Available online at www.scholarsresearchlibrary.com

Scholars Research Library

Scholars Research Library

Central European Journal of Experimental Biology, 2014, 3 (2):1-5
(http://scholarsresearchlibrary.com/archive.html)

Central European Journal of Experimental Biology
Scholars Research Library
ISSN: 2278–7364

Effects of the anaesthetic / tranquillizer treatments (Ketamine, Ketamine+Acepromazine, Zoletil) on selected plasma biochemical parameters in laboratory rats

Heithem Bougherara and Omar Bouaziz

Laboratoire de Gestion de la Santé et Productions Animales, Institut des sciences Vétérinaires, Université Constantine 1, Algeria

---

ABSTRACT

Anaesthetics currently used, such as ketamine and Telitamine may differently affect a number of physiological parameters include glucose, urea, creatinine, alkaline phosphatase, AST, and ALT.and its effects have been widely studied in particular the influence of anesthetic molecules on plasma biochemical parameters in a variety of animal species (rabbits, rats, mouses ...).The aim of our study was to compare the effect of three anesthetic protocols on certain plasma biochemical parameters order to have a protocol that has the finest effects. We conducted on 35 rats (Rattus norvegicus) divided into seven groups of 05 different individuals anesthesia under standardized conditions .Three protocols were tested, ketamine alone (K), ketamine + Acepromazine (K-A) , Tiletamine + Zolazepam (Z) . It seemed possible that these protocols do not generate significant changes in blood biochemical parameters of rats used in this study (GLUCOSE, UREA, CREATININE, AST, ALT, ALP) except that urea was observed an increase in values whose the levy is made in day 0 (D0) and 120 minutes after administration , which guide us to a suspicion of possible effect of general anesthesia regardless of the protocol on the renal function in laboratory rats . Given the importance of variations observed results, it is difficult to exclude any influence of the injection of ketamine - acepromazine , ketamine alone or tiletamine - zolazepam on these variations. We must remain vigilant in the interpretation of the analyte during sedation in these protocols.

***Key words**: effects anesthesia- Ketamine-Zoletil- laboratory rats- blood biochemistry*

INTRODUCTION

In veterinary medicine it is necessary to use restraints (chemical restraint) for the realization of various examinations and sampling blood safely to the vet and with minimal stress to the animal. The choice of protocol to use should take into account the possible interference drug use with examinations and the influence of these anesthetics on different organs of the animal.

Effects of general anesthesia on plasma biochemical parameters been studied in several animal species such as rabbits [6], monkey [10], dog [7], cat [11], the results of these studies are quite variable from one item to another.

It is important to know the existence, nature and magnitude of these modifications to correctly interpret the analyzes after plenum or anesthesia, the choice of protocol can be a very important parameter influencing the results.

A balanced anesthetic protocol is a combination of several drugs to obtain both an easy to control unconsciousness , analgesia and a powerful myorelaxation facilitating the act to achieve. Anesthetic protocol (choice of drugs and doses) minimizing the risk of anesthesia.

Anaesthetics currently used, such as ketamine and Telitamine may differently affect a number of physiological parameters include the glucose , urea, creatinine , alkaline phosphatase, AST , and ALT .

The objective of this study was to compare the effects of three anesthetic protocols (ketamine, ketamine + acepromazine, zoletil) and their influence on some biochemical parameters in laboratory rats in order to have the molecule and the anesthetic protocol has less effect.

MATERIALS AND METHODS

This study was conducted on 35 laboratory rats breed Rattus norvegicus (albinos) (originally Institut Pasteur Algiers). Rats are females elderly (3-5 months), weighing between 180 and 280 g. In the laboratory, the rats were placed in plastic cages with stainless steel lid, equipped with bottles. A thick layer of wood chips is deposited at the bottom of the cages and renewed every 3-4 days and more often for experienced animals and females term so they can make their nest. cages are cleaned and sterilized once or twice per week. The rats were fed daily with a food granules and receive water in abundance.

The rats were bred in the animal house of the Institute of Veterinary Sciences El Khroub, Constantine University 1. Study was conducted from March to July 2013.

