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Sedative and analgesic effect of Butorphanol-xylazine-ketamine anesthesia in rabbits

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Abstract
This study was conducted to evaluate the effects of intramuscular (IM) administration of Butorphanol-Xylazine-Ketamine combination for diagnostic and surgical procedures in rabbits. Five rabbits were included in present study undergoing surgical procedures. Basic physiological parameters, analgesic and sedative scores were recorded at 0, 10, 20, 30, 40, 60. Single intramuscular injection of butorphanol (0.1 mg/kg)-xylazine (5 mg/kg)-ketamine (15 mg/kg) was given. The parameters like rectal temperature (RT), depth and rate of respiration (RR), heart rate (HR), oxygen saturation (Spo2) and reflexes were recorded. Butorphanol found to improve sedation and postoperative analgesia of xylazine-ketamine combination in rabbits.

Keywords: Sedative, analgesic effect, Butorphanol-xylazine-ketamine anesthesia, rabbits

Introduction
For many of years the rabbit anaesthesia was a task and was considered as fear within veterinary practice due to the higher mortality rates seen in rabbits compared to the other small domesticated animal. Nowadays advances being seen in as rabbit medicine and surgery. Anaesthesia is a reversible technique that aims to provide a quick, safe, effective, and affordable means of chemical restraint so that medical or surgical procedures can be carried out with the least amount of stress, pain, discomfort, and hazardous side effects to patients or anaesthetists (Haque and Lucky, 2019) [7]. For successful surgical procedures, anaesthesia is required to establish desired sedation, analgesia, and muscular relaxation (Nesgash *et al*., 2016) [1].

Ketamine hydrochloride is a dissociative anaesthetic with sympathomimetic action in the central nervous system (CNS). When administered alone, it causes insufficient muscular relaxation and a persistent pain reflex. Muscle hypertonicity, myoclonus, convulsions, and a dose-dependent decrease of heart function are all possible side effects (Mahmud *et al*., 2014). Therefore, ketamine is usually administered in combination with other medication classes such as benzodiazepines and alpha2 adrenergic agonists to reduce these undesirable and restrictive effects (Özkan *et al*., 2010) [4].

The combination of alpha2-adrenergic agonists and opioids provides a multimodal pain management with superior analgesia, considerable opioid sparing, fewer side effects, and overall patient satisfaction (Peng *et al*., 2015) [13]. Multimodal analgesia is defined as the concept of simultaneous administration of two or more analgesics of various classes to provide the most effective analgesia (Robertson and Taylor, 2004) [17]. For intramuscular (IM) anaesthetic induction, pre-mixed combinations of an opioid, dissociative, and alpha2-adrenergic agonist are commonly used (Kreisler *et al*., 2020) [14].

Therefore, the goal of this study was to determine, anaesthetic and postoperative analgesic effects of butorphanol-xylazine-ketamine in rabbits.

Materials and Methods

Selection and preparation of the patients

The present study was conducted on 6 healthy rabbits undergoing surgical procedures presented to Bai Sakarbai Dinshaw Petit Hospital for Animals (BSDPHA) affiliated with Mumbai Veterinary College, Parel. Accurate weight measurement is also extremely important in rabbits as even small inaccuracies can result in an under/over dosage of large percentages. The patients were not kept off feed, as rabbits should not be starved prior to anaesthesia, the risk of vomiting is nil due to the rabbit's inability to vomit (Varga, 2014) [20]. Regurgitation has (rarely) been reported (Parkinson *et al*, 2017) [12]. Fasting can actually be disastrous as there is the potential for slowing of gut motility and subsequent stasis.
This study was approved by the Ethical Committee.

