

## VARIATIONS OF GLYCAEMIA AFTER ALFAXALONE INDUCTIONS IN RABBITS. PARTIAL RESULTS.

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### **Abstract**

*Alfaxalone is a neurosteroid with general anesthetic properties. His steroid structure, analog with progesterone, might have an influence on patient glycaemia. The aim of our study was to assess variations of glycaemia after alfaxalone induction.*

*For this study we used 7 female adult laboratory rabbits premedicated with fentanyl (0.0125 mg/kg) and droperidol (0.625 mg/kg) intramuscular. Alfaxan<sup>®</sup> was administered intravenously at a total dose of 3mg/kg by a constant rate infusion over 60 seconds using a syringe pump. Blood samples were drawn prior to and at 2, 4, 6, 10, 15, 20, 30 after induction by an indwelling catheter in the central auricular artery for instant blood glucose determination. Mean value of arterial blood glucose recorded was 154,36 mg/dl (81-262) with the highest peak at minute 4 after induction.*

*Glucose variation remained within normal limits with the highest value at minute 4. Other studies showed an increased in plasmatic glucose after progesterone administration. Women using the progesterone-T intrauterine device showed blood glucose increased after three hours. A study made on rats showed an increase of blood glucose 30 minutes after progesterone administration.*

*The theory that alfaxalone may influence plasmatic glucose have to be further studied on a higher number of animals, however is interesting the fact that in minute four after induction when rabbits suffered the most profound cardio-respiratory depression, blood glucose was at the peak. More extensive monitoring and a pharmacokinetic study are needed to comment accurately on alfaxalone effects on rabbits.*

**Key words:** alfaxalone, blood glucose, rabbit.

### **INTRODUCTION**

Alfaxalone is an analog of progesterone with neuron-active properties. It is registered for use in dogs and cats as Alfaxan<sup>®</sup>. It was also tested with good results on horses, ruminants, rabbits and other small mammals, reptiles and even amphibians. The study wants to demonstrate alfaxalone action over blood glucose level in rabbits because of its steroid structure.

## MATERIALS AND METHODS

Six healthy young adult rabbit females conducted the research, all normal laboratory white breed. Food and water were not withheld prior to premedication. They were kept in a controlled environment. All rabbits were premedicated with the same dose of fentanyl 0.0125mg/kg (Sublimaze<sup>®</sup>, 50µg/mL) and droperidol 0.625 mg/kg (Droleptan<sup>™</sup>, 2.5 mg/mL) (Canellas J. et al., 1996; Strack L.E. et al., 1968; Tillman P. et al., 1983; Walden N.B., 1978) intramuscular in the lumbar region 15 minutes prior to cannulation and kept in a special contention box. Both ears were shaved and disinfected with chlorhexidine soap and alcohol to be prepared for vein and artery cannulation. For catheterization we used 22G catheters (blue) (Diehl K.H. et al., 2001; Morton D.B. et al., 2001; Sjøberg J.G. et al., 2003). Vein catheterization was realized over lateral auricular vein and was used for anesthetic induction. Arterial catheterisation was realised over central auricular artery and it was used for blood sampling (Tutunaru A.C. et al., 2012).

Induction was produced using alfaxalone (figure 1) 3 mg/kg (Alfaxan<sup>®</sup>, 10 mg/mL) was administered intravenously through a 22G catheter in the lateral auricular vein by a constant rate infusion over 60 seconds using a syringe pump (Marsh M.K. et al., 2009).

