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CLINICAL STUDIES ON THE EFFECT OF GLYCOPYRROLATE, XYLAZINE, ACEPROMAZINE, DEXMEDETOMIDINE AND BUTORPHANOL IN DIFFERENT COMBINATIONS ON PROPOFOL- ISOFLURANE ANAESTHESIA IN DOGS

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ABSTRACT

The present study was conducted to compare the effect of pre-anaesthetic combinations such as glycopyrrolate-xylazine-butorphanol, glycopyrrolate-dexmedetomidine-butorphanol and glycopyrrolate-acepromazine-butorphanol on propofol induction and isoflurane maintenance general anaesthesia in 18 dogs of either sex presented to the Department of Veterinary Surgery & Radiology, College of Veterinary Science & Animal Husbandry, Kamdhenu University, Junagadh for varieties of surgeries. A combination of glycopyrrolate, xylazine and butorphanolwas given intramuscularly @ 0.01, 0.5 and 0.2 mg/kg b.wt glycopyrrolate, dexmedetomidine and Butorphanol @ 0.01, 0.005 and 0.2 mg/kg b.wt. and glycopyrrolate, acepromazine and butorphanol @ 0.01, 0.05 and 0.2 mg/kg b.wt. in three different groups as a pre-medication 15 minutes prior to induction with propofol administered intravenously "to effect'' and maintained with isoflurane in oxygen. Acepromazine group had good quality of sedation, abolished palpebral and pedal reflexes, response to intubation as compared to xylazine and dexmedetomidine groups. The mean dose propofol used for induction was non-significantly low in the acepromazine group followed by dexmedetomidine and xylazine groups. The mean vaporizer setting for maintenance, total quantity of isoflurane consumed was non-significantly low in dexmedetomidine group followed by acepromazine and xylazine groups. Among all the groups, xylazine and acepromazine had significantly lower in hemoglobin and PCV and non-significantly higher lymphocytes at recovery when compared to the base values. All the three groups had non-significantly low in TLC and high in neutrophils values at recovery time when compared to the base values. The heart rate showed non-significant reduction in xylazine group, non-significant higher in acepromazine group following pre-medication. During the maintenance period, heart rates remained within clinically normal range which could be due to less isoflurane required. The respiratory rate showed non-significant reduction following pre-medication and increased non-significantly during induction and maintenance in all the three groups. The rectal temperature showed non-significant decrease throughout the period when compared to the base values attributed to the hypothermic effects of general anaesthesia. The MAP remained non-significantly higher during the maintenance period in all the three groups compared to the base values and decreased non-significantly at recovery which could be due to hypertensive effects of general anaesthesia. The SpO_2 values showed non-significant increase following pre-medication and non-significant reduction towards the base values following recovery in all the three groups. The ECG did not any abnormality except for slight increase in QRS duration and T wave amplitude in xylazine group. The serum biochemical parameters like serum creatinine, BUN, AST and ALT remained within normal range, whereas serum glucose increased significantly in dexmedetomidine and acepromazine groups and non-significantly in xylazine group. The acepromazine group showed better sparring effect in dogs induced with propofol, whereas dexmedetomidine showed better sparing effect in dogs maintained with isoflurane. The recovery time was non-significantly lowered in dexmedetomidine group followed by acepromazine and xylazine groups which could be due to dexmedetomidine produced smooth and fast recovery compared to xylazine but complete recovery was faster in acepromazine group compared to the other two groups. The complete recovery time was non-significantly lowered in acepromazine group followed by dexmedetomidine and xylazine groups. The recovery was smooth, fast and uneventful without any complication during observation periods in all the groups. Among all the three groups, significant difference at various observation periods in any parameters was not observed. Hence, it is concluded that the glycopyrrolate-dexmedetomidine-butorphanol with propofol induction and isoflurane maintenance was better followed by glycopyrrolate-acepromazine-butorphanol and glycopyrrolate-xylazine-butorphanol anaesthetic protocol for different orthopedic and soft tissue surgeries in dogs.

KEYWORD: Dogs, Isoflurane, Preanaesthetics, Propofol.

INTRODUCTION

Anaesthesia is an integral part of surgery and a successful surgery can be performed only with a safe anaesthesia. Veterinary anaesthesia is still in a growing stage in which the surgeon itself should play the role of an anaesthetist when compared to human anaesthesia. Unlike humans our patients are more fractious and we need to use general anaesthesia for most of our surgical and diagnostic procedures. Veterinarians are fortunate in a respect that now older and less practicable anaesthetics have been replaced by compounds those are very effective and safe when used properly. No single anaesthetic agent can produce all these effects, hence in practice a combination of drugs is used to produce surgical anaesthesia, each having its own mode of action. Orthopedic surgery is associated with considerable tissue manipulation and induces severe peri and post-operative pain. Balanced anaesthesia in soft tissue surgery and orthopaedic procedures optimize outcome and minimize the risk and the cost of anaesthetic drugs used (Hall *et al*., 2001).

The inhalation agents are widely used in veterinary medicine and the main advantages are their elimination independent of the hepatic and renal systems, reduced biotransformation, in addition to low rates of morbidity and mortality when compared to other anaesthetic drugs. However, inhalation anaesthesia also has some disadvantages, including need of expensive and bulky apparatus and the danger of chronic exposure of operating room personal to low concentration of volatile anaesthetic agents. In spite of all these shortcomings, inhalation anaesthetics offer comparative safety as they provide better control over the depth of anaesthesia and facilitate early recovery (Tranquilli *et al*., 2007).

Pre medication plays an important part of any balanced anaesthesia protocols which helps in preparing the patient for surgery, enhances intraoperative cardiovascular stability, provides perioperative analgesia and aids in smooth induction and recovery from anaesthesia. It also reduces the dose of induction and maintenance anaesthetic drugs with expected reduction in adverse effects. In order to optimize the advantages afforded by premedication, it is important to select the premedicants based on the need of an individual patient, rather than using a single 'blanket' protocol. Drugs those have analgesic, sedative, muscle relaxant and anticholinergic properties are selected in veterinary pre medication protocols. It is an essential component of balanced anaesthesia as it facilitates restraining of animal for smooth induction, to increase the duration of surgical anaesthesia and to help in smooth recovery from anaesthesia (Hall *et al*., 2001).

