Thyroid Pathological Consequences Induced by Caffeine in Female Rats

Noora S. ghalib[1], Abbas A. Khudhair[1], Kassim F. Abdulkareem[2]

[1]Assist. Lec, [2]Assist.Prof, Department of Clinical Laboratory Sciences, College of Pharmacy, University of Basrah, Iraq

Abstract

Objective: this study was designed to investigate the histopathological changes induced by caffeine on thyroid, liver and kidneys in female rats. Caffeine is a central nervous stimulant of methyl xanthine class of drugs, it has many hormonal and metabolic effects.

Method: twenty-four adult female rats was split in to four equal categories of 6 rats in each group as the following: Group1,control group received distilled water only by oral gavage. Group2, received 35mg\kg of caffeine solution. Group3, received 75mg\kg of caffeine and Group4, received 150mg\kg of caffeine. The experiment continued for 40 days. After 24 hours of the end of experiment, the animals were sacrificed and blood has been withdrawn from vena cava to prepare serum for hormonal analysis, whereas liver, kidneys and thyroid were excised and fixed in formalin solution for histopathological processing.

Results: caffeine ingestion cause significant reduction in thyroid function (reduction in T3, T4 and TSH) in all treated groups compared to control group in addition histopathological study show enlargement of thyroid follicle with thinning of lining epithelium of acini, vacuolation of both renal tubules, hepatocytes and vascular congestion of these organs.

Conclusion: Caffeine consumption in high doses causes many histologic and hormonal effects in the studied organs.

***Key words**: caffeine, thyroid hypo-function, histopathology, toxicity.*

Introduction

Caffeine is a chemical substance of methyl xanthine class of medications. Coffee is the main caffeine containing beverage used worldwide and is commonly associated with many health complications[1].Caffeine is absorbed rapidly from the gastrointestinal tract and reach to whole body tissues to give plasma concentration peaks at 30 to 60 minutes[2]. The mode of caffeine action is by blocking the hydrolysis of c-GMP, c-AMP and antagonism of adenosine[3,4], therefore, caffeine may alter hormone levels. It is reported that several hormonal secretion has been affected by high level of caffeine administration including thyroid hormones and pituitary gonadotrophins[5].With respect to kidney, caffeine has mild diuretic action by decreasing proximal tubules reabsorption[6].

The present study aims to evaluate thyroid gland, liver and kidneys in female rats by three doses caffeine.

Materials and Methods

The experiment was accomplished in the laboratory animals' house of College Pharmacy\ University of Basrah, by means of 24 white rats weighing 150-200 gram. Animals were kept in special cages for two weeks to accommodate laboratory conditions at room temperature between 20-25ºC. The nutrient for rats was commercial pellet. Rats were divided into 4 equal groups of 6 animals for each. All animals were given caffeine by oral gavage as follows: Group 1 (control group) were given distilled water. Group 2 were given 35mg\kg caffeine. Group 3 were given 75mg\kg caffeine and Group 4 were given 150mg\kg caffeine solution for 40 days, at the end of experiment the animals were

sacrificed to obtain the thyroid, liver and kidney to prepare histological slides and blood has been withdrawn from vena cava to collect serum for hormonal tests. The data were expressed as mean ± Standard deviation (SD). ANOVA analysis used in this study, using computerized SPSS v23, ($P < 0.05$) considered significant result.

Results

Effect of caffeine on serum level of thyroid hormones T3, T4, TSH (M ± SD) (N = 6)

Hormones Groups	T3	T4	TSH
control	2.35 ± 0.31	55.8 ± 10	0.01 ±0.066
Caffeine 35mg	2.24 ± 0.28	66.4 ± 14.7	0.004 ±0.001
Caffeine 75mg	1.84 ± 0.199	62.4 ± 23.2	0.014 ±0.018
Caffeine 150mg	1.75 ± 0.197	58.9 ± 10.3	0.006± 0.003
LSD	0.199	10	0.001

The above table indicate that treatment with caffeine cause significant decrease in T3 ($p= 0.014$) and non-significant change in T4 ($p = 0.7$), TSH ($p = 0.4$) in all treated groups compared to control group.

Histopathological Results

Caffeine 35 mg\kg

Thyroid: there is flattening of the lining epithelium of most thyroid acini which are filled with light pinkish colloid indicating decrease thyroid activity, whereas other fields reveal destruction of many thyroid follicles.

Kidneys: show pale glomeruli due to low cellularity as well as mild epithelial destruction in the proximal tubules with vascular congestion.

Liver: shows dilation of both the liver sinusoids and central venules with congestion and early degenerative changes manifested by formation of large cyst within liver parenchyma.

Caffeine 75mg\kg

Thyroid: The follicles appear more dilated, larger follicles packed with light color colloid with no inflammation.

Kidneys: shrinkage in glomerular tuft, marked vascular congestion and increase in degenerative changes with vacuolation of some renal tubules.

