# CLINICAL AND HEMATOLOGICAL STUDY OF THE EFFECT OF A MIXTURE OF OLIVE OIL AND COD LIVER OIL ON STAGES OF INDUCTION AND RECOVERY OF XYLAZINE, KITAMINE OR COMBINATION OF KETAMINE AND XYLAZINE IN RABBITS

Rana K. Abdulsamad, Jinan A. Bannay, Ibrahim MH AL Rashid

Department of Surgery and Obstetrics, College of Veterinary Medicine, University of Basrah,Basrah,Iraq.

Keyword: Ketamine, Xylazine, Cod liver oil, Olive oil.

Corresponding Author: dr.ibrahimveterinary@gmail.com

# ABSTRACT

The study showed that the effect of the combination of olive oil and whale liver oil on the stage of anesthesia where the results were shortened in the duration of anesthesia, both in the stage of induction or the stage of recovery. Thirty animals were used in this experiment. The experimental animals divided into three groups, each group divided into two subgroups containing five animals. Mix 1 ml olive oil with 1 ml of whale liver oil for 1 week before anesthesia.

1 - Ketamine group (K): injected with Ketamine Hcl in a dose of 20 mg / kg/body weight

2 – Xylazine group (X): injected with Xylazine Hcl in a dose of 5 mg / kg/body weight

3. Ketamine / Xylazine group (K-X): injected with by mixture of Ketamine Hcl in a dose of 20 mg with Xylazine Hcl in a dose 5mg / kg/ body weight.Blood tests showed no changes

### **INTRODUCTION**

Olive oil is a natural product from olive fruits, olive oil chemically composite from many fatty acids such as citric acid, butyric acid, palmitic acid, oleic acid, linolenic acid, meristic acid, allergic acid, and other components as well as vitamin E, wax, fatty alcoholics and  $\beta$ -carotene (1,2,3). Functions of olive oil to diminish free radicals, liberate energy, decreasing cholesterol, decreasing hypotension as well as to distract cancerous cells (4,5).

Cod liver oil is unsaturated fatty acid extract from liver of fishes (6), it is contain a large amount of vitamin A, vitamin D, docosahexaenoic acid, eicosapentanoic acid, cod liver oil occasionally used as a favors and antioxidants additive (7,8).

Ketamine is phencycline derivative components and dissociative anesthesia, which is synthesis in 1956 by Park-Davis. It used in veterinary medicine in 1962 (9). A number of systemic receptors appear interact with ketamine; N-methyl-D-aspartate(NMDA) receptor, opioid receptor, adrenergic receptor, muscarinic receptor, voltage-sensitive calcium ion channel (10). The dose depends on species of animals, age, healthy status and genius (11).

Xylazine is a 2(2,6 dimethylphnyl amino)-4H-5,6-dihydro-1,3 thiamine hydrochloride (12), it is classified as an effective sedative, analgesic, muscle relaxant, immobilizing and hypnotic agent in domestic animals (13).

Balanced anesthesia is better and safety use in rabbits than ketamine or Xylazine alone, for surgical anesthesia in rabbits the effect of combination of ketamine and Xylazine shown by central nervous system mediated through  $\alpha$  2 adrenergic receptors (14).

### **MATERIALS AND METHODS**

Thirty rabbits were used in this study, there were weighing  $2 \pm 0.05$  kg, their aged between 8-9 months. Clinically, the rabbits were examined to ensure the body health. The animals are divided into three main groups, each group had ten rabbits, each main group subdivided into 2 subgroups (treated and control each subgroup had 5 animals). Kitamine group 5 rabbits dosage with oils and 5 rabbits without dosage,

Basrah Journal of Veterinary Research, Vol. 17, No. 3, 2018 Proceeding of 6th International Scientific Conference, College of Veterinary Medicine University of Basrah, Iraq

Xylazine group and K-X combination group same pattern of Kitamine group. Ketamine 20 mg/kg b.w, Xylazine 5mg /kg b.w, K-X combination (K 20mg +X 5 mg) /kg b.w (15). Treated subgroups were dosage by olive oil 1 cc and cod liver oil 1 cc / animal /day for seven day before anesthesia. All animals in treated subgroup were dosage the mixture of oils by syringe 1cc+1cc /animals /day for seven day, after seven days all animals in subgroups were anesthetized by ketamine, Xylazine, and K-X combination.

Blood samples were drone for examination at periods of 5 min, 1 hr, and after recovery, clinical symptoms were recorded such as pedal reflex, needle sensations, and eye reflex at 0, 10, 20, 30, 40, 50, 60, 70, 80, 90, 100 min after injection, symbols (+ or -) were according to response the reflex (-=0, +=10) to knowledge statistical values.

