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Effects of Propofol, ketamine and their combination (Ketofol) as total intravenous anaesthesia (TIVA) on cardiopulmonary parameters in atropine and xylazine premedicated dogs

Basanta Saikia, Hemen Das, Hitesh Bayan, Rahul paul, Analisha Debbarma and Nirmali Sarma

Abstract
The study was conducted in eighteen clinical cases of dogs of either sex. The animals were randomly divided into three groups with six animals in each group. Atropine sulphate @ 0.04mg/kg b.wt. i.m. and xylazine HCl @ 0.5mg/kg b.wt. i.m. route were administered as Premedicants in all the three groups. In group-I, Propofol @ 5mg/kg body weight, in group-II, ketamine @ 5mg/kg body weight and in group-III, Ketofol @ 4mg/kg body weight was administered intravenously for induction after 15 minutes of Preanaesthetic administration. Surgical anaesthesia was maintained for 90 minutes in all three groups viz. group-I, group-II and group-III with propofol @ 2.5mg/kg. b.w., ketamine @ 2.5mg/kg b.wt. and ketofol @ 2mg/kg b.wt. respectively by intermittent bolus injection (IBI) technique.
Physiological parameters like rectal temperature, heart rate, respiratory rate, blood pressure and spO_2 were evaluated before administration of anaesthetic agent (0 minute) then at 15, 30, 60 and 90 minutes during and after administration of anaesthetic agents. The heart rate initially increased and then decreased gradually towards pre-anaesthetic level in all the three groups. The respiratory rate initially decreased and then increased towards pre-anaesthetic level in all the three groups. Both diastolic pressure and systolic pressure remained in a comfortable zone in group-III animals whereas, high blood pressure was recorded in group-II animals and low blood pressure was recorded in group-I animals.

Keywords: Propofol, ketamine, Ketofol, atropine, xylazine and TIVA

Introduction
The non-availability of sophisticated anaesthetic machine and necessary equipment to administer inhalant anaesthetic in the field hospitals make their use practically unfeasible for the field veterinarians. In field conditions intramuscular or intravenous anaesthesia is usually the method of choice, as it can be performed with limited facilities at hand in the animal hospitals. Total intravenous anaesthesia (TIVA) is a technique of general anaesthesia that uses agents given solely by the intravenous route, and in the absence of all inhalation agents (Campbell *et al*., 2001) [2]. The concept of total intravenous anaesthesia (TIVA) is simple. An I/V line is the only prerequisite, and everything needed for general anaesthesia is supplied through this line. The TIVA provides a reliable, rapid, inexpensive and smooth induction of anaesthesia, adequate hypnosis and analgesia as well as rapid, uncomplicated and complete recovery for discharge in "home-fit" condition to the owner within minutes of completion of the procedure. Maintenance of anaesthesia can be obtained by administering intermittent boluses, continuous rate infusion or by target controlled infusion.
In general, propofol induces a rapid smooth induction, followed by a short period of unconsciousness (Morgan and Legge, 1989) [11]. Propofol is rapidly redistributed from the brain and is also efficiently eliminated from plasma (Zoran *et al*., 1993) [17]. Due to these pharmacokinetic properties, it is considered to be a suitable drug for maintenance of anaesthesia by continuous rate infusion (Musk *et al.,* 2005) [12]. Ketamine is a dissociative anaesthetic and it produces dose-related unconsciousness and mainly somatic analgesia (Waelbers *et al*., 2009) [5]. Ketamine possibly increases muscle tone and it induces spontaneous movement and, occasionally, convulsions. To reduce these undesirable effects, it is often used in conjunction with propofol, benzodiazepines, acepromazine or α2-agonists. Ketamine and propofol administered in combination have offered effective sedation for

Gynaecologic, ophthalmologic and cardiovascular procedures. The opposing haemodynamic and respiratory effects of each drug may enhance the utility of this drug combination, increasing both safety and efficacy and allowing reduction in the dose of propofol required to achieve sedation (Daabiss *et al.,* 2009) [3].

The present study was undertaken with the objectives to evaluate the cardiopulmonary effect of propofol, keatamine and their combination 'Ketofol' as a TIVA in atropine and xylazine premedicated dogs.