Glycopyrrolate is a synthetic quaternary ammonium compound, anticholinergic with no central effects. It has a powerful and prolonged antisialagogue activity and is about five times as potent as atropine. Glycopyrrolate blocks peripheral muscarinic receptors, thus inhibiting cholinergic transmission (Hall *et al*., 2001).

Acepromazine is a potent phenothiazine derivative with anti-dopaminergic property that produces tranquilization or sedation and muscle relaxation and decrease spontaneous activity. Preanaesthetic administration decreases the amount of general anaesthetic dose. It has antiemetic, anticonvulsant, antiarrhythmic and antispasmodic properties (Thurmon *et al*., 1996; Gross, 2001). It is used in combination with some opioids in neuroleptanalgesia as it lacks analgesic properties. The drug has marked sedative properties. Other central effects of acepromazine include hypothermia and a moderate anti-emetic effect. It is also said to reduce the threshold at which epileptiform seizures occur (Hall *et al*., 2001).

Xylazine is a typical α_2 adrenoceptor agonist and exerts its effects accordingly. Sedative doses of xylazine decrease heart rate and cardiac output significantly in dogs, while blood pressure and peripheral vascular resistance initially (Kinjavdekar *et al* 2013).

Dexmedetomidine, an α_2 adrenergic agonist and the active optical enantiomer isolated from the racemic compound medetomidine. In dogs and cats, dexmedetomidine produces dose dependent levels of sedation and the intensity of these effects is similar to that produced by twice the dose of Medetomidine. As with other alpha 2 adrenergic receptor agonists, higher doses of dexmedetomidine (20 mcg/kg) may induce profound hypnosis, substantially reducing injectable and inhalant anaesthetic requirements for producing anaesthesia (Kuusela *et al*., 2001).

Opioids are the most commonly used analgesics because they produce excellent intra and post operative analgesia without loss of consciousness. It has also been reported that opioids reduce the MAC (Minimal Alveolar Concentration) of inhalant anaesthetics (Muir *et al*., 2001; Valverde *et al*., 2003).

Butorphanol a synthetic opioid is a partial agonist at μ and an agonist at kappa opioid receptors. Opioids are traditionally included in balanced anaesthesia protocols for their analgesic effects, but they also have sedative effects (Lemke, 2007). Butorphanol is used in cats, dogs for analgesia and sedative combinations with α 2 adrenoceptor agonists (Marini *et al.*, 1992).

Propofol is an intravenous anaesthetic agent unrelated to barbiturates, eugenols, or steroid anaesthetic agents. The active ingredient 2, 6 diisopropylphenol, exists as oil at room temperature. It is rapidly acting agent producing anaesthesia of short duration without side-effects. Inductions are smooth and excitement free. Recoveries are very smooth and rapid. Rapidity of recovery is due to propofol's rapid metabolism (Cullen and Reynoldson, 1993, Ummenhofer *et al*. (1998)).

Inhalant anaesthetics allow precise control of anaesthetic drug concentration at the central nervous system and quick onset and rapid recovery. It also produces unconsciousness, some degree of muscle relaxation but not adequate analgesia. It is reported that procedures carried out under inhalant anaesthetics alone may produce hyperalgesia during the post-operative period because of central sensitization of the central nervous system caused by the surgical trauma. Isoflurane is the most commonly used volatile anaesthetic because it has low solubility index and associated with quick onset of anaesthesia and faster recovery. It depresses cardiopulmonary system in a dose dependent manner but is less arrhythmogenic (Ranpariya *et al*, 2013 and Singh et al 2013).

General anaesthesia with proper combination of best choice preanesthetics, intravenous and inhaled agents allows adequate surgical access to the operative site. It reduces intraoperative patient awareness, allows proper muscle relaxation for longer periods of time. It facilitates complete control of the airway, breathing and circulation. It could be used in such patients those were sensitive to local anaesthetics, could be administered without moving the patient from supine position. It could be adapted easily to procedures of unpredictable duration or extent of surgical procedure as well as it could be administered rapidly and is reversible. Different anaesthetics agents will be very much helpful in future drug of choice for all type of patients which includes elective surgery, high risk patient's surgery, emergency surgery and cosmetic surgeries. It can reduces anaesthetics morbidity and mortality with non-stressful conditions, physiological changes that occur in body composition, the brain, kidney, heart, liver, and lungs produce no or only minimal functional impairment. The present study was planned with the following objectives.

OBJECTIVES

To study the preanaesthetics and clinico-physiological effects of glycopyrrolate-xylazine-butorphanol, glycopyrrolate-dexmedetomidine-butorphanol and glycopyrrolate-acepromazine-butorphanol combinations in clinical cases of dogs. To evaluate the clinico-physiological, haemodynamic and haemato-biochemical effects of these pre-anaesthetic combinations on propofol-isoflurane anaesthesia in clinical cases of dogs. To select the best preanaesthetic combination for propofol-isoflurane anaesthesia in clinical cases of dogs.

MATERIALS AND METHODS

The present clinical study was carried out on eighteen client-owned mixed breed dogs of either sex at the Department of Veterinary Surgery and Radiology, College of Veterinary Science and Animal Husbandry, Junagadh Agricultural University, Junagadh during the year 2016 to 2017. All eighteen dogs selected for present study were treated for variety of major surgeries like elective sterilizations, orthopaedic surgeries, tumour removal, cataract surgeries etc. They were randomly divided into three groups I, II, and III consisting of six dogs in each group. All the dogs were fasted 12 hours and water was withheld for 6 hours prior to surgery. All the surgeries were conducted in a temperature controlled environment with the operation theatre temperature maintained at 20º C. Pre-anaesthetic evaluation was performed by observing the general health status and physical examination. The clinical status of the dogs was assessed by recording Heart Rate, (HR) Respiratory Rate (RR), Rectal Temperature (RT), Mucous Membrane (MM) color, Capillary Refill Time (CRT) and by conducting Haemodynamic and Haematological studies and those animals which are unfit was excluded from the study. The animals in group I were premedicated with a combination of glycopyrrolate (0.01 mg/kg), xylazine (0.5 mg/kg) butorphanol (0.2 mg/kg). This drug mixture was taken in a single syringe and administered IM 15 min. prior to induction. The animals in group II were premedicated with a combination of glycopyrrolate (0.01 mg/kg), dexmedetomidine (0.005 mg/kg) and butorphanol (0.2 mg/kg). This drug mixture was taken in a single syringe and administered intramuscularly 15 min. prior to induction. The animals in group III were premedicated with a combination of glycopyrrolate (0.01 mg/kg), acepromazine (0.05 mg/kg) and butorphanol (0.2 mg/kg). This drug mixture was taken in a single syringe and administered IM 15 min. prior to induction. All three group animals were administered propofol for induction intravenously "to effect'' and maintained with isoflurane in oxygen.

