Natural Remedies Lower Fibrinogen Levels in the Prevention of Atherosclerosis

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Introduction

The purpose of this paper is to present evidence that elevated plasma fibrinogen causes intravascular inflammation, is a result of inflammation, and is part of the clotting factor contributing to CVD [1]. The secondary purpose of this review is to show elevated fibrinogen levels are an early predictor of future CVD. The final purpose of this report is to discuss natural remedies that can lower fibrinogen levels.

Fibrinogen is one of 12 blood clotting factors in the human body. Fibrinogen proteins are soluble proteins that get converted to fibrin, an insoluble protein. The presence of elevated fibrinogen in blood plasma indicates acute and/or chronic inflammation in various parts of the body, most notably, in the cardiovascular system [2].

Fibrinogen appears as a result of inflammation and is a predictor of CVD severity [2]. Endothelial cells line the entire structure of the inner most part of all arteries, veins, and capillaries. The other inner most layers are the tunica intima and the tunica media. Intima Media Thickness (IMT) of the carotid artery can be measured and is a reliable indicator of the presence and severity of CVD [3,4]. Plasma fibrinogen levels have a high relationship with the severity of IMT [5].

Fibrinogen levels rise in the acute phase of post ischemic stroke [6]. Fibrinogen levels that continue to rise in post ischemic stroke result in a poor prognosis [7]. Therefore, fibrinogen testing is done when CVD is suspected and when a CVD incident has occurred. However, fibrinogen testing can also be an early predictor of future CVD. Evidence suggest that fibrinogen levels begin to slowly rise months, even years, as part of the slow progressive clotting patho-physiology cascade in vascular diseases [8]. The presence of fibrinogen levels in the ages 27 to 35 has been singularly linked to IMT 13 years later in the CARDIA study [8].

Fibrinogen and CRP are both proteins that make up plaque. CRP test is a sensitive test for inflammation and is more predictive of cardiovascular risk as suggested by many research papers [2]. Therefore, CRP is the test primarily given to patients. Fibrinogen is part of the clotting factor and there is growing evidence suggesting its presence is equally as revealing as the CRP. Combining the CRP and the fibrinogen test results in what is called CRP/Fibrinogen ratio, which has been shown to be more sensitive and a better predictor of CVD risk than each of these test used alone because of their higher level of sensitivity in detecting Disseminating Intravascular Coagulation (DIV), a condition where fibrin ultimately causes excessive clots leading to multiple organ failure [9].

Warfarin (Coumadin) is an anticoagulant and a common drug of choice in patients with thrombosis [10]. Warfarin reduces clotting factor by functioning as a Vitamin K antagonist [11]. Vitamin K is part of the blood clotting process. Vitamin K antagonists play a role in clot formation by reducing Vitamin K’s ability to form clots. One of the primary functions of vitamin K is to inhibit vascular calcification [12]. It has been suggested that Vitamin K antagonists promote arterial calcification and increase IMT by reducing the function of Vitamin K to prevent calcification [10,11]. In a longitudinal study by Lip et al. [9]
Warfarin elevated fibrinogen levels 0.36 g/l. This side effect of Vitamin K antagonist classification of drugs warrants other means of preventing and reversing atherosclerotic coagulation.

Methods

This article is a review of published, peer reviewed scientific papers that support the reliability of fibrinogen as an indicator of existing CVD, future CVD risk, and natural remedies and methods that studies have shown to be effective in reducing plasma fibrinogen levels. The relevant types of studies ranged from double-blind, scientific review, retrospective study, cohort study, and meta-analysis papers.

There are many laboratory testing methods of assessing the presence of fibrinogen in blood plasma. The Clauss method is a fairly common one. In reviewing literature relevant to fibrinogen it became evident that many researchers did not mention the specific fibrinogen detecting test, rather, they simply mentioned the test results. The reference range for fibrinogen is generally between 1.5 g/l to 4.0 g/l [14]. This paper will discuss effective methods used at lowering plasma fibrinogen measured in g/l and percent reduction relative to base levels of each specific study.

Various non-pharmaceutical methods of intervention exist in the prevention of CVD by reducing plasma fibrinogen levels. These methods can be organized into 3 broad categories of herbs, exercise, and stress reduction. Many of these methods are often combined by natural health practitioners from various health systems including naturopathy, Ayurveda, and TCM.

Intervention 1

Herbs

There are many natural herbal remedies that show benefit in helping to ameliorate high fibrinogen levels. This report includes a small sampling of a few common remedies often prescribed by natural health practitioners. Most of these herbs appear to reduce plasma fibrinogen using different physiological pathways than the vitamin K dependent means of Coumadin (Warfarin), a pathway that is independent on Vitamin K [10].

