

Effects of X-Ray Exposure on Some CMI Regulatory Cytokines in Technicians Serum Samples

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ABSTRACT

Ionizing radiation considered as an immunosuppressive factor upon over dose of exposure. Radiation field workers usually following a periodic checkup to monitor changes in their clinical status. Cell Mediated Immunity (CMI) has an important cytokines that regulate this specific immunological process. This study estimated the Interleukins (IL-2, IL-12 and IL-18) levels in serum samples using ELISA technique. Serum samples were collected from X-ray Technicians (Radiography, Fluoroscopy and Computed Tomography Scan Technicians) working in AL-Muthanna governorate hospitals. A total of (60) technicians and (30) control were involved in this research. Results showed significant decrease in IL-2 levels and increase in IL-18 levels in test groups (technicians) as compared with controls. While, IL-12 levels did not show a difference; all obtained values were within normal range. Overdose of X-ray exposure caused CMI suppression via disturbing the levels of critical cytokines (IL-2 and IL-18) leading to CMI loss regulation.

Keywords: X-Ray technician; IL-2; IL-12; IL-18; CMI and periodic checkup.

INTRODUCTION

The immune system is the guard of human body against infections and cancers; Cell Mediated Immunity (CMI) is an effective hitting arm of the immune system against intracellular parasites, cancerous cells and mutated or transformed cells, hence; disturbance of this specific immune response will lead to make a person more prone to get intracellular parasites or cancers¹.

Ionizing radiation IR is an immunosuppressive factor, it is able to hit immune cells turning them to inefficient cells and that will be reflexed on these cells regulating products which are cytokines². X-Ray is a type of IR which mainly used for medical purposes and under special control. X-Ray technicians are in continuous exposure to this type of IR especially during work load, they undergo a periodic checkup for monitoring personal exposure and that is usually performed seasonally. Periodic checkup includes clinical parameters of direct link with health status like total and differential white blood cells count and seminal fluid general test; for males^{3,4}.

Occasionally; those used parameters are not enough to view clinical status; mainly due to the ability of hematopoietic system to overcome IR effects and recover cells numbers fast upon exposure with time⁵. From this point; immune system health need to be evaluated using immune cells products rather than number. Because these cytokines are responsible for regulation immune responses and direction of immunological reactions^{1,6}.

This study focused on Interleukins which are cytokines produced by leukocytes and effect on other leukocytes. Interleukin-2 (IL-2), Interleukin-12 (IL-12) and

Interleukin-18 (IL-18) have direct relation with CMI effectiveness and can be considered as indicators for CMI function.

MATERIALS AND METHODS

Subjects

A total of (60) X-Ray technicians involved in this study divided on two test groups; they included (Radiography, Fluoroscopy and Computed Tomography Scan or CT scan Technicians), all of them were all healthy adults, non- smokers, both genders but menstruation period was avoided for females to avoid hormones interfere with the immune system. All were working in Al-Muthanna governorate hospitals.

Controls

There were (30) volunteers included in the present study and their results were used for comparison with test groups results. Controls were healthy adults with no history of IR exposure.

Samples

serum samples were collected from both subjects and controls as in⁷

ELISA tests

three kits of Enzyme Immunosorbant Assay (EIA) were used in this study, EIA IL-2, EIA IL-12 and EIA IL-18; manufactured by Biologend (USA); work steps were performed as provided by the company instructions in the leaflets.

Statistical analysis

test groups results were compared statistically with controls to find the level of significance difference as in⁸.

Table 1: Interleukins Levels obtained for Test groups and Controls.

Group	IL-2	IL-12	IL-18
Control	26.41± 4.59	195.11 ±0.19	56.81± 5.38
G1	24.82± 4.10*	195.39± 0.4	491.71 ±137.79*
G2	36.95±5.15 ^a	195.26 ±0.34	692.07 ±93.75*

($M \pm SE$): Mean \pm Standard error. All the levels of interleukins were estimated in (pg/mL.);(Picogram/ milliliter). * : Refers to significant differences comparing with control group at level $p \leq 0.05$.

a: refers to significant difference comparing with the other test group at level $p \leq 0.05$.

RESULTS

X-ray technicians were divided into two test groups, G1 group represented technicians of employment period equal to or less than (5) years, and G2 group represented X-ray technicians whom had employment time over than G1. This grouping was recommended by (Jacob et al., 2013). Hence; G1 had (23) and G2 (37) cases, ELISA tests results are shown in table (1).

Interleukin-2 results showed that acute radiation exposure for X-ray occupational represented by G1 group members caused a significant decrease in IL-2 levels when compared with controls, while IL-2 levels increased significantly in chronic X-ray exposure as in G2 group levels compared with controls and acute exposure; G1 levels.

