Serotonin reuptake inhibitor use is associated with attenuated thrombocytopenia in septic shock

Background: Serotonin reuptake inhibitors (SRIs) are widely used for long-term treatment of depressive disorders. SRI use for more than 21 days reduces platelet serotonin levels by more than 80% in humans and mice. In mice, reduced platelets serotonin levels offer protection from septic shock because platelet serotonin promotes leukocyte recruitment. We analyzed clinical characteristics and outcome in patients with septic shock who consume SRIs to evaluate whether these murine findings would translate into clinically relevant results.

Methods: Registry data from our intensive care center were extracted retrospectively from 2006 – 2010. Septic shock was defined according to Surviving Sepsis Campaign criteria. All SRI-consumers (n=47) with septic shock were compared to all patients with septic shock without SRI premedication (n=461) treated during this period. In a substudy evaluating SRI-induced blood cell changes, neutrophils and platelets from SRI-consumers without septic shock were compared to blood cells from healthy individuals in flow cytometry.

Results: Mortality (45.6% in SRI users vs. 41.5% in non-SRI users, p=0.63), need for catecholamine administration (84.7% vs. 85.4%, p=0.83), and multi organ dysfunction (p=0.63) were similar in both groups. Mean white blood cell count was 15.9±14 x 10^9/L in SRI users and 14.7±20 x 10^9/L in non-SRI users (p=0.67). Thrombocytopenia was less pronounced in SRI users (207±151 x 10^9/L) than in non-SRI users (151±147 x 10^9/L, p=0.015). The expression of several neutrophil surface markers (L-selectin, P-selectin glycoprotein ligand-1, Mac-1, and CD44) in SRI users without septic shock was not significantly different from healthy individuals. The production of reactive oxygen species (ROS) by isolated neutrophils upon stimulation with 100 nM phorbol myristate acetate (PMA) was increased in non-septic SRI users.

Conclusion: Lack of platelet serotonin in SRI users was associated with higher platelet counts in patients with severe septic shock, while mortality and need for catecholamine administration were unaffected by SRI premedication in this single-center registry. Undepleted platelet serotonin stores may therefore be a prerequisite for platelet consumption in septic shock – which could offer novel ways to influence microvascular complications. The impact of SRI use on neutrophil characteristics warrants further investigation, because ROS production appears to be increased in SRI users.