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Deleterious effect of Perfluorooctanoic Acid on Rat Thyroid Gland

Ahmed AbdulhamidAlbakoush; Mohey el-sayedhulail; Emtethal Mamdouh El-Bestawyand Amira EbrahimAlsemeh

Human Anatomy & Embryology Department, Faculty of Medicine, Zagazig University, Egypt.

Corresponding author:Ahmed AbdulhamidAlbakoushEmail:albakkoshahmad@gmail.com

Abstract

Background: Thyroid hormone is critical for the normal physiological function of almost all mammalian tissues. Perfluorooctanoic acid (PFOA) is a manufactured compound which persist in water and soil. The aim of the present study was to evaluate the possible changes in the thyroid gland of adult male albino rats after oral administration of PFOA. Material and methods: twenty male albino rats (150–200 gm) and pathogenically free were obtained from Zagazig university. Animals divided randomly in to two groups, Group I (control) and Group II rat was PFOA and. Serum sample were collected for estimation thyroid hormones and thyroid gland samples were prepared for differ microscopic examination. Results: In our study, a significant decrease in the level of T3 and T4 with a significant increase of TSH in PFOA group compared to control group. . Thyroid gland sections in rats treated with PFOA showed a normal immunohistochemical expression of iNOS, while, in PFOA group showed a staining was stronger and the area of immunoexpression was greater in thyroid gland. Using Toluidine blue stain, thyroid gland sections in control group showed typical thyroid follicles lined with cuboidal epithelium and filled with homogeneous colloid and separated by capillary beds. However, PFOA group showed some follicles are distended with colloid, others appear collapsed. Mast cells in the interfollicular space with variable densities of the colloid staining. Conclusion: These findings suggest that oral dosing in rats with PFOA results in a noticed decrease in thyroid hormones and a structural change in thyroid tissues.

Keywords: Thyroid gland, PFOA, T3 and T4.

INTRODUCTION

Perfluorooctanoic corrosive (PFOA) is a manufactured, profoundly stable perfluorinated compounds with a wide scope of employments in mechanical and shopper items, from mess and water-safe coatings for rugs and textures to inexpensive food contact materials, fireproof froths, paints, and pressure driven liquids **(1).** The carbon–fluoride bonds that describe perfluorooctanoic corrosive (PFOA) and make it valuable as surfactants are profoundly steady, and reports show the broad perseverance of PFOA in the climate and in untamed life and human populaces universally **(2).**

Most tireless natural contaminations are lipophilic and gather in greasy tissues, yet PFOA are both lipo-and hydrophobic, and after ingestion will tie to proteins in serum instead of aggregating in lipids **(3).** The renal leeway of PFOS is irrelevant in people, prompting revealed half-lives in blood serum of 3.8 and 5.4 years for PFOA and PFOS, separately **(4).**Human biomonitoring of the general population in various countries has shown that, in addition to the near ubiquitous presence of PFOA in blood, these may also be present in breast milk, liver, seminal fluid, and umbilical cord blood **(5).**

Endocrine frameworks that might be focuses of endocrine-disturbing synthetics incorporate the nerve center pituitary–thyroid (HPT) hub **(6).** Thyroid chemical is fundamental for the ordinary physiologic capacity of essentially all mammalian tissues. Thyroid chemical status is constrained by a grounded input system, wherein thyroid-invigorating chemical (TSH) animates the thyroid to incorporate thyroxine (T4), which is then changed over, to the organically dynamic triiodothyronine (T3). The pace of arrival of TSH is managed by the nerve center just as by the coursing levels of T3 and T4. Consequently, various physiologic advances, including chemical biosynthesis, transport, digestion, and activity on track cells, are needed for thyroid chemical homeostasis **(7).** Therefore, the aim of this study was to evaluate the possible changes in the thyroid gland of adult male albino rats after oraladministration of PFOA.

MATERIALS AND METHODS

Twenty male albino rats, weighing (150–200 gm) and pathogenically free were obtained from Zagazig scientific and medical research center (ZSMRC), Faculty of Medicine, Zagazig university. Rats were acclimatized for 15 days before starting the experimental proceduresand housed in an animal care facility under room temperature (25 ± 1 °C) with 12-h light/dark cycleswith free access to food and water.

After getting an ethical committee clearance, all the rats were handled in accordance with the standard guide for the care and use of theInstitutional Animal Care and Use Committee, Zagazig University ZU-IACUC.

