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Some Pharmacological Studies on Lamivudine in Rats

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Abstract

The present study was carried out to evaluate the side effects of lamivudine administration and its immunological effect in male albino rats through estimating some hematological parameters, liver and kidney functions, humoral immunity and phagocytic capacity. Forty adult male albino rats were divided into 2 groups (control and treated groups) each of 20 rats. The treated group was orally administered Lamivudine for 60 days in a dose of 9 mg/kg BW once daily. In the current study, all hematological parameters were within the normal range except the packed cell volume which increased at 60 days (45.60±0.87). IgG was increased in the treated group at 15, 30, 45 and 60 days (1183.96±11.64, 1203.58±2.02, 1185±13.27 and 1181.16±11.74, P<0.01, respectively), while IgM did not reveal any significant change. In treated group, there were no significant changes in serum urea and creatinine except after 15 days of drug administration the creatinine level was significantly decreased. Aspartate aminotransferase was decreased (24.00±1.94, P<0.01) after 45 days of drug administration, while alkaline phosphatase did not significantly changed. Alanine aminotransferase was decreased (26.20±1.95, 31.40±1.77, 29±3.39 and 22±1.41, P<0.01) at 15, 30, 45 and 60 days, respectively. The total protein increased at 15, 30, 45 and 60 days of drug administration in the treated group (8.64±0.12, 8.07±0.19, 8.06±0.46 and 8.60±0.22, P<0.01, respectively). Moreover, total globulins were significantly increased at 15, 30, 45 and 60 days of drug administration (4.91±0.13, 4.92±0.35, 4.31±0.26 and 4.34±0.16, respectively). The present results revealed an increase in the phagocytic percent and phagocytic index at 30 (1.12±0.09 and 79.15±3.64) and 60 days (0.93±0.08 and 77.13±4.45) of drug administration, respectively. Based on the current findings, it may be concluded that lamivudine had no serious side effects on hematology, both liver and kidney functions with a promising immunostimulant effect.

Keywords: Hematology, Lamivudine, Creatinine, IgG

Introduction

Hepatitis B virus (HBV) causes acute inflammation of the liver, a symptomatic infection or chronic liver disease. Adult infected with HBV can develop cirrhosis and/or liver cancer in 2-10% [1]. Hepatitis B should be recognized with the viral replication and histological evidence of the active liver which based on the serological and histological analysis that mainly derived from two years studies in HbeAg-positive patients with compensated liver disease [2]. Antiviral drugs are medicines that cure or control viral infections. Historically, the discovery of antiviral drugs has been largely fortuitous. Developing antiviral medicines are difficult, because most of drugs that kill viruses also damage the host's cells [3].

Lamivudine was used for treating the infection caused by human immunodeficiency virus (HIV) or hepatitis B virus. HIV is the virus that causes acquired immune deficiency syndrome (AIDS). Lamivudine was administered with zidovudine (AZT) or with other medications used for treating HIV [4]. Lamivudine was suggested for treating adult patients with compensated chronic Hepatitis B**.** The aim of this study was to investigate the

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lamivudine side effects on liver and kidney functions and some hematological parameters with special reference to its immunological effects in male albino rats.

Material and Methods

Experimental animals and design

Forty adult male albino rats, were divided into 2 homogenized groups (control and treated) each of 20 rats. Lamivudine was orally administered to the treated group for 60 days in a dose of 9 mg/kg BW once daily according to Paget and Parnes [5]. Two blood samples from 5 rats in each group were collected at 15, 30, 45 and 60 days after Lamivudine administration. The first blood sample was collected on anticoagulant [EDTA] for hematological studies and estimating the phagocytic capacity of the drug after 30 and 60 days. The second was collected without EDTA for separating serum. The serum was used for determining liver and kidney function tests and estimating IgG and IgM after 15, 30, 45 and 60 days.

Hematological studies

Erythrocytic (RBC's), Total leucocytic counts (TLC) and differential leucocytic counts were performed using the improved neubauer chamber [6]. The acid hematin method was carried out to determine the hemoglobin (HB) [7]. The packed cell volume (PCV), erthrocyte indices as mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC) were determined with the microhematocrit method [8].

