Close relationship of tissue plasminogen activator-plasminogen activator inhibitor-1 complex with multiple organ dysfunction syndrome investigated by means of the artificial pancreas

ABSTRACT

GT was not significantly related to SRH, coagulopathy and MODS under strict blood glucose control. Hypercoagulability was closely related to MODS and ECI. Among the parameters indicating coagulopathy, tPA-PAI-1 complex, which is considered to originate from ECA, seemed to be a sensitive parameter of MODS and ECI, and might be a predictive marker of MODS. The treatment for reducing hypercoagulability and ECA/ECI were thought to be justified as one of the therapies for acutely ill septic patients.

INTRODUCTION

Introduction Hypercoagulability and decreased fibrinolysis, including increased PAI-1 level, are often found in the clinical field and are considered to be the risk factors of cardiovascular diseases and glucose intolerance, especially in patients with noninsulin-dependent diabetes mellitus (NIDDM) [,]. Most of the acutely ill severe patients also have coagulopathy, and they often have glucose intolerance. The relationships between coagulopathy and organ dysfunction/glucose intolerance in the acute ill phase have not, however, been clearly analyzed. Although there are reports investigating the relationship between coagulopathy and organ dysfunction, and the relationship between coagulopathy and endothelial cell activation/injury [,] in septic patients, there is no report investigating the relationship between coagulopathy and GT in septic patients as far as we know. Moreover, parameters related to coagulopathy are known to be influenced directly by the metabolic factors. For example, glucose, insulin, and fat influence the production of PAI-1, which is the important parameter related to coagulopathy [, ,]. In aforementioned reports, however, metabolic factors, especially blood glucose level (BG) that is usually unstable in the septic state, are not taken into consideration. We have been using the bedside type artificial pancreas (AP) in septic patients with glucose intolerance since 1985 to control BG, to perform effective nutritional support, and to evaluate metabolic disorders including glucose and fat. By strictly stabilizing BG using AP, analyses of the factors including PAI-1 that are influenced by BG are considered to be correctly performed. The purpose of this study is, first, to analyze the relationships between coagulopathy, including abnormal blood PAI-1-related parameters, and glucose tolerance, MODS, and endothelial cell injury. Second was to investigate which parameters related to coagulopathy were most closely related to glucose tolerance, MODS, and endothelial cell injury, in septic patients with glucose intolerance in whom BG was strictly controlled and the glucose tolerance was evaluated with the glucose clamp method by means of AP. We consider that better understanding of the aforementioned relationships and confirming the useful parameters will be helpful for the early diagnosis of the severity of sepsis and for the treatment of the septic patients.

CONCLUSION

We investigated acutely ill septic patients with glucose intolerance in which BG was strictly controlled and the glucose tolerance was measured by the glucose clamp method by means of AP, and obtained the following conclusions. The GT did not significantly relate with blood stress related

hormone levels, coagulopathy and MODS under strict blood glucose control. Coagulopathy characterized by hypercoagulability with decreased fibrinolysis was closely related with MODS and endothelial cell injury. Among the parameters related with coagulation and fibrinolysis, the tPA-PAI-1 complex, considered to originate from activated endothelium, seemed to be a sensitive parameter of MODS and endothelial cell injury, and might be one of the predictive and risk factors of MODS. Finally, the treatment for reducing hypercoagulability and endothelial cell activation/endothelial cell injury was thought to be justified as one of the therapies for acutely ill septic patients. Further investigation will, however, be necessary for clarifying these conclusions because the number of the patients we investigated was limited.