Journal of Animal and Veterinary Advances 7 (12): 1579-1582, 2008
ISSN: 1680-5593

The Effects of Chloramphenicol on Some Biochemical Parameters in Mice

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Abstract: The aim of the study was to investigate the effects of some dose regimens of chloramphenicol on some biochemical parameters in mice for acute and subacute periods. Chloramphenicol was given to the experimental groups at the doses of 100 mg kg^{-1} bw (group 2) and 200 mg kg^{-1} bw (group 3) in drinking water for 7 days. Blood samples were taken from all animals on day 0, 1, 7 and 14 of the study. The hepatotoxic effect of cloramphenicol occurred in groups 2 and 3 with increasing doses of cloramphenicol. Hepatotoxicity in groups 2 and 3 was determined based on the levels of increased activity of ALP, AST and ALT.

Key words: Chloramphenicol, biochemical parameters, antibiotic, hepatotoxity, mice

INTRODUCTION

Chloramphenicol is primarily bacteriostatic metabolized in the liver into the inactive glucuronide. Two types of bone marrow depression may be caused by chloramphenicol: A reversible dose-related interference with iron metabolism and an irreversible idiosyncratic form of aplastic anaemia. The reversible form is likely to occur with high doses, a prolonged course of treatment and in patients with liver disease: Serum iron and saturation of serum iron-binding capacity increases, reticulocytes decreases and vacuolizastion of Red Blood Cell precursors, anaemia, leukopenia and thrombocytopenia develop. The onset may be delayed until after therapy has been discontinued hypersensitivity reactions are uncommon. Optic and peripheral neuritis may occur with prolonged use of chloramphenicol and nausea, vomiting and diarrhea may occur (Schwarz *et al*., 2004; Holt *et al*., 1998; Smith and Weber, 1983).

The aim of this study was to evaluate the effects of chloram-phenicol in mice, with respect to the biochemical parameters.

MATERIALS AND METHODS

This study carried out according to Directive 86/609/EEC on the protection of animals used for experimental and other scientific purposes. The animals were allowed free access to standart laboratory diet in pellet form and drinking water for 3 days before starting the study. In the present study, 90 male Swiss albino white mice, 25-30 g, were used. The mice were separated into 3 groups: A control (Group 1) and 2 experimental groups (Groups 2 and 3). While, the control group received normal mouse ration and drinking water, the experimental groups received chloramphenicol in drinking water for 7 days. Five mL of medicine were administrated to the mice in group 2 for daily. The concentration of medicine was 0.6 mg mL^{-1} and prepared as 100 mg kg^{-1} dose calculation. Therefore, each mouse in group 2, received 3 mg medicine daily. The same procedure was followed for (Group 3). Five mL of medicine were administrated to the mice in group 3 for daily. The concentration of medicine was 1.2 mg mL^{-1} and prepared as 200 mg kg^{-1} dose calculation. Therefore, each mouse

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in group 3, received 6 mg medicine daily. Following administration of cloramphenicol, blood samples were taken from all animals on 1, 3, 7 and 14 days of feeding. In every sampling period, 200 μL of blood was taken from each animal by orbital sinus venipucture.

Biochemical analysis: The blood samples were centrifuged at 825×g for 10 min to separate the plasma. The serum levels/activity of urea, creatinine, triglyceride, ALT (Alanine aminotransferase), AST (aspartate aminotransferase), CPK (creatine phosphokinase) and ALP (alkaline phosphatase) were measured in auto-analyser (ERBA XL 600, India) with TECO diagnostic kits (U.S.A).

Statistical analysis: The data are given as average and standard deviation. Variance analysis and Duncan test were performed in order to evaluate the significance between groups and to determine significant groups.

RESULTS AND DISCUSSION

The biochemical parameters were used to evaluate changes in some tissues, which may have been caused by using antibiotics like other various c-hemical compounds. The changes in biochemical parameters could be the reflections of alterations in some tissues, organs and systems (Table 1). These changes in the parameters and the other findings may be a guide to understanding the effects of cloramphenicol (Barreto *et al*., 2006; Kalender *et al*., 2005; Patterino and Argentino- Storino, 2006).

The significant changes in urea, triglyceride, ALP and ALT activities were observed on the 1st day of study. These changes were as increases of urea level in group 2 and 3 whereas, triglyceride level decreased in group 2; however, there was increase in ALT activity in groups 2 and 3. The changes in ALP activity had 2 aspects: An increase in group 2 and a decrease in group 3. The urea and creatinin levels were taken into account because they indicate kidneys function. In case of deteriotation of kidneys function, there are always increases in combination. Creatinin level was not affected and its level was quite stable throughout the study, therefore, it indicated that kidneys function were normal. On the other hand, the increase in urea level, which was occurred in control and experimental groups, may be originated by increasing catabolic processes due to blood sampling stress. In addition, the increases in urea levels without

Table 1: Biochemical parameters of mice in different treatment groups (mean±S.E.)