Animals divided randomly in to two groups, each group consists of ten rats:Group I (control):rats received water andfoodfor 2 weeks with no intervention. Group II (PFOA):each rat was given PFOA(C1386, Sigma-Aldrich Cairo, Egypt) dissolved in distilled waterin dose of 5 mg/kg BW/ day by gastric gavage for two weeks**.**

At the end of the experimental period for each group, animals were anesthetized by peritoneal injection of thiopental Na 75 mg\kg. The neck was dissected and the thyroid gland from each rat was removed.

Serum sample were collected for estimation thyroid hormones and thyroid gland samples were kept in formalin prepared for differ microscopic examination by using H&E stain and Masson trichrome. iNOS immunostaining was done for detect the oxidative damage.

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Statistical analysis:

Recorded data were analyzed using the statistical package for social sciences, version 21 (SPSS Inc., Chicago, I11inois, USA). Quantitative data were expressed as mean± standard deviation (SD).Differences between mean values of experimental groups were tested with analysis of variance (ANOVA). Tukey's multiple comparison test was carried out as post hoc test of ANOVA.The results were considered statistically significant when the P value <0.05. Different stages of significance were consideredP-value <0.05 was considered significant.P-value <0.001 was considered as highly significant.P-value >0.05 was considered insignificant.

RESULTS

The present study showed that, a significant decrease in the level of T3 and T4 in PFOA group compared to control group. The level of TSH showed a significant increase in PFOA group compared to control group **(Table 1)**.

Examination of H&E-stainedthyroid gland of control rats showed a normal thyroid follicle of dissimilar sizes full of acidophilic colloid and have oval to rounded nuclei. Interfollicular cells and blood capillary are shown normally between the follicles. However, thyroid gland section in the group of rates treated with PFOA showed disruption of thyroid follicles with shape and size. Connective tissue appears to be increased in the stroma between thyroid follicles. Most follicular cells revealed vacuolation. Interstitial hemorrhage is observed **(Figure 1).**

Thyroid gland sectionsin control group showed a normal immunohistochemical expression of iNOS, while, in PFOA group showed a staining was stronger and the area of immunoexpression was greater in thyroid gland**(Figure 2)**.

Using Masson trichrome stain, thyroid gland sectionsin control group showed few collagen fibers between the follicles. However, PFOA group showedexcessive collagen fibers between the follicles**(Figure 3)**.

Table (1): Serum thyroid activity in the studied groups:

Parameters	**Control**	**PFOA**
T3 (ng/ml)	**75.25 ± 2.45**	**28.07± 3.63 ***
T4 (µg/dl)	**6.02 ± 0.58**	**2.93 ± 1.12 ***
TSH (IU/ml)	**3.88 ±0.12**	**11.04 ± 0.89 ***

Values are expressed as mean ± SE, n=10.

***: Significantly difference from control at p<0.05.**

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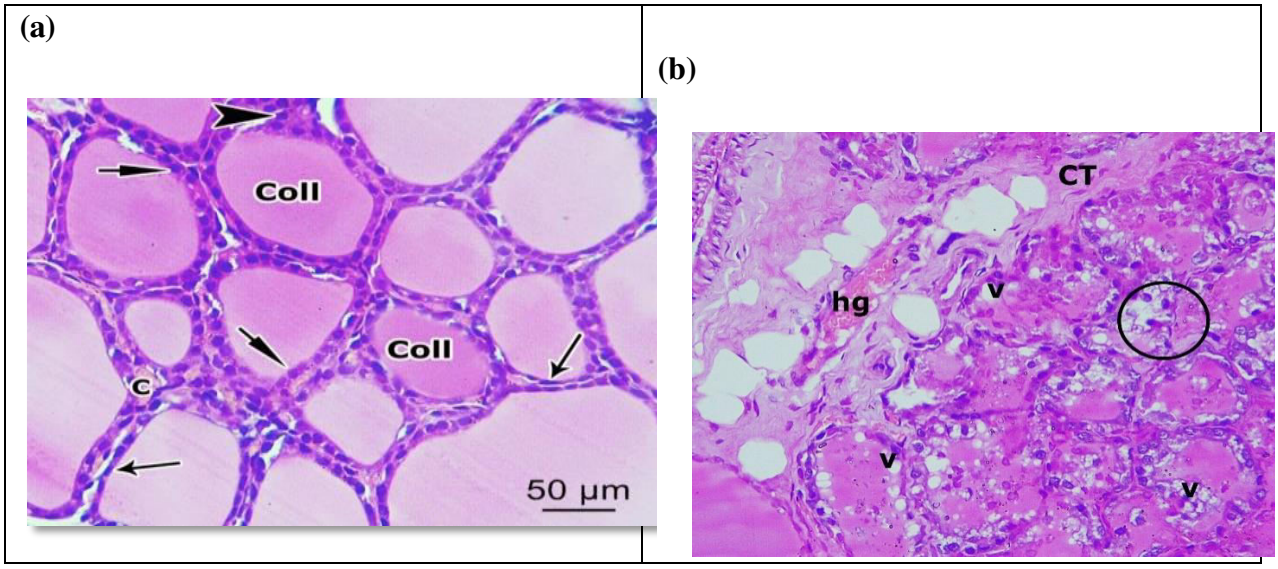

