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THE ROLE OF ENVIRONMENTAL FACTORS ON PLASMA ANTIOXIDANT STATUS AND LIPID PROFILE IN SCHISTOSOMAL CO-INFECTION WITH VIRAL HEPATITIS C AND G

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Abstract

Strong evidence exists for hepatic free radical production in human with liver disease , which may play a role in hepatic fibrogenesis . This work aims to throw light upon link between life style in rural areas and susceptibility to Schistosomal co-infection with viral hepatitis C and /or G. The magnitude og hepatic insult posed by the co-infection was assessed relative to changes in plasma antioxidant status, lipid peroxidation and lipid profile.

Schistosomal cases under study were selected according to the presence of HCV with HGV (GI, n=12)

Or absence GII, n=15) and compared to non-Schistosomal HCV with HGV states (GIII, n=13). Allied age-matched healthy states free of Schistosomiasis and HCV or HGV were taken as controls (GIV, n=10).

Assessment of antioxidant parameters in plasma included α-tocopherol, α-carotene, β-carotene, lycopene, retinol and vitamin C. Malondialdehyde (MDA) representing lipid peroxidation products was involved besides the lipid profile involving triglycerides (TG) , total cholesterol (TC), high density liopprotein cholesterol (HDLc), low density lipoprotein cholesterol (LDLc), very low density lipoprotein cholesterol (VLDLc), apolipoprotein A-I (Apo A-I), and apolipoprotein B (Apo B). Liver function tests evaluated included albumin, total serum bilirubin, enzyme activities of alkaline phosphatase (ALP), alanine and aspartate transaminases (ALT, AST).

A significant reduction of antioxidant parameters was evident in GI with higher magnitude of change than GIII and GII relative to GIV. A similar pattern of alternations was observed in the increment of MDA, TG, TC, LDLc , VLDLc and Apo B as well as S. bilirubin, ALP, ALT and AST, versus a decrement in HDLc , ApoA-I and albumin.

Schistosomal states with HCV and HGV co-infection presented liver function alterations, lower antioxidant status and alterations in lipid profile reflecting the magnitude of hepatic insult. In

Recommendation, antioxidant supplementation should be considered among the therapeutic regimen of such cases. Also, in rural areas, environmental hazards from unhygienic life style practices should be targeted to minimize the rate of hepatic insult by infectious diseases viz schistosomiasis and viral hepatitis.

Introduction

IN rural areas, both schistosomiasis and hepatitis co-infection are more prevalent in lower social classes where parenteral treatment of schistosomiasis contributed to the high prevalence of viral infection [1]. Hepatitis C virus (HCV) and hepatitis G virus (HGV) belong to the same virus family (Flaviviridae)[2,3] with similar mode of transmission (Parenteral or percutaneous). The presence of HGV in man does not appear to be associated with typical clinical sequelae and may be benign nor does it result in the production of antibodies. Currently detection of HGV is performed by PCR[4].

It has been reported that HCV may cause oxidative stress in infected cells[5]. Strong evidence exists for hepatic free radical production in humans with liver disease.It is consistent with the findings of free radical initiated-lipid peroxidation, which may play a role in hepatic fibrogenesis[6]. Free radical mediated liver injury has been associated with lowered vitamin E levels in patients with acute or chronic viral hepatitis consistent to high activity of the disease[7].

Carotenoids and tocopherols, which are major natural protective agents against free radical-mediated damage, expressed lower levels in diseased liver states. Lower hepatic levels of α-and β-carotenes, α-tocopherol and lycopene have been observed in patients with liver cirrhosis[8]. On the other hand, ascorbate can serve as both pro-oxidant and antioxidant whereby at lower concentrations it is prone to be pro-oxidant but at high concentrations, it will tend to be antioxidant[9].

In the present study, we aimed to determine the influence of environmental factors in rural areas involving schistosomal infection with HCV and HGV co-infection on plasma levels of certain antioxidants and lipid peroxidation relative to assessed values of lipid profile and liver function tests. The data were compated to allied non-schistosomal cases in urban areas.

