INNSPUB

International Journal of Biosciences | IJB |
ISSN: 2220-6655 (Print), 2222-5234 (Online)
http://www.innspub.net
Vol. 12, No. 6, p. 123-128, 2018

RESEARCH PAPER OPEN ACCESS

Effect of omeprazole on liver functions of laboratory rat (albino) *Rattus norvegicus*

Suhad Yasin Jassim[1], Rabab Abd Alameer Nasser[2]

Iraq Natural History Research Center and Museum, Bab Al-Muadham, University of Baghdad-Iraq, Faculty of Science, University of Diyala, Iraq

Key words: Drugs, Omeprazole, liver functions, Albino rats, biochemical tests, liver Enzymes.

http://dx.doi.org/10.12692/ijb/12.6.123-128 Article published on June 14, 2018

Abstract

First, the aim of this work was to determine and estimate the effect of Omeprazole drug on liver function in the laboratory rat (Albino) *Rattus norvegicus* by measuring the concentration of alanin aminotransferase (GPT) and aspartate aminotransferase (GOT) enzymes, (18) animals aged (6) weeks and weight of (40-60) g were selected randomly from the animal house of our work place,They were divided into three groups: the first one was administrated (20) mg/kg of drug, second group was given (40) mg/kg and the third group was the control (non treated).The statistical analysis used in this study is the variance analysis test (ANOVA) at ($p< 0.05$) level. After giving medication to animals regularly for three consecutive months without interruption,GPT and GOT enzymes tests were measured and the following results were obtained:Significant increase was observed in the concentration of the GPT enzyme for the second group (40) mg/kg at $p< 0.05$ (43.1167)I u/lcompared with the control group (26.4350) I u/l, while there was no significant difference between the first group (20) mg/kg and the control. As for the GPT test; a significant increase was observed for both dosage groups (20) & (40) mg/kg respectively at $p< 0.05$ (116.7417) (68.9050) I u/l compared with control group (63.5083) I u/l. From the above results it can be confirmed that the long-term use of Omeprazole leads to an imbalance in liver enzymes and this will damage its functions thus this damage will be transmitted to all organs of the body.

* **Corresponding Author:** Suhad Yasin Jassim ✉ suhad.yasin@yahoo.com

Introduction

Omeprazole is classified as a drug belonging to the group of proton pump inhibitors, which plays an important role in the short-term treatment of ulcers infections; reduce acidity of the stomach, and in the treatment of *Helicobacter pylori* infection. Although this type of medicine, known as PPI (Proton Pump Inhibitors) as mentioned earlier, has a great effectiveness and high safety ratio, but its long use may cause some problems (Jassim & Hussin:2016; Hasanin, 2014; Andersson *et al*,1990;).

After oral administration, Omeprazole is absorbed by the gastrointestinal tractand the metabolism processes of the drug occur in the liver which in turn converts the drug into simple substances that can be excreted by urine, for these reasons, taking omeprazole for a long period of time can lead to big liver dysfunction (Cederberg *et al*, 1989).

The liver is one of the largest organs in the body and its function is metabolisms through liver enzymes, which are one of the important terms in the biochemistry, the importance of this enzymes is that in the case of liver infections (hepatitis) note that the level of the rate In the blood rise up before the onset of symptoms and can reach up of 100 times more than normal. High rate of liver enzymes caused by cirrhosis of the liver, hepatitis, hepatic and liver cancer, obesity and drugs lead mainly to liver diseases and imbalance of enzymes *(*Hamada, 1976*)* among these enzymes are : Transamnases; there are two types A- Glutamate pyruvate Transaminase (GPT) or Alanine Transaminase (ALT) B-Glutaamate Transaminase (GOT) or Aspartate Transaminase (AST) These enzymes are present in the liver as well as in other organs of the body, GPT and GOT tests can help to identify diseases and infections that affect the liver where the rate of the enzymes much higher according to damage of liver (Moser,1997 ;Xing *et al,*2006*).*

The aim of this study is to identify the effect of Omeprazole on the function of the liver represented by GPT and GOT enzymes.