Treatment protocol followed

Before induction of anaesthesia, all the rabbits received 100% oxygen via face mask @4L/min (Figure 1), The aim of pre-oxygenation was to replace nitrogen in the functional residual lung capacity, with oxygen. This has a significant positive impact on body oxygen stores and, therefore, tolerance to apnoea is increased (Sirian and Wills, 2009) [18].
The Single intramuscular injection of butorphanol (0.1 mg/kg)-xylazine (5 mg/kg)-ketamine (15 mg/kg) was given. A small gauge catheter was then placed into the marginal ear vein with relative by clipping and preparing the area as dogs and cats.
During anaesthesia in normovolaemic patients received 6 ml/kg/hour fluid when undergoing diagnostic procedures, and rabbits undergoing abdominal surgery, received 10 ml/kg/hour fluid to compensate for evaporative losses and the higher risk of haemorrhage Fluid therapy is extremely important as rabbits have a high metabolic rate and their daily fluid requirement is 100 ml/kg/day maintenance. (Eatwell, 2014) [3].

Basic physiological parameters

Heart rate (HR; beats/ min), respiration rate (RR; breaths/min), rectal temperature (RT) was recorded at 10, 20, 30, 40, 60 min post-induction. The oxygen saturation was evaluated periodically by pulse oximetry.

Sedation and recovery quality assessment

The degree of sedation and anaesthesia in rabbits was scored using a modified numerical rating scale (Rodrigo-Mocholí *et al*., 2016). Poor sedation (0–2), light sedation (4–5), moderate sedation (6–9), and severe sedation (10).

Post-operative observation of pain indicator behaviours:

The post-operative pain was evaluated by distant examination. The pain was scored (0-2), using Rabbit Grimace Scale.

Statistical Data analysis: The data analysis was carried out using turkey pairwise comparison test and Friedman test.

Results and Discussion

Basic Physiological parameters

Heart rate: From 0-10min HR maintained its level then after 10mins it decreased significantly from its initial level attaining the lowest value at 40min and then again increased to attain normal level. Typical heart rates in conscious rabbits lie between 240-280 beats per min (range 125-325 bpm, dependent on size and stress levels), but these may drop to 120-160 bpm after pre-medication (Flecknell, 2000) [5].

Respiratory rate: From 0-10 min RR didn't show the significant change, between 10-20mins it decreased significantly and around 60 min it again attended the normal value. Changes in respiratory rate may indicate excessive or too light anaesthesia and/or hypercapnia, whereas changes in the quality of respirations (e.g. increased effort made by the animal or decrease in rebreathing bag movements) may signal an obstructed airway (Longley, 2008) [10].

Rectal temperature: RT significantly decreased from 0to 10 min and then remained relatively stable until 60 min and at and around 60 min it increased to initial level. Pre-medication all animals causes marked hypothermia. Due to the high surface area to bodyweight ratio in the rabbit, this can be exacerbated further. Temperature management is extremely useful especially in the pre, peri and post-operative periods, can be done using heat pads, foil blankets, forced air warming devices and incubators (Rachel, 2018) [15].

Spo2: From 0-10 min spo2 increased significantly and showed some significant fluctuations in-between. Pulse oximeters require adequate pulsations in order They may therefore be Considered unreliable in patients with decreased blood Pressure and/or vasoconstriction. In addition, it should be emphasized that pulse oximeters measure a pulse but this does not ensure an adequate blood flow (Lawson, 1987) [9].

Sedation and recovery quality assessment

Sedation score: There was significant change in sedation score at various time periods. Till 30 min sedation score steadily increased and then started decreasing slightly. Multimodal regimen by combining a tranquillizer and an analgesic in optimal doses is the method of choice to produce the greatest sedative and opioid action with the fewest adverse effects can solve the Problem (Steagall and Monteiro-Steagall, 2013) [19].

Pain score: The median pain score did not differ significantly throughout the procedures. Our findings are consistent with current research on pre-emptive analgesia for pain management (Goodwin, 1998; Reichert *et al*., 2001) [6, 16]. Pre-emptive analgesia is a novel method to postoperative pain management that seeks to avoid or minimize pain before it starts (Kien *et al*., 2019) [8].