Figure (1): photomicrographs of H&E stained thyroid gland **(a)**control group showing normal follicles full of acidophilic colloid (Coll). Cuboidal epithelial lining the follicles that have oval (short arrow) to rounded (arrow) nuclei. Interfollicular cells (arrowhead) and blood capillary are shown between the follicles. **(b)** PFOA group showinginterstitial tissues areas with hemorrhage (hg) and most of the follicular cells appear disturbed (cicle) and vacuolated (V). Connective tissue area can be seen (CT) **(H&Ex400**).

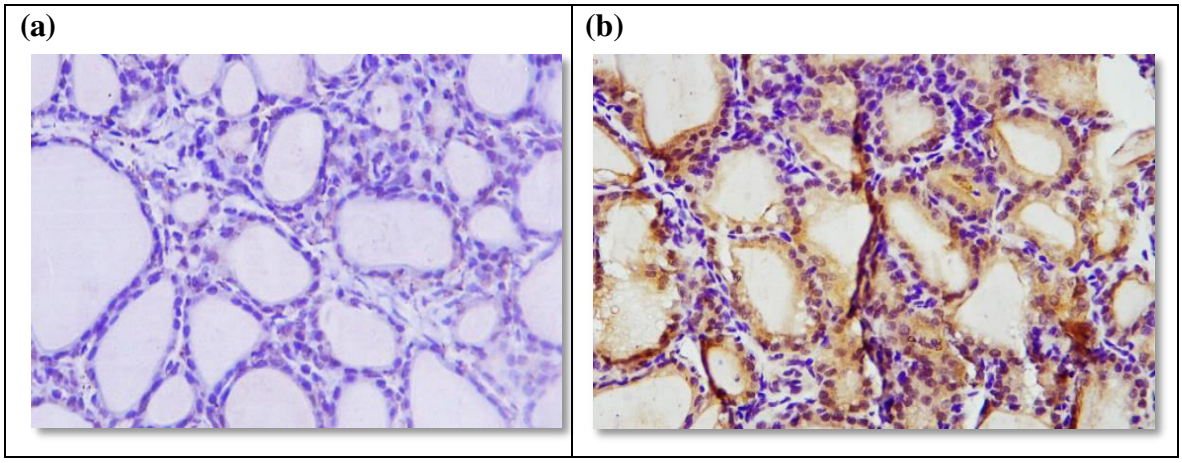

Figure (2):photomicrographs of iNOS immunostaining thyroid gland: **(a)** control group showing normal immunohistochemical expression of INOS in the thyroid gland**. (b)** PFOA group showing staining was stronger, and the area of immunoexpression was greater**(iNOS,X400)**.