Subjects and Methods

The study was conducted on 27 male schistosomal cases (age range 30-45 yr) from rural areas who were selected according to presence of HCV with HGV (GI, n=12) or its absence (GII, n=15) and

compared to non-schistosomal HCV with HGV states (GIII, n=13) from urban areas. Allied healthy states free of schistosomiasis and HCV or HGV were taken as controls (GIV, n=10).

They were subjected to full history taking, thorough clinical examination, abdominal ultrasonography, urine and stool analysis as well as examination of a rectal snip biopsy for detection of bilharzial ova. Liver biopsy was done after taking the consent of the patients to confirm diagnosis. Anti-HCV antibodies were determined by 3rd generation ELISA technique[10]. Liver function tests evaluated included serum albumin[11], total serum bilirubin[12], serum alkaline phosphatas[13], alanine and aspartate transaminases (ALT,AST)[14].

Detection of HCV-RNA was done by polymerase chain reaction (PCR) using Amplicor Kit (Roche Diagnostics, Branchburg, NJ, USA) . HGV was detected by Nested RT-PCR as described by Abe et al .,[15].

Assessment of antioxidant parameters in plasma included α-tocopherol, α-carotene, β-carotene, lycopene and ratinol which were quantitated by reverse phase HPLC technique (Elinder and Walldius) [16] and vitamin C[17]. Malodialdehyde (MDA) representing lipid peroxidation products was determined according to the method of Satoh[18] besides the lipid profile involving triglyceride (TG)[19], total cholesterol (TC)[20], high-density lipoprotein cholesterol (HDLc), low-density lipoprotein cholesterol (LDLc), very low-density lipoprotein cholesterol (VLDLc)[21], apolipoprotein A-I(Apo A-I), and apolopoprotein B (Apo B)[22].

Results

Patients with schistosomiasis and viral hepatitis co-infection HCV+HGV (GI) have a decreased antioxidants level (α- tocopherol, α- caroteine, β-carotein, lycopene, retinol and vitamin C) than those with schistosomal state only G(II) and those with HCV and HGV infection (GIII) compared to normal control (GIV). The decrease was statistically significant with α- tocopherol, β-carotene and vit C ($P < 0.0001$). While lipid peroxidation product (malondialdehyde MDA) was insignificantly higher in GI > GIII>GII compared to normal control with P value >0.005 Table (1).

Plasma lipid profile (TG, TC, LDLc, VLDLc and Apo B) were insignificantly higher in GI> GIII> GII compared to normal control (G IV) with P value > 0.005. While HDLc was decreased and Apo A, was significantly decreased in GI> GIII>GII compared to normal control (G IV) P value < 0.001. Table (2).

Liver function tests (S.bilirubin, ALP, ALT, AST) were increased in GI>GIII, GII compared to normal control (GIV) with statistical significant increase in S alkaline phosphatase values P value <0.001. While S.albumin level was insignificantly decreaseed in GI>GIII>GII compared to normal control with P value P>0.005. Table (3)

Table (1): Plasma levels of antioxidants and lipid peroxidation product in the groups under study. Data are Mean ± SD.

Biochemical Parameter	Schistosomal states + HGV with HCV GI (n=12)	Schistosomal States GII (n=15)	HGV with HCV states GIII (n=13)	Control Group GIV (n=10)	F-value (P)
a-Tocopherol (µg/mL)	4.89± 0.90 (II,III,IV)*	6.32± 1.04 (IV)*	5.72± 1.00 (IV)*	7.78± 1.70	11.96 (<0.0001)
a-Carotene (µg/mL)	0.057±0.007 (IV)*	0.081±0.012 (IV)*	0.074±0.009 (IV)*	0.099±0.022	7.70 (0.0003)
ß-Carotene (µg/mL)	0.01±0.004 (II,III,IV)*	0.13± 0.03	0.11± 0.02	0.17± 0.06	48.26 (<0.0001)
Lycopene (µg/mL)	0.062±0.013 (IV)*	0.086±0.03 (IV)*	0.07±0.02 (IV)*	0.12±0.05	7.76 (0.0002)
Retinol (µg/mL)	0.37±0.09 (IV)*	0.44±0.11* (IV)*	0.40±0.10 (IV)*	0.56±0.12	6.73 (0.0007)
Vitamin C (µg/mL)	14.2±4.6 (II,III,IV)*	28.6±8.4 (IV)*	24.8±7.9 (IV)*	38.6±9.5	18.62 (<0.0001)
Lipid Peroxidation Product (µmol MDA/mL)	2.13±0.52 (II,IV)*	1.68±0.36 (IV)*	1.91±0.45 (IV)*	1.29±0.42	7.37 (0.0003)

