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Dissertation Title : A study on a quantitative assay for protein C activity, the regulator of blood coagulation, based on a chromogenic method mimicking the blood coagulation cascade.

Dissertation Abstract

Protein C is a vitamin K-dependent plasma protein and its activated form, activated protein C, plays a vital role in regulating blood coagulation reactions. Some inherited protein C deficiencies are known risk factors for deep vein thrombosis. Currently, there are two methods for measuring protein C activity: chromogenic and clot-based methods. The chromogenic method is not affected by anticoagulants but cannot detect deficiencies caused by less interaction between activated protein C and its co-factors, such as phospholipids. Otherwise, the clot-based method is affected by anticoagulants, but can detect deficiencies that cannot be detected by the chromogenic method. The test results are recommended in units of IU/mL; however, some laboratories still use percentage of the standard. The relative expression is difficult to understand, and the quality of the applied standards must be clarified, but this has not been revealed. The approved reference interval is approximately 60–140% in Japan; therefore, the need for standardization is recommended in some academic societies.

The chromogenic method and principle of blood coagulation cascade events were combined to improve the limitations of the test and provide quantitatively expressed protein C activity levels. A calibration curve for protein C activity ($y = -0.0132x + 0.14$, $R^2 = 0.9987$, $n = 10$) was obtained, and the results were expressed as optical absorbance and concentration of prepared protein C (μg/mL). Furthermore, we compared the correlation coefficient of the calibration curve between our method and a reagent kit approved in Japan. The difference was not significant in the z-test, and noninferiority was observed ($r = -0.9993$ vs. $r = 0.9899$, $n = 10$, $\alpha = 0.05$, $p > 0.99$). Using this new method, it was shown that the quantitative protein C activity measurement with plasma samples containing the physiological range of protein C concentration (2–6 μg/mL), and the possibility of expression of protein C activity as μg/mL equivalent according to the protein C contained in the control plasma.