Chapter 5

Concluding remarks

β-Thalassemia is an inherited hemoglobin disorder characterized by reduced synthesis of β-globin chain. The clinical course distinguishes this heterogeneous disease in two main subtypes: thalassemia major (TM) and thalassemia intermedia (TI). TI has a later clinical onset with a milder anemia that does not require transfusions at least during the first few years of life. The clinical picture of TI patients who have not received transfusions or have occasionally received transfusions is dominated by the consequences of chronic hemolytic anemia, tissue hypoxia, and their compensatory reactions, such as bone deformities and fractures, extramedullary hemopoiesis, spleen and liver enlargement, hypercoagulability, and **pulmonary arterial hypertension** (PAH). These complications, especially the latter two, are getting more frequent and severe over the years.[1]

PAH is a common cardiovascular complication in thalassemic patients. It is a progressive disease that causes exercise limitation, right ventricular failure, and death. The previous study found that almost 60% of 110 TI patients had developed PAH.[2] Its prevalence in Thailand was 43%.[3] Thrombi in small pulmonary arteries was reported 44% in hemoglobin E/β thalassemia (E/β-Thal) autopsies.[4] PAH in thalassemia could be due to increased pulmonary vascular resistance, increased pulmonary blood flow from chronic anemia and the oxidative stress.[2] Furthermore, the principle pathogenesis of PAH in thalassemia are platelet activation and the coagulation cascade.[5-11] Therapeutic strategies for dealing with PAH in thalassemia are controversial.[2] We studied PAH in thalassemia using Doppler echocardiography (ECHO) to estimate the pulmonary artery systolic pressure (PASP) in these patients. Our results showed that the prevalence of PAH (PASP > 35 mmHg) in thalassemia was 29.0 %. The other studies in Thailand have been reported its prevalence 10-43%.[3,12] Moreover, the risk indicators of PAH in these patients were E/β-Thal and post splenectomy status that were similar to the recent research.[3,12,13]

Furthermore, we studies the effect of low dose acetylsalicylic acid (ASA) on thalassemia with PAH by comparison of the clinical outcomes and PASP between these patients for whom ASA 81 mg daily was and was not prescribed after 1 year. This study found that the low-dose ASA may not have a beneficial effect on PASP after 1 year of treatment of PAH in thalassemia. The outcomes of this study were similar to those of a randomized clinical trial of ASA and simvastatin for PAH, which concluded that the results did not support the routine treatment of patients with PAH with these medications.[14] In contrast to the previous study reported that

there was a rise of arterial PaO_2 after high-dose ASA administration in thalassemia patients with PAH,[14] we found that oxygen saturation rose in the patients who had received low-dose ASA but without statistical significance.[15]

In addition, the authors have reported that there were benefits of chronic blood transfusion in E/β-Thal with PAH. The results of this study support the treatment of thalassemic patients with PAH with chronic blood transfusions, according to a case report that showed that correction of hypercoagulability and amelioration of PAH by chronic blood transfusions was seen in an E/β-Thal patient.[16]

Management of PAH is symptomatic and supportive. Acetylsalicylic acid[14,17] and an anticoagulant[9,18] are also prescribed by the experts. Response to treatment is poor and the survival of patients of NYHA functional class III to IV is about 1 to 2 years. The current therapies for PAH in thalassemia include the use of sildenafil[19,20] and bosentan,[21] however, a large cohort of patients on these drugs are needed before definite recommendations.

Conclusion

This thesis primarily focused on the cardiovascular complication PAH in thalassemia. PAH is one of the most common cardiac complications. Prevalence of PAH in thalassemia was 29% in our study. Clinical indicators were E/β-Thal and postsplenectomy status. The results of this thesis would have potential benefits to the patients and the physicians. The physicians could screen PAH in high-risk patients include postsplenectomy status and E/β-Thal by using ECHO, noninvasive tool to detect PAH. ASA effect for PAH in thalassemia is inconclusive in this study, metaanalyses or randomized clinical trial may be warranted. Chronic blood transfusion in 12 months shows benefit for exercise capacity improvement, PASP and clinical outcomes in thalassemia patients without serious adverse events. Longer follow up should be conducted for further study. According to clinical practice guidelines for diagnosis and management of thalassemia syndromes,[22] ASA has benefit for PAH complication prevention especially in splenectomized patients with thrombocytosis. The authors have suggested that the PAH development can be prevented and treated by starting transfusion and chelation therapy early in life for patients with thalassemia.

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