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Original Research Article

Plasma Concentration of Interleukin-6 and the Risk of Future Myocardial Infarction

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Conflict of interest: Nil

Abstract

Background: Interleukin-6 (IL-6) is a key player in tissue damage and inflammation. There aren't many epidemiological studies examining IL-6 is impact on atherogenesis, though. Methods: In a prospective study involving 1000 seemingly healthy men, we assessed baseline plasma concentrations of IL-6 in 500 participants who later experienced a myocardial infarction (MI) and 500 study participants who were age- and smoking-matched but did not report vascular disease. **Results:** Men who later experienced a MI had median IL-6 concentrations that were greater than males who did not. Men in the highest quartile at entry had a relative risk that was 2.5 times higher than those in the lowest quartile (95% CI 1.5 to 4.5, P0.005); for each quartile increase in IL-6, there was a 38% increase in risk. The risk of future MI increased with increasing quartiles of baseline IL-6 concentration (P for trend, 0.001) (P0.001). When accounting for additional cardiovascular risk factors, this connection remained substantial, was persistent over extended durations of follow-up, and was apparent in all low-risk populations, including nonsmokers. C-reactive protein (P0.001) was the greatest predictor of IL-6 in these data, but even after controlling for it, the association between IL-6 and eventual risk persisted (P0.001).

Conclusion: Elevated levels of IL-6 are linked to an increased risk of future MI in men who appear to be in good health. Hence, our findings are consistent with an early role for cytokine-mediated inflammation in atherogenesis.

Keywords: Plasma, Interleukin-6, Myocardial Infarction.

Introduction

Throughout the past few decades, a lot of studies has been done to better understand the function of inflammation in the progression of cardiovascular disease. An extreme inflammatory response is seen in myocardial infarction (MI), which is necessary for cardiac healing but also plays a role in the etiology of post-infarction remodeling and heart failure [1]. Lastly, even in individuals without overt plaque rupture or acute tissue trauma, higher

levels of IL-6 and other acute-phase proteins have been observed in those with acute coronary syndromes [2-4]. In light of these findings and the theory that atherosclerosis is primarily a chronic inflammatory condition [5]. we looked into the possibility that persons who appear to be in good health but are at risk for myocardial infarction may have elevated plasma levels of IL-6. We also looked to see if there was any association between IL-6 and later vascular risk that was altered by other cardiovascular risk factors, such as chronic inflammation marker levels.

Methods

We conducted a prospective, case-control study of 1000 patients at Rama Medical College in Hapur, Uttar Pradesh, to determine if IL-6 could predict myocardial infarction. 1000 male patients between 40 and 85 without a history of myocardial infarction, stroke, transient ischemic attack, or cancer participated in a randomized, double-blind, placebo-controlled trial of aspirin (325 mg PO every other day) and b-carotene (50 mg PO every other day) for cardiovascular disease and cancer prevention in the Health Study. Participants were asked to submit baseline blood samples between June and November 2022. These EDTA-preserved samples were stored at 280°C. Blood was drawn from trial participants taking active oral aspirin. Myocardial infarction was confirmed if symptoms matched WHO guidelines and diagnostic cardiac enzymes or ECG changes were elevated.Controls produced appropriate baseline plasma samples and did not develop the vascular disease during follow-up. Controls were randomly assigned to trial participants who met age (61 years), study follow-up (6-month intervals), and smoking status requirements (past smoker, current smoker, or never smoked). The Wilcoxon rank-sum test was used to determine the significance of median values between cases and controls because IL-6 levels were skewed. After categorizing the study sample into IL-6 quartiles based on control values, we calculated the relative risks of future myocardial infarction using logistic regression. This analysis required age and smoking matching.

Result

The low-risk subgroups of nonsmokers, those without a history of hypertension, hyperlipidemia, diabetes, or obesity, and those without a family history of early myocardial infarction also showed differences, as shown in Table 1.