In this study, cardiac puncture was used for rats under anesthesia by which the levy is to (D0), the sacrifice of the animal slaughtered for the control rats and levies (D7) in unanesthetized rats. Three anesthetic protocols were studied. Anesthetics used are: (Ketamine alone Ketamine + Acepromazine, Tiletamine + Zolazepam.)

The parameters analyzed are as follows: Glucose, Urea, Creatinine, ALT (alanine aminotransferase), AST (aspartate aminotransferase), ALP (alkaline phosphatase)

Experimental design

Animals were randomly assigned to three treatment groups (n=10 per group):

Ketamine (K) (100 mg/kg IM), Ketamine +Acetylpromazine (acépromazine) (K-A) (30-75 mg/kg +2.5-3 mg/kg IM) , Tiletamine/zolezepam (zolétil) (Z) (20 mg/kg IM).

The doses and the administration route were based upon pre-liminary studies and a review of previous anaesthetic studies involving laboratory rats [2].

Blood samples were obtained at three time points:

Before injection, and at 120 min and 7 days after injection of the anaesthetics.

Blood was placed into heparinized tubes, the analyzes were conducted in a private medical laboratory,the plasma biochemical parameters were measured by the controller (RX © DAYTONA Clinical Chemistry Analyser from the Randox RX Series).

Statistics

All results were stored and reported in an Excel file, the analysis statistic was based on descriptive statistics, analyzes of variance, calculations Correlation and regression analysis using Excel and program (STATITICA.5.5 student version Copyright © StatSoft France1984 2013) the comparison of means is made using the statistical program (Minitab ® 15.1.30.0), Data for plasma ALT, AST, ALP, GLUCOSE, UREA, CREATININE, concentrations and were analysed using a two-way analysis of variance (ANOVA) with repeated measures in each group to assess changes with time. A value of $p < 0.05$ was considered significant.

RESULTS

The results of plasma biochemical parameters of protocol K, K+A and Z are shown in Tables 1, 2 and 3 respectively. Most haematological findings were within normal reference ranges for the species.

In the day 0 (D0)

An increase ($P < 0.05$) in plasma glucose was observed at 120 min in the Z group (Table 3)
No significant changes in plasma ALT, AST, ALP, CREATININE were observed in any group.

An increase (P < 0.05) in plasma UREA was observed at 120 min in the K, K+A and Z groups (Table 1, 2, 3) Twenty-four hours after induction of anaesthesia, these values had returned to control levels.

Table 1

KETAMINE (K)							
K (D0)	**active number**	**Mean**	**Minimum**	**Maximum**	**Variance**	**Ec-Type**	**Er-Type**
GLUCOSE	**5**	**1,228**	**1**	**1,34**	**0,02087**	**0,144465**	**0,064607**
URER	**5**	**0,61***	**0,42**	**0,76**	**0,0191**	**0,138203**	**0,061806**
CREA	**5**	**9,414**	**8,47**	**10,66**	**1,24913**	**1,117645**	**0,499826**
AST	**5**	**246,4**	**177**	**303**	**3350,8**	**57,8861**	**25,88745**
ALT	**5**	**63,2**	**46**	**94**	**351,7**	**18,75367**	**8,386895**
ALP	**4**	**120,5**	**74**	**162**	**1429,667**	**37,81093**	**18,90547**
*All values are expressed as mean SEM. * P <0.05 indicates signiicant difference from the control values*							

Table 2

KETAMINE + ACEPROMAZINE (K+A)							
K+A (D0)	**active number**	**Mean**	**Minimum**	**Maximum**	**Variance**	**Ec-Type**	**Er-Type**
GLUCOSE	**5**	**2,17**	**0,39**	**3,6**	**1,65705**	**1,287265**	**0,575682**
URER	**5**	**0,896***	**0,79**	**1,07**	**0,01288**	**0,11349**	**0,050754**
CREA	**5**	**10,082**	**6,71**	**14,31**	**9,09057**	**3,015057**	**1,348375**
AST	**5**	**269**	**181**	**382**	**5205**	**72,14569**	**32,26453**
ALT	**5**	**73**	**38**	**90**	**430**	**20,73644**	**9,273618**
ALP	**5**	**191,6**	**134**	**245**	**1995,3**	**44,66878**	**19,97649**
*All values are expressed as mean SEM. * P <0.05 indicates signiicant difference from the control values*							

