

## **The Sedative and Analgesic Potentials of Dexmedetomidine Hydrochloride using Constant Rate Infusion Technique in Rabbit**

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**Target Audience:** Farm Animal Handlers, Veterinarians and Animal Scientists

### **Abstract**

*This study evaluated the effective sedative and analgesic doses of dexmedetomidine hydrochloride in rabbits using the Constant Rate Infusion (CRI) technique. Eight healthy adult New Zealand White rabbits with an average weight of  $1.93 \pm 0.33\text{kg}$  were used for the study. They were starved of food but water was provided 30 minutes before the study. The CRI infusion was prepared in 500ml bags of lactated Ringer's solution. Each of the rabbits received an initial dose of  $20\mu\text{gkg}^{-1}$  dexdomitor<sup>®</sup> intramuscularly at the thigh muscle. The procedure was repeated using  $40\mu\text{gkg}^{-1}$ . Venous access was secured thirty minutes later, the fluid was connected to the cannula and was set to flow at daily fluid maintenance rate of  $90\text{mlkgday}^{-1}$ . Neither sedation nor analgesia was achieved with  $20\mu\text{gkg}^{-1}$ . Slight to moderate sedative effect was achieved at  $40\mu\text{g/kg}$  with significant reduction in heart, pulse and respiratory rates. In conclusion,  $40\mu\text{g/kg}$  of dexdomitor<sup>®</sup> intramuscularly produced mild to moderate sedative effect which may be used for chemical restraint of rabbits. The initial loading doses of  $20\mu\text{g/kg}$  and  $40\mu\text{g/kg}$  dexmedetomidine hydrochloride did not give any analgesic effect.*

**Keywords:** Analgesia, Dexmedetomidine Hydrochloride, Rabbit, Sedation, CRI

### **Description of the problem**

Rabbits are small mammals in the family *Leporidae* of the order *Lagomorpha*, found in several parts of the world (1). They are small, furry mammals with long ears, short fluffy tails and strong, large hind legs. They vary in colour and size, ranging from 1 to 7 kilograms depending on the breed (2)

Rabbits are easily stressed and the stress can be caused by pain, disease, unfamiliar surroundings, transport, rough handling or proximity of potential predators such as dogs, cats or ferrets.

Hence, many rabbit patients are already stressed by their underlying disease (3).

Dexdomitor<sup>®</sup> (dexmedetomidine hydrochloride) is a synthetic  $\alpha$ -2 adrenoceptor agonist with sedative and analgesic properties (4). Dexdomitor<sup>®</sup> is a potent and highly selective  $\alpha$ -2 adrenoceptor agonist with sympatholytic, sedative, amnestic, and analgesic properties (5). Dexdomitor<sup>®</sup> is indicated for use as a sedative and analgesic agent which can be used for chemical restraint to facilitate clinical examinations, clinical procedures,

minor surgical procedures and minor dental procedures. It is suitable for sedation and analgesia during perioperative periods: as premedication, as an adjunct for general and regional anaesthesia, and as post-operative sedative and analgesic agent. Atipamezole chloride (Antisedan) is the reversal agent of dexdomitor<sup>®</sup>.

A constant rate infusion (CRI) is a dosing regimen used to deliver a constant amount of a particular drug per unit time (6). The intravenous administration of drugs through constant rate infusions allows a consistent blood concentration hence producing analgesia with fewer peaks and troughs with overall lower doses being used, and therefore, fewer side effects (7).

Very little work has been done on the use of dexdomitor<sup>®</sup> in rabbit considering the fact that the use of rabbit in researches and as meat animal is gaining grounds in our contemporary world. This work is aimed at determining the sedative and analgesic potentials of dexdomitor<sup>®</sup> in New Zealand White rabbits.

### Materials and Methods

Eight apparently healthy adult rabbits with an average weight of  $1.93 \pm 0.33$  kg were used for this study. They were acclimatized for three weeks and each rabbit was starved of food but water was provided 30 minutes before the study.

A 500ml bag of lactated Ringer's solution for constant rate infusion was prepared by adding  $68.78 \mu\text{g}$  of dexdomitor<sup>®</sup> into the bag to give a dosing of  $1 \mu\text{g}/\text{kg}/\text{hr}$ . An initial loading dose of  $20 \mu\text{kg}^{-1}$  of dexdomitor<sup>®</sup> was injected intramuscularly through the thigh

muscle. The procedure was repeated using a loading dose of  $40 \mu\text{g}/\text{kg}$ . The bag of fluid was connected to the intravenous cannula and allowed to flow at a rate in drops/second depending on the specific weight of the rabbits. The fluid was allowed to flow for one hour. A daily fluid maintenance of  $90 \text{ml}/\text{kg}/\text{day}^{-1}$  was used (8).

The baseline values for the heart, pulse and respiratory rates and rectal temperature of the rabbits were taken with the electrodes on the Multi-parameter patient monitor. Each rabbit was monitored continuously for one hour for all the physiological parameters using the patient monitor and records of the parameters were taken every 10 minutes.

The analgesic effect was monitored using the Numerical rating scale (NRS). Variables used were heart rate, ventilation, comfort of animal and response to pin-prick at the paw of the hind limb.

