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Experimental Studies on General Anesthesia Following Blood Loss: Ketamine Hydrochloride and Sodium Pentobarbital Anesthesia in Bled Dogs

2. Effects of Ketamine Hydrochloride on Electrocardiograms and Blood Pressures in Bled Dogs

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Introduction

Ketamine hydrochloride is a rapid acting, non-barbiturate, non-narcotic dissociative agent which does not exert any toxic effects on the vital organs and has a broad margin of safety. Ketamine hydrochloride produces excellent analgesia rapidly without depression of circulation and has little effects on respiration. These qualities would be of value in emergency situations where hemorrhage is severe, and rapid action without depression is needed[20]. Corssen et al.[2] have recommended ketamine for short lasting or minor surgery in debilitated, poor risk patients. Also, a clinical impression of greater safety for the high risk patient was gained from ketamine hydrochloride[10], and ketamine hydrochloride (Ketanset) was found to be a simply applicative and not dangerous drug in sick cats[3]. A number of clinical observations of ketamine in dogs have been reported, [5~7,10~12,17,18] but few reports have been made on the effects of this drug after blood loss.

There are a few works on the effects of ketamine on electrocardiograms (ECG) in healthy dogs, [7,8,16,17] but the works which dealt with the effects of this drug on ECG after hemorrhage have not been done.

This experiment designed to investigate the effects of ketamine anesthesia after bleeding on electrocardiogram, electroencephalogram (EEG) and blood pressure.

Materials and Methods

Fourteen healthy, about one year-old mongrel dogs of both sexes, weighting about 10 kg were used in this study. The experimental dogs were divided into 2 groups, 7 dogs in each group: Group I (Ketamine hydrochloride) and Group II (Blood loss+Ketamine hydrochloride).

Blood volume of 2 percent of body weight was drawn from the jugular vein by means of sterile disposable syringe.

Ketamine hydrochloride (Ketalar 50, Parke Davis San Kyo Co., Ltd.) was administered intramuscularly at the rate of 30 mg/kg of body weight in both healthy and bled dogs.

Blood pressures were recorded from the canulated aorta (A.P.), pulmonary artery (P.A.P.) and right ventricle (R.V.P.), using Visigraph FR-201 (Sanei Instrument Co., Ltd.).

The standard limb lead II, the augmented limb lead aVR and the precordial leads V_3 and V_4 were taken for ECG and bipolar scalp leads, i.e. derivation between left frontal (LF) and right frontal (RF), derivation between left occipital (LO) and right occipital (RO) for EEG. The recordings were

Table 1. Changes in Interval and Amplitude of ECG Waves (Lead II) in Group I (Ketamine Hydrochloride)

		Before Administration	After Administration				
			5 min	20 min	40 min	90 min	24 h
Interval (s)							
R-R	Mean	0.907	0.357**	0.429**	0.376**	0.327**	0.911
	SD	0.195	0.031	0.053	0.067	0.071	0.104
P-Q	Mean	0.093	0.074*	0.075*	0.073*	0.069	0.095
	SD	0.011	0.013	0.011	0.014	0.009	0.014
QRS	Mean	0.062	0.055	0.056	0.060	0.063	0.060
	SD	0.007	0.023	0.009	0.008	0.009	0.009
Q-T	Mean	0.251	0.193**	0.212**	0.197**	0.185**	0.252
	SD	0.009	0.017	0.011	0.019	0.026	0.007
Amplitude(mV)							
P	Mean	0.058	0.128*	0.106*	0.120*	0.124*	0.068
	SD	0.040	0.058	0.046	0.040	0.051	0.041
R	Mean	0.652	0.634	0.708	0.744	0.717	0.850
	SD	0.155	0.183	0.198	0.201	0.188	0.181
T	Mean	0.070	0.058	0.052	0.050	0.052	0.090
	SD	0.018	0.040	0.045	0.043	0.044	0.049

Remarks; **: $p<0.01$, *$p<0.05$

performed using 6 channels polygraph with bioamplifier type (Sanei Instrument Co., Ltd.). The placement of the attaching of electrodes was determined from the anatomic landmarks. The interval and amplitude of ECG waves were analyzed statistically in lead II, using Student's "t_n test.