The scientist⁹, and his team stated that irradiation of whole human body caused acute irradiation syndrome and usually leads to suppression of immune function due to alteration of cytokines release; like IL-2 increase in levels.

The researcher¹⁰ reported that IL-2 production by T-cells is reduced in atomic bomb survivors after ionizing radiation exposure, these findings supporting the present results since acute exposure caused significant elevation in IL-2 levels in G1 members.

Interleukin-2 is the most important immune response modulating factor as stated by¹¹, when they investigated IL-2 production by lymphocytes in radiation occupational blood samples and the interleukin levels increased immediately after radiation exposure.

The author² demonstrated that acute exposure to radiation influenced on X-ray technicians and caused a significant increase in IL-2 levels. These results are consonant with the results of the present study.

From another view;¹² and his colleagues concluded; during their experiment upon chronic irradiation effects; that this method of ionizing radiation exposure caused increase in natural killer cells cytotoxicity due to IL-2 levels increase in response to chronic radiation exposure, these findings support the present result of G2 group since chronic IR exposure caused a significant elevation in IL-2 levels.

Another important study accomplished by¹³, they searched about X-ray radiation biological effects on medical staff, they found that IL-2 levels significantly increased upon continuous exposure due to increase in aberrant cells frequencies in these occupational blood; very same to this study finding.

Outcomes of IL-12 did not show a relation between X-ray exposure and the cytokine levels in technicians serum samples, since; no elevated nor decreased levels recorded

in both test groups G1 and G2. All results were within normal accepted values and no significant difference obtained between test groups and controls.

Despite of the fact that IL-12 is the cytokine that is responsible for differentiation of T-cell into Th1 and usually increased during Th1 immune response; as concluded in many previous researches. The present study outcomes showed different results. The scientists¹⁴ evaluated different cytokines production and their expression in response to ionizing radiation and attributed their increase due to radiation induction of these cytokines expression.

An opposite opinion was stated by¹⁵ they concluded that irradiation caused reduction in IL-12 production. The authors¹⁶ suggested the cytokine IL-12 as a treatment for avoiding radiation exposure damage on immunological barriers in skin. The authors¹⁷ concluded that IL-12 levels can differ post gamma radiation exposure in dose dependent manner, whereas, IL-12 levels increased in low dose of radiation and decreased in higher dose.

Interleukin-18 results showed a very obvious and strong relation to radiation exposure since this cytokine levels increased significantly in serum samples of test groups comparing with controls.

The scientist¹⁸ suggested using of IL-18 as a biomarker for radiation exposure since its levels increased significantly in laboratory animals after irradiation in relation to radiation injury severity. Other supportive results were obtained by¹⁹; they investigated the relation between X-ray irradiation and IL-18 levels in mouse and found that IL-18 levels increased as its expression increase in macrophages after irradiation with both high-dose and low-dose of X-ray. Also; as stated by²⁰; that ionizing radiation induced IL-18 secretion by activation of its production pathway in macrophages of mouse, which is consistent with present study results.

These outcomes may related to this cytokine role as antitumor factor during CMI, many scientists suggested this interleukin as therapy for cancer patients because its activity during cancer fighting and altered cells resulted from IR exposure. The authors,²¹ prepared a vaccine using gene therapy technique when they transfected lung cancer cells with a cloned plasmid liposome containing IL-18 producing genes, they found; after irradiation; this vaccine induced antitumor efficacy by enhancing cytotoxic activity of NK cells, moreover; cancer cells stopped their proliferation process.

A research team²² investigated about the biomarkers for radiation injury and they found IL-18 levels increased after irradiation with γ -radiation showing a direct

correlation with the absorbed dose in experimental animals.

Gamma radiation induces changes in the surface receptors of the influential cells in the immune system including macrophage, dendritic cells and lymphocytes due to chromosomal aberration, mainly during chronic radiation exposure hence altered cells appear in high frequencies. Moreover, these changed cells will be either in early apoptosis status or un-functional cells by they are not able to receive or send messages; by secretion or induction; via cytokines that modulate immune responses in human body⁵ as a consequence for all that as stated by this author, the immune system will suffer from suppression and weakness and many recurrent infections will be common and cancerous cells will appear; mostly in X-ray technicians of long occupation period. This opinion is illustrated and discussed in expansion by⁵ in his research on radiation exposure consequences on human body; and the results he discussed were very similar to our findings and the opinion he presented was supporting to our outcomes in that IL-18 is the most appropriate cytokine to be tested periodically for people working as X-Ray technician with continuous IR exposure.

CONCLUSIONS

Overdose of X-ray exposure caused CMI suppression via disturbing the levels of critical cytokines (IL-2 and IL-18) leading to CMI loss regulation; moreover; these two cytokines can be used as biological indicators in X-Ray technicians periodic checkup indicating for ionizing radiation overdose of exposure.

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