### Results and Discussion

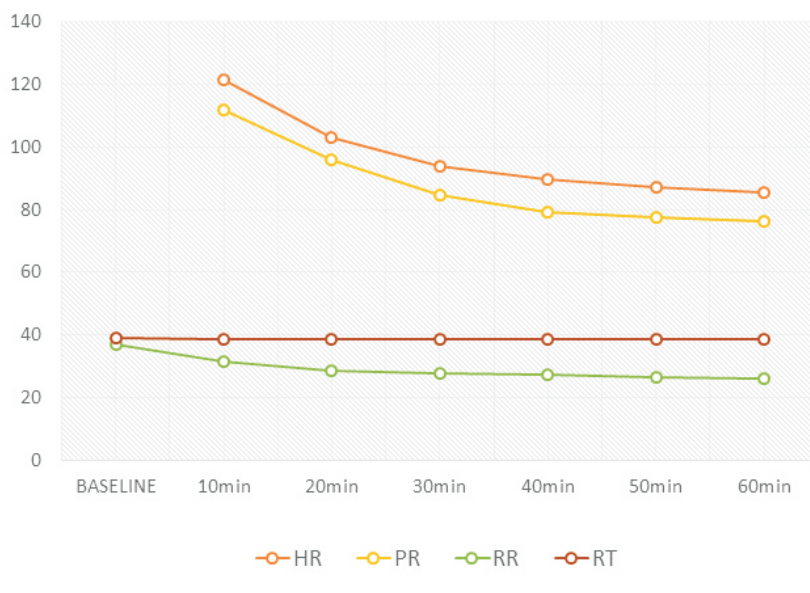
Sedation was not achieved at a loading dose of  $20 \mu\text{g}/\text{kg}$  in seven of eight rabbits but was achieved at a loading dose of  $40 \mu\text{g}/\text{kg}$  in all the rabbits. The onset of drug action observed for those administered with  $40 \mu\text{g}/\text{kg}$  was between 19 to 25 minutes which was reflected in the disinterest of the rabbits in their environment and the progression of their posture from standing to sternal recumbency while peak effects were observed 30 minutes thereafter. Also, a mild to moderate sedation was achieved with a loading dose of  $40 \mu\text{kg}^{-1}$  in seven of eight rabbits as reflected in the body

posture. The rabbits were either on sternal or lateral recumbency. This is as reported by (9) in cats.

The study shows a significant decrease in the heart and pulse rates in beats per minute,  $85.6 \pm 7.1$  and  $76.2 \pm 10.03$ , in sedated rabbits compared with the baseline values of  $124.3 \pm 7.6$  and  $84.5 \pm 10.04$  respectively. This agrees with the work of (5) who reviewed dexdomitor® in pediatric patients. It is observed that

the rate of reduction in the heart and pulse rates was stronger in the initial 40 minutes post dexdomitor® administration (Figure 1). This is thought to be due to the initial rise in plasma concentration of the drug after induction. Attainment of steady state due to the constant rate of infusion is also thought to be responsible for the steady reduction subsequently.

Slight reduction in the respiratory rates



**Figure 1: Graphical representation of the mean heart rate (HR), pulse rate (PR), respiratory rate (RR) and rectal temperature (RT) in rabbits administered with 40µg/kg of dexmedetomidine gluconate**

**Table 1: Sedation Scale in rabbits administered with 20µg/kg and 40µg/kg dexmedetomidine gluconate**

	R1	R2	R3	R4	R5	R6	R7	R8	Mean
Rating 20µg	0	0	0	0	1	0	1	0	0.25±0.46
Scale 40µg	1	2	3	2	2	2	2	1	1.88±0.64

**KEY:**

Alert	No Motor deficits, equivalent to pre-baseline	0
Mild sedation	Cannot stand, can remain sternal, may struggle	1
Moderate Sedation	Can raise head, usually laterally recumbent	2
Heavy sedation	Non response, cannot raise head	3

to  $26.0 \pm 1.22$  breaths/minute was observed compared to the baseline value of  $37.0 \pm 1.87$  breaths/minute in sedated rabbits. This is also as reported by (5) who worked on pediatric patients. There was no observable effect on the rectal temperature throughout this study even though (9) reported a significant reduction at 90 minutes post administration in the rectal temperature in cat.

### Conclusion and application

Sedation was not achieved with  $20\mu\text{g}/\text{kg}$  of dexmedetomidine hydrochloride.  $40\mu\text{g}/\text{kg}$  of dexdomitor<sup>®</sup> intramuscularly produced mild to moderate sedative effect which may be used for chemical restraint of rabbits. The initial loading doses of  $20\mu\text{g}/\text{kg}$  and  $40\mu\text{g}/\text{kg}$  dexmedetomidine hydrochloride did not give any analgesic effect.

### Recommendation

Further studies using  $60\mu\text{g}/\text{kg}$  and  $80\mu\text{g}/\text{kg}$  of dexmedetomidine hydrochloride should be carried out in rabbits to determine the most appropriate dose that is required to achieve surgical plane of anaesthesia and analgesia.

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