Observation was made before administration, 5 min, 20 min, 40 min, 90 min and 24hr after administration in Group I and before blood loss, 30 min after blood loss, 5 min, 20 min, 40 min, 90 min and 24 hr after administration in Group II.

Results

Ketamine Hydrochloride in Healthy Dogs (Group I): The remarkable changes in interval and amplitude of ECG waves (lead II) were found (Table 1). The interval of R-R, P-Q and Q-T showed a significant decrease. The preanesthetic value of 0.907 ± 0.195 sec in R-R interval fell to 0.357 ± 0.031 ($P<0.01$) 5 min after administration and to 0.327 ± 0.071 ($P<0.01$) 90 min later. The P-Q interval in healthy dogs was 0.093 ± 0.011 sec, but from 5 min after injection to 40 min the interval was 0.074 ± 0.013 sec to 0.073 ± 0.014 ($P<0.05$). At the stage of recovery, 90 min after injection a high significant decreased value of 0.069 ± 0.009 ($P<0.01$) was recorded. The changes of Q-T interval were similar to the trends of R-R interval. The preanesthetic Q-T interval of 0.251 ± 0.009 sec decreased significantly ($P<0.01$) to 0.193 ± 0.017, 0.212 ± 0.011, 0.197 ± 0.019 and 0.185 ± 0.026, at 5 min, 20 min, 40 min, and 90 min after injection of the anesthetics, respectively. Among wave amplitudes, the P wave showed a slight significant increase ($P<0.05$).

The changes of ECG and EEG following ketamine hydrochloride anesthesia are shown in Fig. 1. At the induction stage of ketamine the P wave showed a considerable increase. There were cases showing a decrease in amplitude of the R wave, while the S wave deepened in precordial leads V_3 and V_4. The T wave showed a decrease or an increase in

