INFLUENCE OF ACETYLSALICYLIC ACID ON HEMATOXOTOXICITY OF BENZENE

JOANNA KOWALÓWKA-ZAWIEJA, BARBARA ZIELIŃSKA-PSUJA, JĘDRZEJ PRZYSTANOWICZ, and KARINA SOMMERFELD

Poznan University of Medical Sciences, Poznań, Poland
Department of Toxicology

Abstract
Objectives: The aim of the study was to evaluate the influence of acetylsalicylic acid (ASA) on benzene hematotoxicity in rats.

Materials and Methods: The study was carried out on rats exposed for 2, 4 and 8 weeks to benzene vapour at a concentration of 1.5 or 4.5 mmol/m³ of air (5 days per week, 6 hours per day) alone or together with ASA at the doses of 5, 150 or 300 mg/kg body weight (per os).

Results: Benzene at a concentration of 4.5 mmol/m³ caused a slight lymphopenia, granulocytosis and reticulocytosis in blood. In bone marrow traits of megaloblastic renewal, presence of undifferentiated cells and giant forms of granulocytes as well as an increase in myeloperoxidase and decrease in chloroacetate esterase activity and lipids content were noted. ASA (150 and 300 mg/kg b.w.) influenced some of hematological parameters, altered by benzene intoxication. ASA limited the solvent-induced alteration in blood reticulocyte count and in the case of bone marrow in the erythroblasts count. Traits of megaloblastic renewal in bone marrow were less pronounced. Besides, higher activity of myeloperoxidase and the decrease in the level of lipids in granulocytes were noted.

Conclusion: Our results suggest that ASA limited the benzene-induced hematotoxicity.

Key words: Benzene, Acetylsalicylic acid, Interactions, Hematotoxicity, Blood, Bone marrow

INTRODUCTION

Occupational exposure to benzene is a frequent cause of chronic toxicity, which may result in induction of aplastic anemia and neoplastic processes, including leukemias, as well as breast and lung tumors. Proliferative disorders of the hemopoietic system, which most frequently develop in humans exposed to benzene, include chronic myeloid leukemia, acute myeloid leukemia, lymphoblastic leukemia, malignant lymphoma and multiple myeloma. Development of tumors of the hemopoietic system reflects the damage to bone marrow pluripotential stem cells, which leads to anemia, leukopenia or thrombocytopenia and, then, to fully symptomatic aplastic anemia or myeloid leukemia [1,2].

The mechanism of benzene hematotoxicity is not clear yet. One theory stresses the importance of active benzene metabolites and cellular DNA adducts, particularly inherited in somatic cell lines, which cause inability of the cells to react to cytokines, resulting in excessive proliferation. Chromosomal aberrations induced by binding active benzene metabolites to DNA may also lead to oncogenes activation or antioncogenes inactivation [3–5].

Another hypothesis is associated with stimulatory functions of the bone marrow microenvironment. Cytotoxic damage of bone marrow stromal cells and macrophages, in particular induced by benzene and its metabolites, affects their capacity to control proliferation and differentiation.
ASA inhibits inflammatory processes by prostaglandin and nitric oxide production, which may result in reduction of hematotoxic effects of benzene [17,22,25]. The aim of our study was to investigate the effect of oral acetylsalicylic acid administration on hematotoxicity of benzene after inhalation exposure.

MATERIALS AND METHODS

Animals

The studies were performed on male Wistar rats. The animals originated from the breeding farm of the Department of Toxicology, Poznan University of Medical Sciences. The body weight of each rat was 230±15 g. The rats were housed in controlled light conditions (12 h light : 12 h dark), at 22°C and relative humidity of 60±10%. The animals were fed with standard laboratory chow with free access to tap water.

Treatment protocols

The animals were subjected to inhalatory exposure to benzene (Sigma-Aldrich) vapour at a concentration of 1.5 mmol/m³ (37 ppm) or 4.5 mmol/m³ (112 ppm). The exposure took place in a dynamic toxicological chamber for 5 days a week, 6 h every day, for a period of 2, 4 or 8 weeks. Concentration of the solvent inside the toxicological chamber was monitored by gas chromatographic analysis of air samples with 30 min intervals (packed column Supelco: 5% DIDP/5% Bentone 34 on 80/100 Chromosorb W Naw, 6'×1/8" SS, column temperature 80°C, carrier gas flow 20 cm³/min, FID detector, sample volume 10 cm³). Before each exposure, the rats received an aqueous suspension of ASA (Sigma-Aldrich) administered p.o. at a dose of 5 mg/kg b.w. (1/300 DL₅₀) or 150 mg/kg b.w. (1/10 DL₅₀) or 300 mg/kg b.w. (1/5 DL₅₀). On the 3rd day after exposure cycle termination, blood was sampled from the heart of superficially anesthetized rats. In the blood, hemoglobin concentration, hematocrit...