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Study of xylazine ketamine and diazepam in two different combinations as general anesthesia in dog based on vital parameters, top up and duration of recovery

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Abstract
About 40 dogs of various breeds weighing between 8 and 21kg and age above one year brought at Animal Medical Centre, Chuchepati, Kathmandu were included as sample. The selections of dogs in two different groups were done on priority basis. Treatment one as xylazine ketamine combination on first 20 dogs and Treatment two i.e. xylazine ketamine diazepam was used as anesthesia in other 20 dogs. Respiratory rate and Heart rate were significantly higher in the xylazine–ketamine-diazepam group than xylazine-ketamine between 10 and 30 minutes and at 25 and 30 minute respectively. The difference in duration of recovery, top up volume, and surgery duration were non-significant between two treatments. The depressing cardiopulmonary effect on dogs was lesser in xylazine–ketamine-diazepam group than xylazine-ketamine. Thus, use of xylazine–ketamine-diazepam combination is preferred to xylazine-ketamine on cardiopulmonary compromised animal.

Keywords: Anesthesia, cardiopulmonary, surgery.

Introduction
Anesthesia plays immense role in veterinary field from minor handling of the animals to major operations. Inhalant anesthesia is popular for major surgeries and is considered safe but in the developing countries like Nepal use of inhalant anesthesia is rare. Total intravenous anesthesia is common in many veterinary hospitals and animal birth control campaigns in Nepal. Anesthetic drugs act by alternating behavior of receptors distributed to many regions of the body and then they act on multiple organs. If in case major organs like heart, liver and lungs have some abnormalities, these drugs have side effects leading to failure of the organs and then death. Death was reported in dog as being primarily of cardiovascular cause accounting for 34% and secondarily due to the respiratory failure contributing to 20% in UK [1]. Overall risks of anesthetic and sedation-related death in dogs were 0.17%. The risk was estimated to be 0.05% and 1.33% in healthy and sick dogs, respectively [1].
Ketamine, a dissociative anesthesia, is popular in veterinary field because of its ability to suppress chronic pain at sub anesthetic dose [2, 3]. The most common intraoperative complications reported were hypotension, bradycardia, desaturation, and cardiac arrhythmias in anaesthetized dogs with Ketamine [4]. Similarly, the postoperative period is the most common crucial time for dogs. Most postoperative deaths were reported within 3 hours of termination of the procedure. Potential complications that occur include regurgitation, aspiration, hypothermia, vomiting, pain, hyper salivation, neurologic excitement, dysphoria, and respiratory and cardiovascular depression [5].
The purpose of this study is to compare commonly used combinations ketamine-xylazine and Xylazine –ketamine –diazepam in Nepal on the basis of top up volume and vital parameters. This study compares and evaluates these two combinations and finds the suitable one to conduct major surgeries for each individual. This study was conducted with an intension to explore measures to improve the comfort and quality of life of companion animal; dogs. No research on comparison of these combinations of anesthesia till now has been updated in Nepal.

This study helps to prepare strategy to overcome the upcoming unfortunate risks that may arrive at any time when conducting major surgeries

Materials and Methods

Source of data

Purposive clinical sample size of 40 dogs, admitted in the Animal Medical Centre, Chuchepati for major surgeries were considered for this study using. The dogs brought for neutering were reported healthy on the basis of clinical examination. Adult dogs of age group between 1and 8 and weight 7-21 kg brought at the hospital for surgeries like neutering were selected.

Sampling method

Since the study was conducted in a private clinic it was almost impossible to apply scientific research model for sampling. The selection of dogs in two different groups was done on priority basis. The two treatments applied were; xylazine-ketamine-iazepam was used as anesthesia in first 20 dogs and xylazine-ketamine combination on last 20 dogs. 40 dogs were grouped into two treatments 1 and 2. Treatment 1 refers to xylazine ketamine combination and treatment 2 refers xylazine ketamine and diazepam combination. Each group contains 20 dogs.