Determination of immuno-globulins

The procedure using serum samples consists in an immunoprecipition in agarose between an antigen and its homologous antibody [9].

Kidney and Liver function tests

Serum urea level was estimated according to the method of Chaney and Marbach [10]. While, serum creatinine level was determined colormeterically [11]. Colorimetrical method was used to estimate the serum transaminases (aspartate aminotransferase (AST) and alanine aminotransferase (ALT)) [12] and alkaline phosphatase (ALP) [13]. While, serum total protein was estimated according to the method of Weichselbaum [14].

Phagocytic capacity of the drug

It was estimated according to the method described by Boyum [15].

Statistical analysis

In order to assess the influence of Lamivudine on different biochemical and immunological measurements, independent samples t-test (Welch t-test in cases of unequal variance) was used. Homogeneity of variance of sample groups was checked using Levene's test. Analysis was done using Statistical Package for Social Sciences version 22.0 (SPSS IBM Corp., Armonk, NY, USA). Results are reported in means ± SEM (Standard Error of Mean), probability values were indicated by * when $P < 0.05$ and ** when $P < 0.01$. The statistical analysis was based on the intention-to-treat population.

Results

Lamivudine elicited a significant decrease of RBC's count, HB, MCHC, TLC and neutrophil counts, with a significant increased in MCV and MCH which showed macrocytic anemia after 30 days of drug adminstration. There were no significant changes in all tested parameters except an increase in PCV (45.60±0.87) after 60 days of Lamivudine administration (Table 1). IgG revealed a significant increase (1183.96±11.64, 1203.58±2.02, 1185 ± 13.27 and 1181.16±11.74) after 15, 30, 45 and 60 days of Lamivudine administration, respectively while IgM was non-significantly changed (Table 2).

Table 1: The Effect of lamivudine given orally into male albino rats once daily at a dose of (9 mg/kg b.wt.) for 30 and 60 days on some hematological parameters and cellular immunity (Mean ± S.E, n = 5)

Parameters	Control	Treated 1[a]	Control	Treated 2[b]
RBCS[c](10^6 / mm^3)	6.85± 0.07	4.82±0.17**	6.90± 0.12	7.44±0.32
Haemoglobin (gm%)	13.23± 0.14	11.16±0.16**	13.00±0.28	13.60±0.48
PCV[d] (%)	43.00±0.57	40.33±0.33*	40.00±0.57	45.60±0.87**
MCV[e] (FL)	62.90±1.49	83.84±3.82*	61.95±2.04	61.49±1.59
MCH[f] (Pg)	19.28± 1.2	23.19±0.88*	18.59±0.40	18.28±0.17
MCHC[g] (%)	31.42± 0.6	27.69±0.56*	30.59±0.33	29.79±0.42
TLC[h]($x10^3$ / mm^3)	7.51± 0.26	4.79 ±0.53*	7.14±0.08	6.79±0.42
Neutrophil ($x10^3$ /mm^3)	2.38± 0.19	1.34± 0.44**	2.13±0.06	2.02±0.16
Eosinophil ($x10^3$ /mm^3)	0.14± 0.02	0.37± 0.03	0.33±0.01	0.29±0.03
Basophil ($x10^3$ /mm^3)	0.13±0.01	0.09 ± 0.005	0.11 ± 0.008	0.11 ± 0.006
Lymphocyte ($x10^3$/mm^3)	3.23± 0.08	2.94± 0.12	3.52±0.12	3.24±0.28
Monocyte ($x10^3$ / mm^3)	1.06± 0.06	1.04± 0.04	1.00±0.003	1.15±0.07

[a] Treated 1: after 30 days of drug administration; [b] Treated 2: after 60 days of drug administration; [c] RBCS: red blood cells; [d] PCV: packed cell volume; [e] MCV: Mean corpuscular volume; [f] MCH: Mean corpuscular haemoglobin; [g] MCHC: Mean corpuscular haemoglobin concentration; [h] TLC: Total leucocytic counts; * Significant at $P < 0.05$ and ** Significant at $P < 0.01$.