Complications

Several anaesthetic emergency conditions such as apnoea or severe respiratory depression (<4 breaths per minute), upper airway obstruction, hypovolaemia, hypo- and hyperthermia, bradycardia and cardiac arrest (Yvonne, 2014). No such complications were noted as the proper anaesthetic management in this study, including careful and continued monitoring of the patient, allowed better control over anaesthetic depth and duration, resulting into decreased risk of emergency situation.

Table 1: Data regarding the parameters studied

Time (Min)	HR	RR	RT	Spo2	Sedation score	Pain score
	Mean				Median	
0	176.66 [a]	33.00 [ab]	101.88 [a]	97.00 [bc]	0.31	0
10	162.33 [b]	35.50 [a]	100.38 [b]	100.00 [a]	2.89	0
20	149.16 [bc]	29.00 [d]	99.83 [b]	98.66 [ab]	4.89	0
30	152.50 [bc]	30.16 [cd]	99.43 [b]	96.00 [c]	9.89	0
40	137.16 [b]	30.16 [cd]	99.81 [b]	98.33 [ab]	8.56	0
60	152.50 [ab]	32.16 [bc]	100.66 [ab]	98.16 [ab]	6.81	0
P- value					0.00	0.500

Means that do not share a letter are significantly different

Fig 1: Pre-oxygenation

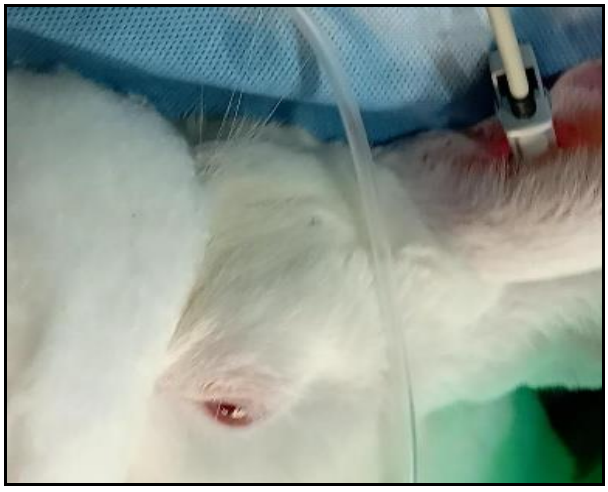

Fig 2: Measurement of SPo2 with pulse oximeter attached

Fig 3: Positioning for surgical procedure

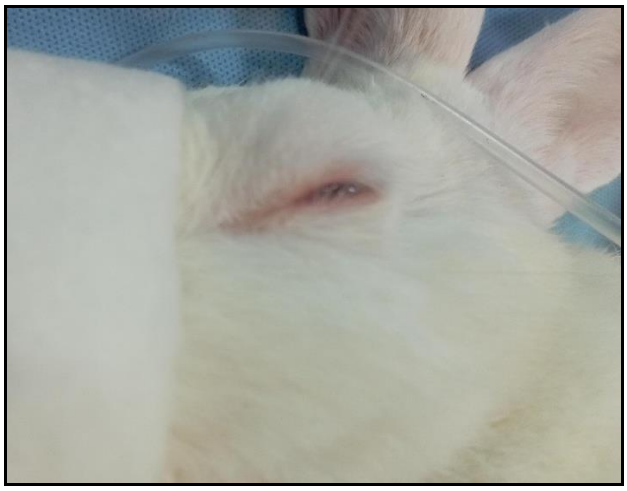

Fig 4: Evaluation of sedation score and pain intra-operatively

Conclusion

Balanced anaesthetic protocols, in particular become commonplace in rabbit medicine, minimizes the risks associated with anaesthesia. It is concluded that intramuscular injection of a Combination of butorphanol, xylazine and ketamine produces a multimodal anesthesia with adequate sedative, analgesic, behavioral, and clinical effects in rabbits undergoing surgical procedures.

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