Quench Academy of Medical Education and Research
Annals of Medical Physiology
www.amphysiol.com

Original Research Article

Effect of aspirin administration on body weight and liver enzymes in male rats

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Article history

Received 17 November 2021
Revised 13 December 2021
Accepted 14 December 2021
Online 31 December 2021
Print 31 December 2021

Keywords

Acetylsalicylic acid
ALP
ALT
Aspirin
AST
Rat

Abstract

The present study was conducted to evaluate the effects of aspirin on body weight and some liver enzyme in rats. The study was done in Veterinary Medicine College, Baghdad University. We used seventy two male rats and randomly divided into three groups (24 in each group). Group-1 was considered as control, Group-2 animals were treated by 40 mg/kg body weight (low-dose) of asprin and the Group-3 was treated by 100 mg/kg body weight (high-dose) of aspirin. The results showed no significant difference in bodyweight gain from 0 to 10 days in all groups, while the low and high-dose asprin treated rats showed decline in bodyweight gain on day 20 and day 30 of aspirin treatment. The liver enzymes, AST and ALT, increased significantly in high-dose of aspirin treated group on day 20 and 30 while the ALP was increased on all time-points in high-dose asprin treated group.

Introduction

Aspirin (acetylsalicylic acid [ASA]) is a non-steroidal anti-inflammatory drug (NSAID) which is cheap, easily available and has wide applications in medical science such as anti-pyretic, analgesic, anti-inflammatory action and anti-platelet action in coronary artery disease. Aspirin is a safe drug in low doses but can cause adverse effects at high doses. Some of the severe adverse effects of high dose of aspirin are caused by necrosis of blood vessels **[1]**. Long term usage of aspirin may cause liver and renal toxicity. Aspirin disrupts the formation of prostaglandins in the body by targeting cyclooxygenase **[2,3]**. Aspirin is involved in the interference of various cancers signaling pathway, sometime used for regulation of tumor suppressor genes, hence long term usage of aspirin in prevention of many types of cancer is envisaged. The absorption of aspirin is rapid after orally administration in the stomach and proximal small intestine by non-ionized passive diffusion at pH of 2-4 **[4,5]**. About sixty percent of therapeutic concentration of aspirin is bound to plasma proteins. The metabolism of aspirin is via conjugation in the liver to salicyluric acid and salicylic acid **[6]**. Aspirin excretion mainly occurs in the kidney by glomerular filtration processes, the half-life of aspirin ranges from 14-20 minute **[7]**. The lethal dose of aspirin with acute oral LD50 value is about 0.9 g/kg in rats, the aspirin poisoning in rats from lethal dose range from mild to severe presentation like hepatitis, nephritis and shock **[8]** and the chronic toxicity of aspirin like delirium and cardiac failure **[9]**. Chronic toxicity of aspirin in mice occurs at dose of 3 to 20 times the tolerated dose up to a year **[10,11]**.

Materials and Methods

Seventy two male rats (Rattus norvegicus) were used with an average body weight of 200±10 gram. All animals housed in cages measuring 50 X 50 cm at animal house in Veterinary Medicine

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DOI: https://doi.org/10.23921/amp.2021v5i3.00051
Print ISSN: XXXX-XXXX
Online ISSN: 2456-8422

College of Baghdad, Iraq. Animals were exposed to similar environment and feeding for climate management and acclimatization two weeks pre-treatment. Rats were feed by protein diet and distilled water. Possibility of animals having any infection was eliminated by giving a course of systemic antibiotics to make sure that they are healthy before the beginning of the study.

The rats were divided to three groups (24 in each group) randomly as following:

Group-1 (control): Administration of 0.5 ml of normal saline (0.9% NaCl) by oral gavage per day

Group-2 (low-dose): Administration of 0.5 ml of 40 mg/kg body weight of aspirin by oral gavage per day

Group-3 (high-dose): Administration of 0.5 ml of 100 mg/kg body weight of aspirin by oral gavage per day

This experiment was carried for thirty days and at different time-points and at the end of experiment we measured the following parameters:

1) The body weight using digital electronic balance
2) Liver enzyme (Alanine transaminase [ALT], Aspartate transaminase [AST] and Alkaline phosphatase [ALP])

Collection of blood samples

The blood samples (about 5ml) were collected in a plain tube and allowed to clot at room temperature, and then the sample was centrifuged at 3000 rpm for 15 minute. The serum samples then separated was stored in polyethylene tube at -20°C till the measurement of the liver enzyme.

Statistical analysis

We used IBM SPSS version 25.0 (IBM Corporation, Armonk, NY, USA). Descriptive and inferential statistics were used. The significance level was set at $p<0.05$.

Results

Body weight

The results showed a significant decline ($p<0.05$) in body weight gain in low-dose aspirin group and high-dose aspirin group at day 20 and 30 compared to control group as depicted in **Table 1**.