Materials and Methods

The study was conducted in eighteen clinical cases of dogs those were brought for elective overiohysrectomy or castration. The animals were randomly divided into three groups with six animals in each group. Atropine sulphate @ 0.04mg/kg b.wt. i.m. and xylazine HCl @ 0.5mg/kg b.wt. i.m. route were administered as premedicants in all the three groups. In group-I, propofol @ 5mg/kg body weight, in group-II, ketamine @ 5mg/kg body weight and in group-III, ketofol @ 4mg/kg body weight was administered intravenously for induction after 15 minutes of preanaesthetic administration. Surgical anaesthesia was maintained for 90 minutes in all three groups viz. group-I, group-II and group-III with propofol @ 2.5mg/kg. b.w., ketamine @ 2.5mg/kg b.wt. and ketofol @ 2mg/kg b.wt. Respectively by intermittent bolus injection (IBI) technique.

The animals were evaluated for the following physiological parameters before administration of pre-anaesthetic agent (0 minute) thereafter at 15, 30, 60 and 90 minutes of injection of anaesthetic agents. The parameters were. Heart rate, Respiratory rate, Systolic pressure and Diastolic pressure and Haemoglobin oxygen saturation. Statistical analysis was performed using windows based statistical package *viz* Microsoft Excel and SPSS. Prior to the conduct of experiment, Institutional Animal Ethics Committee approval was obtained for this study.

Result and Discussion

Heart rate

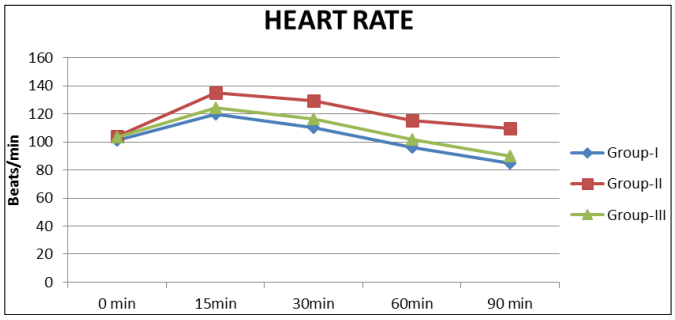

Fig 1: Effect of anaesthetic treatment on heart rate (beat / min) at different time interval in dogs.

Heart rate increased after the administration of atropine and xylazine in all the groups. This is in accordance with the earlier studies in which anticholinergic atropine and glycopyrrolate were found capable of reversing alpha-2-agonist-induced bradycardia in dogs and caused tachycardia (Alibhai *et al*., 1996) [1]. In earlier studies, pre-emptive administration of an anticholinergic was found to prevent the bradyarrhythmias associated with an alpha-2 agonist (Lemke, 2004; Sinclair *et al.,* 2002) [10,14] and to lead to an initial tachycardia (Lemke, 2004) [10]. Therefore, the increase in heart rate after the administration of xylazine might be due to the vagolytic effect of atropine. Significant increase (P<0.05) in heart beat was observed in group –II from 15 minutes till the end of observation than group-I and group -III. This might be due to cardiac stimulatory effects of ketamine (Nusory, 2011) [13], which remained increased for some time as also reported by Kumar *et al.* (2014) [8]. Similar findings were also reported by Hellebrekers *et al.* (1998) [5] who observed higher heart rate during TIVA, in a group of dogs receiving ketamine compared to a group of dogs receiving propofol.

Respiratory rate

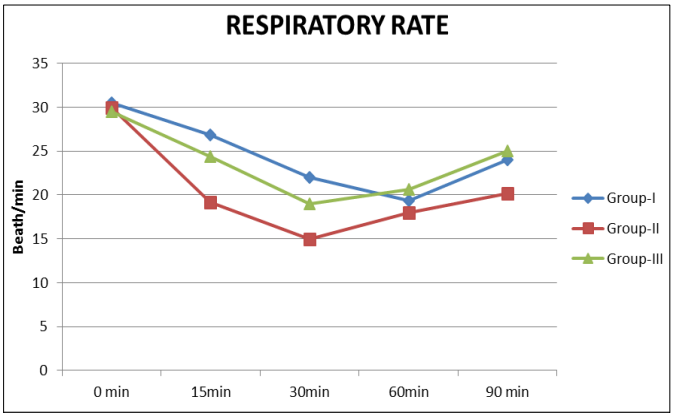

Fig 2: Effect of anaesthetic treatment on respiratory rate (breath / min) at different time interval in dogs

Significantly decrease (P<0.05) of respiratory rate was observed in the animals of group-II than group-I and group -III. There was no significant variation between group-I and group-III. This might be due to combined effect of xylazine and ketamine. Xalazine produce direct depression of the respiratory centres in the brain (Kumar *et al*. 1974) [7]. Ketamine is also a cause of respiratory depression and was observed after bolus administration, often followed by a "apneuistic" breathing pattern, which is characterized by periodic breath holding on inspiration followed by short periods of hyperventilation (Kastner, 2007) [6].