RESULTS

Balanced anaesthesia in orthopedics and soft tissue surgeries used to optimize outcome and minimize the risk and cost of anaesthetic drugs. Hence, present study was undertaken to evaluate the clinicophysiological, haemodynamics and haemato-biochemical effects of glycopyrrolate-xylazine-butorphanol, glycopyrrolate-dexmedetomidine-butorphanol, and glycopyrrolate-acepromazine-butorphanol combination on propofol induction and isoflurane maintenance anaesthesia in clinical cases of dogs. Total eighteen dogs of either sex were used selected and divided into three groups as a Group I, Group II and Group III of six dogs in each group. All the dogs were operated for different surgeries like Intramedullary pinning, cross pinning, bone plating, amputation, tumour excision, ovariohysterectomy etc. The selected dogs under study weighed an average of 20.44 ± 2.22 kg (Mean ± SE) with maximum weight 36 kg whereas the lowest weight recorded was 7 kg from different breeds of canines. The average range of age was 70.11 ± 11.45 months (Mean ± SE) with the higher limit of 156 months (13 years) and lower up to 4 months was recorded. None of the animals of all the three groups showed any complication during premedication. Among all the three groups none of the animals showed vomiting after premedication. Glycopyrrolate decreased the incidence and severity of bradyarrhythmias in dogs and butorphanol maintained the normal heart rate without any complications. All the animals of three groups had

no sedation effect at base (0) time but slight to profound sedation shown at 10 and 15 min. interval after premedication and profound sedation was noticed after 15 min.

In the Group I at 10 min. interval 2 dogs (33.33 %) of the animals had no, slight and moderate sedation followed by at 15 min. 1 dog (16.66 %) had no sedation, 5 dogs (83.33 %) showed moderate sedation. In the Group II at 10 min. interval 5 dogs (83.33 %) showed slight sedation and 1 dog (16.66 %) showed moderate sedation followed by at 15 min. interval 1 dog (16.66 %) showed slight sedation and 5 dogs (83.33 %) showed moderate sedation whereas in the Group III at 10 min. interval 6 dogs (100 %) showed moderate sedation followed by at 15 min. 4 dogs. (66.66 %) showed moderate sedation and 2 dogs (33.33 %) showed profound sedation. In present study observed that moderate sedation prior to induction of anaesthesia made easy handling and surgical preparation of the animals.

In all the three groups combination pre-medications produced moderate and deep sedation with excellent analgesia and muscle relaxation quite enough to perform intubation after propofol induction. During present study group III in which glycopyrrolate -acepromazine-butorphanol combination produced profound sedation in 6 dogs (100 %) after 15 min. Relaxation of the jaw measured as per muscle relaxation, was scored by observing the resistance to opening of the jaw while pulling apart the lower and upper jaws. In the present study all the animals in the three different groups had not relaxation of jaw at base (0) time but jaw tone was significantly abolished at 10 and 15 min. after premedication and completely abolished in all three groups after 15 min.

In the Group I at 10 min. interval 2 dogs (33.33 %) not allow to open the jaw and 4 dogs (66.66 %) showed resistance to open jaw followed by at 15 min. interval 2 dogs (33.33 %) showed resistance to open jaw 4 dogs (66.66 %) showed less resistance to open the jaw. In the Group II at 10 min. interval 3 dogs (50.00 %) showed resistance to open the jaw, while 3 dogs (50.00 %) showed less resistance to whereas in the Group III at 10 min. interval 2 dogs (33.33 %) showed resistance to open jaw and 4 dogs (66.66 %) showed less resistance to open jaw but at 15 min. interval 5 dogs (83.33%) showed less resistance to open jaw and 1 dog (16.66 %) showed no resistance. In the present study sedation prior to induction of general anaesthesia made the easy handling and intubation of the animals.

All the animals in the three different groups showed intact and strong palpebral reflex at base time (0) but palpebral reflex was significantly decreased at 10 and 15 min. interval after premedication and completely abolished after 15 min. after propofol induction and isoflurane maintenance. In the Group I at 10 min. interval 2 dogs (33.33 %) showed intact and strong palpebral reflex while 4 dogs (66.66 %) showed intact but weak reflex followed by at 15 min. interval 1 dogs (16.66 %) showed intact and 5 dogs (83.33 %) showed very weak reflex. In the Group II at 10 min. interval 1 dog (16.66 %) showed intact reflex, 4 dogs (66.66 %) showed intact but weak and 1 dog (16.66 %) showed very weak reflex. After 15 min. interval 1 dog (16.66 %) showed intact but weak and 5 dogs (83.33 %) showed very weak palpebral reflex. Whereas in the Group III at 10 min. 2 dogs (33.33 %) showed intact but weak, and 4 dogs (66.66 %) showed very weak and at 15 min. interval all six dogs (100 %) showed very weak palpebral reflexes. In the present study all the animals in three different groups showed intact and strong pedal reflex at base (0) time interval but reflex was significantly abolished at 10 and 15 min. interval after premedication and completely abolished after 15 min. interval. In the Group I at 10 min. interval 1 dog (16.66 %) showed intact and strong palpebral reflex and 5 dogs (83.33 %) showed intact but weak reflex. After 15 min. interval 1 dog (16.66 %) showed intact and strong reflex 5 dogs (83.33 %) showed intact but very light reflex. In the Group II at 10 min. interval 4 dogs (66.66 %) showed intact but weak reflex and 2 dogs (33.33 %) showed intact but very light reflex. After 15 min. intervals 6 dogs (100 %) showed intact but very light reflex whereas in the Group III at 10 min. intervals 3 dogs (50 %) showed intact but weak reflex and 3 dogs (50 %) showed intact but very light reflex. After 15 min. intervals 6 dogs (100 %) showed intact but very light pedal reflex.

