Turkish Journal of Medical Sciences

Volume 42 | Number 3 Article 13

1-1-2012

Plasma lipid levels in patients with acute bacterial infections

MOHAMMAD NASSAJI

RAHEB GHORBANI

TÜBİTAK

Original Article

Turk J Med Sci
2012; 42 (3): 465-469
© TÜBİTAK
E-mail: medsci@tubitak.gov.tr
doi:10.3906/sag-1011-1278

Plasma lipid levels in patients with acute bacterial infections

Mohammad NASSAJI[1], Raheb GHORBANI[2]

Aim: To assess the impact of acute bacterial infections on plasma lipid levels and to determine the value of plasma lipid measurements in the diagnosis of acute bacterial infection.

Materials and methods: A cross-sectional study was conducted involving 112 patients with acute bacterial infections admitted in hospital and 112 healthy individuals as controls. Levels of total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein, and triglycerides were measured in blood samples of all subjects. Mean levels of serum lipids were compared in both groups.

Results: Both groups were matched based on age (P = 0.10), sex (P = 0.789), BMI (P = 0.515), and history of diabetes mellitus (P = 0.231). Compared with control subjects, in patients with acute bacterial infections, significantly lower levels of total cholesterol (P = 0.013) and high-density lipoprotein cholesterol (P = 0.001) were found. There was no statistically significant differences in triglycerides (P = 0.194) and low-density lipoprotein (P = 0.075) serum levels between patients and controls.

Conclusion: These results suggested that acute bacterial infections are associated with decreased serum cholesterol and high-density lipoprotein level. Therefore plasma lipids levels may serve as indicators of acute bacterial infections.

Key words: Acute bacterial infections, lipoproteins, cholesterol, triglycerides

Introduction

Lipids, such as cholesterol and triglycerides, are insoluble in plasma. Circulating lipid is carried in lipoproteins that transport the lipid to various tissues for energy utilization, lipid deposition, steroid hormone production, and bile acid formation (1). Plasma lipoproteins are divided into 5 major classes based on their relative density: chylomicrons, very low-density lipoprotein (VLDL), intermediate-density lipoprotein (IDL), low-density lipoprotein (LDL), and high-density lipoprotein (HDL) (2). Besides their role in lipid transport, lipoproteins participate in innate immunity, which is the first line of host defense against invading microorganisms (3). In addition, anti-inflammatory effects of lipoproteins, especially HDL, have been demonstrated both in vitro and in vivo studies (4). Circulating lipoproteins bind and detoxify lipopolysaccharide and toxins of gram-negative and lipoteichoic acid of gram-positive bacteria (5,6).

Infection and inflammation produce a variety of profound changes in plasma lipid and lipoprotein concentration, composition, and function. Many of the changes are induced by cytokines that are released during infections and inflammations (7,8).

Received: 15.11.2010 – Accepted: 29.05.2011

[1] Department of Infectious Diseases, Fatemieh Hospital, Semnan University of Medical Sciences, Semnan - IRAN
[2] Department of Biostatistics, Social Medicine, Semnan University of Medical Sciences, Semnan - IRAN
Correspondence: *Mohammad NASSAJI, Fatemieh Hospital, 17 Shahrivar Blvd, Semnan - IRAN*
E-mail: hnassaji@yahoo.com

In patients with infection, decreases in the serum levels of total cholesterol (TC), LDL, and HDL and increase of serum triglyceride (TG) have been reported in most studies. These changes were independent of the underlying disease or infectious agents (9,10). The effects of infections on TG metabolism are similar in all animals, whereas changes in cholesterol metabolism differ between rodents and primates. In rodents, there is an increase in serum total cholesterol levels and hepatic cholesterol synthesis, whereas nonhuman primates and humans have either no change or a decrease in serum cholesterol and LDL levels. HDL levels are decreased in both rodents and primates during acute illness. The mechanisms underlying this species difference are not known (11,12).

Finally, infections produce alterations in the composition and function of lipoproteins, including changes in sphingolipid concentrations, decreased reverse cholesterol transport, and increased oxidation of lipids (8).

It has been proposed that the changes in lipids and lipoproteins metabolism that occur during infection induce anti-inflammatory effects that contribute to the host defense (13).

Markers that will be able to differentiate the inflammatory response of infection from other types of inflammations would be helpful. There are still controversies regarding the change in plasma lipids during acute infections. The diagnostic accuracy of plasma lipid routine measurements for infection needs further investigation. Moreover, whether in patients with acute bacterial infections plasma lipids could help to differentiate bacterial from nonbacterial diseases remains unknown. In most previous studies one bacterial infection or patients with severe infection were evaluated and most of these studies did not include a control group. Therefore, we designed this study to investigate the change in concentrations of TC, TG, HDL, and LDL in patients with acute bacterial infections and compare them with those of healthy subjects. We hypothesized that plasma lipids can serve as a marker to differentiate acute bacterial infections from other acute conditions.