Table 1: Effect of acetylsalicylic acid (aspirin) on body weight

Parameter	Treatment	Periods of treatment (in days)			
		0	10	20	30
Body weight (in gm)	Control (Normal saline)	195.10 ± 1.14^{a}	256.31 ± 0.43^{A}	320.09 ± 1.90^{a}	339.24 ± 1.64^{A}
	Low-dose (40 mg/kg body weight aspirin)	193.23 ± 2.34^{a}	250.21 ± 1.65^{A}	273.35 ± 2.76^{b}	289.21 ± 2.65^{B}
	High-dose (100 mg/kg body weight aspirin)	198.51 ± 1.88^{a}	250.29 ± 1.75^{A}	190.71 ± 2.86^{C}	174.84 ± 1.90^{C}

The superscript small alphabets refer to significant difference at ($p\leq0.05$) among days of treatment

Table 2: The effect of acetylsalicylic acid (aspirin) on liver enzymes

Parameter	Treatment	Periods of treatment (in days)		
		10	20	30
Aspartate transaminase [AST] (IU/L)	Control (Normal saline)	31.32 ± 1.23^{a}	33.02 ± 1.09^{B}	31.75 ± 1.22^{c}
	Low-dose (40 mg/kg body weight aspirin)	30.09 ± 2.08^{a}	30.43 ± 1.32^{B}	49.32 ± 3.87^{b}
	High-dose (100 mg/kg body weight aspirin)	31.05 ± 0.11^{a}	45.61 ± 2.11^{A}	63.02 ± 2.33^{a}
Alanine transaminase [ALT] (IU/L)	Control (Normal saline)	11.17 ± 1.87^{A}	13.08 ± 1.76^{C}	11.50 ± 1.05^{c}
	Low-dose (40 mg/kg body weight aspirin)	10.76 ± 2.07^{A}	21.91 ± 2.05^{B}	31.01 ± 3.64^{b}
	High-dose (100 mg/kg body weight aspirin)	14.42 ± 1.21^{A}	36.11 ± 2.07^{A}	48.44 ± 2.55^{a}
Alkaline phosphatase [ALP] (IU/L)	Control (Normal saline)	51.10 ± 1.10^{b}	55.08 ± 4.85^{B}	52.66 ± 3.64^{C}
	Low-dose (40 mg/kg body weight aspirin)	52.11 ± 3.77^{B}	57.12 ± 2.63^{B}	79.34 ± 2.99^{B}
	High-dose (100 mg/kg body weight aspirin)	61.33 ± 4.11^{a}	78.19 ± 3.33^{A}	81.45 ± 2.66^{a}

The superscript small alphabets refer to significant difference at ($p\leq0.05$) among days of treatment

Liver enzymes

Baseline data for liver enzymes collected from three groups is shown in **Table 2**. The result showed significantly increased ($p \leq 0.05$) in AST enzyme especially in high-dose group on day 20 and day 30 (45.61±2.11, 63.02±2.33 respectively) compared with the control group (33.02±1.09, 31.75±1.22 respectively). Also there appears to be significant increase in AST in low-dose group on day 30 (49.32±3.87) compared to the control group (31.75±1.22).

Table 2 shows significantly increased ALT enzyme concentration on day 20 and 30 in low and high doses of aspirin groups compared with day 10 and also compared with the control group.

Alkaline phosphatase (ALP) enzyme significantly increased in high-dose group on day 10 and 20 (61.33±4.11, 78.19±3.33 respectively), while the results on day 30 treatment of aspirin in both low and high dose group appeared significantly increased (79.34±2.99, 81.45±2.66 respectively) compared to control group (52.66±3.64).

Discussion

Acetylsalicylic acid (aspirin) used as anti-inflammatory drug have side effects as gastrointestinal symptoms, liver damage and renal toxicity. In the present study, we showed that the administration of aspirin with low-dose and high-dose for 10 days, 20 days and 30 days to rats lead to derangement of liver enzymes and interference with body weight gain. Aspirin induced liver toxicity is clear as the metabolism and biotransformation of aspirin occur in liver, sometimes culminating in apoptosis of hepatocytes **[12]**. The changes at the level of serum proteins may also cause damage to liver. In the present study, elevation of alanin aminotransferase (ALT) found is similar to the study done by Abdel-salam **[13]**. The findings of present study in which the serum levels of aspartate aminotransferase (AST), alanine aminotranseferase (ALT) and alkaline phosphatase (ALP) increased in high-dose aspirin administration for 10 days, 20 days and 30 days shows functional damage to the liver but the mechanism of acetylsalicylic acid causing this damage cannot be elucidated as liver toxicity after aspirin administration need several days to develop the symptoms according to a group of researchers **[14]**. A study group reported that administration of aspirin with low-dose daily decreases the progression of fibrosis in rat liver **[15]**. One study advocated that liver toxicity induced by aspirin could be an outcome of idiosyncratic metabolic reaction because aberrant metabolism of the drug may cause aggregation of toxic metabolites in hepatocytes thereby binding to cell proteins leading to abnormalities **[16]**. Administration of aspirin upto doses of 40 mg/kg in rats lead to decrease body weight gain while doses more than 100 mg/kg lead to mild sinusoidal congestion suggesting that aspirin at higher doses is hepatotoxic as evident by elevation in serum alanine aminotransferase, aspartate aminotransferase and alkaline phosphatase.

Conclusion

In conclusion ,the results of study shows the chronic administration of aspirin lead to hepatotoxic in rats , large-scale studies maybe needed to know the chemo preventive effect of aspirin on liver toxic development, liver toxic associated to aspirin is un common adverse effect it is important to be vigilant to the hepatotoxicity, aspirin causes blocking certain chemical processes in the body that cause inflammation, taking of aspirin with high dose for 30 days can lead to hepatic problems and problems in the histological architecture at the liver which is recommended that aspirin should not be taken at extended duration than normally, the antioxidant supplementation may be beneficial to the people who using aspirin for long periods.

Declarations

Ethical consideration

This study received ethical approval and consent from the Ethical Committee, Medical Technical Institute, Middle Technical University, Iraq.

Funding

This study was self funded.

Disclosure of relationships and activities

Authors have declared that no conflicting interests exist.

Acknowledgements

The authors would like to thank all who supported the study.

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