*Comparison between individual groups using LSD (least significant difference) at 5% level of significance.
MDA = malondialdehyde.

Table (2): Plasma levels of lipid profile in the groups under study.
Data are Mean ± SD.

Biochemical Parameter	Schistosomal states + HGV with HCV GI (n=12)	Schistosomal States GII (n=15)	HGV with HCV states GIII (n=13)	Control Group GIV (n=10)	F-value (P)
Triglycerides (mmol/L)	1.19± 0.046 (II,IV)*	0.83± 0.31	0.98± 0.39 (IV)*	0.69± 0.21	6.70 (0.0007)
Total cholesterol (mmol/L)	7.02±1.82 (II,IV)*	5.07±1.74	6.12±1.82 (IV)*	4.45±1.32	5.11 (0.0037)
HDLc (mmol/L)	0.97±0.32 (II,IV)*	1.39±0.46 (IV)*	1.26± 0.42 (IV)*	1.87±0.57	7.67 (0.0003)
LDLc (mmol/L)	3.77±0.89 (II,IV)*	2.84± 0.74 (IV)*	3.28±0.81 (IV)*	2.21± 0.63	8.06 (0.0002)
VLDLc (mmol/L)	0.42±0.19 (II,IV)*	0.28±0.12	0.36±0.14 (IV)*	0.23±0.09	4.14 (0.0107)
Apo A-1 (mg/dL)	105±25.4 (II,IV)*	138±34.6 (IV)*	121±31.7 (IV)*	171±41.0	7.83 (0.0002)
Apo B (mg/dL)	131±28.4 (II,III,IV)*	87.3±21.4 (IV)*	99.7±24.1 (IV)*	65.9±17.2	15.41 (<0.0001)

* Comparison between individual groups using LSD (least significant difference) at 5% level of significance.
HDLc = high-density lipoprotein-cholesterol.
LDLc = low-density lipoprotein-cholesterol.
VLDLc = very low-density lipoprotein-cholesterol.
Apo A-1 =apolipoprotein A-1.
Apo B = apolipoprotein B

Table (3): Liver function tests in the groups under study.
Data are Mean ± SD.

Biochemical Parameter	Schistosomal states + HGV with HCV GI (n=12)	Schistosomal states GII (n=15)	HGV with HCV states GIII (n=13)	Control Group GIV (n=10)	F-value (P)
Aldumin (g/dL)	2.2±0.90 (IV)*	2.8±0.94	2.5±0.91	3.4±1.20	2.97 (0.0403)
Bilirubin (mg/dL)	1.02±0.40	0.89±0.31	0.93±0.35	0.67±0.22	2.16 (0.1039) NS
ALP (IU/dL)	11.2±3.9 (II,III,IV)*	6.51±2.5 (IV)*	8.10±3.30 (IV)*	4.10±1.40	11.37 (<0.0001)
ALT (IU/L)	50.2±18.1 (II,IV)*	36.8±13.2	42.4±15.5 (IV)*	27.6±8.90	4.78 (0.0052)
AST (IU/L)	53.4±18.5 (II,IV)*	38.7±13.8	45.2±16.4 (IV)*	28.9±9.20	5.26 (0.0031)

* Comparison between individual groups using LSD (least significant difference) at 5% level of significance.
ALP = alkaline phosphatase
ALT = alanine transaminase
AST = aspartate transaminase
NS = not significant

Discussion

In view of environmental factors and inadequate hygienic measures in rural areas, individuals with lower socioeconomic standard pertain higher susceptibility to infection with Schistosoma mansoni. Consequently, an immunosuppressed status may potentiate furthermore their susceptibility to co-infection with viral hepatitis C and G.