Pre-anaesthetic Management

Pre-anesthetic evaluation was based upon clinical and physical examination to check health status of dog. Dogs within inclusion criteria were deprived of food for at least 12 hours and water for six hours. Weight of dog was taken before physical and clinical examination. Heart rate was measured by stethoscope, respiration rate per minute by excursion of thoracic muscles and then temperature was taken by digital thermometer. Packed Cell Volume was checked in those appearing anemic and pale mucous membrane. In group 2, dogs were sedated with xylazine at the dose of 1 mg/kg.

Induction of anesthesia

Induction of anesthesia was done by ketamine and diazepam at the rate1:1 intravenously in treatment 2 and Xylazine-ketamine at ratio 1: 2 in treatment 1 intravenously. Both combinations at the dose rate 1ml/ 10 kg body weight were injected. Ketamine at the dose rate 2.5 mg/ kg body weight, diazepam at the rate 0.25 mg/ kg body weight and xylazine at the dose rate 1 mg/ kg body weight were injected.

Post sedative preparation

Immediately after sedation clipper was used to clip the hair around the surgical site. Depending upon procedure, type of surgery, and possible blood loss warm 0.9% normal saline or lactated Ringer's solution was administered at the rate of 5-10 ml/kg/hour. Meloxicam at the rate 0.2 mg/ kg subcutaneously, and Ceftriaxaone at the rate 30 mg/kg were administered by slow intrfavenous infusion. Preparation of the site was done first by shaving and then scrubbing by savlon. The surgery room was prepared with heater to maintain temperature and in case of loadshedding warm water was used to dip the intravenous pipe line. The dog was then shifted to the surgery room. The site was sprayed with iodine and finally by spirit. The surgery was started, meanwhile every records were noted on the animal medical centre- anesthesia log.

Maintenance of Anesthesia

Maintenance of anesthesia was done by mixture of ketamine and diazepam at the ratio 2:1 in both group intravenously. Dose was 0.1 / kg body weight.

During surgery

Continuous monitoring of the patient, recording of heart rate and respiration rate at regular intervals of five minutes were done during surgery. The depth of anesthesia was assessed by parameters; pedal reflex, eye reflexes, jaw tone, heart rate, and respiration rate.

Post-surgery

After successful completion of surgery, recovery was recognized by vocalization, struggling, and presence of head righting reflex. But complete recovery was recorded when animal becomes able to stand for the first time. Enrofloxacin at dose rate of 10 mg/kg body weight was administered intramuscularly post-surgery.

Calculated anesthetic indices

- Surgery Duration: Time period from first incision to the closure of incision
- Recovery Duration: Time period between last top up to the first attempt of animal to stand in the cage
- Top up volume: Total amount of top up required maintaining depth of anesthesia throughout the entire period of surgery.
- Heart rate, respiration rate and temperature recorded before administration of anesthetic drugs
- Heart rate and respiration rate recorded after surgery at five minutes interval up to 30 minutes.
- Heart rate, respiration rate, and temperature during recovery and post-surgery were recorded.

Statistical analysis

Data thus collected was entered in MS-Excel 2007 and then copied to SPSS 20 version.

Average of respiration rate and heart rate; during surgery at five minute interval up to 30 minute, post-surgery, and during recovery were calculated. An independent T test was used to test the significance of difference of mean of heart rate, respiration rate, temperature at different time interval between treatment 1 and treatment 2. A t- test was again used to test the significance of difference of mean of top up, surgery duration, and recovery duration in between treatment 1 and 2. An unequal variance was assumed and P value was calculated at 95% of confidence interval.

Result

The result obtained was analyzed carefully using IBM SPSS. Figure no 1 shows average temperature before surgery, after surgery and during recovery in two treatments. Higher temperature was recorded in treatment 1 than treatment 2 before surgery and after surgery.