The serum urea and creatinine showed no significant changes except after 15 days of drug administration in treated group, the creatinine levels was significantly decreased (0.39 ± 0.05). Lamivudine provoked a high significant decrease in the ALT (26.20 ± 1.95 , 31.40 ± 1.77, 29.00 ± 3.39 and 22.00 ± 1.41) at 15, 30, 45 and 60 days after drug administration, respectively while ALP were non-significantly changed when compared with the control values in all testing periods. AST was non-significantly changed in all sampling time except after 45 days of drug administration it was significantly decreased (24.00±1.94).

Table 2: The Effect of lamivudine given orally into male albino rats once daily at a dose of 9 mg/kg BW for 15, 30, 45, 60 days on humoral immunity (Mean ± S.E, n = 5)

Time(days)	IgM (mg/dl)		IgG (mg/dl)	
	Control	Treated	Control	Treated
15	20.80 ± 3.28	21.68 ± 4.29	928.86 ± 20.65	1183.96±11.64**
30	23.22 ± 3.09	21.90 ± 4.20	932.90 ± 11.82	1203.58±2.02**
45	23.22 ± 3.09	22.78 ± 4.47	931.18 ± 20.28	1185 ± 13.27**
60	18.52 ± 3.19	18.10 ± 4.19	925.50 ± 20.07	1181.16±11.74**

* Significant at $P < 0.01$.

The Lamivudine administration elicited no significant changes in albumin throughout the experiment. The total protein increased at 15, 30, 45 and 60 days after drug administration in treated group (8.64±0.12, 8.07±0.19, 8.06±0.46 and 8.60±0.22, $P<0.01$, respectively). Total globulins were significantly increased at 15, 30, 45 and 60 days of drug administration (4.91±0.13, 4.92±0.35, 4.31±0.26 and 4.34±0.16, respectively) (Table 3). The present results revealed high significant increase in phagocytic percent (1.12 ± 0.09 and 1.11± 0.75) and phagocytic index (79.15 ± 3.64 and 77.13 ± 4.45) at 30 and 60 days after drug administration, respectively (Table 4).

Table 3: The Effect of lamivudine given orally into male albino rats once daily at a dose of 9 mg/kg BW for 15, 30, 45, 60 days on some kidney and liver function parameters

Parameters	Time (days)							
	15		30		45		60	
	C	T	C	T	C	T	C	T
Creatinine (mg/dl)	0.51 ± 0.007	0.39 ± 0.05*	0.50 ± 0.01	0.44 ± 0.02	0.50 ± 0.03	0.41 ± 0.05	0.46 ± 0.01	0.43 ± 0.03
Urea (mg/dl)	31.20 ± 2.13	27.80 ± 2.43	34.60 ± 1.95	33.40 ± 3.57	29.31 ± 2.24	25.20 ± 2.45	31.54 ± 1.74	27.80 ± 2.15
Alk. Ph[a] (U/L)	96.80 ± 5.40	87.20 ± 4.95	96.00 ± 3.24	87.40 ± 3.57	101.00 ± 4.39	97.80 ± 3.80	96.60 ± 5.60	93.60 ± 5.74
ALT[b] (U/L)	41.20 ± 1.49	26.20 ± 1.95**	41.20 ± 1.49	31.40 ± 1.77**	38.20 ± 1.49	29.00 ± 3.39**	29.31 ± 2.24	22.00 ± 1.41**
AST[c] (U/L)	32.60 ± 3.58	29.00 ± 2.82	27.80 ± 3.62	30.60 ± 2.40	40.60 ± 1.77	24.00 ± 1.94**	29.40 ± 3.50	26.00 ± 2.77
Total Protein. (g/dl)	7.24 ± 0.09	8.64 ± 0.12**	6.78 ± 0.21	8.07 ± 0.19**	6.42 ± 0.26	8.06 ± 0.46**	7.22 ± 0.58	8.60 ± 0.22*
Albumin (g/dl)	3.53 ± 0.12	3.78 ± 0.12	3.32 ± 0.14	3.36 ± 0.14	3.44 ± 0.12	3.54 ± 0.16	3.49 ± 0.16	3.76 ± 0.09
Total Globulins (g/dl)	3.71 ± 0.16	4.91 ± 0.13**	3.76 ± 0.18	4.31 ± 0.26*	3.80 ± 3.36	4.92 ± 0.35**	3.73 ± 0.48	4.34 ± 0.16*

[a] Alk. Ph: AlkalinePhosphatase; [b] ALT: Alanine transferase; [c] AST: Aspartate-aminotransferase; * Significant at P < 0.05; ** Significant at P < 0.01; C: control group; T: treated group.