In present study all the animals in the three different groups not permitted entry of endotracheal tube at base (0) time but response was significantly abolished at 10 and 15 min. interval after premedication and completely abolished after 15 min. propofol induction. In the Group I at 10 min. interval 2 dogs (33.33 %) not permitted endotracheal tube and 4 dogs (66.66 %) allowed. At 15 min. intervals 1 dog (16.66 %) not permitted endotracheal tube, 3 dogs (50 %) allowed endotracheal tube but chewed and 2 dogs (33.33 %) showed difficult endotracheal intubation with coughing symptoms. In the Group II at 10 min. intervals 4 dogs (66.66 %) allowed endotracheal tube but chewed and 2 dogs (33.33 %) showed difficult endotracheal intubation with coughing. After 15 min. interval 6 dogs (100 %) permitted endotracheal intubation with coughing whereas in the Group III at 10 min. interval 2 dogs (33.33 %) allowed endotracheal intubation but chewed and 4 dogs (66.66 %) found difficulty during endotracheal intubation mainly due to coughing. At 15 min. interval 6 dogs (100 %) found difficulty during endotracheal intubation with coughing.

Intravenous catheterization of the cephalic vein was successfully undertaken on all the animals of the three different groups prior to induction of anaesthesia under the effect of pre-anaesthesia without any resistance shown from all 18 dogs. Eighteen dogs from three different groups were induced with propofol

administered slowly I/V 15 min. after administration of the pre-anaesthetics. None of the complications were observed in all three different groups during induction of anaesthesia and none of the animals showed any signs of convulsions or apnea after induction of anaesthesia with propofol. Mean effective dose of propofol used for induction in the Group I, Group II and Group III was 3.43 ± 0.24, 3.00 ± 0.12 and 2.81 ± 0.09 mg/kg b.wt. respectively. The induction doses of propofol used for the Group II and Group III were non-significantly lowers than Group I. There were no significant differences among the groups for the requirement of induction agent. The Group III showed minimum dose followed by Group-II and Group-I. In present study propofol administered slowly I/V till it sluggish all reflexes and complete jaw relaxation.

In present study all the dogs in three different groups were intubated successfully after propofol induction with the help of a laryngoscope. In the present study all the dogs in three different groups were immediately shifted to the surgery table and connected to the anaesthetic machine after induction and intubation. None of the animals showed breath holding or any type of complication during the initial times of inhalant anaesthesia and the vaporizer settings were changed according to maintain the surgical plane of anaesthesia.

Mean values of body temperature were non- significant between the groups at different time before premedication and values recorded was 103.15 ± 0.35° F, 101.88 ± 0.30° F and 102.81 ± 0.52° F in the Group I, Group II and Group III respectively. In the present study body temperature were decreases non-significantly from pre-medication values at 60 min. after induction and toward the base value at the recovery time and values recorded were 102.03± 0.59° F, 101.25 ± 0.51° F and 101.4 ± 0.56° F in the Group I, Group II and Group III respectively. Body temperature after recovery in the groups were 102.45 ± 0.43° F, 100.85 ± 0.46° F and 101.48 ± 0.48° F respectively. In the present study change in body temperature showed a slight decrease 15 min. interval after premedication which was statistically non-significant.

In the Group I premedication produced non-significant decrease in the respiratory rate at 10 min. interval after pre-anaesthetic (24 ± 3.94 compared to 27.16 ± 3.28 and 29.66 ± 1.30 compared to 32 ± 1.15/min) which upon 15 min. of induction produced a statistically non-significant further decreased compared to base values (23 ± 3.13 compared to 27.16 ± 3.28 and 29.33 ± 1.35 compared to 32 ± 1.15 /min in group I and Group II. In the Group III upon 20 min. interval of induction respiratory rate increased non-significantly compared to base value (36.33 ± 3.69 compared to 34.8 ± 3.63/min). changes in respiratory rate was non-significant during entire observation period between groups except in the group III there was higher respiration after 5 min. of induction which was lowered in the group I and group II upon induction when compared to the basal respiratory rate. In the present study, in all three different groups there was non-significant decrease in respiratory rate during isoflurane maintenance period, and which was increased non-significantly from 5 min. onwards till recovery time. Respiratory rate showed a non-significant reduction in the Group I and Group II as compared to the Group III.

In the present study during isoflurane maintenance all the three different groups showed a similar degree of dose dependent respiratory depression throughout the maintenance period. However the values were within normal range and adequate to maintain normal ventilation. Isoflurane induced respiratory depression was not evident even at 1.5 MAC but at 2 MAC produced marked respiratory depression.

There was non-significant changes occur in mean heart rate among all three different groups. In the Group I, the premedication produced a non-significant decrease in the mean heart rate at 15 min. interval after premedication (123.67 ± 09.68 compared to 133.33 ± 11.64 beats/min) which upon induction produced a further increase and further decrease after 30 and followed by 60 min. of induction and maintenance when compared to base values and increased further onward recovery period not reach base values.

In the Group II non-significant changes in the mean values of heart rate at different time intervals and remain within normal range while in group III there was non-significantly increase in mean values of heart rate (147.5 ± 11.99 compared to 132.83 ± 8.190 beats/min) compared to base value at 15 min. interval of premedication administration could be due to glycopyrrolate which induces tachycardia followed by reduction in heart rate (137 ± 10.15 and 137 ± 10.15 beats/min) at 45 and 60 min respectively after isoflurane maintenance and increased onward 5 min. interval till recovery. In the present study the heart rate showed a non-significantly decreasing and non-significantly increasing trend in Group I, Group II and Group III respectively.

In the present study during isoflurane maintenance all the dogs in three different groups showed a non-significant decrease in heart rate as compared to induction. From induction to recovery there were consistent non-significant reductions in heart rates in all the dogs in three different groups.

