EUROPEAN ACADEMIC RESEARCH
Vol. VII, Issue 6/ September2019

Impact Factor: 3.4546 (UIF)
DRJI Value: 5.9 (B+)

ISSN 2286-4822
www.euacademic.org

Assessment of Immunological Changes in Workers Occupationally Exposed to Low Levels of Ionizing Radiation

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Abstract

Long-term of low-dose ionizing radiation exposure may produce adverse health effects. The immune system is recognized to be extremely radiosensitive; consequently it is vulnerable to radiation. The aim of this study is to investigate the effect of low levels of ionizing radiation on immune responses in angiography workers chronically exposed to ionizing radiation. The study population consists of 36 workers occupationally exposed to ionizing radiation; 18workers less than a 5 years working period (group 1) and 18 workers more than a 5 years working period (group 2). The control group consists of 20subjects with no exposure to ionizing radiation. The concentrations of immunoglobulins Ig A, M and G and cytokine production such as tumor necrosis factor-α (TNF-α) and interferon-γ (INF-γ) were determined in blood serum. The results revealed that in group 1, the levels of IgA, IgM, IgG, TNF-α and IFN-γ were slightly higher than the control levels. In group 2, IgG was slightly higher, but IgM, TNF-α and IFN-γ were slightly lower than the control levels. The results showed also that, in workers of group 2 (more than 5 years) the levels of IgM, IgG, TNF-α and IFN-γ were significantly lower than in workers of group 1 (lower than 5 years). It is concluded that the immune system may have an adaptation mechanism for coping with occupational radiation exposure in workers of group 2.It is advised to perform a periodic check-up on the immune functions in radiology workers to detect any early changes in the immune system.

Keywords: Low-doses ionizing radiation, X-ray, TNF-α, INF-γ, Immunoglobulins, Occupational workers.

INTRODUCTION

It is well recognized that ionizing radiation has adverse health effects contingent on dose of radiation and length of exposure (Brant and Helms, 1999).Radiation impairment to the cells of the body depends on how sensitive the cells are to ionizing radiation (Alnahhal et al., 2017). The most susceptible cells are those that are difficult or impossible for them to repair any injury that may happen during cell division. The cells of the immune system are among the most greatly radiosensitive cells in the body(Manda et al., 2012).Although genomic instability are the most vital concerns of ionizing radiation, studies have explored that exposure to ionizing radiation can intensely affect immune system responses, leading to variations in the normal functions of immune responses (Georgakilas et al., 2015).

Consequence of high-dose radiation was clearly recognized on immune-suppression in both experimental and epidemiological studies (Harrington et al., 1997and Pandey et al., 2005).On the other hand, the impacts of low doses of ionizing radiation on the immune system show a great variability between different individuals and species (Manda et al., 2012).Also, long-term low doses exposure can produce variations in the sub-population composition of the circulating immunocompetent cells along with a decline in their functional activity (Chang et al., 1999).

Since greater exposure to ionizing radiation occurs from new man-made sources (Torkabadi et al., 2007), the consideration of the biological consequences of exposure to low-dose radiation is becoming important for humans. Health risks from radiation exposure in a large occupational part of population are obviously of special concern.

Along with the benefits of these technologies, fluoroscopy-guided procedures include radiation that increases concerns about the radiation-related health risks to patients and workers. While radiation management mainly focuses on minimizing the radiation dose of patients (Miller et al.,2010), the risk of radiation exposure is also inevitable among medical radiation workers (Ko et al., 2018).

There is a growing indication concerning immunological changes induced by low-dose radiation. The effect of occupational exposure to low levels of ionizing radiation in humoral immunity in radiation workers has been investigated. Earlier studies have shown that total immunoglobulins were lower in exposed workers compared with controls, representing the importance of taking suitable measures to protect radiology workers from exposure to ionizing radiation (Godekmerdan et al., 2004).

Cytokines, as vital mediators for immune cells communication, could be up- or down-regulated by low-dose radiation (Hayashi et al.,2005; Attar et al., 2007; Bogdandi et al., 2010; Gazin et al., 2004 and Wan et al., 2006). Nevertheless, the dysregulated expression of a distinct cytokine after irradiation does not adequately implicate its relationship with the pathogenesis (Schaueet al.,2012).

