

# STUDY ON MEMBRANE FLUIDITY IN CHRONIC MYELOID LEUKEMIA AND MYELOPROLIFERATIVE NEOPLASMS AND MEDICATION INFLUENCES.

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**Background** Patients with chronic myeloproliferative neoplasms (MPN) have a variety of structural and functional abnormalities of platelets. The patients with JAK2-positive MPN have a higher incidence of venous thrombosis compared with noncarrier. Platelet function is influenced by changes in membrane fluidity (MF) which has an important role in the expression of platelet receptors and in modulating the activity of protein membrane. The aim of our study was to determine whether presence of JAK 2 mutation influences platelet MF and if changes of MF may be correlated with the treatment of these patients. **Materials and Methods** We present a retrospective study on 36 cases MPN (20 JAK2-positive MPN) and 14 CML admitted in Colentina Clinical Hospital Bucharest. The determination of platelet membrane fluidity was performed by fluorescence anisotropy measurements using as marker 1-(4-trimethylammoniumphenyl)-6-phenyl-1,3,5-hexatriene p-toluenesulfonate (TMA DPH). We analyzed the fluorescence anisotropy of platelet membrane and correlate the result of with different kind of treatment. **Results and Discussion** Patients with MPN and JAK2 mutation present have a high level of fluorescence anisotropy (equivalent to high fluidity of platelet membrane) than the JAK-negative group. Median value for JAK2 positive MPN group 148.5 95% CI for median value (141-152.8)) vs JAK2 negative MPN group 132 (126.4-137.5)  $p = 0.0009$ . There are no differences between CML and MPN group. Our results confirm that fluorescence anisotropy is influenced by medication taken. We observe that MPN patient who have taken

Hydroxiurea alone had a high level fluorescence anisotropy than patient who have taken association Hydroxiurea and Anagrelid; median value and 95% CI for median value 151 (137.1-158.6) vs 136 (126-137.5)  $p=0.03$ . At the beginning Anagrelid was used as inhibitor of platelet aggregation and after that it was observed its effect in decreased count of platelet. Its effect is inhibitor of phosphodiesterase, blocking megakaryopoiesis and represses proplatelet formation. In recent clinical studies it was not observed any differences in prevention of thrombotic complications MPN patients in treatment with Hydroxiurea and Anagrelid. Patient who have treatment with tyrosin kinase inhibitor (TKI) - Sprycel or Glivec, had a low level of fluorescence anisotropy, median value and 95% CI for Hydroxiurea group 151 (137.1-158.6) vs TKI group values 138 (124.4-147.8)  $p=0.04$ . No differences of fluorescence anisotropy was observed between group of MPN patients who received JAK inhibitor (Jakavi) and group MPN with Hydroxiurea treatment or between TKI inhibitor group and Jakavi group. **Conclusion** Presence of JAK 2 mutation in MPN patient is associated with low fluidity of platelet membrane. In literature this group of MPN patient had frequently thrombotic complication. We have to observe in the future if this group with high level of fluorescence anisotropy had a high risk of thrombosis. Association of Anagrelid or TKI inhibitor is associated with lower level of fluorescence anisotropy value. Both medications Anagrelid and TKI inhibitors influence protein with high role in signaling transduction. It must observe if the modification of MF influences proplatelet formation and Anagrelid effect in decreased level of platelet count.