Blood pressure is the best single indicator that reflects elements of health of the cardiovascular system under anaesthesia. Blood pressure values were derived using automatic NIBP monitoring cuff connected to the multiparamonitor at forelimb. A more complete picture of the effects on the cardiovascular system by anaesthesia would have been produced by measurement of central venous pressure, cardiac output and systemic vascular resistance.

After 15 min. interval of premedication mean values were 126.83 ± 5.01, 119.5 ± 10.57 and 118.33 ± 4.65 mmHg respectively in the Group I, Group II and Group III which was non- significant groups. Mean values of systolic blood pressure were 126.5 ± 5.01, 120.83 ± 10.0, and 118.33 ± 4.65 mmHg respectively in Group I, Group II and Group III. Non-significant reduction in systolic blood pressure continued to 15 min. interval of premedication in Group II and Group III and after onwards the mean values increased non-significantly and reached near the basal range at 15 min and 30 min after induction (121.5 ± 10.36 and 119.6 ± 8.32 mmHg) in the Group II and Group III respectively and further increased at 30 and 45 min. of induction in the Group I, Group II and Group III respectively. The mean values of systolic blood pressure at recovery in the Group I, Group II and Group III were 134.16 ± 9.25, 128 ± 10.46 and 123.83 ± 7.63 mmHg respectively while recovery values showed a non-significant decrease to the base value of systolic blood pressure in all the groups. Systolic blood pressure increased non-significantly in Group I and decrease non-significantly in the group II and Group III after 15 min of premedication and showed a non-significant decrease onward recovery toward but not reach the base values in Group I and Group II where as in Group III increased non-significantly toward the base value onward recovery.

Mean values showed decreasing trend at induction time which was non-significant were 84.33 ± 3.91 and 77.33 ± 10.28 compared to 84.5 ± 4.25 and 77.6 ± 9.86 mmHg in Group I and Group II while mean values non-significantly increased were 66.83 ± 3.59 compared to 66 ± 3.43 mmHg in Group III. Diastolic Blood Pressure (DBP) showed a similar pattern of non-significant increase from induction time interval to 45 min. interval of anaesthesia were (91.66 ± 12.95, 102.16 ± 10.98 and 71.83 ± 6.92 mmHg respectively) in the Group I, Group II and Group III. The recovery values were 86 ± 8.1, 86 ± 7.32 and 76.33 ± 7.36 mmHg in the Group I, Group II and Group III respectively shown non-significantly increased from the base values. There was no significant difference reported in diastolic blood pressure among all three different groups.

Mean values of mean arterial pressure showed non-significant decrease at 15 min. intervals of premedication were 92.33 ± 10.45 and 83.5 ± 3.95 compared to 92.83 ± 9.93 and 83.66 ± 3.98 mmHg in the Group II and Group III respectively whereas non-significant increase were 96.83 ± 4.40 compared to 96 ± 4.29 mmHg in group I compared to the basal level values. Mean Arterial Pressure (MAP) showed non-significant decrease at 15 min of induction in the group I were 95.16 ± 4.99 compared to 96 ± 4.29 mmHg and non-significantly increased the values at 15 min of induction were 93.66 ± 10.06 and 84.16 ± 3.77 compared to 92.83 ± 9.93 and 83.66 ± 3.98mmHg compared to basal values in Group the II and Group III. Non-significant increased MAP at 45 min. of induction were 104.83 ± 12.79, 116.33 ± 10.22 and 87.83 ± 6.83 mmHg in Group I, Group II and Group III respectively. At the recovery, MAP values increased non-significantly which were 100.5 ± 8.83, 100.33 ± 8.36 and 89 ± 6.11 mmHg respectively in the Group-I, Group-II and Group-III respectively.

In Group-I, Group-II and Group-III showed a non-significant increase in SpO_2 at 15 min. intervals of premedication were 96.33 ± 0.61, 97.83 ± 0.54and 97.83 ± 0.47 % respectively in as compared to the basal level values were 96.16 ±0.90, 94.83± 2.0 and 97.16± 0.402 % respectively. The Saturation Percentage of Oxygen ($SpO_{2)}$ showed non-significant increase from induction to 15 min. interval of anaesthesia were 96.5 ± 0.5, 98 ± 0.36 and 97.5 ± 0.71 % respectively in the Group-I, Group-II and Group-III. At 30 min. interval SpO_2 non-significant increased after induction were 97.00 ± 0.36, 97.00 ± 0.36 and 97.33 ± 0.49 % respectively in the Group-I, Group-II and Group-III. At 45 min. interval also SpO_2 increased non-significantly were 96.83 ± 0.54, 97.33 ± 0.49 and 96.33 ± 2.07 % respectively in the Group-I, Group-II and Group-III. The recovery values altered non-significantly from the base values were 97.16 ± 0.87, 96.83 ± 0.70 and 98.16 ± 0.16 % respectively in the Group-I, Group-II and Group-III. In the present study SpO_2 showed non-significant changes within normal physiological limit from induction values to 30 min. interval till end of observation. In isoflurane maintenance SpO_2 increased gradually and showed non-significant increase after 30 min of induction and decreased non-significantly during the recovery period without any clinical signs of hypoxia. All the animals maintained with inhalant isoflurane anaesthesia and allowed to breathe isoflurane mixed with 100 % oxygen hence the changes obtained with SpO_2 were of low clinical significance.

In the present study all the dogs in different groups were placed in right lateral recumbency and ECG was recorded using lead II system on paper with a electrocardiograph. The paper speed and sensitivity were set to 25mm/sec and 1 mV, respectively. Heart rate was counted from the ECG recording, and respiratory rate was measured by observing thoracic excursions.

The incidence of cardiac arrhythmia was not statistically significant among treatments. In the present study animals of all three different groups not showed any abnormality in ECG except for a slight increase in QRS duration and T wave's amplitude in Group I and prolongation of QT interval and ST elevation observed in Group III after propofol induction while in Group-II normal ECG recorded. In the present study prolongation of QT interval, P amplitude after induction, PR segment and ST elevation after five min. of induction was observed in acepromazine group, however it is clinically acceptable. Biphasic T waves were also present in dogs after induction until the end of the anaesthetic period which was in accordance to Group III.

In the present study all haematological parameters namely haemoglobin, packed cell volume, total Leucocytes count decreased non-significantly from base values during induction and maintenance in all animals in the Group I, Group II and Group III.