Oxidative stress of radiation induces higher expression of some markers of inflammation such as adhesion molecules and cytokines, which when interacting with cell's surface receptors induce specific mechanisms and stimulate immune responses (Gyuleva et al., 2018).It has been shown that production of pro-inflammatory cytokines such as interleukin 1ß (IL-1ß) pro-inflammatory cytokine, TNF-α and interleukin 6 (IL-6) were induced by exposure to ionizing radiation (Zhouetal., 2001 and Hayashi et al., 2005). As well, previous studies stated that cytokines, including interleukin-1(IL-1), TNF-α, and IFN-γ play a crucial role in chronic oxidative

damage following exposure to ionizing radiation (Yahyapour et al., 2018).

Aim of study

The objective of this work was to assess the effect of low-doses ionizing radiation on blood serum immunoglobulins A, M, and G (IgA, IgM and IgG) and cytokine production such as TNF-α and INF-γ in radiation workers.

MATERIAL AND METHODS

Subjects

Subjects were 36 physicians in vascular surgery department in El-Mataria teaching hospital. Their occupational exposure due to angioplasty procedures was routinely monitored by reading their film badges read every two months. Their exposure to ionizing radiation was assessed during previous year and they had no recorded over-exposure in their personnel documents. None of the subjects exceeded the International Commission on Radiological protection ICRP-specified dose limits. The control group consisted of 20 subjects from other hospital departments who were not exposed to radiation.

Subjects were divided into two categories: group 1 were workers more than 5years working in radiology; group 2 were workers that had less than 5 years working in radiology. The cases and controls were matched in age, gender and smoking status. Their overall health status was assessed by a questionnaire. They were basically healthy. The demographic characteristics of groups were illustrated in table 1. All persons were informed about the aims and scope of the study and gave their informed consent prior to their inclusion in the investigation. The volunteers were selected according to current International Program on Chemical Safety (IPCS) guidelines.

Experimental Design

5 ml of venous blood samples were obtained from each volunteer. Serum was obtained to determine immunoglobulins and TNF-α and INF-γ levels by centrifuging at 5,000 rpm for 10 min under ambient temperature.

Blood serum IgA, IgM and IgG concentrations were determined by the immunodiffusion technique (BINDARID TM Kit; the Binding Site Group.Birmingham, B15 1QT., U.K).Serum TNF-α, and INF-γ were assessed by the Enzyme-Linked Immunosorbent Assay (MyBioSource, China).

Statistical analysis:

All statistics were performed in SPSS version 20 software. Significant differences among groups were evaluated using one-way analysis of variance (one-way ANOVA); a significant p-value was considered when it was less than 0.05.

RESULTS

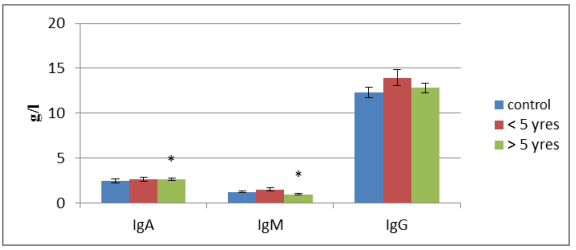
Data on humoral immunity parameters of the study groups are summarized in Figure 1. The results showed that the concentrations of immunoglobulins A,M and G were slightly increased with folds change by 1.07, 1.22 and 1.14 respectively, in workers of group 1 compared to control group with no significant differences detected.

Furthermore, IgA and IgM levels showed a non-significant decrease with fold change by0.82 and 0.79 respectively, in workers of group 2 when compared with the control group. Unlike IgA and M, the IgGlevel showed a non-significant increase (12.80 g/l) in group 2 when compared with that of control group (12.28 g/l).

The current results showed that IgA, IgM levels were significantly decreased in workers of group 2 when compared with respective workers of group 1. Whereas, this decrement

was non-significant in IgG levels with 0.92 fold changein group 2 when compared with that of workers of group 1.

