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Clinico-Physiological Effects of Ketofol 1:2 in Canine Orthopaedic Patients

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A B S T R A C T

Aim of this study to look out the suitability of single syringe mixture of ketamine and propofol (ketofol 1:2 as 7.5 mg per ml) as induction and constant rate maintenance agent (300 µg/kg/minute) in atropine sulphate, dexmedetomidine and butorphanol premedicated orthopedic patient of dogs. This study was done in Indian veterinary research institute, Izatnagar on client owned dog with proper consent. Clinic-physiological and anaesthetic parameters were recorded pre and during study at various time periods. From that it was concluded that less dose of induction (2.57±0.23 mg/kg) with very effect on heart rate and respiratory drive. So its use may be recommended in orthopaedic patients.

Introduction

Propofol is a phenolic compound increases effects of gamma-amino benzoic acid activity (GABA) in turn used as an induction and maintenance anaesthetic agent in both human and veterinary patients. Less harm to the metabolic system and short context-sensitive half-life after continuous rate intravenous infusion and smooth recovery are among the advantages of this drug (Wamaitha *et al*., 2019). Hence it's widely used for emergency and critical patient ward. But limitation of the drug may be its post-induction apnea, cardiovascular complications and absence of analgesia. On flip side ketamine is a dissociative agent acts majorly via N-methyl-D-aspartate (NMDA) antagonist. It has good analgesic and merely user friendly for veterinary anaesthesia. But catalepsy, violent recovery and spontaneous activities are undesirable (Kurdi *et al*., 2014 and Sharma *et al*., 2017). Recent decade ketofol as a blender of ketamine and propofol evidenced that it nullifies side effects of one another with appropriate ratios (Martinez-Taboada, and Leece, 2014 and Saikia *et al*., 2019). In this study we will discuss about effect of single

syringe mixture ketamine and propofol in induction and maintenance on six orthopaedic patients of dogs.

Materials and Methods

This was a prospective blinded clinical anaesthetic study on six randomly chosen (irrespective of age, sex, breed and body weight) ASA (American Society of Anesthesiologists) classified class II (Mayhew *et al*., 2019) dogs with tibial fracture besides normal heamoglobin and Packed cell volume in which plating will be done. Animals were fasted for 12 hours and undergone clinical examination before start of procedure. The premedication, induction and maintenance of anaesthesia done as following:

Initially Atropine sulphate@ 0.04mg per kg body weight administered intramuscularly, after 5 minutes of above drug dexmeditomidine @ 15 µg per kg body weight and butorphanol @ 0.2 mg per kg body weight administered intramuscularly on either side of epaxial muscle of a patient. Ten minutes after that induction was carried out by single syringe mixture of ketofol 1:2 (5 mg ketamine + 2.5 mg propofol combined as 7.5mg/ml) and maintenance of anaesthesia done in ketofol 1:2 constant rate infusion @ 300 µg/kg/minute in added make up volume 10 ml per kg per hour of surgical maintenance fluid (Normal saline) up to the end of last skin suturing. First induction bolus of intravenous dose started 0.5 mg ketofol per kg body weight for 20 seconds, then after 30 seconds evaluated induction based on absence of pedal reflex. As its induction dose continue till the complete abolition of pedal then the dose of induction calculated by adding quantity used against body weight. Clinico-physiological parameters heart rate, respiratory rate, arterial saturation of oxygen, temperature and observational subjective parameters (Jena *et al*., 2014) pedal reflex (measure of depth of analgesia), palpebral and corneal reflex (measure depth of sedation) were recorded 0 minute (min), 15, 20, 30, 45, 60, 75, 90, 105, 120, 135, 150, 165, 180 minutes after administration of atropine sulphate. Duration of surgery (from a start of skin incision to end of last skin suturing), duration of anaesthesia (from a complete abolition of pedal reflex to complete regain of pedal reflex) recovery time (from stoppage of constant rate of infusion into regain of pedal reflex) sternal recumbency time (from stoppage of constant rate of infusion into going to sterna position) standing time (from stoppage of constant rate of infusion into standing) was recorded. In statistical analysis, parametric data and non-parametric data tested and analysed and with Friedman test and Repeated measures ANOVA for different time and results were depicted in Mean±Standard Deviation.

Results and Discussion

From a table 1 (Physiological parameters) Heart rate (beats per minute) was within the normal physiological range throughout the study period. Respiratory rate were significantly lower than pre during initial period of induction and maintenance. This mild depressive respiration pattern may stimulate heart rate. Moreover atropine and ketamine has synergistic in accordance with increased heart rate (Thejasree et al., 2018). Similar trend heart rate noticed in ketofol 1:2 on human orthopaedic patients when compared with cri of propofol (Sabertanha et al., 2019). Oxygen saturation of haemoglobin evidences that significant drop at induction and immediately after induction. There after results were within acceptable limits. Temperatures were drop down post-induction and significant trends noticed after 30 minutes to till the end of 180 minutes after atropine administration. Although it's not uncommon during general anaesthesia warming of patient necessary as need arises.

