

PLASMA LEVEL OF LIPID PEROXIDATION, TOTAL SULPHYDRYL GROUPS AND NITRIC OXIDE LEVELS IN CANCER PATIENTS IRRADIATED ON DIFFERENT ANATOMIC FIELDS: A CASE–CONTROL STUDY

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Aim: The aim of this study was to evaluate the effect of radiotherapy on lipid peroxidation, total sulfhydryl groups (RSH) and nitric oxide (NO·) levels in plasma of cancer patients treated on different anatomic sites, and to compare the results with control subjects. **Methods:** 89 patients with various malignancies and 33 healthy control subjects were recruited for the study. Cancer patients were grouped according to the irradiation portals (head and neck, thoracic, breast, abdominal and pelvic). Two blood samples before and after the completion of the fifth week of radiotherapy were collected from each patient. **Results:** Plasma levels of malondialdehyde (MDA) and NO· of cancer patients before irradiation were found higher than those in control subjects. After irradiation, a marked lipid peroxidation increase was demonstrated as well as the significant decrease of plasma RSH level. **Conclusion:** The alterations of the parameters indicate enhanced oxidant stress and point to the necessity of antioxidant prophylaxis upon application of radiotherapy.

Key Words: cancer, lipid peroxidation, malondialdehyde, nitric oxide, radiotherapy, total sulphhydryl groups.

Radiation therapy (RT) has still been considered to be one of the most popular and important tools to cure cancer. In radiotherapeutic practice, the radiation dose is chosen primarily on the basis of maximum dose tolerated by the normal tissues in the irradiated volume rather than local tumor control as the radiosensitivity of normal tissues adjacent to the tumor limits therapeutic gain [1].

One of the consequences of the radiation is the production of free radicals due to indirect effect of water radiolysis [17]. The process of lipid peroxidation is one of the oxidative conversion of polyunsaturated fatty acids to several products including malondialdehyde (MDA) and lipid peroxides [18]. The production of large amounts of nitric oxide (NO·), a free radical, has been implicated as a cytotoxic factor in a variety of pathophysiological processes [6]. Glutathione (GSH) is known to function as an important antioxidant in the detoxification of xenobiotics, carcinogens, free radicals and maintenance of immune functions as a nonprotein thiol [15]. By this way, GSH also acts as a cosubstrate in the enzymatic repair of radiation damage [10]. Considerable evidence points to the fact that intracellular non-protein sulphhydryl compounds play an important role in the cellular response to ionizing radiation, and the alterations in blood glutathione levels were also suggested to be used as an index of tumor response to therapy [8,15].

The effect of ionizing radiation on surrounding normal cells may differ in various irradiated sites. Therefore, a

study was undertaken to evaluate the effect of radiotherapy on plasma MDA level as the last step of lipid peroxidation, total sulphhydryl group (RSH) and NO· levels of cancer patients treated on different RT field localizations, and to compare the results with control subjects.

PATIENTS AND METHODS

Patients and controls. The protocol for the study was approved by the Ethic Committee of Gazi University Faculty of Medicine, and informed consent was given by each patient. 89 patients with current histopathological proof of cancer without distant metastasis (stage II–III) to whom a course of irradiation was planned were randomly selected from outpatients attending Radiation Oncology Department of Gazi University Faculty of Medicine, Ankara, from November 2002 through April 2003. Eligibility required age ≥ 18 yr and Karnofsky Performance Status $\geq 70\%$. Patients with a history of previous RT to the same region were ineligible. Patients were divided into five groups according to their irradiated sites: group 1 ($n = 12$) head and neck RT, group 2 ($n = 13$) thoracic RT, group 3 ($n = 32$) breast RT, group 4 ($n = 17$) abdominal RT, and group 5 ($n = 15$) pelvic RT. The patient group included 46 women and 43 men (mean age \pm standard error of mean (SEM), 51.24 ± 1.07 years). A detailed clinical history of the subjects was collected by personal interview, and clinical examinations were performed. The tumor stagings were done as per American Joint Committee on Cancer TNM Staging [7].

The control group consisted of 33 healthy volunteers (17 women and 16 men; mean age \pm SEM 52.61 ± 1.72 years). These subjects were confirmed free of disease on the basis of clinical history, physical examination and routine laboratory tests.

Radiotherapy. All patients received 50 Gy in 25 fractions of external beam RT to the primary tumor/

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Abbreviations used: CI — confidence intervals; GSH — glutathione; MDA — malondialdehyde; NO· — nitric oxide; RSH — total sulphhydryl groups; RT — radiation therapy; SEM — standard error of mean.

УРОВЕНЬ ПЕРЕКИСНОГО ОКИСЛЕНИЯ ЛИПИДОВ И СОДЕРЖАНИЕ СУЛЬФИДРИЛЬНЫХ ГРУПП И ОКСИДА АЗОТА В ПЛАЗМЕ КРОВИ ОНКОЛОГИЧЕСКИХ БОЛЬНЫХ ПРИ ОБЛУЧЕНИИ РАЗЛИЧНЫХ ПОЛЕЙ: ИССЛЕДОВАНИЕ МЕТОДОМ “СЛУЧАЙ — КОНТРОЛЬ”

Цель: оценить эффект радиотерапии на содержание малонового диальдегида как маркера перекисного окисления липидов, уровень общих сульфгидрильных групп и оксида азота в плазме крови онкологических больных при облучении различных полей в сравнении со здоровыми донорами. **Методы:** в исследовании участвовали 89 онкологических больных и 33 здоровых донора. Группы больных были сформированы в зависимости от локализации облучения (голова и шея, торакальный отдел, молочная железа, абдоминальный отдел и тазовая область); образцы крови были взяты у больных до проведения радиотерапии и после пятинедельного курса радиотерапии. **Результаты:** до радиотерапии уровень малонового диальдегида и оксида азота в плазме крови больных был выше такового здоровых доноров; после радиотерапии у больных было отмечено как выраженное повышение уровня перекисного окисления липидов в плазме крови, так и статистически значимое снижение содержания сульфгидрильных групп. **Выводы:** изменение указанных параметров свидетельствует об усилении окислительного стресса и необходимости антиоксидантной профилактики при использовании радиотерапии. **Ключевые слова:** рак, окисление липидов, малоновый диальдегид, оксид азота, радиотерапия, общие сульфгидрильные группы.