Material and methods

(18) laboratory rats (albino) aged (6) weeks and weight of (40-60) g were obtained from the Animal House of the Iraq Natural History Research Center and Museum - University of Baghdad , The rats were placed in their own cages in the laboratory at (24± 1°) and (12:12h) light, there were fed on commercial standard pelletsdiet and tap water (Koolhaas, 2010).

The animals were divided into three groups each one containing (6) rats (n=6), group (1) was the control (untreated), group(2) was administered orally (20mg/kg) and group(3) was administered with a dose of (40 mg/kg) once daily. The duration of experiment was three months.

Samples

3ml of blood was withdrawn by a sterile syringe from the animal after anesthetizing and stabilizing it on the anatomy site,the blood was placed in test tubes inside the centrifuge at a speed of 3000 cycles per minute for 15 minutes.

Then take the serum and keep it at (° 20-) until use. The serum was used to measure the level of alanin aminotransferase (GPT/ALT), (Segal and Matsuzawa,1970) and aspartate aminotransferase (GOT/AST) (Itoh and Srere, 1970; Schumann *et al*, 2002*)*. The results were then stabilized and statistical analysis was carried out.

Statistics

The statistical processes calculated for the results of this study are using the variance analysis test (ANOVA) at ($p< 0.05$) (McDonald, 2014)

Results and discussions

Means, Std. Deviation and Std. Error of (GPT) test values Summarized in Table 1 which shows that there is no significant differences at $p< 0.05$ in the test values of the group given (20) mg/kg of the drug compared to the control group, While a significant difference was found for the group that was administrated (40) mg / kg with compared to the

control Table 2, with significant differences between groups (20) and (40) mg/kg, respectively,as shown in Table 3.

This conclusion is in line with the findings of many researchers, where (Bian *et al*, 2017) confirmed the existence of a significant link between acidity drugs and liver diseases.These results contradict the findings of the (Francavilla *et al,* 1989) who observed no effect for both of famotidine and omeprazole on the liver, (Cheng, 2013) noted the presence of anti-inflammatory effects by inhibitors of acidity, but recommended researches to find out their other effects, while (KINUTHIA, 2017 said that Omeprazole can cause a defect in the liver, which has been demonstrated in the present work as the drug's effect on the liver's effectiveness in the rat.

Table 1.(Means, Std. Deviation and Std. Error of (GPT) test values).

	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum
					Lower Bound	Upper Bound		
Cont	6	26.4350	6.29485	2.56986	19.8290	33.0410	17.38	33.55
20mg	6	25.5267	5.94288	2.42617	19.2900	31.7633	19.25	33.21
40mg	6	43.1167	7.83339	3.19797	34.8960	51.3373	33.67	53.21
Total	18	31.6928	10.45592	2.46448	26.4932	36.8924	17.38	53.21

Table 2.(ANOVA).

	Sum of Squares	Df	Mean Square	F	Sig.
Between Groups	1177.022	2	588.511	12.953	.001
Within Groups	681.525	15	45.435		
Total	1858.547	17			

(Dependent Variable: cont).

When the drug was administered at a dose of (20) mg, there was no significant effect on the value of the enzyme compared to the control group, But when the dose given to the animal is increased to (40) mg of omeprazole for three consecutive months, there was a significant increase in the value of the GPT enzyme compared to the control group at $p< 0.05$.

Table 3. Multiple Comparisons.

LSD

(I) VAR00004	(J) VAR00004	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
1.00	2.00	.90833	3.89166	.819	-7.3865-	9.2032
	3.00	-16.68167-*	3.89166	.001	-24.9765-	-8.3868-
2.00	1.00	-.90833-	3.89166	.819	-9.2032-	7.3865
	3.00	-17.59000-*	3.89166	.000	-25.8849-	-9.2951-
3.00	1.00	16.68167*	3.89166	.001	8.3868	24.9765
	2.00	17.59000*	3.89166	.000	9.2951	25.8849

*. The mean difference is significant at the 0.05 level.

This means that there is a very clear impact ofthis drug on the liver, which is expected after the knowledge of the side and negative effects of Some medications include omeprazole on the organs of the body, especially the liver, which metabolisms

processes completely, occurs *(*Regardh *et al,* 1985*;* Cederberg *et al,* 1989*)*.