Materials and methods

Adult patients older than 16 years with acute bacterial infections admitted to Fatemieh hospital in Semnan Province of Iran, between June and December of 2009, were considered for inclusion in the study. Acute bacterial infections included in this study were pneumonia, acute pyelonephritis, bacterial dysentery, and cellulites. The control group was selected from the healthy adult population. Informed written consent was obtained from all subjects before enrollment. The study protocol was approved by the Research Council and Ethical Committee of the Semnan University of Medical Science.

Both groups were matched based on age, sex, body mass index (BMI), and diabetes mellitus. Individuals with a history of hyperlipidemia, diseases that can cause secondary hyperlipidemia, concomitant acute illness, and history of infection or who received treatment with lipid-lowering drugs within the previous month were excluded. Acute bacterial infections were diagnosed according to standard clinical, laboratory, and radiographic criteria by a board-certified specialist in infectious diseases. Baseline assessment included collection of demographic data, BMI, history of diabetes mellitus and, in patients, the type of bacterial infection.

In all subjects, the day after admission, an overnight fasting venous blood sample was taken and serum levels of total cholesterol, triglyceride, HDL, and LDL were measured with a colorimetric method (Biomerieux photometer, France). Normal levels based on the kit used were: cholesterol 130-200, TG <150, HDL 40-70, LDL<130. Mean levels of serum lipids were compared between the 2 groups.

Statistical analysis was performed by chi-square, Student's t test, multivariate analysis and Bonferroni test using SPSS for Windows version 16.0. P values of less than 0.05 were considered statistically significant.

Results

A total of 112 patients with bacterial infections who fulfilled the inclusion criteria and the same number of controls were enrolled. Of the 112 patients included, 41 (36.6%) had pneumonia, 26 (23.2%) bacterial dysentery, 24 (21.4%) acute pyelonephritis, and 21 (18.7%) cellulitis. The time from onset of symptoms

until sampling in 93.8% was less than 48 h and, in 6.2% of patients, it was 48-96 h.

Sex, BMI, history of diabetes mellitus, and mean (± SD) age for patients and the control group are listed in Table 1. There were no significant differences in age, sex, BMI, and history of diabetes mellitus.

Multivariate analysis showed that mean serum levels of cholesterol (P = 0.013) and HDL-C (P = 0.001) were significantly lower in patients compared to controls. However, there was no significant difference between mean serum levels of triglyceride (P = 0.194) or LDL (P = 0.075) between the groups (Table 2).

Discussion

In the present study, we found that levels of cholesterol and HDL were significantly lower in patients with acute bacterial infection than they were in healthy control subjects. Levels of TG and LDL tended to be lower in patients but did not show significant differences compared with controls.

The exact pathophysiology underlying the change in the level of serum lipids in severe illness and infection has never been fully understood. Different mechanisms, including imbalance between synthesis and utilization of plasma lipids, usage of lipids to restore damaged cell membranes, and interaction of cytokines and

Table 1. Characteristics of patients with bacterial infections and control groups.

Characteristic	Study group				P-value
	Case		Control		
	Mean ± SD*	%	Mean ± SD	%	
Sex					
Female	-	52.7	-	50.9	0.789
Diabetes mellitus					
+	-	6.3	-	10.7	0.231
Body mass index					
<18.5	-	3.6	-	2.7	0.515
18.5-24.9		39.3		42.9	
25-29.9		36.6		41.1	
30≤		20.5		13.4	
Age	53.9 ± 20.3		49.9 ± 15.1		0.100

* SD: Standard deviation

Table 2. Mean ± standard error (SE) and difference of serum lipids between patients with acute bacterial infections and control group.

Serum lipid	Study group		Difference between 2 groups		
	Case	Control	Mean ± SE	P-Value	95% CI**
	Mean ± SE*	Mean ± SE			
TG	133.3 ± 13.5	158.0 ± 13.6	24.7 ± 18.9	0.194	(–12.6, 62.0)
Cholesterol	147.5 ± 6.4	170.0 ± 6.3	22.2 ± 8.9	0.013	(4.6, 39.7)
HDL	41.2 ± 0.8	45.2 ± 0.8	4.0 ± 1.1	0.001	(1.8, 6.3)
LDL	80.1 ± 5.4	93.6 ± 5.4	13.5 ± 7.6	0.075	(–1.4, 28.4)

* Standard error **CI: Confidence interval

bacterial toxins with lipids have been discussed (14-16). Several clinical and experimental studies suggest that high circulating levels of different cytokines may be responsible for the decrease in cholesterol levels in acute illnesses (17). Furthermore, one important mechanism leading to the decrease in HDLC is consumption through bacterial substances, particularly lipopolysaccharide (LPS) and other endotoxins (6,18). Another reason for the decreased serum HDL levels might be elevated secretory phospholipase A2 activity and serum amyloid A levels, which increase during acute bacterial infections and result in increased catabolism of HDL-C (19). Finally, lipoproteins may be redistributed from the intravascular to the extravascular compartment due to inflammation-induced capillary leakage. Preliminary data indicate that, due to the high molecular mass of lipoprotein, in normal situations, only small amounts of lipoproteins can be found in the extravascular fluids (3,17).

