Statistical Analysis of Glanzmann's Thrombasthenia in Japan

K.	Kojiro	Yasunaga
S.	Shosaku	Nomura

First Department of Internal Medicine, Kansai Medical University, Osaka, Japan
Kojiro Yasunaga, First Department of Internal Medicine, Kansai Medical University, 1-Fumizonochō, Moriguchi, Osaka 570 (Japan)

Glanzmann's thrombasthenia (GT) is a well-defined inherited disorder of platelet function [1-3]. GT has an au-tosomal recessive inheritance and is characterized by the absence of ADP-induced platelet aggregation. It is caused by a deficiency or abnormality of the membrane glycopro-teín (GP) IIb/IIIa complex, with bleeding occurring due to defective platelet haemostatic plug formation. We have carried out nationwide surveys of congenital platelet function disorders in Japan on four occasions (in 1976, 1981, 1986 and 1991). There were 98 patients in 1976, 160 in 1981, 178 in 1986, and 192 in 1991. Bleeding symptoms appeared at around 3 years of age in 60% of GT patients in all four surveys. The most common symptoms were epistaxis (70.7% in 1976, 70.8% in 1981, 70.2% in 1986, and 70.4% in 1991) and pur-pura (63.9% in 1976, 62.4% in 1981, 62.7% in 1986 and 61.9% in 1991). These were followed in descending order by oral mucosal bleeding, genital bleeding, excessive bleeding after tooth extraction, haematemesis and me-laena, excessive bleeding following trauma, and haematu-ria. In all 4 surveys, laboratory studies showed that the platelet count was normal in these patients, while the bleeding time was prolonged and ADP-induced aggregation was absent or decreased by more than 90%. The most interesting results were the mortality rate and the age distri-bution. The mortality rate was 6.8% in 1976, being slightly higher than that for haemophilia and related disorders (4.4% of 3,193 patients in 1976). The reason for this difference may be the lack of an effective haemostatic drug for GT patients, while coagulant factor therapy can be utilized for haemophilia. The mortality rate of GT patients has slowly declined since that time, with the standardized mortality ratios for age and sex showing a similar pattern (table 1).

Table 1. Changes of the mortality rate of GT patients

Year
Mortality rate   Standardized mortality ratio¹

%
age
sex
1976
6.8
1.76

1.89
1981
6.3
1.51
1.70
1986
5.5
1.13
1.59
1991
4.9
0.83
1.44

Standardized mortality ratio = Observed number of deaths/expected number of deaths $\times$ 100.
Expected deaths were calculated as the sum of the class-specific death rates (stratified for age and sex) in a standard population (general Japanese population) times the number of patients in each class.

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The age distribution was as follows. In 1976, patients under 15 years accounted for 63.3% and those over 30 years comprised 4.5%. In contrast, patients under 15 years comprised 41.3% and those over 30 years accounted for 24.5% of GT patients in 1991. This shift to a higher age distribution appears to have occurred because haemostatic management [4] has decreased the death rate for young GT patients. In the past 20 years, our understanding of the pathophysiology of GT has made remarkable progress, with both biotechnology and genetic engineering studies providing information on the conformation of GPIIb/IIIa [5-7]. Despite such progress in fundamental research, the clinical features of GT have shown little change. However, our results show that the mortality rate of GT is currently decreasing and the age distribution is shifting to an older one. These four nationwide surveys performed in Japan suggest that if GT patients are supported carefully, many episodes of serious haemorrhage can be prevented, with a consequent decrease in mortality and improvement of the quality of life.

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