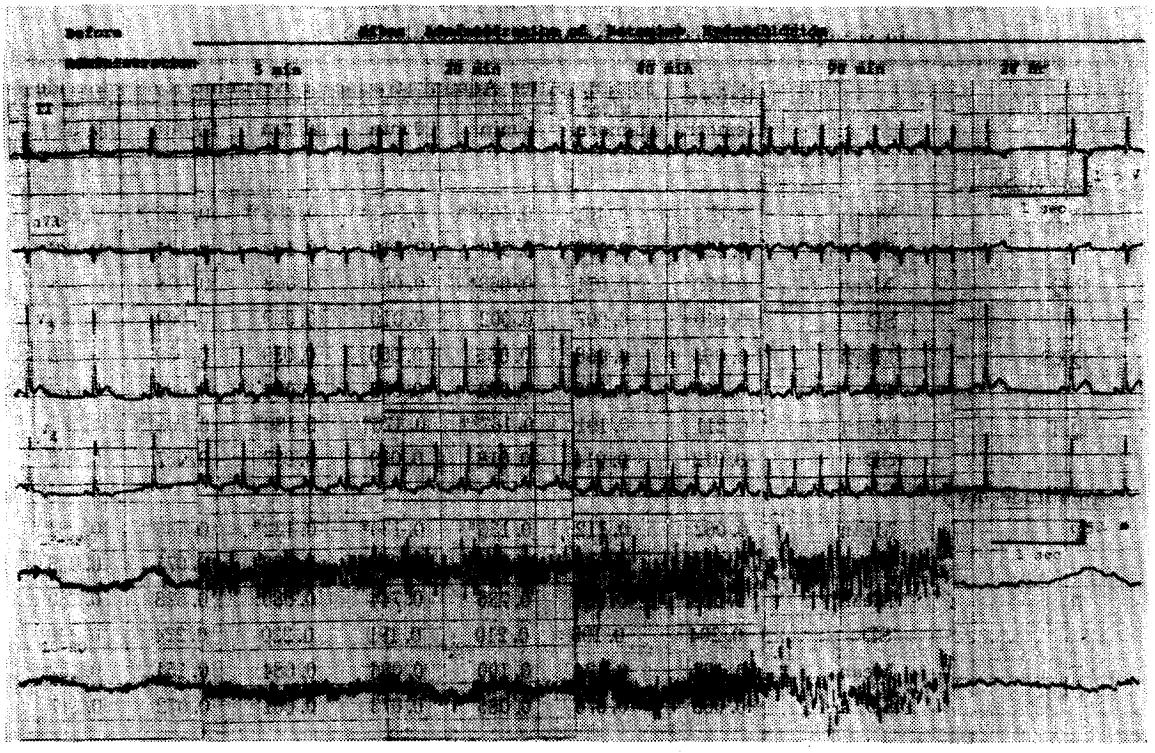

Fig. 1. Changes in ECG and EEG in group I.

the amplitude. There was a tendency of depression of the ST segment in leads II, V_3, V_4 and/or to rise up in lead aVR. The cardiac rhythm was sinus rhythm with tachycardia in all cases. During the maintenance of anesthesia the P wave revealed a sharp increased shape and the ascended P wave was more remarkable at the recovery stage. The amplitude of the R wave was not changed in leads II and aVR, but it was decreased in leads V_3 and V_4. The deepened S wave which occurred in the stage of induction continued also during anesthetic stage. A tendency to decrease in amplitude of T wave (leads V_3 and V_4) was found. Diphasic or two peak pattern in T wave was associated with the decrease of amplitude, while there were cases showing an increase in the amplitude of T wave in leads II and aVR. The depression of S-T segment which appeared in the induction stage was continued during anesthesia. In general, sinus rhythm was observed during anesthesia. Twenty four hours after injection ot ketamine, the P wave, QRS complex and S-T segment were all similar to the pattern before administration, and the T wave was almost like the preanesthesia in most cases.

An electroencephalographic pattern before anesthesia exhibited fast waves of 18 to 23 Hz with moderate voltage of 20 to 30μV. From the onset of anesthesia a multiple spike wave complex with high voltage was observed. The amplitude 20 min after administration revealed a tendecny to decrease more than that at the 5 minutes. The increase in amplitude started again 40 min after injection and the increase of amplitude was more apparent 90 min later. During ketamine anesthesia EEG pattern of high voltage and fast activity was noticed and was more predominent in frontal leads than in occipital leads. During ketamine anesthesia right ventricular pressure showed a gradual decrease, but no change in pulmonary arterial pressure was observed. A slight decrease in aortic pressure was acknowledged 20 min after giving ketamine (Fig.2).

Ketamine Hydrochloride in Bled Dogs (Group

Table 2. Changes in Interval and Amplitude of ECG Waves (Lead II) in Group II (Hemorrhage+Ketamine Hydrochloride)

		Before Hemorr.	30 min. after Hemorr.	After Admini stration of Ketamine Hydrochloride				
				5 min	20 min	40 min	90 min	24 h
Interval(S)								
R-R	Mean	0.676	0.461	0.306**	0.363**	0.388**	0.335**	0.587
	SD	0.129	0.106	0.070	0.110	0.132	0.124	0.129
P-Q	Mean	0.079	0.071	0.063*	0.069	0.068	0.068	0.078
	SD	0.010	0.007	0.002	0.010	0.009	0.009	0.009
QRS	Mean	0.063	0.058	0.056	0.059	0.059	0.059	0.062
	SD	0.007	0.008	0.009	0.005	0.004	0.004	0.007
Q-T	Mean	0.211	0.191	0.167**	0.175*	0.180*	0.169**	0.198
	SD	0.012	0.014	0.018	0.019	0.027	0.057	0.012
Amplitude(mV)								
P	Mean	0.062	0.112	0.136*	0.130*	0.122*	0.136*	0.084
	SD	0.026	0.055	0.054	0.056	0.052	0.071	0.045
R	Mean	0.688	0.684	0.736	0.744	0.680	0.628	0.760
	SD	0.204	0.195	0.210	0.191	0.220	0.234	0.246
T	Mean	0.102	0.124	0.100	0.086	0.084	0.151	0.132
	SD	0.068	0.076	0.086	0.073	0.061	0.072	0.117