Table 3

ZOLETIL (Z)							
Z (D0)	**active number**	**Mean**	**Minimum**	**Maximum**	**Variance**	**Ec-Type**	**Er-Type**
GLUCOSE	**5**	**1,548***	**1,22**	**1,77**	**0,05297**	**0,230152**	**0,102927**
UREA	**5**	**0,626***	**0,32**	**0,87**	**0,04363**	**0,208878**	**0,093413**
CREA	**5**	**8,696**	**6,92**	**11,07**	**4,01383**	**2,003455**	**0,895972**
AST	**5**	**174**	**84**	**410**	**18706**	**136,7699**	**61,16535**
ALT	**5**	**53,6**	**31**	**98**	**716,3**	**26,76378**	**11,96913**
ALP	**3**	**171**	**92**	**297**	**12163**	**110,286**	**63,67365**

*All values are expressed as mean SEM. * P <0.05 indicates signiicant difference from the control values.*
In the day 7 (D7)

No significant changes in plasma ALT, AST, ALP, GLUCOSE, UREA and CREATININE were observed in any group.

DISCUSSION

In our study, it was observed that the anesthetic protocol based on the use Ketamine alone induced no effect on the biochemical parameters except urea which there is an increase of the values obtained at day 0 and 120 minutes after injection , Comparing our results with the results of the nearest studies from ours seems to highlight differences:

The glucose values obtained are close to those of a study on rabbits showed no change [13]. However, in domestic carnivores increased blood glucose was observed [7].

For urea, it was observed an increase of its values. In contrast, Kumar [7] reports no change in dogs. concerning Ketamine alone, no change in creatinine values has was observed which confirms the results of the study by Kumar [7] working on carnivores.

The single administration of ketamine in rats confirmed the absence of significant changes in ALT and AST. This result is comparable to that reported by Muir [8] in cats. By cons in goats, a significant increase was observed [4]. In monkeys, there was a significant decrease in values of PAL [3]. On the contrary an increase was reported by Van der Merwe [14].

On Ketamine + Acepromazine protocol, no significant changes in clinical chemistry parameters tested were observed except increased values of blood urea. This result is comparable to that reported by Regnier [11] in a study on cats but with a protocol consisting of acepromazine alone.

The use of ketamine with diazepam shows different results depending case: In rabbits, a significant increase in ALT, AST, blood urea and creatinine is described. These last two changes are more sources of clinical misinterpretation since the values are outside the range of usual values [6].

Some authors have demonstrated a toxic effect on the liver cells by diazepam [12].

It is possible that the use of ketamine in combination with diazepam may highlight a possible effect on the liver [5]. Diazepam may be responsible for increasing values of ALT, AST, blood urea and creatinine.

Regarding Tiletamine + protocol Zolazepam, increased blood sugar and uremia was observed, but no change was observed in AST, ALT, creatinine and PAL. The data on the effects of the protocol on Tiletamine + Zolazepam blood parameters are very rare. To our knowledge, only one study has been reported by Peinado [9] on a kind of Spanish ibex interval for which no reference exists. It is therefore difficult to assess the actual effects of the drug and more for domestic carnivores to extrapolate the observations.

The increase in urea levels recorded in our study could be the result a short-term effect on renal function. Indeed, the increase in blood urea was reported by Gonzalez [6] in rabbits using the protocol diazepam ketamine (10, 60 and 120 minutes), and the protocol ketamine-xylazine at 10 and 120 minutes. This would explain the lack of increase of urea in rats on the 7th day after administration in all protocols.

But it is impossible, given the importance of variations, to exclude influence of the injection of Ketamine + Acepromazine, ketamine alone or ZOLETIL ® on the renal and hepatic function. We must remain vigilant when interpreting these results in accordance with our sedation protocols.

The comparison of results obtained in our study and those of other authors can explain these variations: It is possible that the effect of anesthetics on the biochemical parameters are in the first few minutes (30-60 minutes) after administration. In effect Farhadi [5] reports an increase in glucose levels in rabbits 30 to 60 minutes after intramuscular administration of ketamine, followed by a decrease after 90 minutes.

