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

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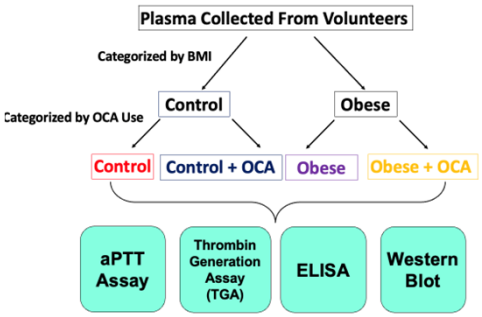
Introduction

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.

Methods



Results

aPTT, TGA, and ELISA Assays

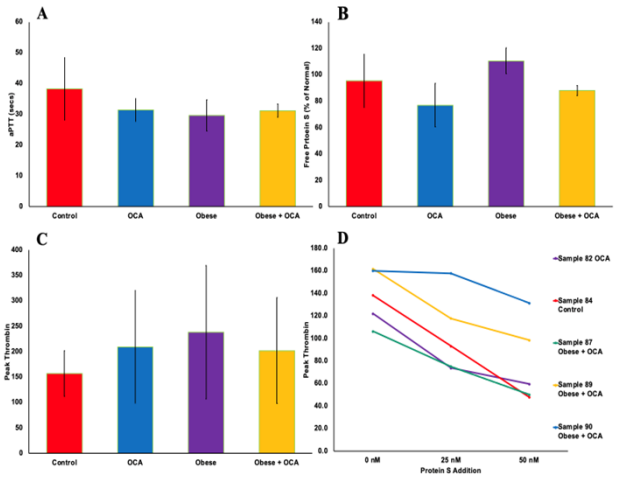


Figure 1: Clotting function tests results; (A) aPTT, (B) ELISA, (C) TGA, (D) TGA modified with added PS.

Western Blot Assay

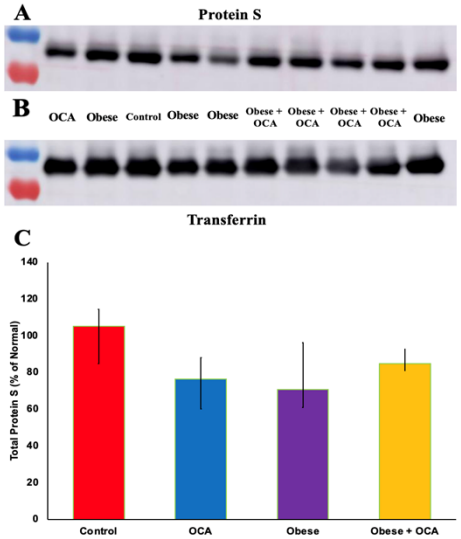


Figure 2: Immunoblot results; (A) Protein S bands, (B) Transferrin Control bands, (C) graphic results of band intensities based on volunteer group.

Conclusion

- Individuals who were considered obese, had OCA use, or both had a shorter aPTT clotting times and higher thrombin generations compared to controls.
- Free PS levels were measured by ELISA and observed that free PS levels of the subjects on OCA are significantly lower than controls
- Total PS levels in OCA, obese, and obese + OCA samples are significantly lower compared to the controls.
- Overall, the use of OCA and obesity contribute to hypercoagulability due to shorter clotting times, low free and total PS levels, and high thrombin generation.

Future Perspectives

- More participants are needed to provide a more representative sample.
- Determine if the binding protein of protein S, C4b, contributes to differences in Free and Total Ps.

References

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