Hypolipoproteinemia as Biological Marker in Acute Leukemia

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ABSTRACT:

BACKGROUND:

Acute leukemia is a clonal hematopoietic malignant disease that arises from malignant transformation of an early hematopoietic stem cells .Seeking for biochemical markers that are associated with acute leukemia may help us for better understanding of the leukemic process &improve our lines of management.Hypolipoproteinemia is one of these markers&it is the target of this study.

OBJECTIVE:

To study the association between the hypolipoproteinemia &acute leukemia &the ability of using hypolipoproteinemia as a biological marker that is helpful in follow up of acute leukemia.

PATIENT&METHODS:

A total of fifty patients with acute leukemia diagnosed by blood film&bone marrow examination were compared with control group of twenty healthy persons regarding fasting lipid profile(TC total cholesterol,LDL low density lipoprotein,HDL high density lipoprotein,TG triglyceride).

RESULTS:

In this study there is close association between hypolipoproteinemia&acute leukemia. The mean values of lipoproteins were significantly lower in patient with acute leukemia compared to control group(P value is 0.0001 for total cholesterol&0.045 for triglyceride).

CONCLUSION:

These data suggest that hypolipoproteinemia could be useful as a marker for follow up of acute leukemia.

KEY WORDS: acute leukemia, hypolipoproteinemia

INTRODUCTION:

Acute leukemia is a hematological malignancy characterized by an uncontrolled proliferation of immature lymphocyte &myelocytes &their progenitors. Acute leukemia is classified into acute lymphoblastic leukemia &acute myeloblastic leukemia based on morphological ,cytogenetic ,cell surface &cytoplasmic markers &molecular studies[(1)].The monitoring of the response to cytotoxic therapy &subsequent follow up of leukemic patient is usually performed with periodic clinical examination ,complete blood picture ,bone marrow examination &recently by detection of minimal residual disease using PCR technique. Some biochemical parameters that are associated with leukemia may help us in the follow up of leukemic patients&improve our line of management. Hypolipoproteinemia is one of the biochemical markers that are associated with acute leukemia it may represent the biological difference between malignant &normal cells that help us for selectively destroy the tumor cells by chemotherapy[(2)],in addition hypolipoproteinemia may reflect disease activity . Lipoproteins are macromolecule complexes that carry hydrophobic plasma lipids, particularly cholesterol&triglyceride ,in the plasma . Lipoproteins consist of a core of insoluble cholesterol esters&TG surrounded by proteins,phospholipids &free cholesterol. A family of proteins, the apolipoproteins,also occupies the surface of lipoprotein play a crucial role in the regulation of lipid transport &metabolism[(3)].the Lipoproteins are classified according to their densities which in turn reflects their size ,two are large ,TG-rich complexes;which are chylomicrones&VLDL.Two smaller Lipoproteins contain mostly cholesterol;which are LDL&HDL[(4,5)].Hypolipoprotenemia may occur in other hematological malignancies like chronic myeloid leukemia &myeloid metaplasia with splenomegaly ;hypolipoproteinemia also occurs in

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solid tumors like gastrointestinal,breast&lung cancer,it is also seen in severe hyperthyroidism ,uncontrolled AIDS ,lipid storage disease ,tuberculosis&malaria[3].

PATIENT &METHODS:

This study was performed at the national center for hematological disease at yarmouk hospital from august 2003 to august 2004.Fifty patients with acute leukemia(at presentation or relapsed)(age range 11-58 years ,mean 31.06±14.06;30 males&20 females where included).Any patient with diabetes or renal impairment ,thyroid disease or family history of lipid disorders or on statins was excluded from the study. Control group were twenty healthy volunteers(age range18-58, mean 34.5±14.5;13male&7female).Patients were fasting for 12hours ,5 ml of blood was taken ,centrifuged for 10 min.&the plasma was examined.Direct measurement of TL,TG&HDL was done by spectrophotometer using the wave length 500nm while LDL was calculated from the following equation: LDL=TC-(HDL+TG/5).All measures were in mmol/l.normal ranges of TC is(3.9-6.5mmol/l),TG (0.9-2.4) ,HDL(0.9-1.4)&LDL(1.8-4.3).The lower normal value was used as the cutoff point that discriminate hypolipoproteinemia from normal. Statistical analysis was carried out using SPSS-11.5(statistical package for social sciences-version 11.5).Data were presented in simple measure of frequency ,percentage ,mean ,standered deviation&range(minimum-maximum values).The significance of different means (quantitative data from different groups &from control group)was tested using analysis of variance(ANOVA)for more than two groups &using independent student –t-test for difference between two means, while different percentages(quantitative data from different groups &from control group)were tested using chi-square test (x2-test).Statistical significances was considered whenever the P value was less than 0.05.[6]

RESULTS:

This study data showed significantly greater percentage of patients who have low TC(58%)&lowLDL(34%) compared to the control group (15%&10%respectively)&no significant differences could be demonstrated regarding TG&HDL levels between the patients&the control group(table 1).The results also show significantly lower mean values of lipoproteins in patients compared to the control group:TC mean (3.76±0.62 versus 4.96±1.0mmol/l),TG mean (1.71±0.71 versus 2.11±0.78mmol/l),LDL mean(2.31±0.65 versus2.91±0.94mmol/l),HDL mean (1.11±0.33 versus 1.62±0.51mmol/l)(table2).There were significantly low levels of TC&HDL seen in patients with AML compared to ALL(table 3).The white cell count &blast count have no influence on the level of lipoproteins table(4).