Diastolic pressure

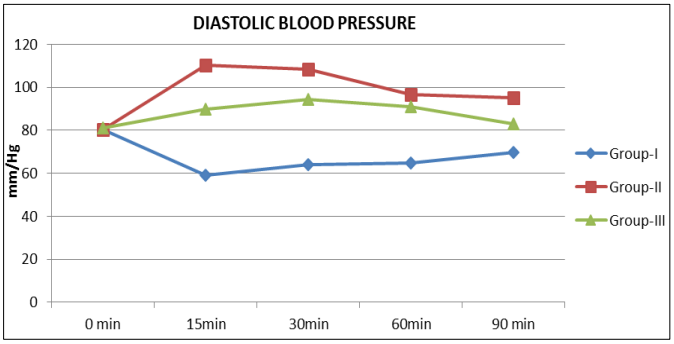

Fig 3: Effect of anaesthetic treatment on diastolic blood pressure (mm hg) at different time interval in dogs.

Significantly higher (*P*<0.01) diastolic pressure was observed in group –II during TIVA while in group-I animals a significant lower (P<0.01) diastolic pressure was recorded for entire period of TIVA after induction.. Group-III animals showed a consistent diastolic pressure during entire period of anaesthesia which might be due to positive synergistic effect of propofol and ketamine when combined together (Larisa *et al.,* 2010) [9].

Systolic blood pressure

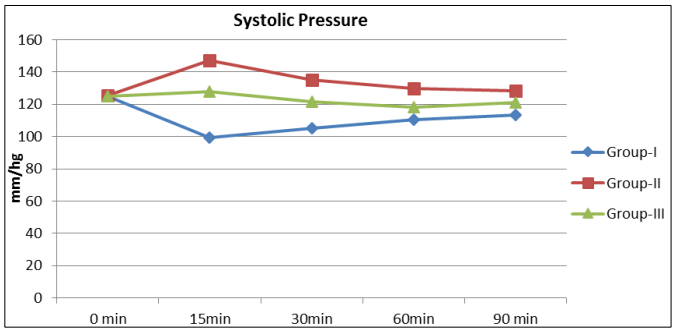

Fig 4: Effect of anaesthetic treatment on systolic blood pressure (mm hg) at different time interval in dogs.

Significantly higher (P<0.01) systolic pressure same as diastolic pressure was observed in group –II during TIVA while in group-I animals a significant lower (P<0.01) systolic pressure was recorded for entire period of TIVA after induction. Group-III animals showed a consistent systolic pressure during entire period of anaesthesia which might be due to positive synergistic effect of propofol and ketamine when combined together (Larisa *et al.* 2010) [9].

Oxygen saturation of haemoglobin (SPO_2)

The Oxygen saturation of haemoglobin (%) of three different treatment groups at different time intervals have been depicted in Fig.5

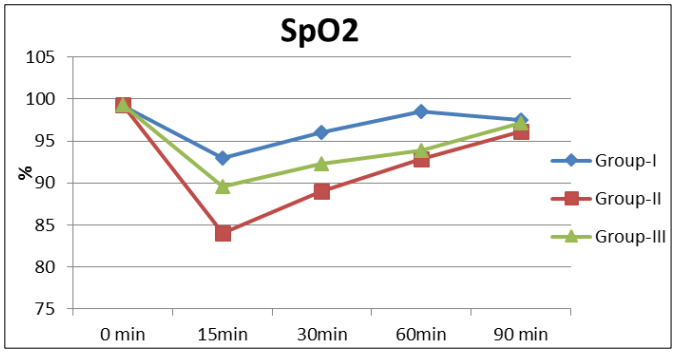

Fig 5: Effect of anaesthetic treatment on Spo_2 (percentage) at different time interval in dogs.

There was significant difference (P<0.01) of SPO_2 among the three experimental groups only at 15 and 30minutes, after that till end of experiment no significant difference was recorded among the groups. In group II significant decrease (P<0.01) of SPO_2 was observed as compared to Group-I and group-III. It might be due to decrease in respiratory rate which occurred as a result of cumulative effect of xylazine and ketamine in early phase of anaestheia. In addition to this vasoconstriction property of xylazine and ketamine might also lead to low pulse oximeter readings (Watkin *et al*., 1987) [16].

Conclusion

The heart rate initially increased and then decreased gradually towards pre-anaesthetic level in all the three groups. The respiratory rate initially decreased and then increased towards pre-anaesthetic level in all the three groups. Both diastolic pressure and systolic pressure remained in a comfortable zone in group-III animals whereas, high blood pressure was recorded in group-II animals and low blood pressure was recorded in group-I animals.

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