Table 4: The effect of lamivudine given orally into male albino rats once daily at a dose of 9 mg/kg BW for 30, 60 days on phagocytic capacity (Mean ± S.E, n = 5)

Time(days)	Phagocytic index		Phagocytic Percentage	
	Control	Treated	Control	Treated
30	0.92±0.11	1.12± 0.09 **	46.64±6.39	79.15±3.64 **
60	0.93±0.08	1.11± 0.75 **	47.89 ±4.37	77.13±4.45**

** Significant at P < 0.01

Discussion

Lamivudine has been used for treating chronic hepatitis B at a lower dose than for treating HIV/AIDS. It improved the seroconversion of e-antigen positive hepatitis B and also improved histology staging of the liver [16]. Lamivudine used also for HIV patients with highly active antiretroviral therapy (HAART) medication [2].

The obtained findings revealed that Lamivudine has untoward side effects on the hematological parameters even in the presence of anemia (macrocytic anemia), leukopenia and neutropenia on the 30th day of Lamivudine administration. Anemia and leucopenia disappeared on the 60th day of Lamivudine administration. The results of the present study were comparable with Umar *et al*. [17] who studied the effect of Lamivudine on rats' hematology for 40 days using 2mg daily dose/rat and they found no hematological disorders except a significant increase in PCV.

In this study, Lamivudine had no effect on IgM, but IgG levels increased significantly. This might be attributed to short half-life of IgM (1-6days) and long half-life of IgG which may reach 24 days [18], therefore IgM disappeared from blood samples taken after 15 days. The previous observations were reported also by Chen and Tsai [19], who studied the Lamivudine response of IgM anti-HBC chronic Hepatitis B, and they found that lamivudine in chronic case of Hepatitis B can produce low response of IgM according to antigenic number and virulence.

The results of the current study revealed that Lamivudine had no critical effect on the serum creatinine or urea level, so it has good tolerability and high safety profile on the kidney. Similar observations were reported by Ron *et al*. [20] who studied the effects of Lamivudine in a daily dose of 100mg for treating the acute Hepatitis B patients. The authors concluded that Lamivudine had no serious effects on kidney of Hepatitis B patient.

Concerning liver functions, Lamivudine caused normalization of liver enzymes which might be attributed to its protective mechanism on hepatocyte. These results go hand in hand with those mentioned by Nagamatsu *et al.* [21]. They reported that the administration of Lamivudine prevented further damage of the liver and so caused normalization of the liver enzymes by using 100mg Lamivudine as a single dose in HBeag +ve patients for 6 months. There were no changes in serum albumin levels, while the total protein and total globulins were significantly increased. These results also endorsed those obtained by Liaw *et al.* [22]. They evaluated the effect of Lamivudine in Hepatitis B patients with advanced liver disease by using 100mg Lamivudine (436 patients and 215 controls) for 5 years and found a normalization of serum albumin and significantly increased in total protein and globulins.

Our results revealed highly significant increase in phagocytic activity. These results might be indicated that Lamivudine can restore function of dendtritic cells which is antigen presenting cells and has a rule in increasing the activity of monocytes through regulation of major histocompatability II (MHC II) expression [23]. Moreover, restore the function of phagocytosis through inhibiting the cyclic adenosine monophosphate (cAMP) production by inhibiting the adenylatecyclase enzyme [24]. Zheng *et al*. [23] had investigated the effect of Lamivudine in restoration of the phagocytic activity and

function of the monocyte in HBV patient. They detected a high significant increase in monocyte activity and phagocytosis by activation of dendritic cells function.

Conclusion

Based on the current findings, it may be concluded that Lamivudine had no serious side effects on hematology, both liver and kidney functions with a promising immunostimulant effect.

Conflict of Interest

The authors declare no conflict of interest.