DISCUSSION:

This study data show a significant lower mean value of lipoproteins(TC ,HDL,LDL,TG)in patients with acute leukemia compared to control group .Patients with acute myeloid leukemia had significantly lower mean values of TC&HDL compared with acute lymphoid leukemia patients. In this study we also found that the white blood cells count &blast count had no influence on the level of lipoproteins.There were many studies prove the association between hypolipoproteinemia & acute leukemia&return of normal lipoprotein homeostasis following remission achieved by cytotoxic drugs.Budd& Ginsberg [7]measured plasma TC,LDL,HDL in32 patients with either acute non lymphoid leukemia or chronic myeloid leukemia in blastic crisis &the values were lower than control group,remission in six subjects was associated with significant increase in total cholesterol level. Reverter[8]&Marini [9]reported similar results.Aixala [10]studied two groups ;either normal control or patients with hematological diseases (lymphoma,myeloma, chronic myeloid leukemia , or chronic lymphoid leukemia)concluding that cholesterol&its fraction may be biochemical markers of disease &play an important role in tumor cell metabolism.Baronis [11]study result suggest a close correlation between acute leukemia&TC&its fraction&considered as a reliable markers of complete remission; similar results proved by other two studies involving acute lymphoblastic leukemia[12,13].

The hypocholestrolemia associated with acute leukemia is explained by different hypothesis;Vitols S [14]suggested that this is due to elevated LDL receptor activity in malignant cells,siguard V [15] also said that leukemic cells have increased receptor mediated uptake of LDL,this is proved also by Rensen [16].Adifferent mechanism was suggested by Tatidis[17] showing that hypocholestrolemia in acute myeloid leukemia is due to decreased conversion of cholesterol to bile acid resulting in decreased intestinal absorption of cholesterol.Lenz [18]demonstrated that the deprivation of cholesterol decrease the velocity of growth &alter the composition of the cell membrane.Vitol[19]discovered that simvastatin

impairs mitogen induced proliferation of malignant B-lymphocytes.Tatidis[20]found an elevated uptake of LDL by leukemic cells.another two studies[21,22]showed that low serum lipids was corrected in remission.

Table 1: Frequency & percentage of hypolipoproteinemia in leukemic patients compared to control group

lipoproteins	Control(n=20)		Leukemic(n=50)		P value
	No.	%	No.	%	
Low TC	3	15	29	58	0.001**
Low TG	-	-	1	2	0.524
Low LDL	2	10	17	34	0.041*
Low HDL	4	20	9	18	0.846

TC total cholesterol/ TG triglyceride/ LDL , HDL low& high density lipo.

Table 2: Mean levels of lipoproteins In leukemic compared to control

lipoproteins	Control(n=20)	Leukemic(n=50)	P value
TC mmol/l mean±SD	4.96 ± 1.0	3.76± 0.62	0.0001**
TG mmol/l mean±SD	2.11± 0.78	1.71± 0.71	0.045*
LDL mmol/l mean±SD	2.91± 0.94	2.31± 0.65	0.004**
HDL mmol/l mean±SD	1.62± 0.51	1.11± 0.33	0.0001**

(*)significant (**)highly significant

Table 3: Comparison of lipoprotein levels in ALL vs. AML

Lipoproteins	Lymphoblastic (n=16)	Myeloblastic (n=34)	P value
TC(mmol/l) mean±SD	4.02± 0.75	3.64± 0.52	0.045*
TG(mmol/l) mean±SD	1.84± 0.80	1.64± 0.67	0.386
LDL(mmol/l) mean±SD	2.35± 0.74	2.30 ± 0.61	0.788
HDL(mmol/l) mean±SD	1.30± 0.44	1.01± 0.23	0.003**

Table 4: Comparing some hematological parameters with cholesterol level in leukemic patient

Mean of hemat. parameters	Patients with low TC(n=29)	Patients with normal TC (n=21)	P value
%of blast	39.38 ± 32.09	47.10± 34.09	0.418
WBC count(x1000)	37.31± 64.26	26.86± 32.21	0.497

CONCLUSION:

Hypolipoproteinemia is associated with acute leukemia.Cholesterol &its fraction constitute an interesting biological marker in hematological malignancies which can represent a valuable parameter (although secondary) in follow up of these malignancies.

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