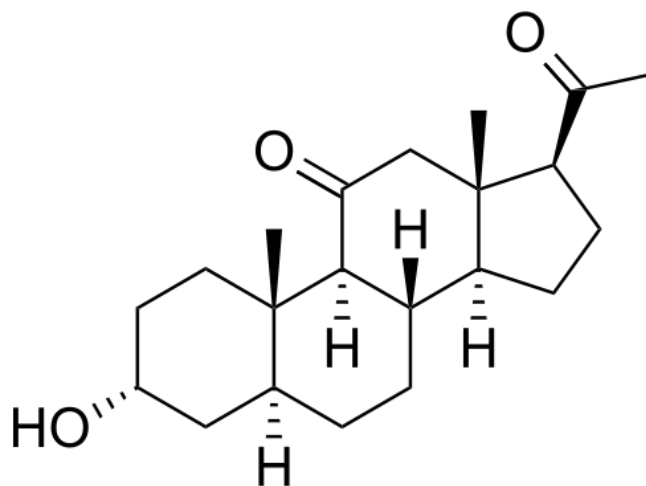


Figure 1. Alfaxalone chemical structure

All rabbits were intubated using blind technique with 3.5 mm endotracheal tubes and they breathed spontaneously room air. Respiratory function was assessed by measuring respiratory rate, the oxygen saturation of hemoglobin in the peripheral blood (SpO<sub>2</sub>) and the end-tidal CO<sub>2</sub> (EtCO<sub>2</sub>). Cardiac function was assessed by measuring heart rate using a pulse oximeter. The level of anesthesia was monitored by evaluating ear and paw pinch reflex, as well as ocular signs such as nystagmus, exophthalmia and the loss of palpebral and corneal reflexes.

Arterial blood samples were taken before alfaxalone induction and in minute 2, 4, 6, 10, 15, 20, 25 and 30 after induction. Glicemia was assessed using a classical glucometer (Ascensia® Contour® Blood Glucose Meter, Bayer®).

## RESULTS AND DISCUSSIONS

Arterial blood glucose mean value was 154.36 mg/dL (range: 81-262) with the highest peak at minute 4 after induction (Figure 2).

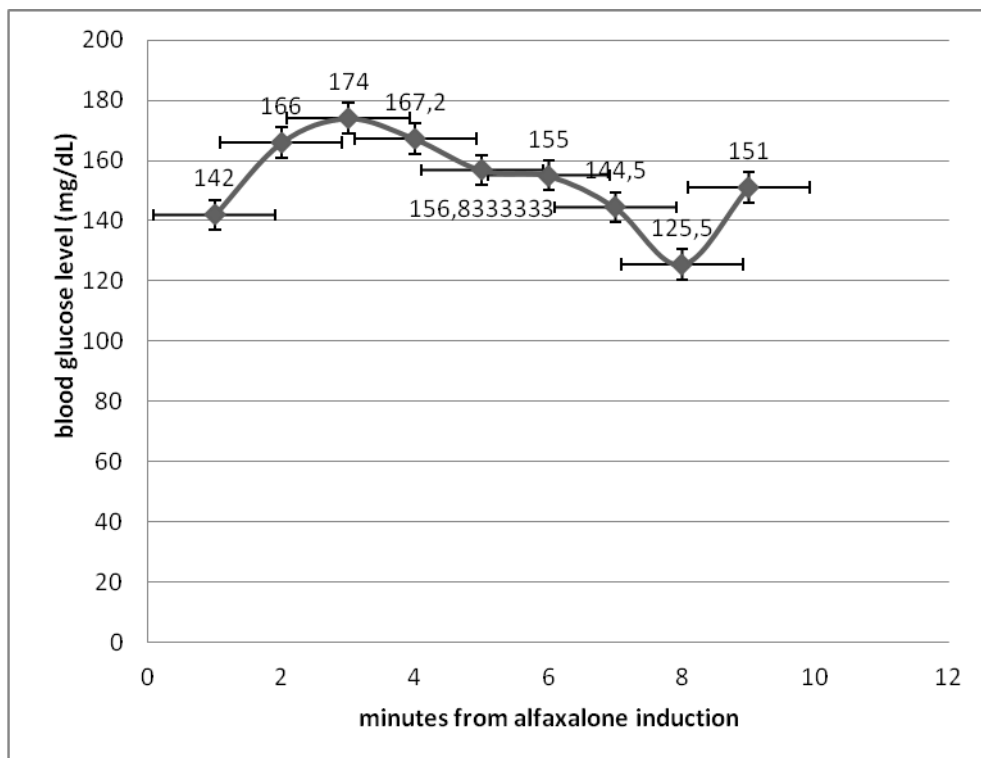


Figure 2. Blood glucose variation before and after alfaxalone induction

The mean respiratory rate recorded was 39 breaths/minute (range: 16-65). Two rabbits showed apnea after induction for ten seconds and respectively two minutes. Oxygen saturation ( $SpO_2$ ) had a mean value of 91% (range: 42-100). The minimum values were recorded in those two rabbits which suffered of apnea in minute 2-4 after induction. Mean end tidal  $CO_2$  recorded ( $EtCO_2$ ) was 24.8 mmHg (range: 13-37). Mean heart rate recorded was 198 beats/minute (range: 115-300) with the lowest value at minute 4 after induction.

