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"The Effects of Obesity and Estrogen Based Contraceptive Use on Protein S Levels and Clotting Function in Pre-menopausal Women"

Protein S (PS) is an essential natural anticoagulant whose deficiency is a major contributor to acquired hypercoagulability [1]. Acquired hypercoagulability causes myocardial infarction, stroke, and deep vein thrombosis in millions of individuals [2]. Many factors affect plasma PS level; most prominently, the female hormone estrogen alters PS level by suppressing PS gene transcription via the estrogen receptor α (ERα) [3]. Thus, women who use estrogen-based oral contraceptive agents (OCA) experience a decrease in PS level. This contraceptive-induced PS decrease enhances the risk of thrombosis by 3-fold (4). Decreased plasma PS is also associated with obesity; obesity elevates the risk of thrombosis by 2.5-fold [5]. Dramatically, the risk of thrombosis increases as much as 24-fold in obese subjects who use OCA [6]. This study is aimed to determine whether there is a downregulation of PS in premenopausal obese women on estrogen-based contraceptives compared to the controls.

We collected blood samples from 10 volunteers who were pre-menopausal women of varied BMI and OCA use. 5 mL blood samples from the subjects were collected into citrated (3.2 %) tubes and centrifuged to isolate PPP (platelet poor plasma). 5 additional plasma samples were used from a previous study to normalize our data. We used different assays using the PPP to determine the clotting parameters of the samples: Activated Partial thromboplastin Time (aPTT), Thrombin Generation Assay (TGA), Enzyme-Linked Immunosorbent Assay (ELISA), and Western Blot. We analyzed the data using Microsoft Excel and Image J.

We observed that individuals who were considered obese, had OCA use, or both had a shorter aPTT clotting times and higher thrombin generations compared to controls. We determined free PS levels by ELISA and observed that free PS levels of the subjects on OCA are significantly lower than controls. However, due to small sample size, we could not assess the exact levels of free PS in the obese or obese+OCA samples. Finally, we determined (using immunoblot) that total PS levels in OCA, obese, and obese+OCA samples are significantly lower compared to the controls.

Our data indicates that use of OCA and obesity contribute to hypercoagulability due to shorter clotting times, low free and total PS levels, and high thrombin formation.

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