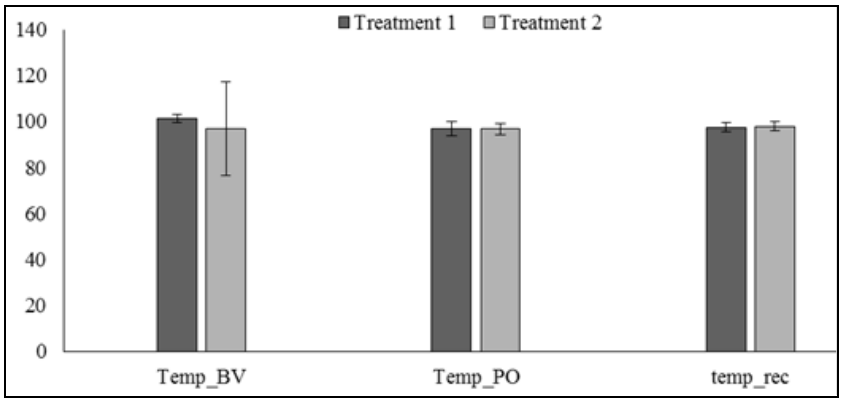

Fig 1: Graph shows average temperature level with standard deviation in both treatment.

Table no 1. Shows the non-significant difference in temperature recorded; before surgery, after surgery, and during recovery in between two treatment.

Table 1: Independent T test done to determine significance of difference of temperature between treatment 1 and treatment 2 before anesthesia, after surgery and during recovery.

Temperature	P value	Decision
Temp_BV	.361	Non-significant
Temp_PO	.616	Non-significant
Temp_recovery	.547	Non-significant

Table 2. Shows significant difference in respiration rate was seen between treatment one and treatment two when anlaysed using independent T- test. Respiration rate was found significantly higher in treatment two than in treatment one during 10, 15, 20, 25 and 30 minute after surgery at p value of 5% significance.

Table 2: Table showing independent T- test between respiration rate of Treatment 1 and 2

Respiration Variable	Treatment 1 (n=20)		Treatment 2 (n=25)		T-test
	Mean	Standard deviation	Mean	Standard deviation	
BT –R	35.35	11.54522	37.95	12.97558	Non-significant
5 min	18	6.867161	25.6	15.74601	Non-significant
10 min	19.1	7.580446	33.4	21.04982	Significant
15 min	20.95	8.964697	30.7	15.21806	Significant
20 min	19.75	8.390941	30.45	15.58162	Significant
25 min	20.45	7.394699	30.15	15.98774	Significant
30 min	19.72	8.358198	31.35	18.36838	Significant
Post-surgery	25.95	10.77754	32.25	14.082	Non-significant
Recovery	30.9	11.77821	32.25	14.082	Non-significant

Figure no 2. Indicates minimum respiration rate was found to be 18 ± 6.86 on an average in treatment one after five minute of surgery. Also maximum respiration rate was found to be 35.35±11.54 in treatment one before surgery. Minimum respiration rate 25.6±15.74 at five minutes after surgery and maximum was 37.95±25.0345 post surgery in xylazine-ketamine-diazepam group.

The figure no 2. Indicates respiration rate decreases just after five minutes after beginning of surgery and start increasing after 25 minutes of surgery in xylazine-ketamine-dizepam group.

