BIOLOGICAL DOSIMETRY APPLIED TO TREATMENT WITH ^{131}RADIO-IODINE IN THYROID CANCERS

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This study had 2 objectives :
Firstly to compare the number of unstable chromosomal anomalies (dicentrics, rings and fragments) obtained by the method of conventional cytogenetics with the number of translocations revealed by in situ hybridization (FISH) and secondly to estimate the mean whole body dose after treatment with 3.7 GBq (100 mCi) of ^{131}I.

MATERIALS AND METHODS

Dose effect curves in vitro were generated by the method of counting unstable anomalies and by the FISH method, using peripheral lymphocytes of healthy donors. Both curves were fitted by the linear-quadratic model. Conventional Cytogenetics was carried out on slides containing metaphase spreads stained by Giemsa. Only complete metaphases (46 centromeres) were scored for dicentrics, rings and fragments under a light microscope (1).

Hybridization in situ was carried out using a modified procedure of Pinkel et al (2). The technique was applied to chromosome 4 by means of a specific probe. Chromosome 4 was chosen because of its large size which facilitates the scoring of translocations. The FISH slides were read under a fluorescent microscope using blue light emission and filters for green and red fluorescence.
The pair of chromosome 4 had been labelled by the green fluorescence of Fluorescein isothiocyanate (FITC) and the other chromosomes of the genome counterstained with propidium iodide.
Scoring of dicentrics and translocations was done on a patient blood sample 24 hours before and then 4 days after the administration of ^{131}I.

The number of dicentrics was directly compared to the standard curve.
Since chromosome 4 represents 6,23 % of the total genome, the number of translocations obtained by FISH was extended to cover the whole genome by the following formula (3).

$$F_h = 2\, f_s\, (1 - f_s)\, F_b$$

were F_h is the translocation fraction found by hybridization, f_s the conterstained fraction of the genome and F_b the transloction fraction observed by G-banding which is set equal to 1.

PATIENTS

Patients had been treated with 3.7 GBq (100 mCi) of ^{131}I. The mean total body dose was 0.54 Gy (95 % CI : 0.45 - 0.61 Gy) by chromosome 4 painting. A close relationship was found between total body retention of ^{131}I at day 4 after ^{131}I treatment and the estimated dose by conventional cytogenetics and chromosome 4 painting. In contrast, no relationship was found between the uptake of ^{131}I in thyroid remnants and distant metastases and the dose estimated by biological dosimetry.

RESULTS

The ratio of translocations to dicentrics induced by ionising radiation is supposed to be 1, because a dicentric chromosome as well as a chromosomal translocation is the result of 2 successive events. However, we found that induced translocations were 3-8.4 times more frequent than dicentrics for each dose of irradiation ; this agrees with earlier findings (3).
When comparing the number of chromosomal aberrations found by FISH or conventional cytogenetics with the dose effect curve obtained by in vitro, exposure of normal peripheral lymphocytes, the total body dose was

estimated to be significantly higher than the estimation based on MIRD (4). Some aberrations (dicentrics and translocations) were found before ^{131}I treatment and no known previous exposure to irradiation may explain this.

DISCUSSION

The estimated mean total body dose is 2 to 4 times higher than that based on MIRD calculations (0.13 Gy) (4). In fact, MIRD calculations were derived from individuals with normal thyroid function and normal metabolic activity. Thyroid cancer patients are hypothyroid at the time of ^{131}I administration. The hypothyroid status decreases the renal clearance of radioiodine and thus increases the whole body dose which can explain the discrepancy between the MIRD estimation and the values found by biological dosimetry.

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