Remarks; **: $p<0.01$, *: $p<0.05$

II): The changes in interval and amplitude of ECG waves in lead II after ketamine hydrochloride anesthesia in bled dogs are shown in Table 2. Ketamine hydrochloride affected greatly the R-R interval of the bled dogs. The prehemorrhagic R-R interval was 0.676±0.129 sec, but the R-R interval was 0.306±0.070, 0.363±0.110, 0.388±0.132 and 0.335±0.124, at 5 min, 20 min, 40 min and 90 min after injection of anesthetics, respectively. These all were high significant differences ($P<0.01$). The P-Q interval of 0.079±0.010 sec before hemorrhage fell to 0.063±0.002 ($P<0.05$) 5 min after administration, and thereafter the interval increased a little. QRS complex showed little change. The Q-T interval of 0.211±0.012 sec before hemorrhage decreased after injection of anesthetics in bled dogs. During anesthesia the Q-T interval showed a decrease at the level of 5 %, while the value was 0.167±0.018 sec ($P<0.01$) and 0.169±0.056 ($P<0.01$), at 5 min and 90 min after administration, respectively. The amplitude of P wave showed a significant increase ($P<0.05$), but amplitude of T and R wave was slightly affected by ketamine hydrochloride.

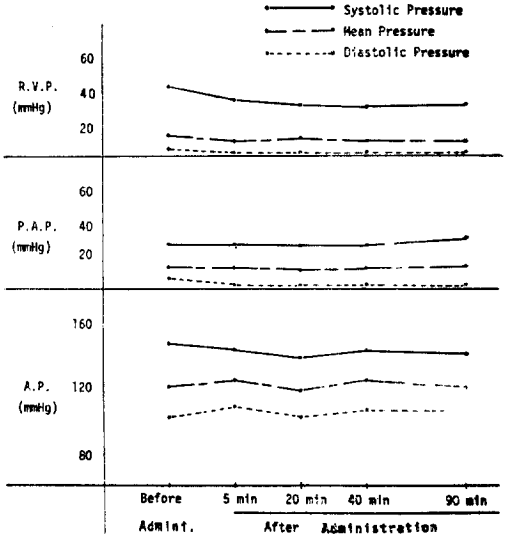

Fig. 2. Changes in blood pressures in group I.