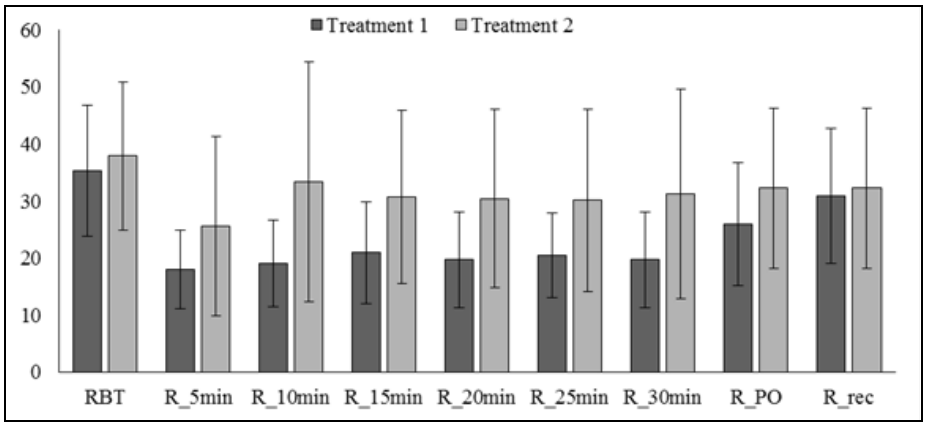

Fig 2: Graph shows average respiration level with standard deviation in both treatments.

Figure no 3. Indicates least heart rate was 84±22.655at post-surgery and maximum of 118.25 ± 25.63 before surgery in treatment one. The minimum heart rate 99.1 + 25. 0345 and maximum 123.35 + 22.19833 before surgery in treatment two. In both group minimum heart rate found to be after surgery and maximum before administration of anesthetic drugs. Figure no 3. Shows heart rate decreases all over the period of surgery and becomes minimum at post surgery.

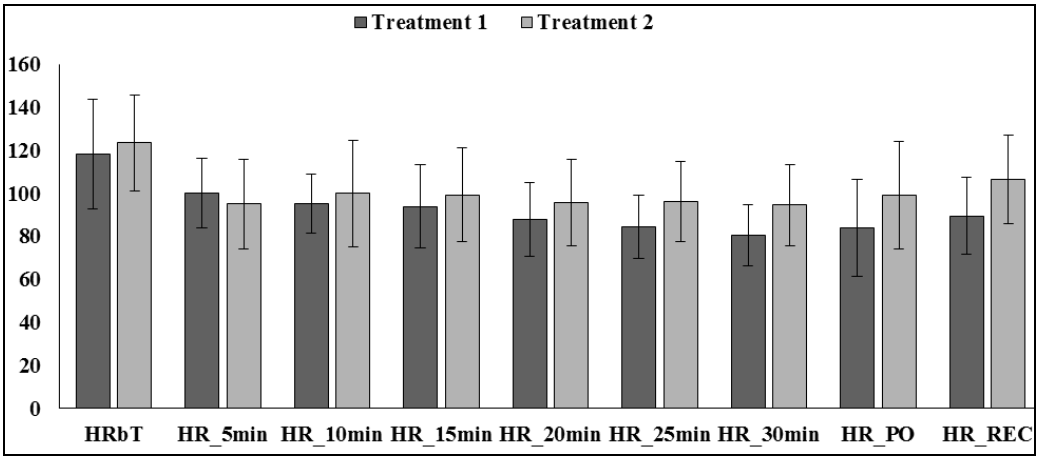

Fig 3: Graph shows average heartrate level with standard deviation in both treatment.

Xylazine and ketamine has greater depression on heart rate than xylazine-ketamine-diazepam at 25 and 30 minute after surgery which is statistically significant at 5% level of significance is indicated by Table no 3.

Table 3: Shows independent T- test between heart rate of Treatment 1 and 2

Heart rate Variable	Treatment 1 (n=20)		Treatment 2 (n=25)		T-test
	Mean	Standard deviation	Mean	Standard deviation	
BT –R	118.25	25.63	123.35	22.19833	Non-significant
5 min	100	16	94.95	20.944	Non-Significant
10 min	95.15	13.8	99.9	24.72991	Non-Significant
15 min	93.9	19.22	99.25	21.84123	Non-Significant
20 min	87.8	17.14	95.65	20.06903	Non-significant
25 min	84.25	14.73	96.15	18.57637	Significant
30 min	80.5	14.73226	94.45	18.91386	Significant
Post-surgery	84	22.655	99.1	25.0345	Non-significant
Recovery	84	18.07	106.55	20.49255	Non-significant

Table no. 4. Shows top up volume was greater in treatment two than in treatment one but this difference was not statistically significant at P value of 5% level of significance, Surgery duration and recovery duration were lesser in treatment two than in treatment one. This difference was statistically non-significant at 5% level of significance.