Mean haemoglobin concentration values before premedication were 15.47 ± 1.81, 13.45 ± 1.39 and 12.55 ± 1.27 g/dl respectively in the Group I, Group II and Group III. After 15 min. interval of induction mean Hb values were 14.10 ± 1.24, 12.38 ±1.42 and 10.4 ±0.98 g/dl respectively in the Group I, Group II and Group III. At 60 min. interval of anaesthesia mean Hb values were observed to be 11.71 ± 1.69, 11.75 ± 1.43 and 9.38 ± 0.76 g/dl respectively in the Group I, Group II and Group III. Mean Hb at recovery were 10.29 ± 1.82, 11.05 ± 1.40 and 8.69 ± 0.63 g/dl respectively in the Group I, Group II and Group III. Haemoglobin concentration in Group I and Group III decreased significantly at recovery time when compared to base values while in the Group II Hb decreased non-significantly. In the present study minimum haemoglobin concentration was observed at recovery time in all the three groups which was non-significant in between all three different groups. Non-significant decrease in Hb concentration observed may be due to combine effects of premedication drugs, propofol induction with continuous administration of ringer lactate during isoflurane maintenance.

Mean PCV values before premedication were 44.41 ± 2.92, 41.27 ± 2.7 and 36.18 ± 3.41 % respectively in the Group I, Group II and Group III. After 15 min. interval of induction values were 40.67 ± 2.89, 43.15 ± 6.03 and 30.83 ± 2.85 % respectively in the Group I, Group II and Group III. At 60 min. interval of anaesthesia values were 35.21 ± 4.41, 38.67 ± 4.34 and 28.86 ± 1.86 % respectively in the Group I, Group II and Group III. Mean PCV values at recovery time were 30.13 ± 4.86, 36.64 ± 4.20 and 27.30 ± 1.48 % respectively in the Group I, Group II and Group III respectively. PCV of the Group I and Group III significantly decrease at recovery time when compared to base values while non-significantly in the Group II. In the present study PCV showed non-significant difference between all three different groups from premedication to recovery time and minimum PCV was observed at recovery. Mean TLC values before premedication were 21. 46± 2.86, 23.93 ± 6.50 and 24.35 ± 4.91 (x 10^3 / µL) respectively in the Group I, Group II and Group III respectively. After 15 min. interval of induction mean TLC were 17.15 ± 1.25, 19.98 ± 4.45 and 21.41± 5.29 (x 10^3 / µL) respectively in Group I, Group II and Group III. At 60 min. interval of anaesthesia mean values of TLC were 16.12 ± 1.57, 17.71 ± 4.56 and 20.41± 5.32 (x 10^3 / µL) respectively in the Group I, Group II and Group III.TLC values at recovery time were 14.51 ± 1.30, 16.53 ± 4.56 and 19.0 ± 5.6 (x 10^3 / µL) respectively in Group I, Group II and Group III. TLC decreased non-significantly in all three different groups throughout observation period. In the present study non-significant increase from base level to premedication followed by a non-significant decrease from induction to recovery in all the groups and minimum value of TLC was recorded at recovery time.

Mean values of neutrophils and lymphocytes were non-significant. Mean values of neutrophils (N) recorded maximum at 60 min. interval in the Group I and Group II and at recovery time in Group III. In the present study non-significant changes were observed in all three groups. All the animals undergone surgical interventions had stress and associated neutrophilia seen at different time intervals. In the Group III mean values of lymphocytes increased non-significantly in acepromazine groups and in the Group I and Group II non-significant variation recorded in DLC. In the present study mean values of neutrophils before premedication were 67.21 ± 9.96, 58.88 ± 8.82 and 69.06 ± 4.99 % respectively in the Group I, Group II and Group III. After 15 min. interval of induction neutrophils values were 67.03 ± 9.88, 62.81 ± 7.68 and 62.68 ± 3.90 % respectively in the Group I, Group II and Group III. At 60 min. of anaesthesia neutrophils values were 69.87 ± 9.93, 64.33 ± 10.10 and 64.33 ± 10.10 % respectively in the Group I, Group II and Group III. Neutrophils values at recovery time were 69.16 ± 10.95, 63.41 ± 11.26 and 70.26 ± 5.48 % respectively in the Group I, Group II and Group III. In the present study mean values of lymphocytes (L) before premedication were 24.61 ± 10.2, 28.18 ± 8.83 and 19.8 ± 3.65 % respectively in the Group-I, Group-II and Group-III. After 15 min. of induction lymphocyte were 25.18 ± 10.4, 25.15 ± 7.44 and 26.35 ± 2.66 % respectively in the Group I, Group II and Group III. At 60 min. interval of anaesthesia lymphocytes values were 25.37 ± 10.6, 25.62 ±8.77 and 25.62 ± 8.77 % respectively in the Group I, Group II and Group III. Lymphocytes values at recovery were 26.96 ± 11.3, 28.25 ± 10.0 and 31.87 ± 8.29 % respectively in the Group I, Group II and Group III.

In the present study changes in the number of eosinophils, basophiles and monocytes were recorded negligible which can be attributed to the fact that very few number of cells were observed on peripheral blood smear examination. In the present study serum biochemical parameters namely, serum creatinine, blood urea nitrogen, alanine aminotransferase and aspartate aminotransferase not show any significant changes during the entire study indicating that the drug combinations which was used not have any adverse effects on organ functions. Mean serum creatinine values showed non-significant changes between the groups at all the intervals of base (0 min), 15 min, 30 min, 60 min. and 120 min. interval time. In all three different groups not showed significant changes and remain within normal range during entire observation period. In the present study mean values of serum creatinine before pre-medication were 0.079 ± 0.018, 0.090 ± 0.008 and 0.104 ± 0.024 mg/dl respectively in the Group I,

Group II and Group III. After 15 min. interval of induction serum creatinine values were 0.067 ± 0.015, 0.093 ± 0.0079 and 0.10 ± 0.029 mg/dl respectively in Group I, Group II and Group III. At 30 min. interval of anaesthesia serum creatinine values were 0.10 ± 0.020, 0.091 ± 0.0099 and 0.11 ± 0.028 mg/dl respectively in the Group I, Group II and Group III. At recovery time values of serum creatinine were 0.305 ± 0.22 03, 0.093 ± 0.010 and 0.11 ± 0.029 mg/dl respectively in Group I, Group II and Group III.

