International Journal of Agriculture and Environmental Research

ISSN: 2455-6939

Volume: 06, Issue: 04 "July-August 2020"

ORAL ADMINISTRATION OF THE ENVIRONMENTAL POLLUTANT ATRAZINE HERBICIDE AND ITS IMPACTS ON THYROID STIMULATION HORMONE (TSH) ASSESSED BY (*WISTAR RATS*), AND ITS IMPLICATIONS ON HUMAN COMMUNITY

[1]Daradkeh S.M, [2]Abdelgadir M.I, [3]Awad Eljeed B.A.,
[4]Daradkeh M.S, [5]Murwan K. Sabahelkhier

[1,2]Nursing Department, Alghad International Colleges for Applied Health Sciences, Qassim, Saudi Arabia

[3]Chemistry Department, Faculty of Science, Bakht Er-Ruda University, White Nile State, Sudan

[4]Faculty of Veterinary Medicine, Jordan University of Science and Technology, Jordan

[5]Department of Biochemistry and molecular biology, Faculty of Science and Technology, El Neelain University, Khartoum, Sudan

DOI: https://doi.org/10.51193/IJAER.2020.6409

ABSTRACT

Twenty Wistar rats were divided into 4 groups; 3 groups were orally administered by different doses of the herbicide atrazine; (27.3, 38.5, and 42.0 mg/kg b.w), while the 4th served as control. Animals were freely accessed to tab water, and basal diet. Metal cages were interval cleaned twice a week. Cages were kept in 15 C degree. Increased concentrations ($p \leq 0.05$) of thyroid stimulating hormone (TSH) compared to control were observed through the course of the experiment. Each mole of sprayed atrazine was found to increase TSH and T3 and decrease FT4. Increasing moles of other sprayed herbicides was found to increase T4, while others resulted in increased levels of TSH, stated [9]. The NOAEL was 50 ppm, equal to 3.2 and 3.34 mg/kg bw/day in males and females, respectively [14].

Keywords: Atrazine, Epidemiological, and Adverse health effects, TSH, Cytochrome P450, Overexpression, Perturbateurs, Endocriniens.

1. INTRODUCTION

Epidemiological studies assessing potential adverse health effects attributed to atrazine exposure are of great interest. While occupational exposures typically occur due to manufacturing or field

 Copyright © IJAER 2020, All rights reserved

ISSN: 2455-6939

Volume: 06, Issue: 04 "July-August 2020"

application, environmental exposures may arise from residual spray drift or most commonly from the consumption of contaminated drinking water. It was found that the presence of atrazine was associated with fetal growth impairment and small head circumference [5]. In human epidemiological studies, significant changes of serum lipid levels occur as a result of thyroid dysfunction, and a significant reduction in PON1 activity was observed in both hyperthyroid and hypothyroid patients, stated [1]. An additional study examining Iowa farmers found urinary levels of atrazine mercapturate were associated with the amount of atrazine applied to crops [2]. Atrazine (ATZ) metabolism by human liver microsomes (HLM), cytochrome P450 (CYP) isoforms, and human liver (HL) S9 fractions, was investigated using HPLC/PDA and LC/MS/MS. CYP-dependent metabolites from pooled HLM are desethylatrazine (DEA), desisopropylatrazine (DIA), 1-hydroxyisopropylatrazine (HIATZ), and 2-hydroxyethyl atrazine (HEATZ). DEA and DIA were major metabolites in pooled HLM. CYP1A2 and 2C19, respectively, were major isoforms for DEA and DIA production. CYP3A4, while less active, is generally at high concentrations, produces both DEA and DIA and is significant [8]. Mechanisms for thyroid disruption by pesticides may include interference at the hypothalamic pituitary thyroid (HPT) axis, inhibition of iodine intake by the thyroid gland, increased excretion of thyroid hormones, decreased cellular uptake of thyroid hormones, and up or down regulated expression of thyroid hormone regulated genes [7].

2. METHODOLOGY

Atrazine with different concentrations was prepared in a suitable carrier. Blood samples were collected in a duration of 40 days; 10 days interval, subsequently centrifuged and kept at 5 C degree, till analysis according to the method described by [12]. Data results were assessed as control charts and compared means; one – sample T test in accordance to SPSS version 2019..