Days	Parameters	Group 1	Group 2	Group 3
1	Urea mg dL^{-1}	35.20±5.310^{a}	40.60±5.12^{a}	47.00±8.42^{b}
	Creatinin mg dL^{-1}	41.60±21.19	55.20±6.97	53.80±6.53
	Triglyceride mg dL^{-1}	117.20±5.76^{a}	99.20±3.03^{b}	112.00±6.59^{a}
	ALT IU L^{-1}	69.00±3.31^{a}	84.00±12.62^{b}	81.00±5.24^{b}
	AST IU L^{-1}	105.20±6.37	100.20±16.17	94.50±38.64
	CPK IU L^{-1}	49.00±3.80	43.80±2.28	56.00±50.86
	ALP IU L^{-1}	127.80±15.31^{a}	162.00±19.45^{a}	72.00±66.05^{b}
3	Urea mg dL^{-1}	63.50±4.43^{a}	49.00±21.03^{ab}	114.20±1.48^{b}
	Creatinin mg dL^{-1}	39.25±23.76	38.00±19.26	38.80±14.21
	Triglyceride mg dL^{-1}	72.00±6.97^{a}	81.40±3.36^{b}	84.00±1.41^{b}
	ALT IU L^{-1}	45.25±2.75^{a}	56.80±4.20^{b}	55.50±16.36^{b}
	AST IUL^{-1}	112.75±6.18	89.60±9.04	91.00±16.06
	CPK IU L^{-1}	70.50±8.81	74.00±10.36	49.66±6.35
	ALP IU L^{-1}	123.00±10.32^{a}	131.00±16.77^{a}	134.50±15.92^{b}
7	Urea mg dL^{-1}	131.33±6.80	138.75±8.05	129.00±3.60
	Creatinin mg dL^{-1}	40.00±9.48	36.40±1.42	40.60±15.61
	Triglyceride mg dL^{-1}	106.33±6.65	108.80±14.28	100.66±2.51
	ALT IU L^{-1}	49.00±2.82^{a}	72.00±9.01^{b}	59.70±7.25^{a}
	AST IU L^{-1}	98.00±4.24	92.00±1.41	94.50±2.12
	CPK IU L^{-1}	53.66±9.60	59.00±29.01	47.75±12.09
	ALP IU L^{-1}	151.66±9.07	154.00±11.532	153.00±4.00
14	Urea mg dL^{-1}	133.20±15.64	131.20±3.63	121.40±3.50
	Creatinin mg dL^{-1}	43.00±9.19	36.00±18.06	40.60±15.61
	Triglyceride mg dL^{-1}	101.66±14.57	101.33±20.42	104.33±20.55
	ALT IU L^{-1}	70.40±22.46	76.20±12.51	69.80±2.94
	AST IU L^{-1}	33.80±22.91^{a}	76.00±8.21^{b}	40.00±10.46^{a}
	CPK IU L^{-1}	50.25±4.57	52.25±4.50	47.75±12.09
	ALP IU L^{-1}	103.60±22.41	119.60±25.71	120.20±10.25

^{a,b}The difference is significant in the rows between the groups, which carries different superscripts ($p<0.05$)

alterations in blood creatin levels was most probably related to the rise of protein levels with daily feed intake. In experimental mice, their low blood urea levels on 1st day of study was begun to rise on 3rd day and stabilised on 7th. On the other hand, no differences were observed between groups. The reason for that may be originated the shortness of 3 day adaptation period. Looking at the values on the 3rd day, the increase in urea level continued in Groups 2 and 3. Again, the increases were observed in ALT activities for both experimental groups, on the 1st day, as compared to the control. ALP activity significantly increased in group 3 only. On the 7th day of study, increase was observed in ALT activity in both the experimental groups, as compared to control. This increase was significant in group 2. On 14th day of study, a significant change was observed in AST activity only and that significance was limited to group 2.

According to the results, chloramphenicol caused changes in ALP, AST and ALT that were related to the liver and however, these changes were not persistent as indicated by non-significant changes in the parameters during following periods. Even though, cloramphenicol was given for 7 days, there were no statistically significant increase in the parameters, related to dose and time. However, there was statistically significant increase concerning the changes in urea level in group 3, on the 3rd day. In particular, on 14th day, the significant increases in AST activity only was specific in group 2. However, these changes were not seen in other periods. It was suggested that the damage was reversible. The significant changes in CPK levels were not observed during the study. However, there was a significant increase in AST level of group 2. Despite of this increase, that value should be considered as normal, because of mice normal AST levels range between 30-314 IU L^{-1}. The major toxic effect mechanism of chloramphenicol includes its potential to cause lipid peroxidation (Farombio, 2001). That effect is primarily responsible for toxication and tissue damage and the inhibition of xanthine oxidase and glucose-6-phosphate dehydrogenase are involved in that mechanism. On the other hand, chloramphenicol may lead to changes in the metabolism of other drugs and chemicals in the body by causing inhibition of drug-metabolising enzymes. Therefore, it brought the changes on the toxic effects of those drugs and chemicals (El-Demerdash *et al*., 2004; Farombi *et al*., 2002). The effects of chloramphenicol on tissues and organs, are probably related to this mechanism.

CONCLUSION

The doses and dose regimen of choramphenicol, given to the mice caused changes in some of the biochemical parameters which are related to the liver; however, the biochemical changes were reversible.

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