Int J Drug Dev & Res, Volume 12
DOI: 10.36648/0975-9344-C1-009

Differential effect of iodine bioorganic molecular complex on host defense in balb/c and c57bl/6 mice

Tamara Bukeyeva
Scientific Centre for Anti-infectious Drugs, Almaty

Statement of the Problem: Long experience in the use of various iodine preparations has shown that while possessing pronounced antibacterial and antiviral properties, wide-spectrum antimicrobial activity, and lacking mutagenic and teratogenic effects, they are toxic when introduced to the human body, which significantly narrows the scope of their clinical application. The search for alternative ways to solve the problem of the high toxicity of inorganic iodine compounds has led to the development of iodine-containing organic complexes. And since the 60s of the XX century, the compounds of iodine with various iodophors are being actively examined. The coordination compound of iodine with alpha-dextrin and polypeptides was synthesized at the Scientific Center for Anti-Infectious Drugs JSC, the effect of which on the phagocytic activity of granulocytes and monocytes in BALB/c and C57BL/6 mice was studied. Phagocytosis is considered as one of the major host defense function, which is a fundamental component of the innate immune response /1/. The manifestation of the phagocytic response is a significant indicator of the host antimicrobial reactivity state and overall level of its immune activity.

Materials and methods: A study was performed in the whole blood of 30 BALB/c mice and 30 C57BL/6 mice. The animals of each line were divided into 3 groups of 10 mice, including 5 females and 5 males. Two doses of the drug were used in the study: 1/20 of maximum tolerated dose (MTD) is 125 mg/kg and 250 mg/kg (1/10 MTD) of animal weight. Blood was collected on day 14 after the administration of the drug. The analysis was performed by flow cytometry, measuring the percentage of phagocytizing granulocytes and monocytes that engulfed E. coli bacteria, and phagocytosis intensity (the number of bacteria per cell by average fluorescence intensity). The average fluorescence intensity (AFI) was correlated with the number of bacteria per leukocyte and served as an indicator of the phagocytic activity of individual cells. The data obtained during the study were processed by the method of variation statistics using GraphPad Prism software, version 6.00 for Windows (GraphPad Software, La Jolla California, USA). The arithmetic mean (M) and error of the arithmetic mean (m) were calculated for each sample. The distribution was checked for compliance with a normal one using the Shapiro-Wilk test. A comparison of sample means was carried out by Student's t-test in the case of a normal distribution or by the Kruskal-Wallis test in the case of distribution other than normal. Multiple comparisons were carried out using the Dunn's and Tukey's tests.

Findings: It was shown that a new complex of iodine with bioorganic molecules upon repeated oral administration for 14 days in the examined doses did not affect the phagocytosis in BALB/c mice. It

was established that under the influence of a complex of iodine with bioorganic molecules at a dose of 125 mg/kg, significant differences from the control group were recorded only in the number of phagocytizing monocytes in C57BL/6 mice. The findings indicated that the complex of iodine with bioorganic molecules at a dose of 250 mg/kg increased the phagocytic activity of both granulocytes and monocytes in C57BL/6 mice.

Conclusion & Significance: One of the explanations for the differential effect of a new complex of iodine with bioorganic molecules on different lines of mice may be based on the genetic characteristics of these animals. Macrophages of BALB/c mice are known to be of M-2 type, which inhibits inducible NO synthesis and stimulates cell division. Macrophages of C57BL/6 mice are of M-1 type, which produces NO and inhibit cell division, and increases the cytostatic or cytotoxic activity of phagocytes /2 - 4/. According to the results of the study, we can, therefore, conclude that a new complex of iodine with bioorganic molecules enhances the cellular factors of the natural resistance in the prototype mouse strains Th1 (C57BL/6), but not Th2 (BALB/c). This, in turn, fits into the single mechanism of action of the studied complex, namely, the activation of phagocytic cells through the induction of IFN-γ production and the ability of the complex to switch T cells to the Th1-type response path.

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