Chapter 1

Introduction

Thalassemia is an inherited hemoglobin disorder in chronic hemolytic anemia.[1,2] β-thalassemia, there are two forms of clinical severity: thalassemia major (TM) transfusion-dependent and thalassemia intermedia (TI) non-transfusion-dependent.[1,2] The TM is characterized by severe anemia during the first year of life and requiring long term regular blood transfusion therapy for survival, while the TI has a milder anemia and later clinical onset, permitting survival without life-long regular blood transfusions, and a longer life expectancy.[2]

In Thailand, the incidence of β-thalassemia gene was 2-7% and hemoglobin E was 20-35%, but accounts for 40-50% in the northeast.[3]

Cardiac complications are the main cause of death in thalassemia.[4] Cardiac complications in TM is iron induced heart failure from ventricular dysfunction.[5,6] The standard therapy is considered by the different compliance patients with this therapy have led to conflicting data with point to the left ventricular dysfunction and the pulmonary arterial hypertension.[6,7] While, the cardiac benefits of a lifetime compliance with the standard therapy are unclear. In TI, age related pulmonary arterial hypertension and high cardiac output state with LV remodeling have been reported.[8]

The pathogenesis of pulmonary arterial hypertension, a severe complication in thalassemia, is not well understood. There are currently limited specific data on this disease .

The incidence of pulmonary arterial hypertension was 66%. It was reported a high incidence in TI.[8] We also found in Hb H disease (α-thalassemia). Doppler echocardiography is sensitive and is a noninvasive tool to early detect pulmonary arterial hypertension.

The patients with severe pulmonary arterial hypertension had worse prognosis and high mortality rate. Standard therapy of pulmonary arterial hypertension in thalassemia are controversial.

Scope of the thesis

Research questions in this thesis carried out from the hematological outpatient routine practice to find out the answer of these research question:

1. What are clinical indicators of thalassemic patients with pulmonary arterial hypertension (PAH)?

PAH is the common cardiac complications in β-thalassemic patients.[8,9] PAH was detected in 10% of thalassemia major, and 50% in thalassemia intermedia.[8] Early detection of PAH are effective to decrease mortalities and morbidities in thalassemic patients. There were a few studies identified clinical indicators of PAH in thalassemic patients. PAH could not be early diagnosed with clinical or chest radiograph or electrocardiography. Right heart catheterization (RHC) is costly, invasive and has limited use in only large cardiac centers. Doppler echocardiography (ECHO) is a commonly used to detect this complication because it is a noninvasive and more sensitive tool.[10-12]

The study entitled "Clinical indicators for pulmonary arterial hypertension in thalassemia" was conducted to estimate prevalence of PAH in and to explore important clinical indicators for PAH in these patients. Identification of clinical indicators could be an advantage in providing therapeutic strategies for early detection and prevention of severe PAH.

2. Is acetylsalicylic acid effective for treatment PAH in thalassemia?

PAH is a cardiovascular complication that causes death in thalassemic patients. More studies showed that PAH in thalassemia is associated with platelet activation.[13-15] There was evidence that arterial partial pressure of oxygen of β-thalassemic patients with PAH were improved by antiplatelet administration.[16]

The standard medication for PAH in thalassemia is unclear. Studies of antiplatelet therapy are required for further study. There were few studies of acetylsalicylic acid (ASA) therapy in thalassemia with PAH.[16]

The study entitled "Effect of acetylsalicylic acid on thalassemia with pulmonary arterial hypertension" was conducted to investigate an effect of ASA after 1 year of

follow-up the pulmonary artery systolic pressure of thalassemia patients with PAH to whom ASA was and was not prescribed.

The study of the effect of ASA could be an advantage in providing the treatment PAH in thalassemia.

3. Do pulmonary artery systolic pressure decrease after chronic blood transfusion in thalassemia intermedia with PAH?

The mechanisms leading to PAH in thalassemia involve platelet activation and the coagulation cascade.[14,17-22] The experts have recommened that the PAH complication could be prevented by starting red cell transfusion and iron chelation therapy early in life for patients with thalassemia.[8,9]

The study entitled “Benefits of chronic blood transfusion in hemoglobin E/β thalassemia with pulmonary arterial hypertension” was conducted to investigate an effect of chronic blood transfusions. We compared the pulmonary artery systolic pressure and six-minute walk distance after 12 months of follow-up in β-Thal/Hb E disease with PAH patients who received chronic red cell transfusions versus those who received occasional transfusions.

The study of the effect of chronic blood transfusions could be an advantage in providing therapeutic strategies for PAH in thalassemia.

The philosophical context of clinical epidemiology research including theoretical, data collection, and data analysis design for each study is presented in Appendix A.

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