Table 4: Showing mean of top up volume, surgery duration and recovery duration of treatment 1 and 2.

Data	Treatment 1 (mean)	Standard deviation	Treatment 2 (mean)	Standard Deviation
Top up vol	2.185	1.4272	3.305	2.2116
Surgery Duration	41.7	28.384	36.75	13.8102
Recovery duration	52.05	22.5376	48.7	7.9346

Discussion

Ketamine is popular anaesthetic drug in Nepal, but has some unwanted effects due to which its alone use is prohibited during major surgery. In an attempt to counteract these effects and compensate the lacking properties, past studies have suggested the combination of ketamine with alpha 2 agonist; xylazine [6] and benzodiazepines; diazepam [7]. The depression effect on respiration rate by xylazine-ketamine group is similar to the past studies done in rabbit [8] and Budgerigar [9]. In contrast to this, significant increase in respiration rate at 15 minutes in the Diazepam- ketamine group was reported by Kul in his study [10]. This difference might be due to the use of xylazine as premedication drugs in this study. Xylazine-ketamine-diazepam group shows non-significant changes in respiration rate similar to the findings obtained by Hazra [11]. The significant difference in heart rate has been seen at 25 and 30 minute after surgery which supports the findings of Oguntoye [8]. And also significant depression in heart rate by xylazine- ketamine-diazepam supporting to these findings [11, 12]. Depression in physiological parameters in treatment one is due to the use of xylazine as premedication in this study which stimulates the parasympathetic nerves and inhibits sympathetic nervous system directly depressing the heart rate [13]. Decrease in respiration rate and heart rate in xylazine-ketamine combination is also supported by past study [14]. Decreasing pattern in heart rate from 10 to 60 minutes was observed in dog receiving diazepam and ketamine combination [15]. Difference in rectal temperature between two treatments was statistically non-significant, which is contrast to the result obtained in past study [9]. The past study had reported significant decrease in clocal temperature in first 15 minute in budgerigar after administration of Xylazine ketamine. This difference could be due to greater effect of xylazine ketamine in budgerigar than in dog. Hypothermia is classified as slight (38.49°C–36.50°C), moderate (36.49°C–34.00°C) and severe hypothermia (<34.00°C) [16]. Accordingly, on average patient only suffered from moderate hypothermia. The physiological parameters remained stable during anesthesia in treatment two and smooth recovery was obtained which did not demand the use of yohimbine. But in treatment one bradycardia occurred and atropine was administered through slow IV in six dogs at the dose rate of 0.01 mg /kg body weight. The anesthetic recovery was smooth and complete recovery period was 51.6 and 50.2 minutes on an average for treatment one and treatment two, respectively. The recovery period of dog under treatment XKD was between 20 to 35 minute according Hazra [11] which differs from this findings. This variation occurred because complete recovery or time the dog takes for stand was the priority of this research. The depth of anesthesia was adequate

under both treatments to carry out the operation which was similar to the findings reported by Hazra [11]. No major operative complication was encountered during surgery. Among 40 dogs there was no any report of death. So both combinations can be applied in conducting surgeries in healthy patient

Conclusion

Moderate hypothermia was observed during study so both combinations can be used in cold environment with minimum risk. Xylazine-ketamine-diazepam combination is found to have lesser effect on cardiopulmonary system than xylazine-ketamine combination in dog. As not a single death was encountered during the study period both the combinations are suitable for operating major surgeries but they differs only at the point that xylazine ketamine usage should be considered being more conscious in cardiac pulmonary compromised patient.

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