Fish oil

Vanschoonbeek et al. studied the hypocoagulant effects of 3.0 g of omega 3 fish oil on 25 healthy, borderline overweight, male volunteers for 4 weeks [15]. Their data suggested that fibrinogen was significantly reduced −4.1% ± 3.1%, there is a causal relationship between the lowering of fibrinogen levels and a lowering of thrombin, and this effect was achieved independent of vitamin K [15].

Hartweg et al. [16] reviewed 24 studies on omega 3 fish oils from 1966 to 2008. They studied the data of 1533 participants who took 2.4 g of omega 3 fish oils for 24 weeks. Compared to the control groups their data revealed that fibrinogen levels reduced by 10%.

Mita et al. [17] studies 60 Japanese type 2 diabetic patients who took 1800 mg of eicosapentaenoic acid (EPA) fish oils per day for 2.1 ± 0.2 years [17]. Their data revealed a significant annual decrease of Carotid IMT compared to the control group (mean IMT, -0.029 mm ± 0.112 mm versus 0.016 mm ± 0.109 mm).

Hostmark et al. [18] conducted a double blind study of sixty four men between the ages of 35-40 for 6 weeks divided into two groups. Their data revealed that within 3 weeks of 14 g of omega 3 fish oils there was a significant reduction of plasma fibrinogen of 13.2% compared to the control group of participants that took 14 g of olive oil capsules per day who showed no significant fibrinogen lowering effect [18].

Nattokinase

Hsia et al. conducted a study of 3 groups of participants (Healthy Group, Cardiovascular Group, and Dialysis Group) who took 2 capsules of nattokinase (2000 fibrinolysis units per capsule) daily orally for 2 months. Their data showed that fibrinogen decreased by 9% in the Healthy Group, 7% for the Cardiovascular Group, and 10% on the Dialysis Group [19].

XueFu ZhuYu Decoction

Wang et al conducted a meta-analysis study of XueFu ZhuYu Decoction (XZD) [20]. Their data from a study of 62 participants in XZD group and 62 participants in the conventional antihypertensive group showed that XZD Lowered plasma fibrinogen -0.56 g/l and improved IMT -0.40 mm [20].

Intervention 2

Exercise

Research data in a few studies on exercise and fibrinogen levels have shown that mild to moderate exercise can lower fibrinogen levels [21-24]. Connelly et al. [21] conducted a cross sectional survey of 3967 male participants and found that strenuous exercise, which included jogging, cycling, and fast swimming lowered fibrinogen levels by 15%.

Gomez-Marcos et al. [24] studied 1,284 participants with fibrinogen present showed a decrease of plasma fibrinogen levels was causally related to physical activity. Physical activity was measured by the 7-Day PAR (Physical Activity Recall) method where subjects that performed 30 minutes of moderate activity five days a week or a minimum of 20 minutes of hard activity for 3 days a week reduced plasma fibrinogen levels by -0.162 mg/dl. Elwood at al. [23] performed a cross sectional study of 2,398 men between the ages 50-64 years. Their data showed a strong correlation between High Intensity leisure activities (Jogging, Soccor) and lower fibrinogen concentration by 0.24 g/l in the third of men who were most active in leisure activities.

Intervention 3

Stress reduction

There is a strong statistical correlation between psychological stress over a period of few years, plasma fibrinogen concentration, and CVD in various studies [25-28], Ellis et al. [27] studied 155 healthy men and women who performed standardized behavioral tasks that induced acute psychological and physiological stress resulting in an inflammatory response evident in blood test measuring plasma fibrinogen, tumor necrosis factor (TNF) alpha and interleukin (IL) 6. Individuals that presented with higher plasma fibrinogen concentrations had increased carotid artery stiffness 3 years later [27].

Steptoe et al. [26] show a similar correlation between psychological stress, inflammatory response, fibrinogen, and increased risk of hypertension after an 8 year period. The study focused on the relationship between psychological stress and hypertension along with
the biological impact of acute stress on cardiovascular function and concluded that women had the greater risk.

Wolff et al. [28] in a larger study involving 2164 participants showed that high psychological strain did not predict IMT; however, there data did reveal a linear relationship to plaque buildup.

Lippi et al. [25] studied the morning serum cortisol and fibrinogen levels in 302 patients and found a strong statistical relationship between elevated levels of the two inflammatory markers. They found morning cortisol levels that were higher on the reference parameters equated with higher fibrinogen levels.

Conclusion

The high prevalence of CVD and side effects of conventional medical treatments warrant multimodal methods of intervention. Inflammatory markers like fibrinogen and CRP along with the measurement of IMT has been shown to be clinically viable means of assessing present and future CVD risk. Preventative medicine by way of natural medical systems show promise in helping to ameliorate symptoms and inflammatory markers associated with CVD. This paper presents compelling evidence that natural remedies can play a significant role in the treatment and prevention of CVD and the role of natural remedies should continue to be given scientific attention.

References