### RESULTS

#### **Blood samples**

#### Ketamine group

Table(1) blood parameters in different period								
group	Control group			Kitamine group				
Time	5 min	1 hr	A R	5 min	1 hr	A R		
RBC $10^{12}$ +SD	5.5 ±	5.1 ±	4.1 ±	$5.1 \pm 0.2$	$4.1 \pm 0.7$	$5.1 \pm 0.7$		
	0.3	0.2	0.7					
WBC 10 <sup>9</sup> +SD	$7.0 \pm$	$7.2 \pm 1.1$	9.2±1.6	$10.2 \pm 1.6$	9.2±1.6	$12.2 \pm 1.6$		
	2.1							
HB g/dl+SD	$11.5 \pm$	$10.2 \pm$	9.2 ±	10.2 ±	$8.2 \pm 0.1$	$9.1 \pm 0.1$		
	0.8	0.1	0.1	0.1				
ALT U/L	70	66	80	90	86	75		
AST U/L	33	38	38	44	48*	44		
*Mean and standard deviation, P value $\leq 0.05$								

### Xylazine group

Basrah Journal of Veterinary Research, Vol. 17, No.3, 2018 Proceeding of 6th International Scientific Conference, College of Veterinary Medicine University of Basrah, Iraq

Table(1) blood parameters in different period							
group	Control group			Kitamine group			
Time	5 min	1 hr	A R	5 min	1 hr	A R	
RBC 10 <sup>12</sup> +SD	5.5 ±	5.1 ±	4.1 ±	$5.1 \pm 0.2$	$4.1 \pm 0.7$	$5.1 \pm 0.7$	
	0.3	0.2	0.7				
WBC 10 <sup>9</sup> +SD	$7.0 \pm$	$7.2 \pm 1.1$	9.2±1.6	$10.2{\pm}1.6$	9.2±1.6	$12.2 \pm 1.6$	
	2.1						
HB g/dl+SD	$11.5 \pm$	$10.2 \pm$	9.2 ±	10.2 ±	$8.2 \pm 0.1$	$9.1 \pm 0.1$	
	0.8	0.1	0.1	0.1			
ALT U/L	70	66	80	90	86	75	
AST U/L	33	38	38	44	48*	44	
*Mean and standard deviation, P value $\leq 0.05$							

# Ketamine/Xylazine combination group

Table(1) blood parameters in different period							
group	Control group			Kitamine group			
Time	5 min	1 hr	A R	5 min	1 hr	A R	
RBC $10^{12}$ +SD	5.5 ±	5.1 ±	4.1 ±	$5.1 \pm 0.2$	$4.1 \pm 0.7$	$5.1 \pm 0.7$	
	0.3	0.2	0.7				
WBC 10 <sup>9</sup> +SD	$7.0 \pm$	$7.2 \pm 1.1$	9.2±1.6	$10.2 \pm 1.6$	9.2±1.6	$12.2 \pm 1.6$	
	2.1						
HB g/dl+SD	11.5 ±	$10.2 \pm$	9.2 ±	10.2 ±	$8.2 \pm 0.1$	$9.1 \pm 0.1$	
_	0.8	0.1	0.1	0.1			
ALT U/L	70	66	80	90	86	75	
AST U/L	33	38	38	44	$48^{*}$	44	
*Mean and standard deviation, P value $\leq 0.05$							

## **Clinical symptoms**

# Ketamine group

group	Control group			Treated group			
Time/ min							
	PR	NS	ER	PR	NS	ER	
10	4+	5+	5+	4+	5+	5+	
20	+++	4+	4+	+++	4+	4+	
30	+	++	3+	++	+++	3+	
40	-	+	+	+	++	+	
50	-	-	+	+	++	+	
60	-	+	-	++	+	-	
70	+	+	+	++	+	+	
80	++	+	+	+++	++	++	
90	+++	++	+++	4+	+++	+++	
100	5+	+++	+++	5+	4+	4+	
A R	5+	5+	5+	5+	5+	5+	
PR : pe	edal reflex,	NS: needle se	ensation, El	R: eye reflex,	AR: after re	ecovery	
1		response, ++ se, ++++= c	<b>U</b> 1	,	ery good resp	ponse,	

