STRUCTURAL ABERRATIONS IN BONE MARROW CELLS AFTER TRITIATED WATER ADMINISTRATION IN RATS

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Abstract

Structural aberrations in bone marrow cells were used as a biological test of HTO irradiation.

Three groups of nine rats were used : two groups received a single intraperitoneal dose of 75 and 100 µCi/g HTO ; one group received daily 3o µCi/g HTO for 18 days and 5 animals receiving saline solution served as controls.

Structural aberrations incidence in loo cells for each animal was established using the MOORHEAD and LAM-PO-TANG techniques.

The structural aberrations were of chromatidian (gaps and breaks) and chromosomial type (acentric fragments and translocations).

A relationship between calculated bone marrow dose and structural aberrations incidence was established.

Rats receiving once loo µCi/g HTO (2o rads) have 5.o+2.o p.c. structural aberrations and rats receiving 18 days 3o µCi/g HTO daily (∿ 6oo rads cummulative dose) displayed 7.3±3.2 p.c. structural aberrations. Control rats displayed only o.6±o.5 p.c. aberrations.

1. Introduction

The aim of this paper is to present the alterations in number and structure of bone marrow cells chromosomes, in rats, after unique and repeated administration of tritiated water (HTO).

Chromosomial aberrations were used as a biological dosimeter, due to the great sensitivity mentioned in the literature (BENDER)[1].

2. Material and methods

32 female WISTAR rats were divided in 4 groups. Groups A and B received intraperitoneally 75 and loo µCi/g body weight HTO. Group C received for 18 days intragastric administration of 3o µCi/g HTO. Group D has served as control and received saline solution. Groups A, B and C were of 9 animals and D of 5 animals.

Amersham tritiated water was used, the dilution to 2o

mCi/ml being made with saline solution.

Three animals from groups A and B were killed at 24 hours, 3 and 7 days interval, after HTO administration. From group C three animals were killed at 24 hours, 7 and 14 days after the last intragastric administration of HTO.

A technique combining the methods of MOORHEAD[2] and LAM-PO-TANG[3] was used for emphasizing chromosomes. loo metaphases were analysed for each animal, scoring the aneuploid mitosis and the various types of chromatidian and chromosomial aberrations.

The pattern of normal rat caryotype described by VRBA[4] and FITZGERALD[5] was used.

3. Results and discussions

DAWEY's work shown that RBE of tritium particles for structural aberrations is 1.2 by comparison with ^{60}Co gamma rays.

In our work we have attempted to assess the magnitude of the process of alteration in structure and number of chromosomes and the elimination with the time of altered cells, the selection of damaged cells in renewing cellular systems being well known (FABRIKANT)[7].

We did not notice differences in aneuploid cells between irradiated animals and controls at any interval after irradiation. The maximum occurence of aneuploid cells was 13.6 p.c. and the minimum 9.o p.c., in controls the incidence was 11.2 p.c.

Table 1 - Numerical abnormalities

	GROUPS	Time of study -days-	No. animals	Total cells analyzed	Euploid cells %	Aneuploid cells %
Single Administration	A loo μCi/g	1	3	3oo	87 ±9.3	13 ±9.3
		3	3	3oo	86.4±1.1	13.6±1.1
		7	3	3oo	87.4±2.3	12.6±2.3
	B 75 μCi/g	1	3	3oo	91 ±1.7	9 ±1.7
		3	3	3oo	88 ±3.4	12 ±3.4
		7	3	3oo	9o ±1.1	lo ±1.1
Repeated Administration	C 3o μCi/9/day	1	3	3oo	9o.7±2	9.3±2
		3	3	3oo	87.4±2.3	12.6±2.3
		14	3	3oo	9o ±1.7	lo ±1.7
	CONTROL		5	5oo	88.8±3.6	11.2±3.6

Structural aberrations observed were chromatidian (gaps and chromatid breaks) and chromosomial type (acentric fragments and translocations). The gaps were not scored because these are considered by EVANS[8] reparable lesions.

After single administration of HTO the incidence of chromatidian aberrations (table 2) is not significatively increased.

