Platelets

Prognostic relevance of large-platelet counts in patients with immune thrombocytopenic purpura

In this preliminary study, the value of different platelet parameters, measured by the ADVIA120 Analyzer, in predicting the immediate response to intravenous immunoglobulin or intravenous anti-RhoD was assessed in 31 patients with immune thrombocytopenic purpura. The number of large platelets pre-treatment was the only independent predictor of the 24 hour-platelet increase.

haematologica 2005; 90:1715-1716
(*http://www.haematologica.org/journal/2005/12/1715.html*)

A routinely and rapidly available parameter that would reliably predict immediate response to treatments such as intravenous anti-RhoD (anti-D) and intravenous gammaglobulin (IVIG) in patients with immune thrombocytopenic purpura (ITP) would be helpful in clinical practice. In ITP, both IVIG and anti-D can rapidly increase the platelet count, primarily by slowing the Fcγ receptor-dependent clearance of opsonized platelets[1]. We therefore hypothesized that patients with the highest levels of platelet production would have the largest immediate platelet increase after treatment.

In this preliminary study, a single device, the ADVIA 120 Hematology System (Bayer Healthcare LLC, NY, USA)[2] was used to test different platelet parameters in 31 patients with ITP[3] treated by IVIG or anti-D, and the relationship of those parameters to the post-treatment platelet increase was assessed. Among the 31 patients with chronic ITP (26 adults, median age 31 years, range: 11-68), 17 received IVIG at a dose of 1 g/kg in a 3-5 hour-infusion, and 14 received intravenous anti-D (WinRho SDF; Cangene, Winnipeg, MB, Canada) at a dose of 50 (n=5) or 75 (n=9) μg/kg. Ten of the patients receiving IVIG had previously undergone a splenectomy. The following platelet parameters were measured just before (T_0), 24 hours (T_1), and 7 days (T_7) after treatment: platelet count, mean platelet volume, mean platelet mass, number of large platelets (LP), platelet distribution width, and platelet-crit. Platelet counts and large-platelet counts were expressed as absolute numbers $\times 10^9$/L. Large platelets were identified on the basis of their size (20-60 femtoliter). The platelet count (Plt) and mean platelet volume were available simultaneously in all patients pre-treatment (T_0), LPT_0 was available for 30/31 patients. At 24 hours, the platelet count ($PltT_1$) was available for 25/31 patients, and for 29/31 on day 7±2 after treatment ($PltT_7$). To test the relationship between the above platelet parameters measured at T_0 and the platelet count increase in the first 24 hours (T_1-T_0) and the first 7 days (T_7-T_0), a linear regression analysis was performed using the SPSS® software package. χ^2 testing with the Yates' correction was also used to investigate the relationship of two variables. Since multiple analyses were performed, a p value ≤0.025 was considered statistically significant. The median platelet count before treatment ($PltT_0$) was 17×10^9/L (range:2-62) with 27/31 counts ≤30×10^9/L. As shown in Figure 1, the platelet increase at 24h ($PltT_1$-T_0) was strongly correlated with the number of large platelets at T_0 (r=0.689, p value =0.0002). The only three platelet increases <10×10^9/L had no large platelets at T_0 (Figure 1). When the IVIG and anti-D groups were analyzed separately, the correlations between LPT_0 and $PltT_1$-T_0 were still significant (p values = 0.0006 and 0.014, respectively). When mean platelet volume at T_0 was considered, there was only a trend towards a positive correlation with T_1-T_0 platelet increase (p=0.0762). The other platelet parameters had no relationship with the T_1-T_0 platelet increase. No significant correlation was found for any of the platelet parameters with the platelet increase at day 7 (p=0.061 with LPT_0). Except for the longer duration of ITP which correlated with the T_1-T_0 platelet increase (p=0.035), none of the patient's characteristics (age, sex, bleeding symptoms, previous splenectomy, number of previous treatments with IVIG and/or anti-D, ongoing medication, etc.) was significantly related to the T_1-T_0 platelet increase and/or to the LPT_0.

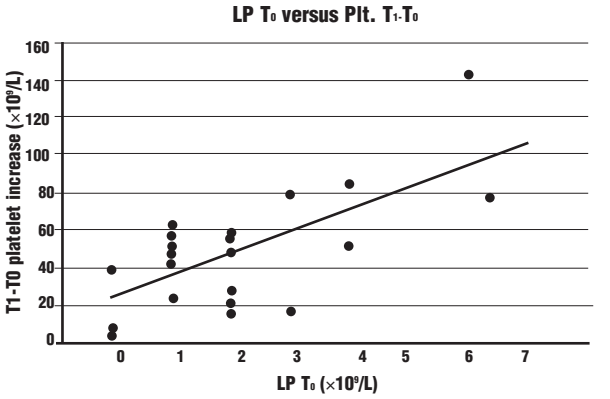

Figure 1. The linear correlation between the number of large platelets before treatment (LPT_0) and the platelet gain 24 hours after the first treatment ($Plt\ T_1$-T_0) in 25 patients with ITP treated with either IVIG (n=14) or IV anti-D (n=8). Both sets of values are expressed as $\times10^9$/L.

In conclusion, in patients with ITP treated with IVIG and with anti-D, the number of large platelets at T_0 was a strong, independent predictor of the immediate platelet increase. LPT_0 accounted for almost 50% of the variance in the T_1-T_0 platelet increase (r=0.69, r^2=0.48). Although this finding cannot be extrapolated to other thrombocytopenic states, such as inherited thrombocytopenias, it does suggest that LPT_0 could be good surrogate marker of platelet production. Two previous studies showed that the rate of large platelets was significantly higher in patients with ITP than in healthy controls[4,5] but the study reported here is the first one showing a relationship of LPT_0 with the acute platelet increase after treatment. That none of the parameters predicted the platelet increase 7 days after treatment is not surprising since by 7 days more complex effects of IVIG[1,6] and anti-D[7] than Fcγ blockade may be contributing to the increase in the platelet count. To confirm these preliminary data, additional studies including a larger number of patients with ITP and other thrombocytopenic states, and comparing the reliability and reproducibility of large-platelet counts with other surrogate markers of platelet production, such as glycocalicin,[8] reticulated platelets,[4] thrombopoietin level,[9] or the immature platelet fraction,[10] are needed.

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Key words: immune thrombocytopenic purpura, platelet production, large platelets, mean platelet volume (MPV), ADVIA 120 Hematology System.

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