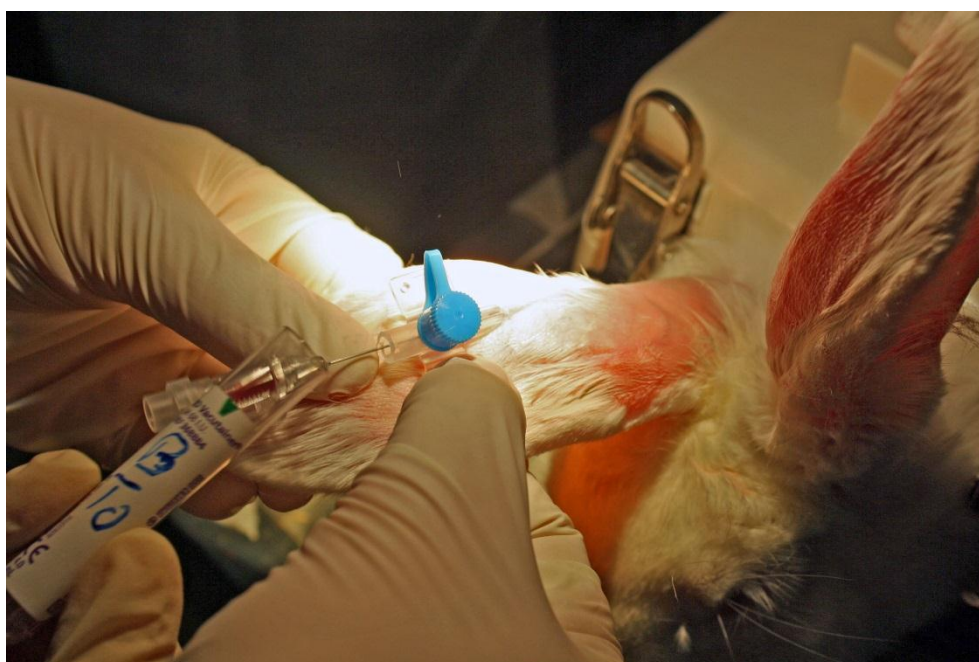


Figure 3. Blood sampling from central auricular artery using a vascular catheter

Alfaxalone is a synthetic neuron-active steroid. In this research we wanted to check for the first time if alfaxalone, as a steroid and a progesterone analog, can modify blood glucose levels. Glucose variation remained within normal limits with the highest value at minute 4, the minute with most pronounced cardio-respiratory depression. Amer et al. (1990) showed that on goats increased glucose levels results from administration of Saffan. Other studies showed an increased in plasmatic glucose after progesterone administration. Women using the progesterone-T intrauterine device showed blood glucose increased after three hours (Spellacy et al., 1978). A

study made on rats by Mei-Po and Yang M.M.P. (1970) showed an increase of blood glucose, 30 minutes after progesterone administration but this study also demonstrates that adrenal medulla is apparently involved in the hyperglycemic effect of progesterone. Another study on rats showed that Althesin<sup>®</sup> injected intra-peritoneal did not modify blood glucose concentration (Mezza et al., 1981).

The theory that alfaxalone may influence plasmatic glucose have to be further studied on a higher number of animals, however is interesting the fact that in minute four after induction when rabbits suffered the most profound cardio-respiratory depression, blood glucose was at the peak. More extensive monitoring and a pharmacokinetic study are needed to comment accurately on alfaxalone effects on rabbits.

## **CONCLUSIONS**

We recorded a blood glucose peak even if it had not exceeded physiological limits correlated with alfaxalone maximum action over cardio-respiratory functions suggesting that alfaxalone influence glucose plasmatic level.

More pharmacological and pharmacokinetic studies are needed over alfaxalone induction in rabbits to demonstrate its effect over blood glucose.

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