Figure 3 shows the changes of ECG and EEG in

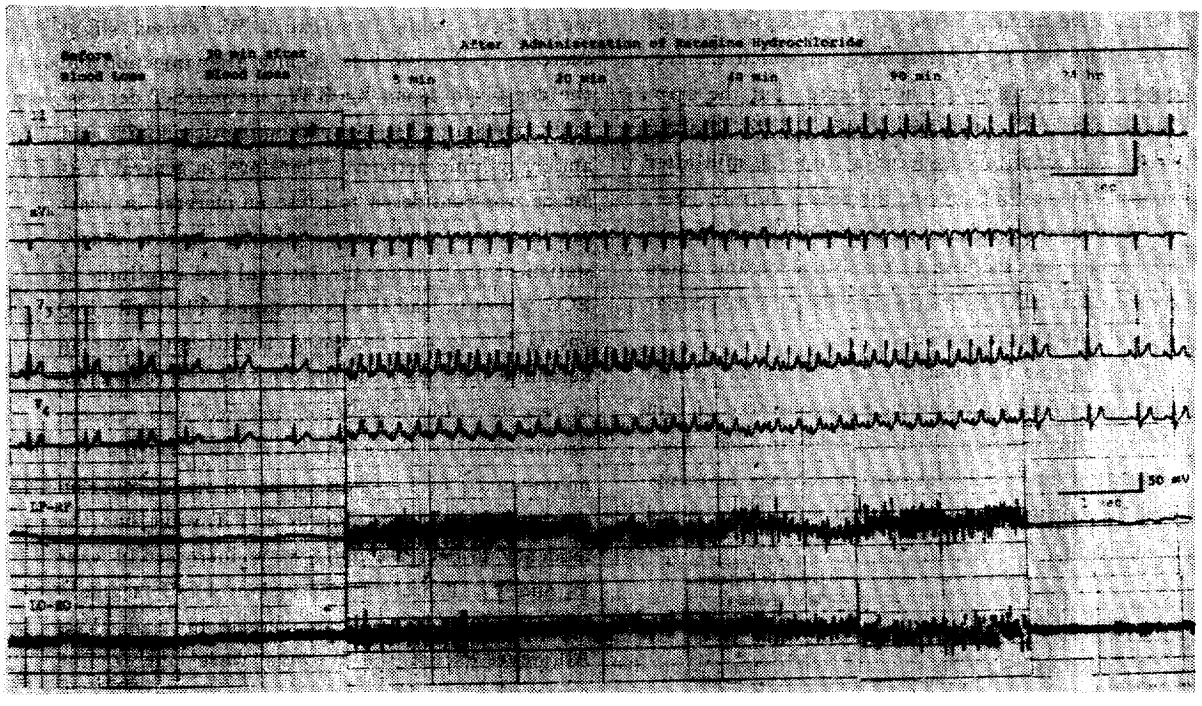

Fig. 3. Changes in ECG and EEG in group II.

the trial periods afteradministration of ketamine in bled dogs. Thirty minutes after hemorrhage the P wave was not greatly altered, but one dog showed a sharp P wave. The amplitude of the R wave decreased in leads V_3 and V_4, and was unchanged in leads II and aVR. In most of the cases amplitude of the T wave increased in leads II and aVR, and in V_3 and V_4 T wave was reduced and a case with two peaks in the T wave was observed. S-T segment depressed particularly in precordial leads. There was sinus rhythm or sinus arrhythmia. At the stage of induction of ketamine hydrochloride in bled dogs, the pattern of P wave was variable. The R wave did not change in leads II and aVR, but decreased in leads V_3 and V_4. In most of the cases the T wave revealed more sharp form than that of 30 min after hemorrhage and showed variable changes. With the induction of anesthesia a decreased tendency in S-T segment was found. Sinus rhythm in all cases was sustained. During the anesthesia, P wave in most of the cases was sharply increased. QRS complex was not different from the initial stage with the course of anesthesia in leads II and aVR. The R wave, which was altered 5 min after injection of anesthetics, began to return to preanesthetic wave from 40 min in precordial leads. There was an increase in amplitude of T wave 5 to 20 min after injection, and more at 40 to 90 minutes. The above change was more remarkable in leads V_3 and V_4 than in leads II and aVR. Five to 20 min after giving the anesthetics, S-T segment showed the deviation of a pot or bow like shape in leads II and aVR, and the S wave became deeper and deeper. The deepened S wave thereafter shortened a little, but at the recovery stage it was again deepeed. Heart rhythm also maintained sinus rhythm during anesthetic stage. Twenty-four hours after ketamine anesthesia in bled dogs P, QRS and T wave were similar to prehemorrhagic pattern in leads II and aVR. In leads V_3 and V_4 waves and QRS amplitude nearly restored to prehemorrhagic wave, but T wave in most cases was still different. S-T segment almost restored prior to the prehemorrhage in leads II and aVR, but in some cases it still remained different.

