Impairment of Primary Hemostasis as an Additional Risk Factor of Haemorrhage in Patients With Newly Diagnosed Acute Myeloid Leukemia (AML): Ukrainian Prospective Study.

Z. Stupakova[1], I. Dyagil[1], Z. Martina[1], A Sergeieva[1], O. Karnabeda[2], U. Melnyk[3], O. Novosad[4].
[1]National Research Center for Radiation Medicine of NAMS of Ukraine, Kyiv, Ukraine
[2] Bohomolets National Medical University, Kyiv, Ukraine
[3]Kyiv City Clinical Hospital №9, Kyiv, Ukraine
[4]National Cancer Institute, Kyiv, Ukraine

Background

Bleeding events in AML are frequent and life threatening, whereas widely used treatment approaches are not always able to satisfy expected outcome. Disturbances in primary link of haemostasis could play an etiologic role in hemorrhagic complications in newly diagnosed AML and might provide as a prognostic factor for further investigation.

Objective

The primary endpoints were a qualitative and quantitative functions of plasma von Willebrand factor (vWF) which include measurements of vWF activity (vWF:ristocetin cofactor [vWF:RCo]), vWF level (vWF:antigen [vWF:Ag]), factor VIII coagulation activity regarding to vWF(vWF:FVIII) and FVIII activity (FVIII) .

Materials & Methods

42 patients with newly diagnosed AML (excluded APL) were included in the study group (21 males and 21 females; median age: 52 years).

The diagnosis of AML established by FAB and WHO classification systems and the plasma samples were collected before the beginning of induction therapy. The grade (G) of bleeding events was assessed according to Modified WHO Bleeding Scale (WHO BS).

Control group included 20 age-matched and sex-matched healthy individuals. Levels of vWF:Ag and vWF:RCo tested on automated latex particle-enhanced immunoassay ACL Elite Pro and ACL TOP 300 (Instrumentation Laboratory). vWF:FVIII and FVIII were measured using a clotting assay with factors deficient plasma by fully automated coagulometer ACL Elite Pro (Instrumentation Laboratory).

Results

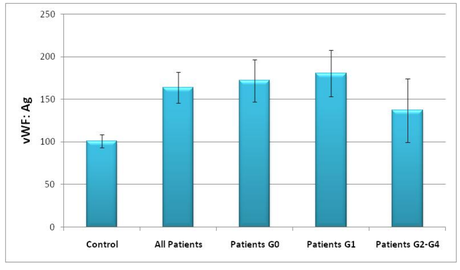
Hemorrhage (G1-4) occur in 53,3 % of patients in the study group during induction therapy. Bleeding episodes in the control group did not arise (G0). The median platelets in the study group was 41,5 versus 260 in the control group ($p<0,05$).

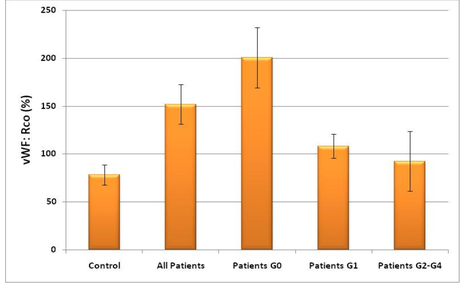
vWF:Ag below normal ranges had been observed in 19% of patients with AML (seven patients) and was associated with the occurrence of severe haemorrhage compared with the patients who had normal vWF:Ag levels and no bleeding episodes ($p=0.012$). It is important to mention, that vWF:Ag levels (median 134, mean 163±18,25) were elevated in most cases (56%) in the main group and probably are associated with a compensatory mechanism for stopping bleeding compared with the control group.

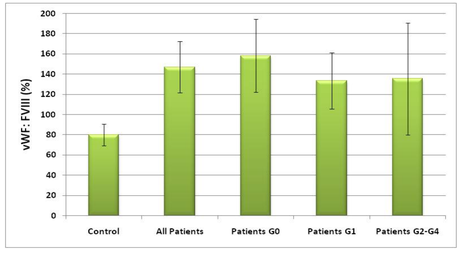
In 23,8% patients with AML we observed levels of vWF:RCo below normal ranges. Among them the most frequent bleeding events were G2 (5/10) 50% and G4 (3/10) 30%, three of them died during the first course of chemotherapy due to gastrointestinal and CNS bleeding. Therefore we found a statistically significant association between a decreased levels of vWF:RCo below normal ranges and the occurrence of severe bleeding episodes (G2-G4) in patients with AML compared with the group that had normal ranges of vWF:RCo and no bleeding episodes (G0) ($p=0,0001$).

Despite decreasing in vWF:RCo below normal ranges in the control group as an accidental finding, bleeding events have not emerged.

Furthermore, low vWF:FVIII ($p=0,033$) and FVIII ($p=0,037$) levels in patients with AML and bleeding episodes G2-G4 had statistic difference compared to non-haemorrhage patients (G0).







Summary

According to our study, vWF:RCo, vWF:Ag and vWF:FVIII were associated with haemorrhage in patients with newly diagnosed AML and could be considered as a predictive factors of bleeding. Further investigation of the role of Von Willebrand factor in this group of patients could provide more specific assessment of hemorrhage as well as implementing of new bleeding assessment scales.