The same results were found in the (GOT) test values, as shown in Table 4, indicating that the differences were significant between the first dose group (20mg/kg) compared with the control group at p< 0.05 (Table 5), As well as between the second dosage group (40mg/kg) with the control group Table 4, There were also significant differences between the two treated groups illustrative in Table 6,It can be said that Omeprazole has a significant effect on liver enzymes because the value of this test was high in both dosage groups.

Table4. (Means, Std. Deviation and Std. Error of (GOT) test values).

	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum
					Lower Bound	Upper Bound		
1.00	6	63.5083	9.07147	3.70341	53.9884	73.0283	50.32	75.26
2.00	6	68.9050	8.86314	3.61836	59.6037	78.2063	58.45	80.31
3.00	6	116.7417	23.41338	9.55847	92.1708	141.3125	95.22	153.25
Total	18	83.0517	28.54066	6.72710	68.8587	97.2446	50.32	153.25

Table5.(ANOVA).

	Sum of Squares	Df	Mean Square	F	Sig.
Between Groups	10302.517	2	5151.258	21.796	.000
Within Groups	3545.165	15	236.344		
Total	13847.682	17			

Dependent Variable: GOT.

This enzyme is an important indicator to determine the health of liver in the body, any increase or decrease in enzyme value over its normal range is evidence of an inflammation or liver dysfunction (Kim *et al,* 2008).

It is worth mentioning that this medicine is given to the patients by the doctor for a short period, In contrast to what happened in the current study where the administration of animals for three consecutive-regular months and this is considered sufficient time to cause damage to some members of the body, especially the liver.

Table6. (Multiple Comparisons).

(I) VAR00011	(J) VAR00011	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
1.00	2.00	-5.39667-	8.87589	.552	-24.3152-	13.5218
	3.00	-53.23333-*	8.87589	.000	-72.1518-	-34.3148-
2.00	1.00	5.39667	8.87589	.552	-13.5218-	24.3152
	3.00	-47.83667-*	8.87589	.000	-66.7552-	-28.9182-
3.00	1.00	53.23333*	8.87589	.000	34.3148	72.1518
	2.00	47.83667*	8.87589	.000	28.9182	66.7552

*. The mean difference is significant at the 0.05 level.

The apparent increase in the values of this enzyme (Aspartate Transaminase (AST)) is evidence of inflammation in the liver and this is what has been mentioned in many studies *(*Sauvet and, *Schouler, 1992;Wei et al, 2013)*. In the case of liver infection or viruses or any other disease, we find that the level of activity of these enzymes in the serum rises even before the onset of symptoms and can be up to 100 times the normal level (Aragon & Younossi, 2010).

Conclusions

In the current study we can come up with the following: Elevated serum GPT & GOT enzymes, when the body is exposed to Omeprazole, In other words, when taking the drug for a long time (three months), the rate of the two enzymes above in the exposed animals increased compared with the control. Since these two enzymes are considered indicators of liver effectiveness, the liver may have inflammation that reduces its function. Studies in this regard are few. In the future, it is possible to expand the study of this drug to include its impacts on the effectiveness of kidney and heart and whether it has other side effects, which are not known especially after taking it for a very long time.

Acknowledgements

First of all, I would like to thank all those who helped me to complete this work, especially Dr. Amer M. Hussin and Lecturer / Mahmoud Hussein Abdul Rahman/ Iraq Natural History Research Center and Museum/ University of Baghdad, My great gratitude goes to my colleague and professor Dr. Ezeddin Albayyar- Faculty of Science/ University of Al-Anbar,

References

Jassim SY, HussinAM.2017. The Effect of Omeprazole Drug on the Blood Picture of Laboratory Rat Rattus Norvegicus, IOSR Journal of Pharmacy and Biological Sciences, Volume 12, Issue 3 Ver. IV, PP 56-59.

Hasanin A H. .2014 Impact of omeprazole on bone remodeling in normal and ovariectomized Wistar rats. Eur Rev Med PharmacolSci, Jul;18(13), 48-56.

Andersson T, Cederberg C, Edvardsson G, Heggelund A, Lundborg P.1990. Effect of omeprazole treatment on diazepam plasma levels in slow versus normal rapid metabolizers of omeprazole, Clin Pharmacol Ther, Jan; **47(1),** 79-85.