Table.1 Clinico-physiological parameters of ketofol 1:2

Table.1	Pre	After premed+Induction + Maintenance and upto 180 minutes												
Time	**0 min**	**15 min**	**20 min**	**30 min**	**45 min**	**60 min**	**75 min**	**90 min**	**105 min**	**120 min**	**135 min**	**150 min**	**165 min**	**180 min**
Heart rate	104.5±5.58	130.33±3.93*	148.17±6.31**	153.83±4.79**	121±3.58	115.5±3.27	110.17±3.19	83.83±7.81	91.5±6.89	83.17±5.88	94.83±3.87	91.83±6.49	91.83±5	91.17±7.96
Resp. rate	22±1.67	18.83±1.47	9±0.89**	9±1.26**	9.17±0.75**	10.83±3.76	12±5.55	10.5±4.28	11.17±3.92	11±3.35	10.5±3.51	12.83±2.71	11.83±2.79	13.5±2.51
spo2	99.5±0.55	98.83±0.41	91.17±1.72**	95.5±2.88	91±4.73	89.83±4.96	95.83±2.64	95.33±2.07	95.17±3.19	95.33±2.16	93.67±3.44	96.83±1.17	98.17±0.75	98.66±0.516
Temperature	102.6±0.63	101.45±1.04	100.78±1.15	99.88±1.06*	99.58±0.84*	99.32±0.81**	99.08±0.75**	98.75±0.87**	98.67±0.78**	97.38±0.84**	97.08±0.98**	95.85±1.12**	95.48±0.82**	95.18±0.68**

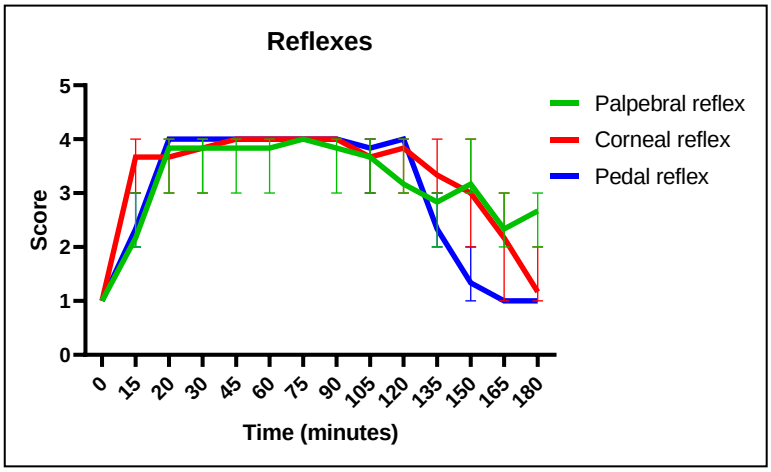
* Represent value of p < 0.05 and ** for p < 0.05

Table.2 Clinical Quantitative Anaesthetic Parameters (Mean±SD)

Dose of Induction (mg/kg±SD)	**2.57±0.23**
Duration Of Surgery (min±SD)	93.67±3.27
Duration Of Anaesthesia(min±SD)	140.17±10.5
Recovery time (min±SD)	31.17±7.94
Sternal recumbency time (min±SD)	63.5±8.17
Standing time (min±SD)	90.33±13.25

* Represent value of P < 0.05 and ** for P < 0.01

Figure.1 Reflex score of pedal, palpebral and corneal reflex in Ketofol 1:2 induced and maintained dogs



From the figure of reflexes score, status of analgesia well in ketofol 1:2 constant rate infusion maintenance period and pattern of regain of pedal reflex also faster than palpebral and corneal reflex. Palpebral and corneal reflex diminishes significantly after premedication to end. Even at the time of end also not gained full palpebral reflex strength than corneal reflex. This may be due to dissociative effect of ketamine as its metabolite (Romagnoli *et al*., 2017) also equally potent and combined depressive activity of dexmedetomidine, butorphanol and propofol some extent. Clinical quantitive anaesthetic parameters of ketofol 1:2 were in table 2. Although comparative study not done with ketamine and propofol, but it was evidenced that dose of induction was very lower than recommended dose ranges of both ketamine and propofol in clinical settings.

In conclusion, ketofol 1:2 Constant rate indusion contribution will be outstanding in orthopaedic patients of dogs. Because of its surgical plane analgesia along with dexmeditomidine and butorphanol, its sustainability in maintaining heart rate, less dose of induction than clinically recommended dose range of both drug alone and preservation of respiratory drive except during induction. Hence it's advised to monitor patient while induction as it inturn may cause hypoxia. Limitation of this study is no comparison and haemodynamic activity were not done. Subsequent research may warrant in this area as it has potential as procedural sedative and day care surgical combo in veterinary as in ICU patients and pediatrics of human.

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