Our findings confirm most other studies reporting that cholesterol and HDL levels decrease in acute infections. In accordance with our findings, Alvarez et al. found that concentration of total cholesterol, HDL and apoproteins decreased during sepsis (10). Similarly, another study showed that HDL-C and total cholesterol levels were lower in critically ill infected patients than they were in non-infected patients (20). Patients with community-acquired pneumonia have had significantly lower total cholesterol and HDL-C in Gruber et al.'s study (21). Vermont et al. reported extremely low levels of total serum cholesterol and HDL in children with severe meningococcal disease who are in the initial phase (22).

In contrast to earlier studies that described hypertriglyceridemia during infections (10,23,24), our study showed no significant difference in triglyceride concentrations in patients with bacterial infections compared to normal subjects. Kerttula et al. found a low triglyceride level in patients with bacterial pneumonia (25). In another study, lower plasma level of triglyceride was reported in patients with severe sepsis (17). In contrast, one study showed slightly elevated triglyceride level in children with pharyngitis; however, no significant difference was observed compared to healthy children (26). Similarly, Gordon et al. reported in their study that, in critically ill patients, the mean triglyceride concentration was higher in patients with an infection compared to patients without infection, but these differences were not statistically significant (27). In another study no significant difference was seen in the serum TG level in critically ill infected patients when compared with non-infected critically ill patients (20). This difference in findings may be due to the type of disease being evaluated and the number of patients.

Some studies showed that plasma LDL-C levels are reduced during infection and inflammation (17,21,22). This is thought to be caused by the host response to infection and inflammation, which might induce LDL-C oxidation resulting in lower serum LDL-C levels (7). In our study, the level of LDL was lower in patients but this decrease was not significant.

The limitations of our study must be pointed out. First, unfortunately, we do not know the pre-admission plasma lipid values of our patients. Second, we did not follow our patients and so we could not determine how long this change in lipid levels persisted. Third, the number of patients enrolled in the study was low. A study with a larger group of patients is recommended.

It was suggested in some studies that increasing the low plasma lipoprotein concentrations that are common during acute illness was a therapeutic option for preventing and treating the clinical syndromes associated with infection (4,16), which warrants further study.

If confirmed in further studies with a larger sample and combined with other clinical and laboratory markers, measurement of plasma lipids, especially cholesterol and HDL, may allow clinicians to target patients with acute bacterial infections. On the other hand, physicians should be reminded that measurement of lipid values in patients with bacterial infections should not be used for cardiovascular risk prediction, since circulating levels of TC and HDL-C may be false-low in such patients.

More studies are needed to explore the potential of plasma lipids compared to alternative measures in monitoring infection and therapy response in patients with bacterial infections. Furthermore, it is recommended that these changes be followed after recovery from infections and serum lipids in patients with bacterial and viral infections be compared.

Conclusion

Low levels of plasma lipids, particularly cholesterol and HDL, may point to acute bacterial infection. This property might be due to an association with the acute-phase response. Therefore decreased plasma levels of cholesterol and HDL may serve as indicators of acute bacterial infections.