References

[1] Viviani, S.; Jack, A.; Hall, A.J.; Maine, N.; Mendy, M.; Montesano, R. and Whittle, H.C. (1999): Hepatitis B vaccination in infancy in the Gambia: protection: against carriage at 9 years of age. Vaccine, (17): 2946-2950.

[2] Libbrecht E.;Doutreloigne J.; Van De Velde, H.; Yuen M.F..; Lai, C.L.; Shapiro, F. and Sablon, E. (2007):Evolution of primary and compensatory lamivudine re-sistance mutations in chronic hepatitis B virus-infected patients during long–term lamivudine treatment. J Clin Microbiol, 45 (12): 3935-3941.

[3] Almela, M.J.; Gonzalez, M.E. and Carrasco, L. (1991): Inhibitors of poliovirus uncoating efficiently block the early membrane permeabilization induced by virus particles. J Virol, 65 (5): 2572-2577.

[4] Chang, T.T.; Gish, R.G.; de Man, R.; Gadano, A.; Sollano, J.; Chao, Y.C.; Lok, A.S.; Han K.H.; Goodman, Z.; Zhu, J.; Cross, A.; DeHertogh, D.; Wilber, R.; Colonno, R. and Apelian, D. (2006): A comparison of entecavir and lamivudine for HBeAg-positive chronic hepatitis B. N Engl J Med, 354 (10):1001-1010.

[5] Paget, S. and Parnes, R., (1964): Evaluation of drug activities and Pharmacometrics. Ed. Laurance and Bacharach, Vol.1.Academic press, New York.

[6] Wintrobe, M.M. (1961): Clinical haematology. 5th Ed. Henry Kimpton, London, 5-30.

[7] Lynch, M.J.; Raphael, S.S.; Meller, L.D.; Spare, P.D. and Inwood, M.J. (1969): Medical laboratory technology and clinical pathology. 2nd Ed. W.E. Saunders co. Philadelphia, London, Toronto.

[8] Schalm, O.W. (1975): Veterinary Haematology. 3rd Ed, Bailliere, Tindall and Cassel Ltd, London.

[9] Nash, D.R. and Heremans, J.F. (1969): A quantitative antibody-binding method for the determination of specific antibody within different immunoglobulin classes. Application to four Ig classes in the mouse. Immunology, 17 (5): 685-694.

[10] Chaney, A.L. and Marbach, E.P. (1962): Modified reagents for determination of urea and ammonia. Clin Chem, 8: 130-132.

[11] Husdan, H. and Rapoport, A. (1968): Estimation of creatinine by the Jaffe reaction. A comparison of three methods. Clin Chem, (4): 222-238.

[12] Reitman, S. and Frankel, S. (1957): A colorimetric method for the determination of serum glutamic oxalacetic and glutamic pyruvic transaminases. Amer J Clin Path, 28 (1): 56-63.

[13] Kind, P.R. and King, E.G. (1954): Colometric method for the determination of serum ALP. J Clin Path, 7: 322-324.

[14] Weichselbaum, T.E. (1946): An accurate and rapid method for the determination of proteins in small amounts of blood serum and plasma. Am J Cli Path 16, Tech. Sect. 10, 40.

[15] Bøyum, A. (1974): Separation of blood leucocytes, granulocytes and lymphocytes. Tissue Antigens, 4(3): 269-74.

[16] Hsu, C.; Hsiung, C.A.; Su, I.J.; Hwang, W.S.; Wang, M.C.; Lin, S.F.; Lin, T.H.; Hsiao, H.H.; Young, J.H.; Chang, M.C.; Liao, Y.M.; Li, C.C.; Wu, H.B.; Tien,

H.F.; Chao, T.Y.; Liu, T.W.; Cheng, A.L. and Chen, P.J. (2008): A revisit of prophylactic lamivudine for chemotherapy-associated Hepatitis B reactivation in non-Hodgkin's lymphoma. a randomized trial. Hepatology, 47 (3): 844-853.

[17] Umar, R.A.; Ladan, M.J.; Hassan, S.W.; Sa`id, Y.; Abbas, A.Y. and Odoulisaeme, I.B. (2007): Administration of antiretroviral drugs (Lamivudine, Nevirapine and Stavudine) has no untoward effects on haematological profile in albino rats. Asian J Biochem, 2 (2): 147-151.

