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Proposal for biochemical dosimeter for prolonged space flights

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Abstract

Radiation dosimetry has been developed by means of physical, chemical and biological methods. A different approach to calculate the absorbed dose is related to the assay in body fluids of some molecules that modify their concentration after irradiation. The salivary glands in humans appear particularly radiosensitive and the effects of ionizing radiation can be evaluated by means of the determination of serum amylase (produced by acinar cells) and Tissue Polypeptide Antigen (TPA, synthesized by ductal cells). Patients submitted to external radiotherapy for tumours localized in the head and neck region show early and late effects on salivary glands. The modification of amylase activity and TPA appear as a progressive statistically significant increase within two days. Levels of 200-300% of baseline value are reached, followed by a rapid return to preirradiation levels. The use of different doses per fraction and fractionation schedules (conventional or multiple daily fractionations) confirm the direct correlation between the absorbed dose and serum amylase and TPA levels. It is worthnoting that the irradiation of pancreas region did not produce any effect on amylase activity. The correlation may be assumed as linear for a short dose range (2-6 Gy) whereas in the range from 0.5 to 10 Gy a sigmoid curve represents the experimental data. Both molecules confirm their capability to quantify the absorbed dose in patients with thyroid carcinoma submitted to metabolic treatment with iodine-131. The effects of radiation are species-specific and are absent in laboratory mammals. The easiness of the determination of serum amylase and TPA lead us to propose the test as biochemical dosimeter for cosmic rays exposure during prolonged staying in the space.

KEYWORDS: Dosimetry, salivary glands, amylase, TPA.

1. Introduction

The prolonged exposure to cosmic radiation during human space flights involves the absorption of a not neglectable dose, with increased risk for acute and late damage.

The search for biological and biochemical parameters to be used in the dosimetry and in the assessment of biological effects is a topic or particular interest. The concentration of some molecules in body fluids can be modified by relatively low dose of ionising radiations [1, 2], thus they can be used to monitor the radiation dose absorbed during space flights.

In humans, differently from usual laboratory animals, the salivary glands show high sensitivity. After irradiation both acinous and ductal cells produce, respectively, an increase of serum aplha-amylase activity and Tissue Polypeptide Antigen (TPA) concentration, caused by cell death [3-6].

During the years several studies have been conducted in our Laboratory to quantify the dose-effect relationship. Patients treated by external radiation therapy, for head and neck tumours, with different fractionation schedules, and by ^{131}I radiometabolic therapy for thyroid cancer have been analyzed [3-7].

Part of the study has been performed with the cooperation of the Department of Radiotherapy and Clinical Biology of the Institute G. Roussy, Villejuif (F), and the Department of Biomathematics of the MD Anderson Cancer Center, Houston (TX, USA).

2. Patients and methods

Patients with head and neck cancer (26 oral cavity, 24 oropharynx, 14 nasopharynx, 8 larynx and 6 paranasal sinus) were treated with γ rays from ^{60}Co unit or 15 MV photons from linear accelerator, through two lateral opposite fields. All salivary glands were included in the irradiated volume.

The following fractionations, conventional or hyperfractionated, have been used:

Schedule	Daily dose (Gy)	Total dose (Gy)	n. of patients
2 Gy 1 time/day	2	60-66	35
1 Gy 3 times/day	3	60-66	13
2 Gy 2 times/day	4	60	5
2 Gy 3 times/day	6	56	20

Blood samples were collected daily before and during the first week, then weekly during the whole treatment. Serum alpha amylase was assayed according to the Street and Close method [3, 4] and TPA by immunometric method [5]

3. Results

The amylasemia shows a statistically significant increase after the first day of treatment, progressively increases during the following 2-3 days, then returns on the control values. At first day, the higher the daily dose the higher the increase that, however, lasts for a shorter time.

The cumulative data from Villejuif and Florence regarding the amylasemia at first day of treatment have been analyzed to obtain the curve better interpolating the experimental points, from 0.5 to 10 Gy. The mathematical model able to describes the fitted values is represented by the following equation:

$$Y = \frac{K \cdot e^{(\beta D+C)}}{1 - e^{(\beta D+C)}} \qquad (1)$$

where Y = the post irradiation amylasemia;
K, C = constants;
β = parameter associated with the dose.

The values obtained by the Florence cases alone were better described by a linear model:

$$Y = 0.07 + 1.83\ D \qquad (2)$$

TPA shows an overlapping behaviour [3]. At day 1 TPA shows a high dose/effect correlation ($r = 0.971$, $p < 0.01$).

4. Discussion

According to the results, salivary alpha-amylase and TPA assayed in the serum respond to the characteristic of a biochemical indicator of radiation injury when head and neck region is exposed to ionising radiation.

The results obtained in a cohort of patients treated with different doses of ^{131}I for thyroid carcinoma showed the capability of these molecules to calculate the dose received by the salivary glands and to justify the acute and late damage after radiometabolic treatments [7].

Recently the amylasemia have been effectively used to monitor the dose received in the Japanese nuclear reactor accident.

Alpha-amylase and TPA appear to be sensible to quite low doses; moreover, sampling and assay are easy, able to show early modification and to evidence an effective dose/effect relationship. For these reasons they can be proposed as indicators of radiation injury during human space flights.

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