# Xylazine group

group	Control group			Treated group			
Time/ min							
	PR	NS	ER	PR	NS	ER	
10	5+	5+	5+	5+	5+	5+	
20	5+	5+	+++	5+	5+	+++	
30	4+	4+	++	4+	4+	++	
40	+++	4+	-	+++	4+	+	
50	++	+++	-	++	4+	-	
60	++	+++	+	++	+++	++	
70	+++	+++	+	+++	+++	++	
80	+++	4+	++	4+	4+	++	
90	4+	5+	++	4+	5+	++	
100	5+	5+	+++	5+	5+	+++	
A R	5+	5+	+++	5+	5+	+++	
PR : pedal r	eflex , NS: 1	needle sensati	ion, ER: ey	e reflex, AR:	after recove	ery	
		response, ++ se, +++++= c			ery good resp	oonse,	

group	Control group			Treated group			
Time/ min							
	PR	NS	ER	PR	NS	ER	
10	4+	5+	5+	4+	5+	5+	
20	+++	4+	4+	+++	4+	4+	
30	+	++	3+	++	+++	3+	
40	-	+	+	+	++	+	
50	-	-	+	+	++	+	
60	-	+	-	++	+	-	
70	+	+	+	++	+	+	
80	++	+	+	+++	++	++	
90	+++	++	+++	4+	+++	+++	
100	5+	+++	+++	5+	4+	4+	
A R	5+	5+	5+	5+	5+	5+	
PR : pedal r	eflex , NS: 1	needle sensat	ion , ER: ey	e reflex, AR:	after recove	ery	
-=no respon ++++: excel		response, ++	• 1	,	ery good resp	ponse,	

#### Ketamine/Xylazine combination group

#### **Statically Analysis**

The data were analyzed statically by used SPSS 18.0 program. Normal values P value  $\leq 0.05$ , the significant values  $\leq 0.005$ .

#### DISCUSSION

The significance olive oil and cod liver oil in process of induction and recovery of anesthesia to decrease unfavorable events in recovery phase and after recovery, the results of treated subgroups compare with control subgroups. There are decrease terminal induction phase time and beginner recovery phase time, this changes reveal to in metabolism activity is differ from control subgroups and treated subgroups. In the present study there are two axials to explain an important this study; first axial, the role of factors which effect on detoxification and depolarization of anesthesia and the second axial the role of activation of these factors which effect on detoxification and depolarization of anesthesia. Detoxification of anesthesia agents toxicity, liver enzymes which play main role to detoxification of anesthetic agents. C-reaction

protein, aspartate transaminase, alanine transaminase and creative kinase are main enzymes to detoxified in rabbits liver, were show the effect of cod liver oil, they were showed significant increase activity when dosage the oil to the rabbits (16,17). Liver enzymes and pancreatic enzymes of the cod liver oil digested to many fatty acids which effect on neurotransmitters such as acetylcholine and dopamine (18,19). Olive oil have many fatty acids and vitamins play important role to activate mitochondria and specific detoxification cell enzymes (cytochrome 450) (20). Neurotransmitters in central nervous system, neurotransmitters in peripheral nervous system and neuromuscular junction those travel nerve impulses and cause sensation (21). The activation cells which response neurotransmitters materials mainly depend on fatty acid in blood stream which similar in cod liver oil (22). Vitamin A and D which support the physiological process in the body. The processes in the present study divided into three parts according to the nature of anesthesia, ketamine is dissociative anesthesia mainly effect on central nervous system, while Xylazine is relaxant and analgesic effects mainly effects on central nervous system, peripheral nervous system and neuromuscular junction, therefore the mixture of cod liver oil and olive oil and their functional process in the body are express on supporting face against to anesthetic agents, but long duration of oils to animals are unfavorable in emergent cases.

### REFERENCES

- Caponio F, Bilancia D, Pasqualon A, Sikoisaka E and Gomasl (2005). Influence of the exposure to light on extra virgin olive oil quality during storge. Eu. Food Res. Tech. 221(2-1): 92-98.
- 2- Salvini N, Sera F, Caruso D, Giavanneilli L, Visioli F, Saiera C, Masala G, Cerati M, Glovacchini V, Gill C and Romani A (2006). Dialy consumption of a high phenol extra virgin olive oil reduced oxidative DNA damage in postmenopausal women. Br. J. Nutr., 95: 742-751.
- 3- Atkinson W, Elmslie J, Lever M, Chambers S and George P.(2008). Dietary and supplementary betaine : acute effects on plasma betaine and homocysteine concentration under stander and post methonine load conditions in healthy male subject. Am. J. Clin. Nutr., 78(3): 577-585.

