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Original research article

The effect of radiotherapy and chemotherapy on osmotic fragility of red blood cells and plasma levels of malondialdehyde in patients with breast cancer

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ABSTRACT

Background: Gamma radiation effects on the erythrocyte membrane from three different functional parts, lipid bilayer, cytoskeleton and protein components. When the red cell membrane is exposed to radiation, it loses its integrity and hemoglobin leaks out. In addition, irradiation leads to lipid peroxidation and the products of this process, leading to hemolysis. The aim of the present study was to measure osmotic fragility (OF) of red blood cells and malondialdehyde (MDA) levels as a marker of oxidative injury in breast cancer patients treated with radiation and chemotherapy.

Materials and Methods: The OF test was performed using different concentrations of a salt solution. The measurement of MDA was done with chemical methods.[11] The sampling was taken during three stages of treatment: first sample was taken before starting chemotherapy, the second sample was taken before radiation therapy and the third sample was taken after radiotherapy.

Results: No statistically significant differences between levels of MDA in these three stages of treatment were observed. However, the comparison of mean levels of MDA showed an increase after radiotherapy. The OF rate did not show significant difference ($P > 0.05$) during the stages of treatment.

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Conclusion: In a standard treatment program of radiotherapy and chemotherapy lipid peroxidation level and OF do not significantly increase.

1. Background

Breast cancer is a major public health problem in the world, with incidence of more than one million a year, and nearly half of it occurs in North America and Europe.[1] In 2012, 1.7 million new cases of breast cancer were diagnosed worldwide, and in the same year 52,2000 women died from it.[2] The prognosis of this disease depends on the tumor characteristics and quality of treatments. These treatments include systemic and local approaches based on chemotherapy and then hormonal interventions to prevent or delay metastasis.[1] Approximately 5–10% of breast and ovarian cancers are hereditary and 30–50% are autosomal dominant mutations. Deleterious gene mutations in BRCA1 and BRCA2 are responsible for hereditary breast cancer.[3]

Gamma rays used in radiotherapy have different biological effects on the membrane of red blood cells. Free radicals that are produced during body irradiation can cause membrane changes including lipid peroxidation, phospholipid hydrolysis and disulfide bridged formation.[4] Also, these changes in the cell membrane may affect the cytoskeleton. The effect of free radicals on the erythrocyte membrane and cytoskeleton can cause defects and hemolysis in the red blood cells and hemoglobin leakage.[5] For evaluation of osmotic fragility of red blood cells and disease diagnosis related to hemolysis osmotic fragility (OF), a test was performed.[6] Patients with breast cancer under adjuvant treatment suffer from a decrease in hemoglobin concentration that in cancer patients has been related to high levels of fatigue and depression with a decrease in physical activity, quality of life and survival.[7] Based on the previous studies, the importance of this test is to confirm that the membrane property and morphology of red blood cells is abnormal.[6]

The free radicals from radiation have a high affinity to the lipid membrane, which may cause damage to the membrane. These damaged lipid molecules are hardly back to the initial state and cause a gap in the cell and disorder in exchanging important intracellular minerals.[8,9] To evaluate the oxidative damage of erythrocyte, malondialdehyde (MDA) was used as a marker for measuring lipid peroxidation levels.[10] The aim of this study was to evaluate the effect of radiotherapy and chemotherapy on the fragility of red blood cells and plasma MDA levels as a marker of oxidative damage.

2. Materials and methods

This descriptive-analytical study was performed in 2013 on 17 patients with breast cancer recently diagnosed and who had followed surgery.

Fasting venous blood was taken for OF and MDA measurement. OF was evaluated by a method using different concentrations of salt solution and MDA was assayed with the chemical method developed by Satoh.[11] The sampling was taken during three stages of treatment: first sample was taken before starting chemotherapy, the second sample was taken before radiation therapy and the third sample was taken after radiotherapy. All patients received the same drug regimen, including Taxotere (docetaxel), Adriamycin (doxorubicin) and cyclophosphamide in chemotherapy. Concerning radiotherapy, all patients received radiation dose of 54 Gy in the chest wall and supraclavicular regions as a standard protocol delivered by the Phoenix radiotherapy machine. This study was approved by the ethical committee of Golestan University of medical sciences and patients participated on a voluntary and conscious basis.

2.1. *Statistical test*

Statistical analysis was performed using the SPSS software (v.16.0). Mean values and standard deviations were calculated for all parameters. Pearson's correlation was used to correlate the markers of oxidative injury (MDA levels and OF). Comparisons between each stage of treatment were done using a t-test.

3. Results

The mean and standard deviation age of the patients was 51.5 ± 1.05 years and the average radiation dose was 4693 ± 219.4 cGy. Plasma level of MDA and erythrocyte OF increased during three stages (Table 1), but no significant statistical difference was observed (Table 2).

Despite of the increasing trend of MDA and OF in each stage compared to the previous stage, no significant difference was found between groups ($P > 0.05$).

4. Discussion

This study evaluated the levels of MDA and OF in patients with breast cancer who had undergone chemotherapy and radiotherapy. The comparison of the mean of MDA levels and OF showed an increasing trend from beginning to end of treatment.

Few studies have been performed on this subject. Some results are in accordance with ours, while some others are contrary to our results. The study performed by Kergonou and colleagues evaluated the effects of gamma radiotherapy on the lipid peroxidation and osmotic fragility of rat erythrocytes. The authors found that MDA levels increased and rat erythrocyte fragility decreased after radiotherapy.[12] In another study performed by Selim and coworkers to assess the effect of radiotherapy on the biophysical characteristics of the