References

1. Mahley R, Wisgraber K, Bersot T. Disorders of lipid metabolism. In: Kronenberg H, Melmed S, Polonsky K, Reedlarsen P, editors. Williams Textbook of Endocrinology. 11th ed. Philadelphia: Saunders; 2008. p.1589-1610.
2. Kwiterovich PO Jr. The metabolic pathways of high-density lipoprotein, low-density lipoprotein, and triglycerides: a current review. Am J Cardiol 2000; 21: 5-10. Review
3. Murch O, Collin M, Hinds CJ, Thiemermann C. Lipoproteins in inflammation and sepsis. I. Basic science. Intensive Care Med 2007; 33: 13-24.
4. Khovidhunkit W, Kim M, Memon RA, Shigenaga JK, Moser AH, Feingold KR et al. Effects of infection and inflammation on lipid and lipoprotein metabolism: mechanisms and consequences to the host. J Lipid Res 2004; 45: 1169-96.
5. Iribarren C, Jacobs DR, Sidney S, Claxton AJ, Feingold KR. Cohort study of serum total cholesterol and in-hospital incidence of infectious diseases. Epidemiol Infect 1998; 121: 335-47.
6. Emancipator K, Csako G, Elin RJ. In vitro inactivation of bacterial endotoxin by human lipoproteins and apolipoproteins. Infect Immun. 1992; 60**:** 596-601.
7. Carpentier YA, Scruel O. Changes in the concentration and composition of plasma lipoproteins during the acute phase response. Curr Opin Clin Nutr Metab Care 2002; 5: 153-8.
8. Khovidhunkit W, Memon RA, Feingold KR, Grunfeld C. Infection and inflammation-induced proatherogenic changes of lipoproteins. J Infect Dis 2000; 181: 462-472.
9. Khosla SN, Goyle N, Seth RK. Lipid profile in enteric fever. J Assoc Phys India 1991; 39: 260-2.
10. Alvarez C, Ramos A. Lipids, lipoproteins and apoproteins in serum during infections. Clin Chem 1986; 32: 142-5.
11. Wu A, Hinds CJ, Thiemermann C. High-density lipoproteins in sepsis and septic shock: metabolism, actions, and therapeutic applications. Shock 2004; 21: 210-21.
12. Sammalkorpi K, Valtonen V, Kerttula Y, Nikkila E, Taskinen MR. Changes in serum lipoprotein pattern induced by acute infections. Metabolism 1988; 37: 859-65.
13. Hardardóttir I, Grünfeld C, Feingold KR. Effects of endotoxin and cytokines on lipid metabolism. Curr Opin Lipidol 1994; 5: 207-15.
14. Fraunberger P, Schaefer S, Werdan K, Walli AK, Seidel D. Reduction of circulating cholesterol and apolipoprotein levels during sepsis. Clin Chem Lab Med 1999; 37: 357-62.
15. Kaminska M, Badzio T, Ksiezopolska-Kaczorowska A, Bako W, Boj E, Przymanowski Z. High-molecular-weight lipoprotein concentrations in pneumonia in children. Problem Med Wieku Rozwoj 1983; 12: 363-75.
16. Gordon BR, Parker TS, Levine DM, Saal SD, Wang JC, Sloan BJ et al. Relationship of hypolipidemia to cytokine concentrations and outcomes in critically ill surgical patients. Crit Care Med 2001; 29: 1563-8.
17. van Leeuwen HJ, Heezius EC, Dallinga GM, van Strijp JA, Verhoef J, van Kessel KP. Lipoprotein metabolism in patients with severe sepsis. Crit Care Med 2003; 31: 1359-66.
18. Ettinger WH, Varma VK, Sorci-Thomas M, Parks JS, Sigmon RC, Smith TK et al. Cytokines decrease apolipoprotein accumulation in medium from Hep G2 cells. Arterioscler Thromb 1994; 14: 8-13.
19. Artl A, Marsche G, Lestavel S, Sattler W, Malle E. Role of serum amyloid A during metabolism of acute-phase HDL-C by macrophages. Arterioscler Thromb Vasc Biol 2000; 20: 763-72.
20. Lüthold S, Berneis K, Bady P, Müller B. Effects of infectious disease on plasma lipids and their diagnostic significance in critical illness. Eur J Clin Inves 2007; 37**:** 573-579.
21. Gruber M, Christ-Crain M, Stolz D, Keller U, Müller C, Bingisser R et al. Prognostic impact of plasma lipids in patients with lower respiratory tract infections – an observational study. Swiss Med Wkly 2009; 139: 166-72.
22. Vermont CL, den Brinker M, Kâkeci N, de Kleijn ED, de Rijke YB, Joosten KF et al. Serum lipids and disease severity in children with severe meningococcal sepsis. Crit Care Med 2005; 33: 1610-5.
23. Deniz O, Tozkoparan E, Yaman H, Cakir E, Gumus S, Ozcan O et al. Serum HDL-C levels, log (TG/HDL-C. values and serum total cholesterol/HDL-C ratios significantly correlate with radiological extent of disease in patients with community-acquired pneumonia. Clin Biochem 2006; 39: 287-92.
24. Henter JI, Carlson LA, Hansson M, Nilsson-Ehle P, Ortqvist E. Lipoprotein alterations in children with bacterial meningitis. Acta Paediatr 1993; 82: 694-8.
25. Kerttula Y, Weber T. Serum lipids in pneumonia of different aetiology**.** Ann Clin Res 1988; 20:184-8.
26. Iscan A, Yigitoglu R, Onag A, Vurgun N, Ari Z, Ertan P et al. Should children with infection be tested for lipid, lipoprotein and apolipoprotein? Acta Paediatr Jpn 1998; 40: 47-51.
27. Gordon BR, Parker TS, Levine DM, Saal SD, Wang JC, Sloan BJ et al. Low lipid concentrations in critical illness: implications for preventing and treating endotoxemia. Crit Care Med 1996; 24: 584-9.