Mean BUN values showed non-significant changes between the groups at different time intervals in Group I and Group III. Non-significant increase in BUN values from pre-medication to 45 min. interval of induction and then afterward decreased to normal after recovery. In Group II non-significant variation observed and BUN values remain within the normal ranges. In the present study mean values of BUN before pre-medication were 4.95 ± 1.31, 5.6 ± 0.38 and 4.86±2.12 mmol/L respectively in the Group I, Group II and Group III. After 15 min. interval of induction BUN values were 6.99±2.09, 5.5±0.32 and 5.50±2.77 mmol/L respectively in the Group I, Group II and Group III. At 45 min. interval of anaesthesia BUN values were 6.80±1.50, 5.25±0.22 and 5.86±2.75 mmol/L respectively in the Group I, Group II and Group III. BUN values at recovery time were 6.14±1.27, 5.11±0.20 and 6.07±2.76 mmol/L respectively in Group-I, Group- II and Group-III.

Mean ALT values before pre-medication were 19.5±4.6, 28.9 ±8.1 and 29.0 ±3.0 IU/L respectively the in Group I, Group II and Group III and after 15 min. interval of induction the ALT values were 27.8 ±7.5, 26.8 ±10.6 and 27.2 ±2.42 IU/L respectively in Group I, Group II and Group III. After 45 min. Mean ALT values were 18.7 ±4.6, 37.4 ±10.1 and 33.5 ±3.3 IU/L respectively in the Group I, Group II and Group III and at recovery time ALT values were 27.1 ±5.7, 32.4 ±7.5 and 31.0 ±4.7 IU/L respectively in the Group I, Group II and Group III.

Mean ALT values showed non-significant changes between the groups at different time intervals in all the groups. Changes in mean ALT values were non-significant from premedication to entire observation periods

Mean AST values were non-significant between the groups at different time intervals in all groups. Mean AST values were non-significantly increased from pre-medication, 15 min. interval of induction and followed by 45 min. interval of induction till recovery time. Mean AST values before premedication were 58.7±16.2, 54.6±8.1 and 44.8±2. IU/L respectively in the Group I, Group II and Group III. Mean AST values at 30 min. interval were 66.0±16.1, 62.9±11.3 and 47.4±4.5 IU/L respectively in Group I, Group II and Group III. At 60 min. interval of induction mean AST values were 66.4±14.3, 83.3±22.5 and 53.3±9.4 IU/L respectively in the Group I, Group II and Group III. Mean AST values at recovery time were 64.4±10.5, 74.4±24.3 and 54.0±9.3 respectively in the Group I, Group II and Group III.

Mean values of glucose before premedication were 4.23±0.62, 4.07±0.48 and 4.12±0.37 mmol/L respectively in the Group I, Group II and Group III. At 30 min. interval before induction glucose values were 4.84±0.64, 4.43±0.37, 4.55±0.37 mmol/L respectively in the Group I, Group II and Group III. At 60 min. interval mean glucose values were 5.27±0.56, 6.16±0.96 and 4.87±0.36 mmol/L respectively in the Group I, Group II and Group III. Mean serum glucose values at recovery time were 6.36±0.88, 8.39±2.06 and 5.29±0.32 mmol/L respectively in the Group I, Group II and Group III. In the present study serum glucose values were significantly increases and maximum values recorded after 60 min. interval of induction and maintenance in the Group II and Groups III but non-significantly increased in Group I.

Total quantity of isoflurane consumed per animal in each group were compared and observed non-significant reduction in the Group II and group III compared to the Group I. Mean isoflurane vaporizer setting used in the Group II for maintaining the surgical plane of anaesthesia (1.53 ± 0.080) was lowest as compared to the Group III (1.66 ± 0.07) and the Group I (1.75± 0.056). Reduction of total quantity of isoflurane consumption and maintenance of animals per hour observed non-significant between all three different groups. In the present study quantity of isoflurane liquid used for maintenance showed a non-significant reduction in the Group II (6.27 ± 0.38) compared to Group III (7.0 ± 0.3) and Group I (7.33 ± 0.22).

In the present study all eighteen dogs in the three different groups were recovered well without any complication. In the present study mean values of duration of anaesthesia were 86.83 ± 9.51, 85.83 ± 5.73 and 79.83 ± 7.03 min. respectively in the Group I, Group II and Group III. The duration of anaesthesia did not change much between the three groups. Duration of anaesthesia in between three different groups was non-significant. In the present study mean values of recovery time (time lapsed from discontinuation of isoflurane administration to extubation) were 5.83 ±0.29, 4.88 ±

0.21 and 5.28 ± 0.12 min. respectively in the Group I, Group II and Group III respectively. The Group II showed less recovery time followed by the Group III and the Group I. Recovery time was observed non-significant between three different groups. At the time of extubation cough reflex or swallowing was noticed. The extubation time in the Group II was less compared to the Group I and Group III could be due to the higher isoflurane vaporizer setting during maintenance and higher volume of isoflurane consumed in the acepromazine and xylazine groups which made more prolonged extubation time.

In the present study mean values of complete recovery time (time lapsed from the discontinuation of the isoflurane administration to the time when the animal stand) were 34.83 ± 1.75, 29.33 ± 1.11 and 26 ± 1.12 min. respectively in the Group I, Group II and Group III which was non-significant between all three groups. Recovery time and complete recovery time were non-significant between all three different groups. The Group III showed faster complete recovery time followed by Group II and Group I. The combination of opioid and sedative/tranquilizer reduce the dose of anaesthetic required for propofol induction and isoflurane maintenance of anaesthesia with faster recovery. The quality of recovery was excellent and uneventful in all animals of all three different groups without any complication.