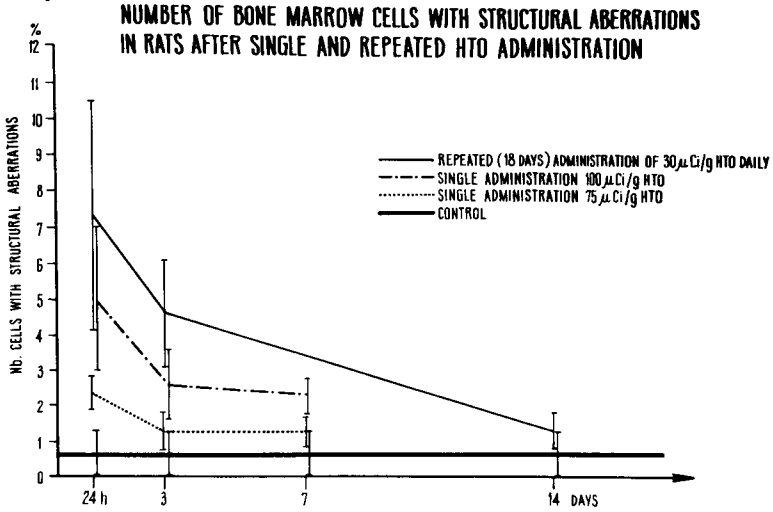
Table 2 - Structural chromosome aberrations

GRUPS		Time of study -days-	Nr. animals	Total cells analyzed	Nr.Chromatid Type Aberrations	Nr.Chromosome Type Aberrations		Cells with structural abnormalities	
					Breaks	Fragments	Translocations	Total	%
Single Administration	A 100 µCi/g	1	3	300	4	9	2	15	5±2 (p o,o25)
		3	3	300	3	3	2	8	2,6±1 (p o.5)
		7	3	300	1	5	1	7	2.3±o.5 (p=o.o2)
	B 75 µCi/g	1	3	300	2	5	-	7	2.3±o.5 (p=o.o2)
		3	3	300	3	1	-	4	1.3±o.5 (p o.5)
		7	3	300	4	-	-	4	1.3±o.5 (p o.5)
Repeated Administration	C 30 µCi/g/day	1	3	300	7	9	6	22	7.3±3.2 (p=o.o25)
		3	3	300	3	lo	1	4	4.6±1.5 (p=o.o2)
		14	3	300	-	3	1	4	1.3±o.5 (p o.1)
D	CONTROL	-	5	500	3	-	-	3	o.6±o.5

The chromosomial aberrations increased significatively after 100 μCi/g HTO, and were gradually eliminated 3 and 7 days later. 75 μCi/g also produce a statistically significative increase after 24 hours and the decrease could be detected 3 days after HTO administration.

The repeated HTO administration produced a higher increase, 7.3 ± 3.2 p.c. of cells with structural aberrations both the chromatidian and chromosomial type being involved. Three days after, cessation of HTO administration, the incidence of chromosomial aberrations is still significatively higher that in controls but 14 days later the elimination of damaged cells is almost complete.

Fig.1.



From the calculation of bone marrow absorbed dose, we obtained for single administration of 100 μCi/g HTO approximately 27 rad, for 75 μCi/g - 20 rad and for repeated administration of 30 μCi/g the cummulative bone marrow absorbed dose was about 600 rad.

The pattern of structural aberrations after single admistration of HTO, shown before, may be related with bone marrow cells irradiation, if we consider that the bone marrow receives an irradiation with a dose rate which attains the maximum a few hours after the HTO administration and decreases gradually during the first days. Such a distribution of irradiation could explain the reason for which 75 μCi/g HTO deliver enough bone marrow dose to produce statistical significative increase of structural aberrations only 24 hours after administration. With 100 μCi/g HTO, the dose obtained after administration produce enough altered cells to be detected until the 7 days.

During daily administration of HTO, the bone marrow dose increases gradually, the tritiated water eliminated in 24 hours being only a part of that administred the following day.

The equilibrium of tritium content in bone marrow with the tritium in blood reached, the dose attains a steady state until

the cessation of administration, afterwards the decrease beging. The production of damaged cells is at the same time partly compensated by elimination of these cells and this explains the figures observed in group C.

From the above discussions we have to conclude that tritiated water irradiation induces in bone marrow system with a cellular population inhomogeneous as structure and division phase, structural aberrations roughly dose dependent.

This fact needs a more accurate establishing on a homogeneous cellular system as periphereal lymphocyte.

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