Changes in EEG following blood olss were rarely

found. Five minutes after giving ketamine in bled dogs there was multiple spiking in which the frequency of the wave was not altered, but the amplitude markedly increased compared to healthy dogs. The amplitude reduced a little 20 min after administration but again increased 40 min later. At 90 min after injection correspond to the recovery stage, an increase in amplitude became more conspicuous. EEG 24 hr after anesthesia were similar to prehemorrhagic period.

The decrease in blood pressure in aorta, pulmonary artery and right ventricle was observed 20 min after giving ketamine hydrochloride in bled dogs. Thereafter their value showed no change as compared to the blood pressure of 30 min after blood loss (Fig. 4).

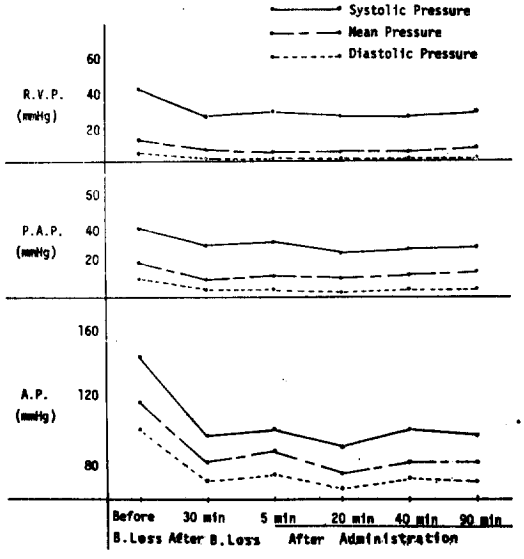

Fig. 4. Changes in blood pressures in group II.

Discussion

There are few works on the ECG changes after administration of ketamine. Tanabe and Nio[16] did not recognize arrhythmia but only tachycardia after ketamine anesthesia, Kosaka et al.[8] also found no change in ECG. Ishihara et al.[7] read a paper in which he showed no change in amplitude after injection of 20 mg/kg B.W., but showed lower amplitude in dogs given 50mg/kg B.W. There was no change on ECG after injection of ketamine of 20 mg/kg B.W., while 30 mg/kg B.W. caused slight decrease of R wave 5 to 10 min after injection and the dog given 40 mg/kg B.W. showed S-T depression[17]. Ketamine has sympathomimetic activity and antiarrhythmic activity. Therefore, in general, ketamine was considered to cause an increase in heart rate ketamine and non-arrythmia. In this study, statistical analysis on the interval and amplitude of ECG waves in lead II was attemped. The R-R, P-Q and Q-T interval decreased significantly during ketamine anesthesia and the decrease was remakable at recovery. The changes of interval were closely associated with those of heart rate. During the maintenance of anesthesia, the P wave revealed sharp ascended form. The R and T wave had the tendency to decrease and S wave increased in leads V_3 and V_4. There was depression of S-T segment in leads II, V_3, V_4 and an increase in lead aVR. All waves except the T wave were almost like preanesthesia in most of the cases 24 hr after injection of anesthetics.

In human being, the preanesthetic α wave became high voltage and a little slow wave 1 min after ketamine administration, while θ wave was observed 4 min after administration and afterwards the wave gradually returned to the preanesthetic pattern[14]. EEG in this study showed high voltage with the induction of anesthesia[13], a moderate to high voltage during the anesthesia, and again high voltage at the recovery stage. The response to ketamine seems to be more prominent infrontal leads than in occipital leads[2,9].

Ketamine hydrochloride caused an increase of blood pressure [2,11,17,20]. A slight decrease was observed in dogs injected over 30 mg/kg[17]. In this study the decrease in right ventricle and aortic pressure during ketamine anesthesia was accorded with Tanaka et al.[17]. Takahashi et al.[15] have reported that in spite of a significant fall in mean systemic arterial pressure, mean pulmonary arterial pressure tended to rise during ketamine anesthesia. Unchange in pulmonary arterial pressure might be associated with pulmonary vasculation resistance.

