Autoimmune Thyroiditis Among Ionizing Radiation Exposed Workers in Cardiac Catheterization Units.

Thesis

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الألتهاب المناعي في الغدة الدرقية بين العاملين المعرضين للاشعاع المؤين في وحدات قسطرة القلب

رسالة
توطئة للحصول على
درجة الدكتوراة فى السموم الأكلينيكية

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LIST OF ABBREVIATIONS

SI :	International system of units
AITD :	Autoimmune thyroid disease
ANC :	Absolute neutrophil count
Anti-TPO :	Anti-thyroxiperoxidase
APC :	Antigen presenting cells
ARS:	Acute radiation syndrome
BCL :	B cell lymphoma
Bq :	Becquerel
C :	Complement
cAMP :	cyclic adenosine monophosphate
CD :	Cluster Differentiation
Ci :	Curie
CT :	Computed Tomography
CTLA :	Cytotoxic T-lymphocyte association-protein
CVD :	Cardiovascular disease
DC :	Dendritic cells
DNA :	Deoxyribo nucleic acid
Dps :	Disintegration per second
E	Effective dose
ECLIA :	Electro-Chemi-Luminescence Immuno-Assay
EDTA :	Ethylene diamine tetra acetate
ELISA :	Enzyme-Linked Immuno-Sorbent Assay
ERCP :	Endoscopic Retrograde Cholangio-Pancreatography
Fc :	Fragment crystalizable
FNAb :	Fine needle aspiration biopsy
GD :	Graves' disease
GJIC :	Gap-Junction Intracellular Communication
GM-CSF :	Granulocyte-Macrophage Colony-Stimulating Factor
Gy :	Gray
HD-IR :	High dose ionizing radiation
HLA :	Human leukocyte Antigen

HLADR :	Human Leukocyte Antigen-antigen D Related
HRP :	Horseradish peroxidase
HT:	Hashimoto's thyroiditis
ICRP :	International Commission on Radiological Protection
ICs :	Interventional cardiologists
IFNγ :	Interferon γ
Ig :	Immunoglobulin
IL :	Interleukin
IR :	Ionizing radiation
KD :	Kilodalton
LD :	Lethal dose
LDR :	Low dose radiation
LET :	Linear energy transfer
MHC :	Major histocompatibility complex
NK :	Natural killer
PBS :	Phosphate-buffered saline
PCI :	Percutaneous coronary intervention
PCNA :	Proliferating cell nuclear antigen
PIP2 :	Phosphatidyl inositol-bisphosphate
PPT :	Post partum thyroiditis
PTH :	Parathyroid hormone
PTPN :	protein tyrosine phosphatases non-receptor
Rad :	Radiation absorbed dose
Rem :	Roentgen equivalent man
RF :	Radiofrequency
ROS :	Reactive oxygen species
Sv :	Sievert
T3 :	Triiodothyronine
T4 :	Thyroxin
TAO :	Thyroid associated orbitopathy
TBAbs :	Thyroid stimulation-Blocking Antibodies
TBS :	Tris-buffered saline
Tc :	Technetium

TCR :	T-cell Receptor
Tg :	Thyroglobin
Th :	T helper
TIPS :	Transjugular intrahepatic portosystemic shunt
TLD :	Thermo-luminescent dosimeter
TMB :	Tetra-methyl benzidine
TNF :	Tumor necrosis factor
TRAIL :	TNF-related apoptosis-inducing ligand
TRH :	Thyrotrophin-releasing hormone
TSAbs :	Thyroid Stimulating Auto-antibodies
TSH :	Thyroid stimulating hormone
TSH-R :	Thyroid stimulating hormone receptor
UR I:	Upper respiratoty tract infection
WR :	Radiation weighting factor

