

Effect of Platelet Transfusion on Hemostasis in Patients with ALL or LLy Receiving PEG-Aspargase

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Introduction/Significance

- PEG-aspargase and glucocorticoids, mainstays of acute lymphoblastic leukemia (ALL) and lymphoblastic lymphoma (LLy) treatment, are risk factors for thrombosis.
- Venous thromboembolism (VTE) is a significant source of disease- and therapy-related morbidity, specifically during induction chemotherapy.
- Many patients require platelet transfusions during therapy, with an unknown impact on VTE risk.

Objective

- To examine the effect of platelet transfusion on the clotting milieu during induction chemotherapy using thromboelastography (TEG) parameters maximal amplitude (MA) and clot strength (G) to determine if changes were predictive of VTE risk.

Study Procedures/Definitions

- 26 pediatric patients with ALL or LLy treated on a Children’s Oncology Group protocol were enrolled from 11/2014 to 1/2020. Demographics illustrated in Table 1.
- Patients eligible for inclusion: 1) received all doses of PEG-aspargase at HDVCH; 2) weighed greater than or equal to 17 kg; 3) were older than 1 year of age and less than 21 years of age at time of enrollment.
- Patients were excluded if they: 1) had AML; 2) did not meet appropriate age or weight criteria; 3) did not or could not receive PEG-Aspargase; 4) had been given systemic thrombolytic therapy within 72 hours of enrollment; or 5) were treated with CRRT.
- Informed consent was obtained for every patient enrolled in the study.
- Complete blood count (CBC), PT, aPTT, fibrinogen and TEG were collected prior to day 4 PEG-aspargase administration, and on days 8 and 15 of induction. These studies were also collected before and within 1 hour after platelet transfusions given during induction. Comparisons between TEG parameters pre- and post-transfusion were made. Heparinase was used in all specimens to neutralize effects of heparin.
- Mixed effects general linear modeling was used for analysis.

Table 1. Demographics and clinical outcomes of 26 enrolled patients

| Variable | Total N=26 | % |
|--|------------|------|
| Age (years) | | |
| 1-5 | 8 | 30.8 |
| 5-10 | 6 | 23.1 |
| 10+ | 12 | 46.1 |
| Gender | | |
| Male | 13 | 50 |
| Female | 13 | 50 |
| Cancer Diagnosis | | |
| Standard Risk (SR) B-cell ALL | 11 | 42.3 |
| High Risk (HR) B-cell ALL | 10 | 38.5 |
| T-cell LLy | 2 | 7.7 |
| T-cell ALL | 3 | 11.5 |
| History of prior VTE | 0 | 0 |
| VTE during Induction* | 2 | 7.7 |
| Pulmonary | 1 | 3.8 |
| Cerebral | 1 | 3.8 |
| Extremity | 1 | 3.8 |
| Bleeding during Induction | 1 | 3.8 |
| Cerebral** | 1 | 3.8 |
| *Extremity VTE and Pulmonary VTE occurred in one patient. | | |
| **Cerebral hemorrhage related to cerebral venous sinus thromboembolism | | |



Design

- Observational, prospective study.

Results

- Of 26 patients enrolled, 11 (5 males, 6 females) received platelet transfusions on or after day 4 of induction. Average age was 7.5±3.5 years with the majority (45.5%) of transfused patients having standard risk B-ALL.
- Increases in MA (26.7±9.8 vs. 46.4±8.6, p <0.001), and G (1.9±0.9 vs. 4.6±1.5, p <0.001) occurred following platelet transfusion (Figure 1A and 1B).
- 10 patients were transfused platelets on or within 96 hours of day 8 and 4 patients were transfused on or within 96 hours of day 15. When compared to 12 non-transfused patients on day 8, (Figure 2A and 2B) and 16 non-transfused patients on day 15 (Figure 3A and 3B), post-transfusion MA and G parameters were not statistically different for transfused patients compared to non-transfused patients.
- None of the transfused or non-transfused patients had significant bleeding. 2 of 26 patients developed VTE. Neither received a platelet transfusion on or after day 4 PEG-aspargase.

Discussion/Conclusion

- Platelet transfusion was associated with statistically significant increases in TEG parameters MA and G, with correction of abnormally low parameters pre-transfusion to the normal range post-transfusion. However, there was no difference in MA and G parameters for patients post-platelet transfusion compared to non-transfused individuals.
- Overall, platelet transfusion did not increase the risk for VTE during induction.