3. RESULTS AND DISCUSSIONS

This study resulted in increased TSH ($p \leq 0.05$) concentrations through the course of the experiment (10th, 20th, 30th, and 40th day), as shown in Figure No.1 and Table No.1. Study results are confirmed by [6] who stated that levels of TSH were significantly higher in traditional farmers than those in non-traditional (organic farmers). [16] found metabolites of ATR delay puberty, by affecting the CNS control of the pituitary gonadal - axis. Atrazine effects on the thyroid gland demonstrated a significant increase in the serum T3 level in male rats treated with 200 mg/kg body weight (bw) [15]. Study results are confirmed by [11] who found histopathological changes in male rats exposed to high doses of atrazine such as hypertrophy of thyroid follicular epithelium and hypertrophy of thyroid-stimulating hormone (TSH)-producing cells in the pituitary gland [14]. A previous study indicated that atrazine can delay the onset of puberty and alter estrous cyclicity in the female Wistar rat, serum T3 concentration was

 Copyright © IJAER 2020, All rights reserved

ISSN: 2455-6939

Volume: 06, Issue: 04 "July-August 2020"

significantly increased at 200 mg/kg bw per day. The mode of action appears to be in altering the secretion of steroids, probably due to disruption of control of pituitary function by the central nervous system [15]. Some pesticides have been reported to act as endocrine disruptors with effects on many systems, including the thyroid system, stated [4]. Atrazine and other herbicides were found to increase TSH, T4 and T3 and decrease FT4 [9], whom our results are in agreement with. It was reported that a significant increase in TSH and T4 due to increased pesticides metabolites in urine. In studies of fish, the insecticide cypermethrin was found to increase serum TSH and decrease T3 and T4 hormones [3], these findings are in agreement with our study results. It was found that small but significant increases in TSH were associated with an increase in the moles of the applied herbicides [13] reported that in men, life time years of herbicide use was associated with increased TSH and decreased FT4, and also that lifetime use of fungicides and the insecticide dithiocarbamate was significantly associated with increasing TSH and decreasing FT4 in men. No significant association between the moles of fungicide or insecticide used and thyroid hormone levels. However, [10] reported a significant increase in TSH and T4 with an increase in an organophosphate insecticide metabolite (dimethylphosphate) in urine. Study results are in agreement with [3], who conducted studies in fish, and found some pesticides result increased serum TSH.

Table 1: Shows Mean difference of TSH concentration in milli-international units per liter. µU/ml Weight in mg/kg bw, and Time in days

One-Sample Test

	Test Value = 0					
	t	df	Sig. (2-tailed)	Mean Difference	95% Confidence Interval of the Difference	
	6.102	15	.000	26.050	Lower	Upper
Weight mg/kg bw	8.660	15	.000	25.000	16.951	35.1494
Days	3.309	15	.005	2.0551	18.85	31.15
TSH µU/ml	3.309	15	.005	2.0551	.73119	3.37893

 Copyright © IJAER 2020, All rights reserved

ISSN: 2455-6939

Volume: 06, Issue: 04 "July-August 2020"

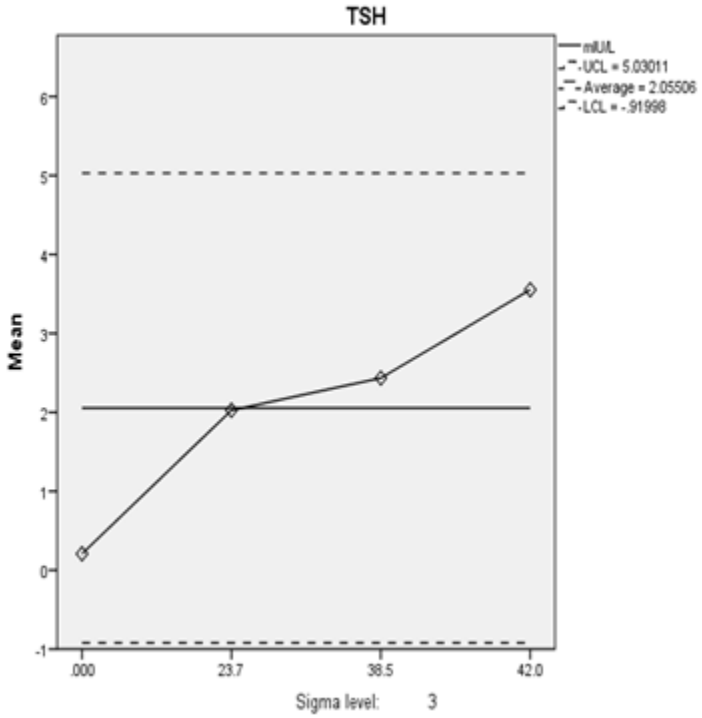

Fig. 1: Mean values of TSH in milli-international units per liter. µU/ml vs Dosage mg/kg bw

4. ACKNOWLEDGEMENTS

Authors gratefully thank Dr. Eljack M. Elamin., the Head administrator of Zagross company for import/ export of agricultural requirements, for providing atrazine reagent, Dr. Mohamed H. Bani Khaled for generous financial participation and encouragements, the family of Meck - Nimir Research Center, Khartoum, Sudan, for encaging experimental rats, and the family of Khartoum educational hospital for sample analysis.