[18] Curtis, J. and Bourne, F.J. (1973): Half-lives of immunoglobulins IgG, IgA and IgM in the serum of new-born pigs. Immunology, 24(1): 147-155.

[19] Chen, J.J. and Tsai, S.L. (2006): Lamivudine response of IgM anti-HBc chronic Hepatitis B patients. Aliment pharmacol Ther, 23 (12):1758-1760.

[20] Reshef, R.; Sbeit, W. and Tur-Kaspa, R. (2004): Lamivudine in the treatment of acute Hepatitis B. N Engl J Med, (343): 1123-1124.

[21] Nagamatsu, H.; Itano, S.; Nagaoka, S.; Akiyoshi, J.; Matsugaki, S., Kurogi, J.; Tajiri, N.; Yamasaki, S.; Koga, H.; Torimura, T.; Kumashiro, R. and Sata, M. (2004): Prophylactic lamivudine administration prevents exacerbation of liver damage in HBe antigen positive patients with hepatocellular carcinoma undergoing transhepatic arterial infusion chemotherapy. Am J Gastroenterol 99 (12): 2369-2375.

[22] Liaw, Y.F.; Sung, J.J.; Chow, W.C.; Farrell, G.; Lee, C.Z.; Yuen, H.; Tanwandee, T.; Tao, Q.M.; Shue, K.; Keene, O.N.; Dixon, J.S.; Gray, D.F. and Sabbat, J. (2004). Lamivudine for patient with chronic Hepatitis B and advanced liver disease. N Engl J Med, 351 (15) :1521-1531.

[23] Zheng, P.; Zhang, D.; Lu, G.; Yang, P.; Qi, Y. and Wang, B. (2007): Effects of lamivudine on the function of dendritic cells derived from patients with chronic hepatitis B virus infection. World J Gastroenterol, 13 (34): 4641-4645.

[24] Azzam, R.; Kedzierska, K.; Leeansyah, E.; Chan, H.; Doischer, D.; Gorry, P.R.; Cunningham, A.L.; Crowe, S.M. and Jaworowski, A. (2006): Impaired Complement-Mediated Phagocytosis by HIV Type-1-Infected Human Monocyte-Derived Macrophages Involves a cAMP-Dependent Mechanism. Aids Research and Human Retroviruses, 22 (7): 619-629.

الملخص العربي

بعض الدراسات الفارماكولوجية علي اللاميڤيودين في الجرذان

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إن الالتهاب الكبدي الوبائي (ب) من أكثر الأمراض المعدية انتشارا في العالم وهو ڤيروس يصيب الكبد. ويعتبرمستحضر اللاميڤيودين من مضادات الفيروسات الجديدة المستخدمة فى هذا المجال ضمن المجموعه المميزه العاليه الكفاءه. لذا أجريت هذه الدراسة لتقييم أهم الأعراض الجانبية لهذا المستحضر (اللاميڤيودين), ودراسة خواصه المناعية في ذكور الجرذان البيضاء. ولقد تم اختبار هذا التأثير من خلال التغيرات في صوره الدم الكامله ووظائف الكبد و الكلى وتأثيره على المناعة المكتسبة وخاصية التهام الميكروبات, وكذلك الجلوبيولينات المناعية م ، ج. تم تقسيم الجرذان (٤٠ جرذ) إلى مجموعتين: المجموعة الأولى وهى المجموعة الضابطة (٢٠ جرذاً) والمجموعة الثانية وهى المجموعة المعالجة (٢٠ جرذاً). وقد تم تجريع الدواء للمجموعة المعالجة لمدة ٦٠ يوماً (٩ مجم/كجم) جرعة واحدة يومياً عن طريق الفم. وعلى أساس النتائج ، نستخلص من هذة الدراسة أن مستحضر اللاميڤيودين الذي يستخدم في علاج مرضى الالتهاب الكبدي الفيروسي ب , لا يسبب أى أعراض جانبية خطيره على صورة الدم ووظائف الكبد والكليتين على حد سواء، وفي نفس الوقت يملك خصائص تنشيطية واعدة للمناعة.