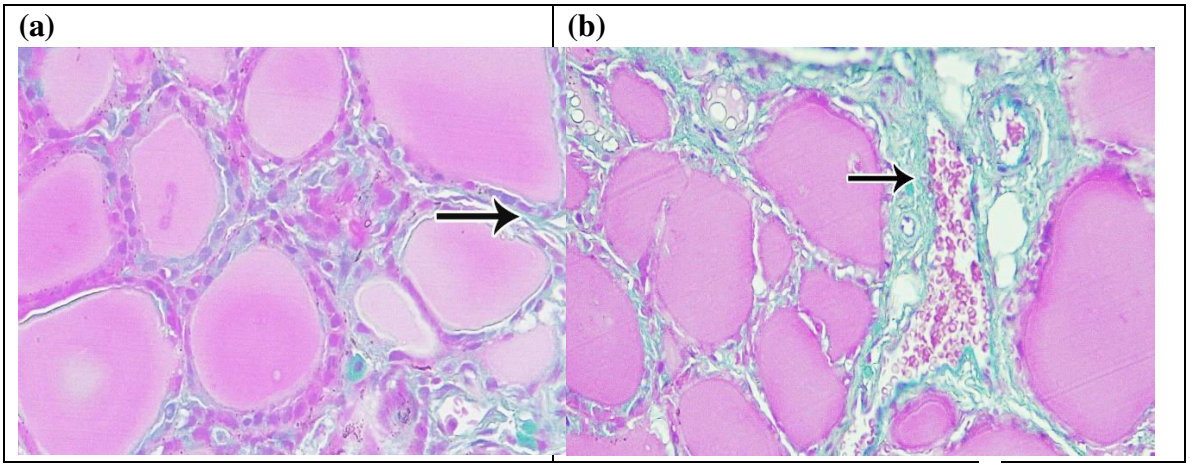

Figure (3):photomicrographs of Masson trichrome stained thyroid gland: (a) control group showing few collagen fibers between the thyroid follicles (arrow). (b) PFOA group showing excessive collagen fibers between the follicles and the blood vessel **(arrows)(Masson trichrome,400×)**

DISCUSSION:

Extrapolations from lab contemplates assessed the dangers presented by PFOA to thyroid capacity in people are convoluted by the outrageous varieties revealed in their toxicokinetic profile between species **(4).** In this way, causing to notice the likely dangers to human wellbeing and interruption to thyroid chemical equilibrium.

The current investigation was expected to assess the potential changes in the thyroid organ of grown-up male pale skinned person rodents after oral organization of PFOA. In our investigation, a huge decline in the degree of T3 and T4 in PFOA bunch contrasted with control bunch, while TSH showed a critical diminishing in PFOA bunch contrasted with control bunch. These concurred with a various report have now shown PFOA to impede thyroid chemical homeostasis in creature examines.

Melancholy of serum T4 and T3 in PFOA-uncovered rodents has been accounted for by a few creators: Lau et al. **(9)**; Luebker et al. **(10)**; Seacat et al. **(11)**, without the corresponding expansion in TSH that would be normal through input incitement. Prior unthinking investigations of fundamentally related perfluorodecanoic corrosive showed that it could lessen serum thyroid chemical levels clearly by diminishing the responsiveness of the HPT pivot and by uprooting flowing thyroid chemicals from their plasma protein-restricting locales**(12).**

An investigation of Yu et al. **(13)** detailed the instruments associated with PFOA - initiated hypothyroxinemia in rodents has demonstrated that expanded formation of T4 in the liver, catalyzed by the hepatic compound uridine diphospho-glucuronosyl transferase (UGT1A1), and expanded thyroidal transformation of T4 to T3 by type 1 deiodinase might be part of the way answerable for the impacts. In contract to our finding, a modest associations between PFOA and thyroid production workers across three production facilities; there were no associations between TSH or T4 and PFOA, and the free hormone levels were within the normal reference range**(14)**.

In our study, there was a pathological change in the tissue of thyroid gland in PFOA group compared to control. These results agree withMelzer et al., **(10)** who concluded

thathigher concentrations of serum PFOA is associated with current thyroid disease in the U.S. general adult population. These results was confirmed withstudies onPFOA that reported enlargement of the liver, disrupting of thyroid tissue , modulation of sex hormone homeostasis, developmental and immune system toxicity, hypolipidemia, and reduced body weight in rodent and nonhuman primate models **(5;8)**.

Another studies explained that PFOA has ability of these compounds to bind to nuclear receptors, including the peroxisome proliferator–activating receptor (PPARα), and to disrupt serum protein ligand binding **(10)**, highlighting PFOA as potential endocrine disruptors **(16)**.

Taken together, these findings suggest that the effects of PFOA on thyroid hormone physiology and thyroid tissue are multiple and complex.

Further studies are needed to establish the mechanisms involved with thyroid disease.

CONCLUSION:

We can conclude that oral dosing Perfluorooctanoic acid (PFOA)in adultrats results in a noticed decrease in thyroid hormones and a structural changes in thyroid tissues.

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