SUMMARY AND CONCLUSIONS

In Group I, animals were premedicated with a combination of glycopyrrolate, xylazine and butorphanol @ 0.01, 0.5 and 0.2 mg/kg b.wt. I/M respectively. In Group II, animals were premedicated with a combination of glycopyrrolate, dexmedetomidine and Butorphanol @ 0.01, 0.005 and 0.2 mg/kg b.wt. I/M respectively and Group III, dogs were premedicated with a combination of glycopyrrolate, acepromazine and butorphanol @ 0.01, 0.05 and 0.2 mg/kg b.wt. respectively I/M 15 min. prior to induction. In all the three different groups the induction of anaesthesia was done with propofol and the maintenance of anaesthesia was done with isoflurane. The quality of sedation, jaw relaxation, palpebral reflex, pedal reflex and response to intubation was superior with acepromazine (Group III) compared to xylazine (Group I) and dexmedetomidine (Group II). In the present study, glycopyrrolate-acepromazine –butorphanol combination had a better sedation quality.

Mean effective dose of propofol used for induction in Group I, Group II and Group III were 3.43 ± 0.24, 3.00 ± 0.12 and 2.81 ± 0.09, respectively. The induction dose of propofol used for acepromazine (group III) was found non-significantly lower as compared to xylazine (Group I) and dexmedetomidine (Group II). Acepromazine and dexmedetomidine showed sparing effect the on induction dose of anaesthesia with propofol. None of the animals showed any complications while induction of anaesthesia in all the three different groups

Rectal temperature showed a non-significant decreasing trend throughout the surgical procedure when compared to the base values in all the three groups. It may be to the hypothermic effects of general anaesthesia. Respiratory rate showed a non-significant decreasing trend after pre-medication and increasing trend during induction and maintenance period throughout the surgical procedure in all the three different groups as compared to the base values. Heart rate showed a non-significant decrease immediately after pre-medication in xylazine (Group I) while, heart rate increased non-significantly in dexmedetomidine (Group II) and acepromazine (Group III). During the maintenance with isoflurane the heart rate at different time intervals remained within normal range. The Heart rate fluctuation throughout the observation period, was non-significant and within the normal range.

The mean blood pressure was high during the maintenance time in all the three groups as compared to the base values and lower at recovery time. Blood pressure fluctuation, throughout observation period, was non-significant and was found within normal range. Blood pressure fluctuations may be due to the hypotensive effects of general anaesthesia. The SpO_2 increased at 15 min. interval of the induction and decreased at the recovery time in all the three groups. SpO_2 fluctuations was non-significant and within normal range. The present anaesthetic protocol the maintenance with isoflurane does not produce any signs of hypoxia throughout observation period in all three groups. In the present study, the animals of all the three groups did not show any abnormality in ECG slight increase in GRS duration and T wave's amplitude in xylazine (Group I) and prolongation of QT interval and ST elevation in acepromazine (Group III) after propofol induction. No abnormality in ECG was found in Group II. Prolongation of QT interval, P amplitude after induction, PR segment and ST elevation and dysphasic T waves was also present in dogs after induction until the end of the anaesthetic period in acepromazine (Group III). The haemoglobin and packed cell volume decreased significantly from premedication to recovery time in xylazine (Group I) and acepromazine (Group III) while non-significant in dexmedetomidine (group II). It may be due to haemodilution with fluid therapy and continuous blood loss during surgery. The total leucocyte count decreased non-significantly at different intervals throughout the observation period when compared to the base values in all three groups. In the differential leucocyte count, lymphocytes values increased in group I and group III when compared to the base values while in group III lymphocytes remained within the physiological limit. Neutrophils values increased at recovery period when compared to the base values in all the three groups, which remained acceptable clinically normal range and there was non-significance difference noticed among the groups at various intervals during the observation period. The serum biochemical parameters remained unaltered throughout the observation period and were non-

significant. However, serum blood urea nitrogen increased in xylazine (Group I) and acepromazine (Group III) while decreased in dexmedetomidine (Group II) at recovery time when compared to the base values. Serum creatinine, serum ALT and serum AST values increased at recovery period when compared to base values. Serum glucose increased significantly in dexmedetomidine (Group II) and acepromazine (Group III) while the change was non-significant in xylazine (Group I) at recovery period when compared to the base values.

In the present study, the mean isoflurane vaporizer setting for Group I, Group II and Group III were 1.75± 0.056, 1.53 ± 0.080 and 1.66 ± 0.07 %, respectively and the average quantity of isoflurane liquid used for maintenance were 7.33 ± 0.22, 6.27 ± 0.38 and 7.0 ± 0.3 ml/hr respectively. The mean vaporizer setting and isoflurane liquid used was lower in dexmedetomidine (Group II) followed by acepromazine (Group III) and xylazine (Group I). The mean changes in isoflurane vaporizer and % of isoflurane used was non-significant in all the three groups. The mean duration of anaesthesia was non-significant between the groups. The recovery time was lowered in dexmedetomidine (Group II) followed by acepromazine (Group III) and xylazine (Group I). The complete recovery time was lower in acepromazine (Group III) followed by dexmedetomidine (Group II) and xylazine (Group I). Complete recovery was faster in dexmedetomidine and acepromazine groups as compared to xylazine groups which could be due to smooth and fast recovery produced by dexmedetomidine as compared to xylazine but complete recovery was faster in acepromazine group as compared to the other two groups.

Glycopyrrolate-xylazine-butorphanol, glycopyrrolate-dexmedetomidine-butorphanol and glycopyrrolate-acepromazine-butorphanol premedication resulted in good sedation, smooth induction and smooth and fast recovery with better anaesthetic sparing effect on the induction agent and isoflurane liquid for maintenance and lower stress response during general anaesthesia in dogs who underwent varieties of surgeries. Hence, their general usage in clinical practice is recommended. Among all the three groups, glycopyrrolate-dexmedetomidine-butorphanol premedication had more sparing effect on isoflurane during maintenance of anaesthesia as compared to xylazine and acepromazine groups. The vaporizer setting showed the lowest values and the clinico-physiological effect were minimal and within the normal range in dexmedetomidine group. Hence, it is concluded that the, Glycopyrrolate-Dexmedetomidine-Butorphanol premedication with propofol induction and isoflurane maintenance was a better combination followed by glycopyrrolate-acepromazine-butorphanol and glycopyrrolate-xylazine-butorphanol anaesthetic protocol for varieties of surgeries in dogs.

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