The S-T segment and T wave changes, a chara-

cteristic of myocardial hypoxaemia developed during the period of hemorrhage. Further deterioration developed in some animals on administrering halothane or ether under this condition[4]. The dogs anesthetized with 40 mg/kg B.W. of ketamine showed the depression of S-T segment[17]. In this work the R-R interval after ketamine anesthesia in bled dogs showed similar trends, and the P-Q and Q-T interval were relatively prolonged as compared to ketamine anesthesia group in healthy dogs. Taran and Szilagyi[19] postulated that a raised QTc was a sign of impairment of the functional integrity of the myocardium. According to the hypothesis the relative prolongation of P-Q and Q-T interval under ketamine anesthesia after hemorrhage might suggest direct action to heart. During anesthesia of ketamine in bled dogs P wave and QRS complex were similar to those of non-bled dogs anesthetized with ketamine. However, the T wave revealed more variable changes and the S wave became deeper. In some cases the changed T wave and S-T deviation of leads V_3 and V_4 were not returned to preanesthetic pattern 24 hr after giving the drug.

EEG changes during ketamine anesthesia in bled dogs were of similar pattern to those after anesthesia to healthy dogs. Changes in amplitude with time of anesthesia were not marked as those in normovolemia.

Virture et al.[20] have reported that administration of ketamine to healthy dogs was followed by a 24% increase of blood pressure, and ketamine rose only 4% in blood pressure of the hypovolemic dogs. Cyclopropane might offer a wider margin of safety for anesthesia in shock than ether or sodium evipal with respect to blood pressure and blood flow through essential vascular beds[1]. In this study, ketamine hydrochloride seems not aggravate blood pressure which was decreased 30 min after hemorrhage. However, the blood pressure decreased slightly 20 min after giving the drugs in bled dogs, and the return to prehemorrhagic pressure seemed somewhat to be prolonged. Non-significant change in blood pressure after ketamine anesthesia in bled dogs might be due to interaction between sympatomimetic action of ketamine and cathecholamine occurred after blood loss. In future the certain mechanism is to be investigated.

In conclusion, ketamine hydrochloride for general anesthsia after blood loss in dogs might offer a wide margin of safety with respect to electrocardiograms and bloodpressures.

Conclusion

During ketamine hydrochloride anesthesia in bled dogs, sinus tachycardia was sustained, but the particular irregularities in cardiac rhythm were not found. As compared to non-bled ketamine group the changes in ECG waves and S-T segment deviation were slightly apparent, and the P-Q and Q-T interval (lead II) were relatively prolonged after ketamine anesthesia in bled dogs.

EEG changes during ketamine anesthesia in bled dogs were of similar pattern to those of the healthy dogs anesthetized with ketamine, but the amplitude was lower than that of non-bled dogs.

Ketamine hydrochloride caused slightly the decrease in blood pressure 20 min after injection in bled dogs but did not aggravate.

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失血時의 全身麻醉에 關한 實驗的硏究 : 失血犬에 있어서 鹽酸케타민과 소디엄 펜토발비탈 麻醉

2. 失血犬에 있어서 鹽酸케타민이 心電圖 및 血壓에 미치는 影響

南 治 州

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초 록

失血犬에 있어서 鹽酸케타민 全身麻醉가 心電圖, 腦波 및 血壓에 미치는 影響을 調査하였던 바 그 成積은 다음과 같았다.

心電圖所見에 있어서는 洞性頻脈이 持續되었으나 心臟調律에는 特異한 變化가 나타나지 아니 하였다. 그러나 健康犬에 있어서 鹽酸케타민 麻醉群과 比較해서 波形의 變化와 S-T 分節의 偏位가 輕微하게 있었으며 P-Q와 Q-T 間隔은 相對的으로 多少 延長 되었다.

腦波는 健康犬에 있어서의 鹽酸케타민 麻醉群과 類似한 樣相을 보였으나, 그 振幅은 약간 減少되었다.

血壓은 麻醉後 약간 下落되었으나 곧 麻醉前으로 恢復되었으며, 惡化되지는 아니하였다.