ABSTRACT

Introduction: It is well known that ionizing radiation IR exposure increases the risk of thyroid cancer; however less is known about its role in development of autoimmune thyroiditis. **Objective:** To assess the effects of occupational exposure to ionizing radiation on thyroid functions and the possibility of having autoimmune thyroiditis. **Methods:** a group of 47 cardiac catheterization workers (19 physicians, 15 nurses and 13 technicians) and another 47 job, age, and sex matched controls were subjected to investigating the serum level of T3, T4, TSH, anti-TPO, Th_1 cytokines (IL2, IFNγ), Th_2 cytokines (IL10) and CD4%. Area monitoring of IR was also done using portable dose rate meter to measure local scattered radiation. Besides, annual personal exposure was monitored by TLD readings over the last 3 years **Results:** Area monitoring showed high level of scattered ionizing radiation inside the cardiac catheterization rooms, although dosimeter readings were within the acceptable level over the three years. Statistically significant higher level of serum TSH, anti-TPO, IL2, IFNγ along with statistically significant lower levels of T3, IL10 and CD4% were found among the exposed compared to control groups ($P<0.05$). Significant positive correlation was detected between the level of anti-TPO and each of cumulative exposure index (CMI) ($r=0.378$ $P<0.05$) ,TSH ($r= 0.876$ $P<0.001$), IL2 ($r=0.847$ $P<0.001$), and IFN γ ($r=0.685$ $P<0.001$). Moreover, a significant negative correlation was found between anti-TPO and each of T3 ($r= -0.814$ $P<0.001$) and T4($r= -0.324$ $P<0.05$). ANOVA and Post Hoc tests showed significantly higher level of anti-TPO and Th_1 cytokines with significantly lower levels of T3, CD4% and IL10 among the physicians compared to control group **Conclusion:** Autoimmune thyroiditis might be one of the hazards that can be attributed to occupational exposure to ionizing radiation especially in cardiac catheterization units.

Key wards: Ionizing radiation- Autoimmune thyroiditis- T3- T4- TSH- Anti-TPO- IL2- IFNγ-IL10 - CD4%.

Introduction

Medical exposure from X-rays and nuclear medicine is the largest man-made source of radiation exposure **(Mettler et al., 2009)**. Such exposure is of significant concern for interventional cardiologists due to increasing workloads and complexity of procedures over the last decade **(Cousins et al., 2013)**. Moreover, those interventional cardiologists encounter much more radiation exposure than most other medical staff due to their working position close to the X-ray beam and the patient (the source of scatter radiation) **(Rehani and Ortiz-Lopez, 2006).**

Radiation exposure can exert a number of adverse effects on many tissues in the body. One of the target organs for radiation-related damage is the thyroid gland as it receives a considerable radiation dose from scattered radiation probably due to its anatomical site **(Eheman et al., 2003)**.

There is a general consensus that there is a high prevalence of thyroid cancer, thyroid nodules formation and thyroiditis in workers who were occupationally exposed to radiation, particularly among X-ray workers and other health staff exposed to radiation in laboratories **(Paolo et al., 2005).** Furthermore, autoimmune thyroid disease has been linked to therapeutic medical radiation, as well as environmental radiation exposure but the mechanisms and pathways involved in that relation remain not well clear **(Brent, 2010)**.

Autoimmune thyroid disease is the most common organ-specific autoimmune disease and characterized by the presence auto-antibodies directed against several major thyroid antigen. Among those, are the Anti-TPO auto-antibodies which found in over 90% of patients with autoimmune hypothyroidism and 70% of patient with Graves' disease **(Hawa et al., 2006).**

Moreover, a dose-response relation between radiation exposure and the prevalence of positive anti-thyroxiperoxidase antibodies was found in some studies **(Vo¨lzke et al., 2005).**

Also, the role of cytokines in the development of autoimmune thyroid disorders has been widely explained **(Stassi and de Maria, 2002)**. In case of Hashimoto's thyroiditis, a Th_1 disease, the cytokine IFNγ appears to play a crucial role in the pathology of the disease while in the Graves' disease, a Th_2 disease, the cytokines IL4 and IL-10 are responsible for the pathology. However, these cytokines could be up- or down-regulated by low dose radiation (LDR) **(Hayashi et al., 2005).**

Ionizing radiation can produce functional alteration of the immune system and breaks self -tolerance with induction of autoimmune disease among that is the thyroid gland which is one of the susceptible organs for the deleterious effect of ionizing radiation. However, the association and pathogenesis of radiation induce autoimmune thyroiditis is still not well clear, therefore, in this work we estimated the level of thyroid hormones, anti TPO and some cytokines searching for that association and possible immune mechanism.