In schistosomal cases with viral hepatitis co-infection (HCV and HGV) it was found a significant reduction in α-,β-carotenes and retinol in coordination with severity of hepatic insult (GI>GIII>GII relative to GIV). This suggests that liver disease interferes with their uptake, excretion, or perhaps metabolism. It aligns with previous reports identifying differential depletion of carotenoids and tocopherols in liver disease[8].

Generation of free radical intermediates with hepatocellular injury may be implicated with both lower plasma levels of the aformentioned antioxidants and higher lipid peroxidation product, malondialdehyde (MDA) in the studied group relative to severity of hepatic disposition. Induction of lipid peroxidation by hepatic free radical initiators has been cited in the literature[23]. A free radicals can damage cellular macromolecules participating in hepatocellular injury when produced in excess.

Carotenoids including α-β-carotenes and lycopene help cells to communicate, facilitate cell growth and protect the body from cancer, in association with their antioxidant capacity[24]. High lycopene consumption has been noted to protect against myocardial infarction by preventing the formation of low-density lipoprotein (LDL) in the blood. Lycopene's protective potency appears to exceed those of α- or β-carotenes, which have been highly touted as antioxidants in recent years[24]. In conformity, the higher values of assessed LDL versus lower levels of high-density lipoprotein (HDL) and apoprotein A-I coodinate with the lower levels of lycopene and α-β-carotenes .

Apparently, the higher induction of reactive oxygen species (ROS) posed by hepatocellular damage initiated by schistosmiasis and hepatitis co-infection would agree with previous reports[25] and coincide with the lower levels of vitamin C and retinol monitored here with. Generally ascorbate is able to serve as an antioxidant in free radical-mediated process. However, at lower levels, ascorbate is prone to be pro-oxidant[9].The higher magnitude posed by (ROS) perpetuated higher lipid peroxidation products potentiating hepatocellular damage with altered lipid metabolism. It confirms reports identifying the development of chronic liver damage to be associated with the onset of lipid peroxidation.

On the other hand, free radical initiated-lipid peroxidation via an effect of aldehydic peroxidation products on kupffer cell and lipocytes may play a role in hepatic fibrogenesis. While cellular damage in human liver disease is probably multifactorial, free radicals may play important roles in initiating and/or perpetuating this damage[6]. A close link between lipid peroxidation and activation of inflammatory cells involving infiltration of neutrophils and of a monocyte-macrophage population in the development of chronic liver disease has been reported[6].

Lower levels of the antioxidant vitamin A have been found in liver disease. Apparently, the lower retinol levels assessed herewith relative to liver affection represent an impact on immune system functions and antioxidant defese status. Its coordination with tocopherol function as a powerful antioxidant appears to be affected together with the antioxidant defense system by ascorbate. Their impact on the oxidation of unsaturated fatty acids by trapping free radicals is probably disoriented in relation to the magnitude of lowered levels versus hepatic damage[26].

In parallel, the observed increments in total cholesterol, TG, VLDL and Apo-B, confirm this aspect relative to influence on lipoprotein metabolism . The assessed alterations in liver function tests reflect the Overt strategy of hepatic insult posed by schistosomiasis and viral hepatitis co-infection in agreement with previous repots[23].

In conclusion, the lower antioxidant defense mechanisms assessed herewith may represent the effect of schistosomiasis on the suppression of the immune system rendering decreased clearance of infection making such patients more vulnerable to supreimposed viral infection. A close observation of antioxidant status with supplementation of therapeutic antioxidant regimens within the therapeutic means of treatment of schistosomal cases with viral hepatitis co-infection. Moreover, continual health education and improvement of hygienic conditions with appraisal of awareness regarding environmental hazards may enable safeguard measures towards lowering the incidence of both schistosomal and viral hepatitis infections.

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