

Co-administration of sulphostin with rifampicin and isoniazid could prevent hematopoietic side effects of the drugs in Balb/c mice

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Background and Aims: Leucopenia and neutropenia are the main hematologic side effects of certain antibiotics used for infectious diseases especially for those prescribed in tuberculosis. Sulphostin, a new compound isolated from streptomyces sp. MK251-43F3, stimulates production of myeloid cells in bone marrow and peripheral hematopoietic centers including spleen and liver. Our goal: from the current study was surveying evidences to answer this question: Could sulphostin co-administration with tuberculosis (TB) drugs restore leukocyte and neutrophil cells counts in the blood or myeloid cell counts in the bone marrow of rifampicin and isoniazid treated mice? Study design: BALB/c mice were divided into several groups of seven animals and received rifampicin (20 mg/kg) with isoniazid (20 mg/kg) (as regular TB medications) or in combination of the two drugs with sulphostin (50 mg/kg). A group of mice were also considered as control with no treatments. Blood samples were collected on day 6 using EDTA as anticoagulant and bone marrow cells were collected from femurs and tibiae by flushing the shaft with buffer and heparin as anticoagulant.

Measurements: Blood total leukocytes and neutrophils were counted using a standard cell counter and myeloid cell fraction of bone marrow was analyzed using flow cytometry assay. Fluorochrome conjugated antibodies for the analyses were as follows: Gr-1-FITC, Ter119-PE together with Hoechst 33342 exclusion staining.

Results: Leukopenia was seen in all mice treated with the TB drugs without sulphostin. A significant reduction in neutrophil ratio was also seen in the same group. Sulphostin co-administration with TB drugs enhanced noticeably leukocyte and neutrophil counts in the blood and myeloid/non myeloid cell ratio in the bone marrow samples.

Conclusions: Our findings revealed sulphostin could interfere with TB drug induced leukopenia and neutropenia. Further studies should be planning to elucidate the involved mechanisms and immunologic outcomes associated with co-administration of the drugs.

Keywords: Rifampicin; Isoniazid; Sulphostin; Leukopenia.