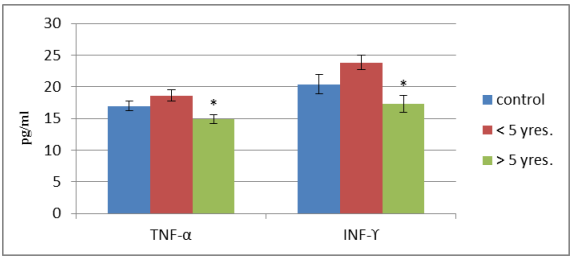
Figure 1: Serum IgA, IgM and IgG(g/l)levels in groups of exposed workers and control group.



*significant with workers lower than 5 years working period

The present results showed that values of TNF-α and IFN-γ were higher with 1.10 folds and 1.17 folds respectively in workers of group 1 as compared with the control group, which were not statistically significant. Contrarily, the lower levels inserum TNF-α and IFN-γ were not significantly decreased with fold 0.88 and 0.85 respectively in workers of group 2 when compared with control group. however, a significant decrease of TNF-α and IFN-γ levels wasobserved in group 2 as compared to that of group1 Figure (2).

Figure 2: Serum TNF-α and IFN-γ (pg/ml) levels in groups of exposed workers and control group.



*significant with workers lower than 5 years working period.

DISCUSSION

Previous studies indicated that whole-body exposure of humans to low doses of ionizing radiation enhances immune function, decreases total cancer mortality rates, and increased life-span (Luckey, 1997). On the other hand, high-dose radiation depresses immune function, increases the incidence of cancer, and induces higher mortality rates (Moss and Eckhardt, 1995).

Most studies have focused on the changes in immunity after exposure to doses >0.2 Gy and asymmetrical patterns are often observed. This is due, in part, to the complexity of the immune system (Zakeri et al., 2010). Godekmerdan et al. (2004); Alnahhal et al. (2017) and Zakeri et al. (2010)stated that the most effective periods which induce immunological changes were 5 years period.

A potential restriction was encountered due to the time between radiation exposure and the detection abnormalities known as the latent period, for example effects of low dose irradiation on genetic abnormalities and immune system cells and its functions (T and B cells) may takes years to appear (Alnahhal et al., 2017).

The present study assessed serum immunoglobulins IgA, IgM, and IgG concentrations as expressing the functional activity of B- lymphocytes. Our results revealed a non-significant increase in serum immunoglobulin IgA, IgM and IgGin workers of group 1 in comparison with control group (Fig. 1).Similar to our results, an increasing of IgA and IgM were found by Rybkina et al. (2018) in radiology employee chronically exposed to external radiation. The results of the IgA level are in agreement with the previous studies of Gyuleva et al. (2018) which found that plasma IgA was elevated with no statistical significant difference in employees working in nuclear power. Furthermore, Japanese authors (Kusunoki et al., 2004; Fujiwara et al., 1994) who performed a long-term

study of atomic bomb survivors, reported elevated serum concentration of IgM.

In considering workers of group 2 with working period over than 5 years, the results showed that IgA and IgM concentrations were lower than in control. These findings are consistent with the results reported by Godekmerdan et al. (2004) who reported that the radiologists with professional service of over 5 years working period demonstrated decreased levels of serum IgA and IgM. As well, the results of IgA and IgM are matched with the results of Serhatlioglu et al.(2004) who found that serum immunoglobulin A and M were in lower concentrations in radiology workers than in controls. Similarly Iakovlev et al. (1991) found that natural and specific immunoglobulin production was decreased.

On the other hand, the results showed that IgG levels were non-significantly increased in group 2 when compared with control group. The same results are achieved with studies conducted by Alnahhal et al. (2017) which explored that the mean level of serum IgG among medical radiographers (working period have at least 5 years' experience) was higher than non-exposed with no statistically significant levels. Zakeri et al. (2010) found a significant increase in serum IgG of interventional cardiologists with at least 5 years employment occupationally exposed to radiation compared to non-exposed group, which is explained by switches of immunoglobulins biosynthesis to IgGisotype. Contrarily, studies performed by Klucinski et al. (2005) reported significant lower concentrations of IgG among radiology employees. Such inconsistency could be due to different exposure rates, duration of exposure and different sample sizes.

In addition, the results showed that there was a trend of decrease in serum mean levels of IgA and IgM (2.01 g/l) and (0.96 g/l) respectively, in workers of group 2 when compared with that of workers in group 1(2.61 g/l) and (1.49 g/l) respectively, with statistical significant levels. Except for IgG

levels that recorded no significant differences between the two groups. These results are matched with reports of Oskouii et al. (2013), which found a statistical significant differences between IgA,IgM levels within working period differences.