Aim of the work

The overall aim of this study is to investigate the effect of occupational exposure to ionizing radiation on the thyroid gland function and the risk for autoimmune thyroiditis development.

objectives:

1. Assess radiation exposure among cardiac catheterization's workers.

2. Assess thyroid gland integrity among ionizing radiation exposed workers in cardiac catheterization units**.**

3. Assess the level of anti-thyroxiperoxiase antibody and its relation to radiation exposure.

4. Assess the balance between Th1 and Th2 immune response through measuring some related cytokines with investigating their relation to radiation exposure.

Background

Radiation is the propagation or emission of energy in the form of particles or waves travelling through space. Electromagnetic radiation is a type of radiation in which there are self-propagating waves, and is further classified on the electromagnetic spectrum based on the wavelength, frequency, or energy of these waves, ranging from radio waves (highest wavelengths, lowest frequencies and energies) to gamma rays and X-rays (lowest wavelengths, highest frequencies and energies) **(ARPANSA, 2011)**.

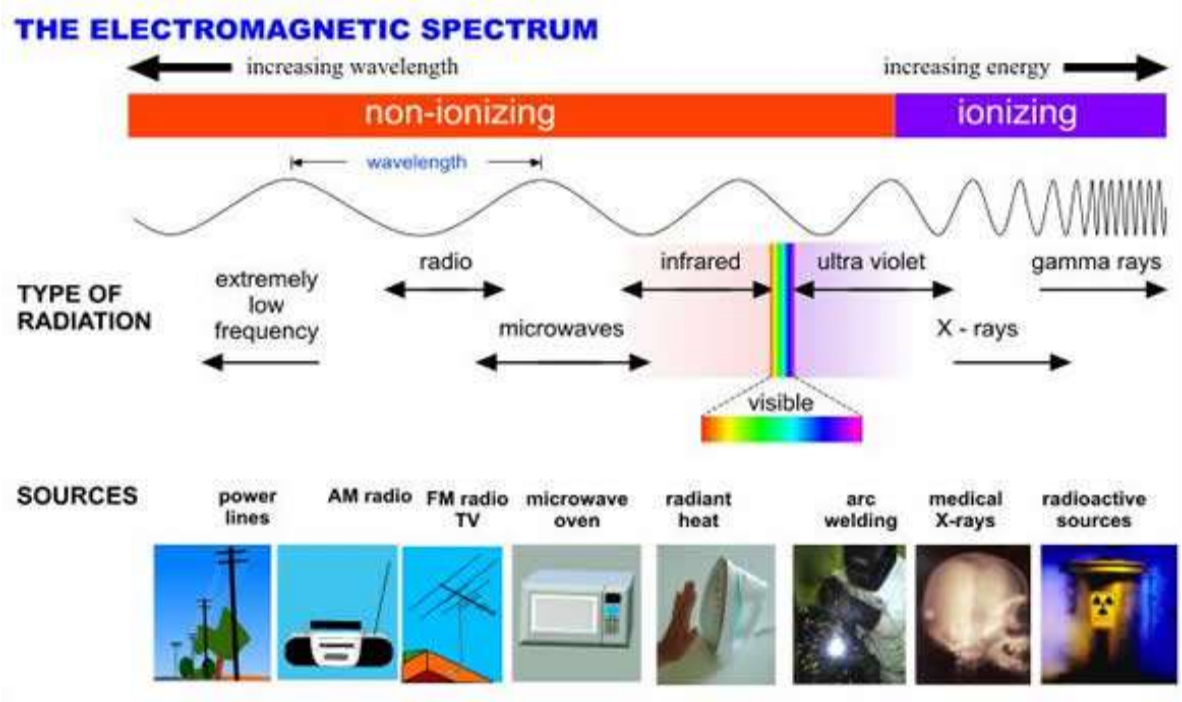

Figure (2:1): The electromagnetic spectrum, **(ARPANSA, 2012).**

Another classification of radiation is the distinction between ionizing and non-ionizing radiation. Ionizing radiation has enough energy to ionize atoms, e.g. to enable an electron to move out of its orbit, whereas non-ionizing radiation does not. Most types of electromagnetic radiation, such as visible light, are non-ionizing, but higher energy electromagnetic radiation such as gamma rays and X-rays is ionizing **(ARPANSA, 2012).**