Cederberg C, Andersson T, Skånberg I. 1989. Omeprazole.Pharmacokinetics and metabolism in man. Scand J Gastroenterol Suppl.**166,**33-40.

Hamada H, Ohkura Y.1976. A new photometric method for the determination of serum glutamate pyruvate transaminase activity using pyruvate and glutamate as substrates. Chem. Pharm. Bull.; **24,** 1865–1869.

Moser I, Jobst G, Svasek P, Varahram M, Urban G.1997.Rapid liver enzyme assay with miniaturized liquid handling system comprising thin film biosensor array. Sens. Actuators B,**44,**377–380.

Xing-Jiu Huang, Yang-Kyu Choi, Hyung-Soon Im, Oktay Yarimaga, Euisik Yoon, and Hak-Sung Kim. 2006. Sensors (Basel). Jul; **6(7),**756–782.

Koolhaas JM. 2010. The UFAW Handbook on the Care and Management of Laboratory and Other Research Animals (Eighth Edition Hubrecht, R. & Kirkwood, J. (eds.). s.n.,) 311-326.

Segal HL, Matsuzawa TL. 1970. Alanine aminotransferase (rat liver). Methods in Enzymology **17A,**153-159.

Itoh H, Srere PA.1970. A new assay for glutamate-oxaloacetate transaminase Anal. Biochem. **35,**405–410.

Schumann G, Bonora R, Ceriotti F, Férard G, Ferrero CA, Franck PFH, Gella FJ, Hoelzel W, Jørgensen PJ, Kanno T, Kessner A, Klauke R, Kristiansen N, Lessinger JM, Linsinger TP, Misaki H, Panteghini M, Pauwels J, Schiele F, Schimmel HG, Weidemann G, Siekmann L. 2002. IFCC primary reference procedures for the measurement of catalytic activity concentrations of enzymes at 37 °C: Part 5. Reference procedure for the measurement of catalytic concentration of aspartate-aminotransferase. Clin. Chem. Lab Med.; **40,**725–733.

McDonald JH. 2014. Handbook of Biological Statistics (3rd ed.). Sparky House Publishing, Baltimore.

Jin Bian MD, Anqiang Wang MD, Jianzhen Lin MD, Liangcai Wu MD, Hanchun Huang, MD, Shanshan Wang MD, Xiaobo Yang, MD, Xin Lu, MD, YiyaoXu MD, Haitao Zhao, MD. 2017. Association between proton pump inhibitors and hepatic encephalopathy A meta-analysis Apr; **96(17),**e6723.

Francavilla A, Panella C, Polimeno L, Di Leo A, Makowka L, Baronel M, Amoruso A, Ingrosso M, Starz TE. 1989. Effect of cimetidine, ranitidine, famotidine and omeprazole on hepatocyte proliferation in vitro, Journal of Hepatology**8,**32-41, Elsevier.

Cheng E. 2013.Proton Pump Inhibitors for Eosinophilic Esophagitis, current Opinion in Gastroenterology. **29(4),**416–420.

Kinuthia E. 2017: Omeprazole Liver Side Effects, Liver strong.com.

Regårdh CG, Gabrielsson M, Hoffman KJ, Löfberg I, Skånberg I. 1985. Pharmacokinetics and metabolism of omeprazole in animals and man--an overview. Scand J Gastroenterol Suppl.108, 79-94.

Ray Kim W, Steven L,Flamm Adrian M, Di Bisceglie. 2008. Serum activity of alanine aminotransferase (ALT) as an indicator of health and disease, Hepatology, **47(7),**1363-1370.

Sauvet P, Schouler L. 1992 Omeprazole and liver function,Rev Med Interne. Sep-Oct; 13(5):359-63. Review. French.

Li W, Zeng S, Yu LS, Zhou Q. 2013Pharmacokinetic drug interaction profile of omeprazole with adverse consequences and clinical risk management. Ther Clin Risk Manag**9,**259–271.

George A, Zobair MY.2010, When and how to evaluate mildly elevated liver enzymes in apparently healthy patients, C level and Clinic Journal of Medicine **7(7)**.

HenryC, Bodenheimer Jr. 2008: Serum activity of alanine aminotransferase (ALT) as an indicator of health and disease **47(4),** 1363–1370.