Production of cytokines is an essential step in immune responses and immune regulation. Inflammation is initiated as a defensive response by the host, but can often result in systemic pathology. The proper regulation of cytokine production is serious in the control and prevention of diverse disease states (Moss et al., 2004).

The present study illustrated a tendency of an increased average levels of TNF-α and IFN-γ but not statistically significant in workers group 1as compared with control group (Fig. 2).These results are in concurrence with another report on angiography personnel exposed to x-ray showing insignificant increase for IFN-γ in study group when compared with control group (Torkabadi et al., 2007). Additionally, inflammatory cytokines production coincide with the study of atomic bomb survivors, in which IFN-γ, IL-10, IL-6, and TNF-α increased expression (Lourenco et al., 2013 and Hayashi et al., 2005). Furthermore, previous in vivo study on mice exposed to low dose γ-irradiation showed that resident peritoneal macrophages produced inflammatory cytokines in response to activation (Ibuki and Goto, 1999).

Inflammatory cytokines, such as IFN-γ, IL-2, IL-6, and TNF-α, increased expression, provide evidence of constant inflammatory responses, while IL-4 is anti-inflammatory cytokine, and an antioxidant restoring homeostasis (Gyuleva et al., 2018).Taking the results mentioned above, it could be observed that immune response favor inflammatory action in workers of group 1 in comparison with control group, which is in harmony with the report by Sun and Liu (1998), who verified that after low dose radiation, the change observed might contribute to a shift in favor of Th1 differentiation. Furthermore, the results are in consonance, to some extent,

with previous report on workers operating x-ray equipment demonstrating significant increase of IL-2 (Th1) and decrease of IL-4 (Th2) in sera of exposed compared to the control group (Hrycek et al., 2002).

The current observations did not reveal statistically significant differences in serum TNF-α and IFN-γ concentrations in group 2 than in control group. Different studies indicate that ionizing radiation causes augmentation of Th2 cytokine production (Field et al., 1997 and Kremer et al., 1996) and suppression of Th1 while decreasing in level of IFN-γ. This suggested in view of the shift in cytokine profile towards a humoral immune response. Another previous study reported by Sheikh Sajjadieh et al. (2012) showed that irritable bowel syndrome in Ukrainian children residing in contaminated area may have stemmed from Th1 to Th2 immune deviation and differential expression of IL-4 and IFN-γ.

Despite, insignificant decrease for TNF-α and INF-γ in the present report, it is reasonable to postulate that decrease in pro-inflammatory cytokine response is along with increase ofIgG in workers of group 2 compared to control group as compromising immune system.

Additionally, a significant serum decrease of TNF-α and IFN-γ in workers in group 2 compared with workers in group 1 was observed, which is in accordance, in some extent, with studies of Gyuleva et al. (2018)who also demonstrated that a slight trend of decreasing of INF-γ was with increasing of cumulative dose. These results were inconsistent with earlier studies performed by Li et al. (2014).

Finally, several reports indicated that low dose ionizing radiation in professional radiation workers (Wall et al., 2006) may stimulate the immune system and potentiate its effector function "radiation Hormesis" (Luckey, 1997). Low dose radiation not only stimulates the immune system but also transforms free oxygen radicals, repairs DNA breakage, and increases longevity.

CONCLUSION

It could be concluded that the immune system of individual exposed to low-dose radiation has adapted to its occupational exposure by reducing the inflammation burden that it observed as the decreasing of the pro-inflammatory cytokines TNF-α and IFN-γ in workers in group 2 compared with workers in group 1 as an immune defense mechanism. In addition, it is advised to perform a periodic check-up on the immune functions in radiology workers to detect any early changes in the immune system.

Acknowledgement
The author greatly appreciates Dr. Tarek Showky Mohamed El-Shanshoury, Consultant in Vascular Surgery, El-Mataria Teaching Hospital, for his help in blood sampling.
I would like to express my sincerest thanks to Dr. Mahmoud Mohamed Ahmed, Radiation Biology Department, National Center of Radiation Research and Technology, Atomic Energy Authority, for his guidance and valuable advice in this work.

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