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Research Article

ALTERATIONS OF LIPID PROFILE LEVELS IN 7,12-DIMETHYLBENZ(A)ANTHRACENE INDUCED ULCERATIVE COLITIS RAT MODEL

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ABSTRACT

Objective: Ulcerative colitis is a type of inflammatory bowel disease is a chronic gastrointestinal disorder characterized by intestinal inflammation and mucosal tissue damage. We examined the lipid profile levels in murine model of 7,12-dimethylbenz(a)anthracene induced ulcerative colitis.

Methods: Serum was separated from whole blood and was used to determine the lipid profile such as total cholesterol (TC), phospholipids (PL), triglycerides (TG), free fatty acids, high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol (LDL-C).

Results: Ulcerative colitis rats exhibit a low level of LDL-C and TC. No significant difference was observed in HDL and TG, and significant difference was observed in PL and free fatty acid serum levels. This communication highlights the lipid profile that occurs in ulcerative colitis.

Conclusion: This study, thus, provides valuable information about the disturbances in the lipids and lipoproteins occur in ulcerative colitis.

Keywords: Ulcerative colitis, 7,12-Dimethylbenz(a)anthracene, Lipoprotein, Low-density lipoprotein, Phospholipids.

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INTRODUCTION

Ulcerative colitis is a type of inflammatory bowel disease in which immune dysregulation promotes development of ulcerations in the lining of the colon [1]. It is characterized by recurring episodes of inflammation limited to the mucosal layer of the colon; it invariably involves the rectum and may extend in a proximal and continuous fashion to involve other portions of the colon [2,3]. Main clinical manifestations of ulcerative colitis are abdominal pain, diarrhea, mucous, bloody, and purulent stools [3,4]. Although the underlying pathogenesis of the disease was still unknown, the widely accepted hypothesis was that the pathophysiology involves an interaction among immunological, genetic, and environmental factors [4]. The inflammatory bowel disease is becoming more common in Asia, but epidemiologic data are lacking [5]. The highest rates have been reported in India particularly ulcerative colitis, Japan, Middle East, and overall rising trends of inflammatory bowel disease are seen in East Asia [6].

METHODS

Animal selection

Male Wistar rats (170-200 g) were obtained from the animal house of Mannuthy Veterinary College, Thrissur, Kerala. Animals were maintained under standard conditions (12 hrs light/dark cycle; 25±3°C, 45-65% humidity) and had free access to standard rat feed and water *ad libitum*. Animals were grouped as control and induced. Induced group was sub-grouped as A, B and induced with 10, and 20 mg/kg body weight of 7,12-dimethylbenz(a)anthracene. Animals were sacrificed on 4^{th}, 8^{th}, 12^{th}, 24^{th}, and 32^{nd} week from the date of induction by cervical dislocation. Animal studies were performed according to the prescribed guidelines of the committee for the purpose of control and supervision of experiments on animals (659/02/a/CPCSEA), Government of India, India.

Biochemical analysis

Heparinized blood was collected for analysis and serum was prepared from whole blood. The homogenates were centrifuged at 3000 g for 15 minutes at 4°C for cytosolic separation. Serum was separated from whole blood and was used to quantify the lipid profile such as total cholesterol (TC) [7], phospholipids (PL) [8], triglycerides (TG) [9], free fatty acids [10], and high-density lipoprotein (HDL) [11]. Low-density lipoprotein (LDL) was calculated using the following formula:

LDLC=TC−HDL+(TGL/5)

RESULTS AND DISCUSSION

Several differences were noted in plasma lipid profile of ulcerative colitis induced rats and control rats (Tables 1 and 2). TC levels were significantly reduced. On 32^{nd} week induced group both 10 mg and 20 mg showed reclined value when compared with control rats (10 mg - 58.67±0.65 mg/dL, and 20 mg - 54.57±0.54 mg/dL vs.

Table 1: Effect of DMBA on the levels of lipoprotein in serum of control and experimental animals

Groups	HDL-C	LDL-C
Group I control	42.65±0.65	23.43±0.21
Group II induced		
A. 10 mg		
1. 4^{th}	42.44±0.45^{a*}	22.14±0.16^{a*}
2. 8^{th}	42.29±0.34^{a*}	19.15±0.23^{a*}
3. 16^{th}	43.14±0.76^{a*}	17.21±0.18^{a*}
4. 24^{th}	42.13±0.89^{a*}	15.27±0.21^{a*}
5. 32^{nd}	41.34±0.23^{a*,c*}	13.91±0.15^{a*,c*}
B. 20 mg		
1. 4^{th}	43.56±0.87^{a*,b*}	20.51±0.21^{a*,b*}
2. 8^{th}	41.65±0.24^{a*,b*}	18.11±0.17^{a*,b*}
3. 16^{th}	42.33±0.77^{a*,b*}	14.16±0.22^{a*,b*}
4. 24^{th}	43.09±1.23^{a*,b*}	12.62±0.18^{a*,b*}
5. 32^{nd}	42.11±0.43^{a*,b*,d*}	10.19±0.19^{a*,b*,d*}