REFERENCES

[1] Azizi F., Raiszadeh F., Solati M., Etemadi A., Rahmani M., and Arabi M. (2003). Serum paraoxonase 1 activity is decreased in thyroid dysfunction. J. Endocrinol. Investing, 26: pp.703–709.

[2] Bakke B., de Roos A.J., Barr D.B., Stewart P.A., Blair A., Freeman L.B., Lynch C.F., Allen R.H., Alavanja M.C., and Vermeulen R. (2009). Exposure to atrazine and selected non-persistent pesticides among corn farmers during a growing season. J. Exp. Sci. Environ. Epidemiol, 19: pp. 544–554.

 Copyright © IJAER 2020, All rights reserved

[3] Bhanu A.P. (2016). Disrupting Action of Cypermethrin onThyroid and Cortisol Hormones in The Serum of Cyprinus carpio. J. Entomol. Zool. Stud. 4: pp. 340–341.

[4] Campos E., and Freire C. (2016). Exposure to non-persistent pesticides and thyroid function: A systematic review of epidemiological evidence. Int. J. Hyg. Environ. Health, 219: pp. 481–497.

[5] Chevrier C., Limon G., Monfort C., Rouget F., Garlantezec R., Petit C., Durand G., and Cordier. (2011). Urinary biomarkers of prenatal atrazine exposure and adverse birth outcomes in the PELAGIE birth cohort. Environ. Health. Perspect, 119: pp. 1034–1041.

[6] Chouichom S. and Yamao M. (2010). Comparing opinions and attitudes of organic and non-organic farmers towards organic rice farming system in north-eastern Thailand. J. Org. Syst. 5: pp. 25–35.

[7] Goldner W.S., Sandler D.P., Yu F., Shostrom V., Hoppin J.A., Kamel F., and LeVan T.D. (2013). Hypothyroidism and pesticide use among male private pesticide applicators in the agricultural health study. J. Occup. Environ. Med. 55: pp. 1171–1178.

[8] Hyun J., Kyoungju C., and Ernest H. (2010). Human metabolism of atrazine. Pesticide Biochemistry and Physiology, 98 (1): pp.73-79.

[9] Kongtip P., Nankongnab N., Kallayanatham N., Pundee R., Choochouy N., Yimsabai J., and Woskie S. (2014). Thyroid Hormones in Conventional and Organic Farmers in Thailand. Int J Environ Res Public Health, 16 (15).

[10] Lacasaña M., López-Flores I., Rodríguez-Barranco M., Aguilar-Garduño C., Blanco-Muñoz J., Pérez-Méndez O., Gamboa R., Bassol S., and Cebrian M.E. (2010). Association between organophosphate pesticides exposure and thyroid hormones in floriculture workers. Toxicol. Appl. Pharmacol, 243: pp. 19–26.

[11] Laws S.C., Ferrell J.M., Stoker T.E., Schmid J., and Cooper R.L. (2000). The effects of atrazine on female Wistar rats: an evaluation of the protocol for assessing pubertal development and thyroid function. Toxicol. Sci, 58: pp. 366–376.

[12] Morimoto K., and Inouye K.A. (1997). Sensitive enzyme immunoassay of human thyroid–stimulating hormone (TSH) using bispecific F(ab')2 fragments recognizing polymerized alkaline phosphatase and TSH. J. Immunol. Methods, 205 (1): pp. 81–90.

 Copyright © IJAER 2020, All rights reserved

ISSN: 2455-6939

Volume: 06, Issue: 04 "July-August 2020"

[13] Piccoli C., Cremonese C., Koifman R.J., Koifman S., and Freire C. (2016). Pesticide exposure and thyroid function in an agricultural population in Brazil. Environ. Res, Vol. 151, pp. 389–398.

[14] Schneider M.G. (1992). 28279 - 3-month oral toxicity study in rats (administration in food). Unpublished report No. 901261 dated 8 May 1992 from Ciba-Geigy Ltd, Stein, Switzerland. Submitted to WHO by Syngenta Crop Protection AG.

[15] Stoker T.E., Laws S.C., Guidici D.L., and Cooper R.L. (2000). The effect of atrazine on puberty in male Wistar rats: An evaluation in the protocol for the assessment of pubertal development and thyroid function, Toxicol. Sci, 58: pp. 50–59.

[16] Stoker T E., Guidici D L., Laws V., and Cooper R L. (2002). The Effects of Atrazine Metabolites on Puberty and Thyroid Function in the Male Wistar Rat. Toxicological Sciences, 67 (I2): pp.198–206.

 Copyright © IJAER 2020, All rights reserved