Table 1: Baseline Plasma Concentrations of IL-6 According to Case and Control Status

	Controls	Cases	P
All participants	1.45	1.75	0.001
Non-smokers	1.34	1.70	0.001
No-hypertension	1.45	1.75	0.002
No-hyperlipidemia	1.40	1.80	0.006
No-diabetes	1.42	1.76	0.001
No-obesity	1.35	1.65	0.006
No family history of CAD	1.45	1.80	0.006

In analyses that controlled for baseline variations in total cholesterol, HDL cholesterol, body mass index, blood pressure, diabetes, a family history of premature coronary artery disease, alcohol use, and frequency of exercise, the relationship between baseline IL-6 level and risk of future myocardial infarction remained unchanged (Table 2).

Table 2: Risks of Future Myocardial Infarction Among Apparently Healthy Men According to Baseline Level of IL-6

	1 (<1.04)	2 (1.04–1.46)	3 (1.47–2.28)	4 (>2.28)	P for Trend
Crude analysis Total cohort					
RR	1.0	1.5	2.5	2.4	<0.001
95% CI	⋯	0.5–2.5	1.5–5.5	1.4–4.5	
P Nonsmokers	⋯	0.2	0.001	0.005	
RR	1.0	1.5	2.5	2.6	0.001
95% CI	⋯	0.5–2.5	1.5–4.5	1.5–4.5	
P	⋯	0.2	0.003	0.01	
Total and HDL cholesterol adjusted Total cohort					
RR	1.0	1.5	2.8	2.3	0.002
95 % CI	⋯	0.7–2.9	1.6–5.4	1.2–4.2	
P Nonsmokers	⋯	0.3	0.001	0.01	
RR	1.0	1.6	2.6	2.5	0.003
95% CI	⋯	0.6–3.0	1.6–5.1	1.5–5.1	
P	⋯	0.2	0.003	0.01	
Fully adjusted Total cohort					
RR	1.0	1.9	3.5	2.3	0.01
95% CI	⋯	0.9–3.9	1.5–6.5	1.3–4.3	
P Nonsmokers	⋯	0.08	0.001	0.03	
RR	1.0	2.0	3.6	2.7	0.007
95% CI	⋯	1.0–4.5	1.6–6.7	1.1–5.7	
P	⋯	0.06	0.002	0.02	

Discussion

These findings suggest that healthy people at risk for future myocardial infarction have significantly higher baseline IL-6 levels. In analyses that controlled for baseline variations in total cholesterol, HDL cholesterol, body mass index, blood pressure, diabetes, a family history of early coronary artery disease, alcohol use, or frequency of exercise, the relationship between IL-6 level and risk did not change. Few studies have examined the function of IL-6 in healthy people at risk for future coronary events. IL-6 levels rise in response to acute ischemia and may indicate plaque instability [6,7]. The elevated IL-6 levels in these results cannot be attributed to acute ischemia because baseline blood samples were taken for the current investigation. Our findings suggest that such effects are common and can be clinically diagnosed many years before the first myocardial infarction if people with a tendency for acute plaque rupture have an elevated inflammatory response [8]. IL-6 levels are elevated in autoimmune diseases like arthritis, Castleman syndrome, psoriasis, mesangial proliferative glomerulonephritis, and inflammatory bowel disease. Atherosclerosis is at least partially inflammatory, according to the data [6]. C-reactive protein and fibrinogen were the strongest predictors of IL-6, which is expected since IL-6 stimulates the hepatic synthesis of acute-phase proteins [9].

Think about these data's limitations. Since we only used one baseline blood sample, we cannot account for IL-6 changes over time.

Our data may also be constrained by IL-6 diurnal variation because our baseline blood samples were not collected at the same time. IL-6 levels are raised by glucocorticoids and catecholamines, and its plasma half-life is 6 hours. Since all of our study participants were taking oral aspirin at the time of blood sample, this medication's effect on IL-6 levels could not have changed our primary findings [10]. IL-6 is produced by unknown stimuli in healthy men at risk for myocardial infarction. IL-6 may be a disease marker, but preclinical atherosclerosis may be an inflammatory stimulus. Since monocyte-derived macrophages are abundant in atherosclerotic plaque and IL-6 gene transcripts are expressed in human atheroma, increased IL-6 production from endothelium and vascular smooth muscle may directly affect plaque proliferation and stability. IL-6 levels rise with infection, which may worsen atherogenesis.

Conclusion

As a result, we think that these findings lend credence to the idea that anti-inflammatory medicines can offer a fresh method for the treatment and prevention of cardiovascular disease.

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