The variation of our results of AST, ALT and ALP with the results of other studies could be due to the protocol used (blood sampling after 120 minutes and 7 days after anesthesia). However, several sampling times (48, 72 hours ...) are needed to evaluate a possible hepatic toxicity [5].

Many factors can affect the biochemical parameters, especially species, genetic factors, microbial environment, age, sex, diet [1].The type of feed used in our breeding (pelleted feeds for rabbits), could be a factor influencing the biochemical parameters analyzed. The use of females in our study and breeding conditions in the animal of our institute can beings parameters that influence the results [1].

CONCLUSION

Our study on the effects of three anesthetic protocols on parameters plasma biochemical laboratory rats shows variations compared to other studies. It seemed to us that these protocols do not generate large changes values of blood biochemical parameters of rats used in this study except urea which there is an increase in values in almost all protocols used, which guide us to a suspicion of any possible effect of general anesthesia of the protocol on renal function in laboratory rats. But it should be noted that the variations observed in the different studies concerning the influence of anesthesia results on blood biochemistry, it is impossible, given the importance of these observed variations, to exclude any influence of the ketamine acepromazine injection, ketamine alone or tiletamine-zolazepam on these variations. We must remain vigilant when interpreting this analyte during sedation according to these protocols.

It might be interesting to perform the same type of study by choosing other protocols, either by changing the route of administration, and even the use of molecules orally acepromazine such as tablets or by studying molecules on which few data exist as to their effects by ZOLETIL example, and it is advisable to increase the number of animals in the testing in order to test the molecules in different phases of time.

REFERENCES

[1] Guy.J le rat de laboratoire 1-reactif biologique .technique de laboratoire 7e édition. Paris : Masson, **1981**. 115 p.
[2] WVU **(** West Virginia university) ACUC Approved Guidelines: Anesthesia and Analgesia in Rats 10/**2011**.
[3] Benett J.S., Gossett K.A., Mccarthy M.P., Simpson E.D. *Veterinary Clinical Pathology*, **1992**, 21:15-18.
[4] Dehghani S., Sharifnia N., Yahyaei M.R., Souri A. Clinical, haematological and biochemical effects of xylazine, ketamine and their combination in caprine and feline. Proceedings of the 4th International Congress of Veterinary Anaesthesia, **1991**, 129-133.
[5] Farhadi N, Rostami H., *Journal of Applied Biological Sciences* 3 (1): 65-67, **2009**
[6] Gonzalez GIL A., Illera J.C., Silvan G., Illera M. *Laboratory Animals*, **2003**, 37:155-161.
[7] Kumar N., Kumar A., Singh B. *Indian Journal of Animal Sciences*, **1989**, 59:815-818.
[8] MUIR W.W. Anesthesia for dogs and cats with cardiovascular disease. Part I. Comp.Contin. Educ. Pract. Vet., **1998**, 20, n° 1, 78-87 .a
[9] Peinado V.I., Fernandez, Arias A., Viscor G., Palomeque J. Haematology of Spanish ibex (Capra pyrenaica hispanica) restrained by physical or chemical means**, 1993.**
[10] Plooy W.J., Schutte P.J., Still J., Hay L., Kahler C.P. *Journal of the South African Veterinary Association*, **1998,** 69:18-21.
[11] Regnier A., Guelfi J.F. Effet de la sédation par la xylazine, l'acépromazine et la kétamine sur l'hémogramme du chat. Revue de Médecine Vétérinaire, **1982**, 133:243- 248.
[12] Strombeck D.R., Guildford W.G. Hepatic necrosis and acute hepatic failure.In: Sm all Anim al Gastroenterology. London: Wolfe Publishing, **1991,** pp 574±92
[13] Suleiman S. and Hanan A. *American Journal of Pharmacology and Toxicology* **2009**, 4 (2):38-45,
[14] Van Der Merwe J., Du Bruyn D.B., Van Der Walt W.H., SLY M.R. *Journal of the South African Veterinary Association*, **1987**, 3:125-128.