Résumé

THE EFFECT OF ANTI-CANCER AGENTS ON THE NUMBER OF LEUCOCYTES IN THE PERIPHERIAL BLOOD AND ON THE HEMOPOIETIC SYSTEM OF THE RABBIT

TANEKAZU HARADA

Department of Surgery, Keio University, Tokyo, Japan (Chief of the Department, Prof. NOBUKATSU SHIMADA)

Leucopenia is one of the most serious side effect of the anti-cancer drugs. I have given nitromin (NMO), mitomycin (MC) and carzinophilin (CZP) on the rabbits and the changes in the number of the leucocytes in the peripherial blood and the pathological changes in liver, spleen and bone marrow were studied. The number of the rabbit used for my study mounted to 112. My conclusions are as follows ;

1) The maximum doses of these anti-cancer drugs are 10 mg/kg for NMO, 500 mcg/kg for MC and 1,000 u/kg for CZP, if they are to be given continuously for over the period of two weeks. Leucopenia in the peripherial blood is more pronounced in the order of CZP, MC and NM.

2) The pathological findings are as follows; In the liver, there is swelling of liver cells and the cytoplasma becomes transparent if the amount of these drugs is given, but the amount of the glycogen will decrease and it becomes atrophic if the large amount of these drugs is given. In bone marrow, the number of megakaryocytes and myelocytes is reduced, and, particularly in the group of the latter, those of mature type cells decrease remarkably. In the spleen, I have found the reduction of the size of the follicles, the disappearance of the germ centers and the dilatation of the sinuses as the amount of the drug increases.

3) The extent of the changes mentioned above is different depending on the anti-cancer drugs as well as on the amount adiministered, but the effect of MC and NMO is fairly similar. For decrease in the number of myelocytes induced by NMO, the mature type cells are most affected. When CZP is administered the decrease in the liver glycogen and hemosiderosis, as general, are pronounced.

4) These pathological changes are similar to those develop after irradiation, and I believe that these changes are not specific to anti-cancer agents,

5) Thu intermittent way of administration is better than continuous way of administration from the stand points of anti-cancer reaction and of prohibiting the side effect of the drugs.

THE INVESTIGATION CONCERNING THE PREVENTION OF LEUCOPENIA PRODUCED BY THE ADMINISTRATION OF ANTI-NEOPLASTIC DRUGS

CHANG I LANG

Department of Surgery, School of Medicine, Keio University
(Director: Prof. NOBUKATSU SHIMADA)

Because of the fetal side effect leucopenia, following the clinical application of chemotherapy to malignant neoplastic diseases, there are many cases in which the sufficient doses of these drugs are unable to be administered. Many investigations have been reported about the prevention of this side effect. In this paper, carzinophilin and mitomydin C were mixed with cobalt-chlorophyllin, vitamin K 3, adrenochrome monosemicarbazone (AC-17), vitamin B 12 and cystine, and the titer of this mixture was measured. The effect of the prevention of leucopenia and of the inhibition of the proliferation of experimental neoplasm were observed, administering this mixture to rats, the decrease of the titer was hardly recognizable by this mixture and the same effect was obtained against the experimental neoplasms with the administration of either carzinophilin and mitomycin C or the mixture. The effect of the prevention of leucopenia was observed among cases received combined therapy of these drugs, though the effect was decreased when the doses of these drugs was too excessive. Histologically the combined therapy of these drugs showed better improvement.

The fact that the combined administration of these drugs did not show any unsatisfactory influence to the anti-neoplastic effect, seems to imply good possibility of the prevention of leucopenia in cases administering such anti-neoplastic substance as carzinophiln and mitomycin C.

EXPERIMENTAL STUDIES ON METHODS OF ADMINISTRATION OF THE ANTITUMOR ANTIBIOTICS

SHIGEHISA HOJYO

Surgical Department of Medical School Keio University, Tokyo

Animal tumors used are YOSHIDA sarcoma, EHRLICH carcinoma and Sarcoma 180. All these tumors are used as the solid type, some part the ascitic type tumors.

Our experimental observations of the intravenous administration of carzinophilin (CZP), mitomycin-C (MC) and nitromin (NMO) were the methods of

administration for consecutive and intermittent as follows.

The method :

CZP

1,000 u/kg/day, 500 u/kg/day, 250 u/kg/day for 6 consecutive days.

500 u/kg/day for 12 consecutive days.

3,000 u/kg/day, 1,500 u/kg/day, 750 u/kg/day twice a week intermittently.

MC

500 mcg/kg/day, 250 mcg/kg/day, 100 mcg/kg/day for 6 consecutive days.

250 mcg/kg/day for 12 consecutive days.

1,500 mcg/kg/day, 750 mcg/kg/day, 300 mcg/kg/day twice a week intermittently.

NMO

10 mg/kg/day, 5 mg/kg/day, 2.5 mg/kg/day for 6 consecutive days.

30 mg/kg/day, 15 mg/kg/day, 7.5 mg/kg/day twice a week intermittently.

The result: The use of much dosage at the early stage was more effective. The intermittent therapy of antitumor antibiotics gave better results as far as the side effects were conserved and antitumor effects than the consecutive treatment.

The antitumor effects are indicated in the shape of diminition of tumor and the survival rate.

The side effects of antitumor antibiotics were investigated on mice and rats, and loss of weight resulted from the consecutive and intermittent application, and histo-pathological of liver after several application.

STUDIES ON THE CORRELATION OF GROUP-ELECTRONEGATIVITY WITH ANTIBACTERIAL ACTIVITY

SHIGERU YAMABE

Research Institute, Kobe College, Nishinomiya, Japan

The first purpose of this paper is to review the electronegativity scales of atoms and atomic groups. The second purpose is to show some applications of these scales to chemotherapeutic agents. It might be anticipated that, instead of structure-activity-relationship, group-electronegativity-activity relationship contributes to the rational approach to potent drugs. For example, the author points out that values of the group-electronegativity of N^1-substituents in sulfanilamide derivatives are required to be 3.00~3.07 for antibacterial activity. According to this hypothesis, compounds with the group, $-\overset{|}{\underset{S}{C}}-$N- as N^1-substituent can be the most promising sulfa-drugs. In the case of chloramphenicol analogs, as shown by HAHN, *et al.*, the dichloracetamide-moiety and the *p*-nitrophenyl moiety are largely electronegative, so that any variation of these two moieties cannot exceed the values of group-electronegativity of chloramphenicol itself and also cannot result in increase of activity.