Values expressed as mean±SD (n=2). *Significant at 5% ($p<0.05$). Group comparison: [a]GII versus GI, [b]GIIB versus GIIA, [c]GIIA5 versus GIIA1, GIIA2, GIIA3 and GIIA4, [d]GIIB5 versus GIIB1, GIIB2, GIIB3 and GIIB4. HDL-C: High-density lipoprotein cholesterol, LDL-C: Low-density lipoprotein cholesterol, DMBA: 7,12 Dimethylbenz(a)anthracene, SD: Standard deviation

Table 2: Effect of DMBA on the levels of lipids in serum of control and experimental animals

Groups	TC mg/dL	Phospholipids mg/dL	TG mg/dL	Free fatty acids mg/dL
Group I control	72.67±3.67	66.33±1.43	40.54±1.12	86.55±2.65
Group II induced				
A. 10 mg				
1. 4th	70.35±0.14a*	73.76±0.44a*	41.12±0.63a*	90.12±0.35a*
2. 8th	67.31±0.26a*	75.44±0.23a*	40.22±0.66a*	94.35±0.67a*
3. 16th	63.22±0.43a*	96.43±0.54a*	41.01±0.82a*	114.51±0.39a*
4. 24th	61.35±0.73a*	97.26±0.89a*	41.12±0.32a*	114.78±0.54a*
5. 32nd	58.67±0.65a*,c*	97.33±0.34a*,c*	40.45±0.52a*,c*	115.78±0.17a*,c*
B. 20 mg				
1. 4th	66.32±0.87a*,b*	75.65±0.45a*b*	40.66±0.35a*,b*	92.45±0.89a*,b*
2. 8th	64.34±0.11a*,b*	78.34±0.56a*,b*	41.44±0.89a*,b*	97.23±0.34a*,b*
3. 16th	60.23±0.29a*,b*	100.28±0.54a*,b	41.39±0.56a*,b*	118.09±0.90a*,b*
4. 24th	57.87±0.32a*,b*	101.56±0.48a*,b*	42.01±0.45a*,b*	124.34±0.48a*,b*
5. 32nd	54.57±0.54a*,b*,d*	102.45±0.22a*,b*,d*	41.45±0.73a*,b*,d*	126.67±0.67a*,b*,d*

Values expressed as mean±SD (n=2). *Significant at 5% (p<0.05), Group comparison: [a]GII versus GI, [b]GIIB versus GIIA, [c]GIIA5 versus GIIA1, GIIA2, GIIA3 and GIIA4, [d]GIIB5 versus GIIB1, GIIB2, GIIB3 and GIIB4, TC: Total cholesterol, TG: Triglycerides, DMBA: 7,12 dimethylbenz(a)anthracene

control - 72.67±3.67 mg/dL). PL, TG, and free fatty acids showed gradual increase in induced group when compare with control rats. From 4th week until 32nd week, the values increased steadily. No significant changes were observed in HDL-C levels in both 10 mg and 20 mg group of induced group. Lowering of LDL-C values was observed in induced group of both doses against control value (13.91±0.15, and 10.19±0.19 vs. 23.43±0.21). The data are expressed as mean±standard deviation. Statistical comparison was done at significance level, $p<0.05$ using SPSS package version 10.0. One-way ANOVA followed by *post-hoc* analysis of least significant difference was performed.

In another study serum concentration of TC, LDL-C was significantly lowered when compared with healthy controls.

On the other hand, no significant changes were observed in HDL-C levels and TG ulcerative colitis, and healthy subjects [12-15]. PL were significantly increased in another study in ulcerative colitis patients when compared with healthy subjects [16]. In our study, free fatty acids were significantly raised from 4th week until 32nd week in experimental rats when compared with control. In another study, there were a significant raise in fatty acids in inflammatory bowel disease [17-19]. In conclusion, ulcerative colitis rats exhibit lower levels of TC and LDL-C compared to healthy subjects. In addition, no significant changes seen in HDL-C and TG. High level of free fatty acids and PL found when compared with healthy rats. This proves the link between the lipid alteration and ulcerative colitis disease. However, more large-scale studies should be carried to reach the robust conclusions about the lipid alterations reported in ulcerative colitis.

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