- 4- Ajuluchkwa NA, Ogechukwu OJ, Ifedioramma OS, Mshelbwala BS and Tochukwu U (2014). Histopathological and Biochemical disrupting effect of escravos crude oil on the liver and heart in chinchilla rabbits. Afr. J. Env. Sci. Tech. 8(3): 203-209.
- 5- Donnelly TM (2004). Disease problems of chinchilla rabbits. In : Quesenbreey KE, Carpenter JW, ed Rerrets, Rabbits and Rodants, Clinical Medicine and Surgery. 2<sup>nd</sup> ed St.Louis MO:Saunder; 255-265.
- 6- Nakbi A, Tayeb W, Grissa A, Issaui M, Chargui I, Ellous M, Miled A and Hammami M (2010). Effects of olive oil and its fractions on oxidative stress and the liver's fatty acid composition in 2,4 Dichlorophenoxyacetic acid treated rats. Nutr. Metab. 7:80.
- 7- Chen W, Tsai C, Yang J J, Liu C T, Kuo WW and Lii CK (2003). The combined effect of garlic oil and fish oil on the hepatic antioxidants and drug metabolizing enzymes of rats. Br. J. Nutr., 89(2): 189-200.
- 8- Gidado A, Zainab A, Hadiza M, Serah D, Anas H, Milala M, Meakins J and Masterson B (2012). Metabolic enzymes activities in fish gills as a biomarkers exposure to petroleum hydrocarbons. J Ethropharmacol. 39,:33-35.
- 9- Smith DJ, Bouchal RL, DeSanctis CA, Monroe PJ, AmedroJB, Perrotti JM and Crisp T (2007). Properties of interaction between ketamine and opiate binding sites in vivo and in vetro. Neuropharmacology 26:1253-1260.
- 10- Lipman NS, Phillips PA, and Newcomer CE.(2016). Reversal of ketamine/xylazine anesthesia in the rabbit with yohimbine. Lab Anim. Sci., 37(4):474-479.
- 11- Stain F, Barjavel MJ, Sandouk P, Plotkine M, Scherrmann JM, and Bhargava NH (1999). Analgesic receponse and plasma brain extracellular fluid pharmakinetics of morphine and morphine-6-beta-D-glucuronidation in rats. J. Pharmocol Exp. Ther. 274: 852-857.
- 12- Kanda T and Hikasa Y (2008). Neurohormonal and metabolic effects of medetommidine compared with Xylazine in healthy cats. Can. J. Vet. Res., 72:278-286.
- 13- Gweba M, Onifade KI, and Faleke OO (2009). Effect of Xylazine sedation on some hematological indices after chloramphenicol pre-treatment in Sokoto red goat. Inter. J. Pharm., 5(1): 76-80.

- 14- Lipman NS<sup>1</sup>, Marini RP,and Erdman SE.(2010). A comparison of ketamine/xylazine and ketamine/xylazine/acepromazine anesthesia in the rabbit. Lab Anim Sci.;40(4):395-405.
- 15- Alrashid IM (2011). A Comparative Study: The Effect of Pulsed and Static Magnetic Field on The Healing of Rupture of Achilles Tendon in Rabbits. J. Bas. Res., 37(4): 56-65.
- 16- Afonne OJ, Onyiarah IV and Orisakwe OE (2013). Toxicity of cheveron escravos crude oil and chemical dispersant on guinea pig testicular function. J. Basic Clin. Physiol. Pharm., 24(4): 321-328.
- 17- Agbogidi OM, Eruotor PG, and Alkparobi SO (2007). Effects of crude oil levels on the growth of maize (*Zea mays* L) Am. J. Food Tech., 2: 529-535.
- 18- Wichmann T, Illing RB, and Starke K.( 2003). Evidence for a neurotransmitter function of acetylcholine in rabbit superior colliculus. Neuroscience.,23(3):991-1000.
- 19- Jimmy Z, Gordon L, and Fain O (1995). Neurotransmitter Receptors of Starburst Amacrine Cells in Rabbit Retinal Slices. J. Neuroscience, 15(7): 5334-5345.
- 20- Bloomfield SA, Miller RF (1986) A functional organization of ON and OFF pathways in the rabbit retina. J Neurosci 6:1-13.
- Wei C, Andrea D, Marian Z, Gilles L, Jean-Real B, and Frangois B. J (1993).
  Effects of Experimentally Induced Ischemia on Dopamine Metabolism in Rabbit Retina. Inves.Ophtha. Visual Science, October 1993, 34,(11): 3140-3149.
- 22- DiPaolo T, Harnois C, and Daigle M. (1996). Assay of dopamine and its metabolites in human and rat retina. Neurosci Lett.,74:250-254.