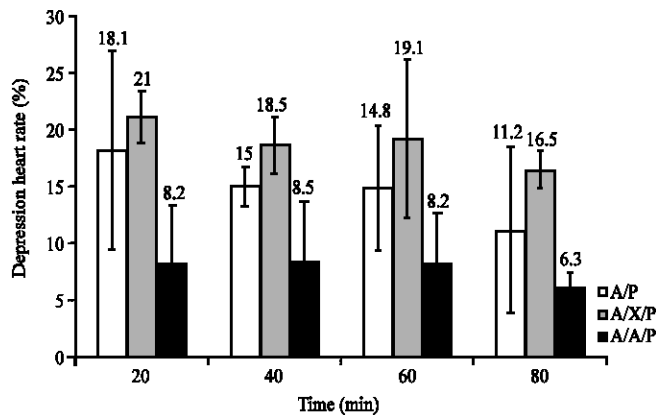


Fig. 2: Percentage depression of heart rate in anaesthetized rabbits

**Physiologic variables:** The percentage depression of the Rr and Hr are shown in Fig. 1 and 2, all drug combinations induced severe respiratory depression greater than 45% from 20-80 min post induction of anesthesia (Fig. 1). No significant ( $p > 0.05$ ) difference was observed in the respiratory effect of all three drug combinations throughout the study. The percentage depression of heart rate in A-A-P group was significantly ( $p < 0.05$ ) lower than those of the atropine-pentobarbitone (A-P) and atropine-xylazine-pentobarbitone (A-X-P) groups (Fig. 2). The percentage Hr depression in groups 1 and 3 were not significantly ( $p < 0.05$ ) different. No significant difference ( $p > 0.05$ ) was observed between the temperature of all three groups (Fig. 3).

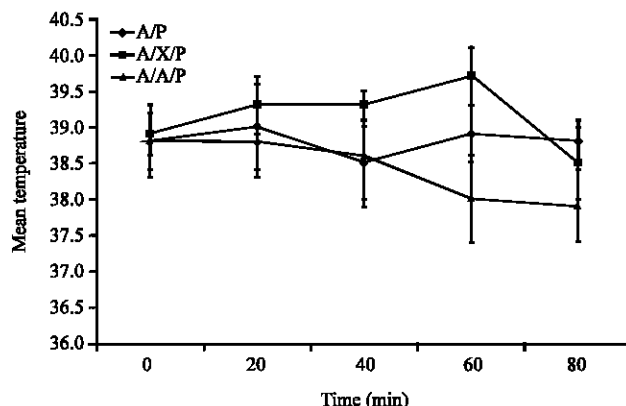


Fig. 3: Mean rectal temperature of anaesthetized rabbits

Table 2: Blood parameters of anesthetized rabbits

Parameters	Groups	Time	
		0 min	30 min
Packed cell volume (%)	1	37.5±3.4	33.2±2.6**
	2	37.2±1.9	33.0±0.7**
	3	38.0±1.5	32.6±5.8**
Red cell count (10 <sup>6</sup> µL <sup>-1</sup> )	1	7.2±0.4	5.9±0.9**
	2	6.9±0.5	5.8±0.3**
	3	6.7±0.7	4.9±1.7**
Total white cell count (10 <sup>3</sup> µL <sup>-1</sup> )	1	6.9±1.1	7.6±1.3**
	2	6.5±3.4	6.1±2.7 <sup>b</sup>
	3	6.8±3.4	6.3±0.9 <sup>b*</sup>

\*Indicates significant (p<0.05) difference from baseline value. Different letters indicates significant (p<0.05) difference between group means

**Hematologic variables:** The RBC and PCV of the rabbits in the three treatment groups were significantly (p<0.05) lower than their baseline values 30 min during anesthesia (Table 2). The WBC counts of the rabbits treated with A-P increased significantly (p<0.05) during anesthesia.

## DISCUSSION

The use of A-A-P drug combination significantly prolonged the duration of pentobarbitone anesthesia in rabbits. The reason for this finding is not known. We may suggest that the anesthetic effect observed in this group may be due to the action of acepromazine. Acepromazine maleate is known to have a rapid onset and long duration of activity up to four hours (Bishop, 2005).

The observed changes in the erythrocyte indices of rabbits are consistent with findings of previous researchers following administration of barbiturates (Graca and Garst, 1957; Elsa *et al.*, 2002), xylazine (Mohammed and Yelwa, 1993; Mohammed *et al.*, 2001; Gweba *et al.*, 2009) and acepromazine (Ballard *et al.*, 1982). We suggest that the reduction in PCV and RBC of rabbits in this study was induced by pentobarbitone, xylazine and acepromazine. Previous researchers have tried to proffer reason for the observed effect of these drugs on the haematocrit of animals studied. Graca and Garst, 1957 and Ballard *et al.* (1982) opined that the decrease in PCV and RBC after the injection of barbiturates and acepromazine may be due to their effect on the spleen. These

researchers are of the opinion that these drugs block receptor input to the spleen leading to its relaxation and subsequent pooling of blood in the spleen. This according to them reduces the amount of RBC in the systemic circulation.

The WBC of rabbits in A-P group increased significantly post treatment. Our finding is in line with that of Elsa *et al.* (2002). These researchers reported an increase in the WBC of rabbits after intra peritoneal injection of amylobarbitone sodium. The reasons for these findings have been given (Moore, 1984).

Pentobarbitone, xylazine and acepromazine are known to have depressant effects on the heart (Svendsen and Carter, 1985; Mohammed and Yelwa, 1993; Mohammed *et al.*, 2001; Busch *et al.*, 2006). It has been suggested that the use of atropine along with acepromazine and xylazine prior to general anesthesia prevents the vagal effect of both drugs (Branson, 2001). Therefore, the finding in the A-X-P group was not expected since atropine was used along side xylazine. The reason for this finding is not known. We may however, suggest that this was due to the synergistic interaction of pentobarbitone and xylazine.

Respiratory depression was observed in the experimental animals. Depression of respiration is however not unique to the use of pentobarbitone but is a common complication of anesthesia in rabbits (Hedenqvist *et al.*, 2003; Eze and Nweke, 2004). Comparing data from this study with those obtained in the previous studies suggests that more respiratory depression occurred after administration of the three pentobarbitone drug combinations. Respiratory depression has been reported in animals given pentobarbitone (Flecknell *et al.*, 1983; Peeters *et al.*, 1988), acepromazine (Popovic *et al.*, 1972) and xylazine (Mohammed and Yelwa, 1993; Mohammed *et al.*, 2001; Gweba *et al.*, 2010). According to Van Praag (2003) and Flecknell (1991) depression of respiration below 30 breaths/min or up to 40% leads to hypoxia, hypercapnea, acidosis and mortality. No mortality was recorded during this study, probably because the experimental rabbits were healthy and did not undergo surgery.

This study showed that administration of the three pentobarbitone drug combinations lead to severe respiratory depression, cardiovascular depression and decrease in the erythrocyte count. Considering the importance of ventilation, circulation and the erythrocytes in ensuring adequate tissue oxygenation during anesthesia, we conclude that the pentobarbitone and its drug combinations are unsuitable for rabbit anesthesia.

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