Liver: showed increased sinusoidal dilation with more obvious degeneration and necrosis of many hepatocytes, congestion of blood vessels and formation of cyst between hepatocytes.

Caffeine 150mg\kg

Thyroid: showed marked fullness of acini by colloid with flattening of lining epithelium and congested blood vessels with no evidence of inflammatory reaction.

Kidneys: there is frank tubular necrosis with extravasation of blood among renal tubules and vascular congestion, other fields showed glomerular ischemia with vacuolation.

Liver: showed formation of larger cyst within parenchyma with excessive degeneration and necrosis of many hepatocytes with no effect on bile tubules and portal triad.

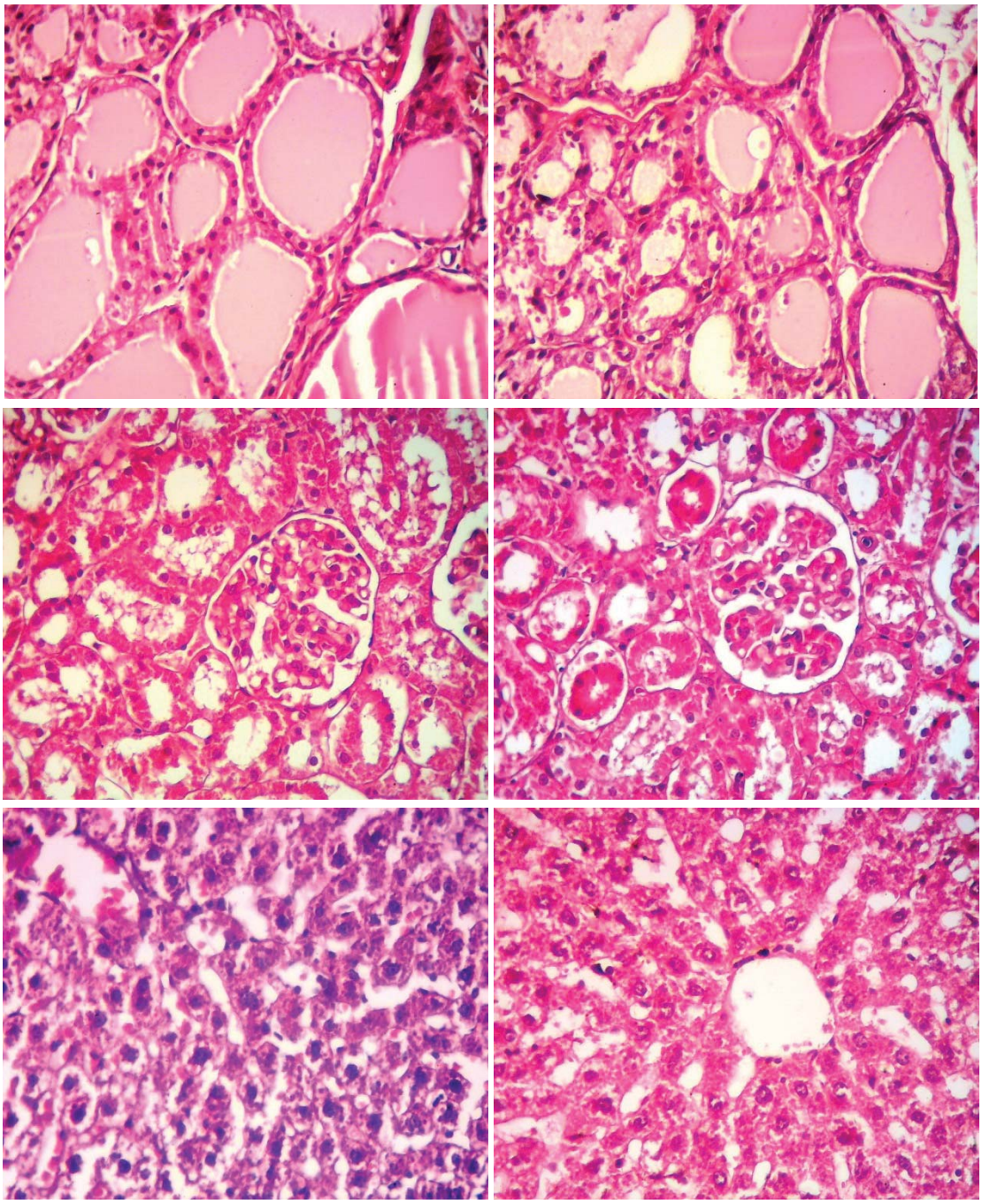

Figure1: show effect of 35mg\kg caffeine on thyroid, kidney and liver in which there is flattening of the epithelium of thyroid follicle, renal show vacuolation of glomeruli and renal tubules, the liver show sinusoidal dilation and vacuolation of hepatocytes.

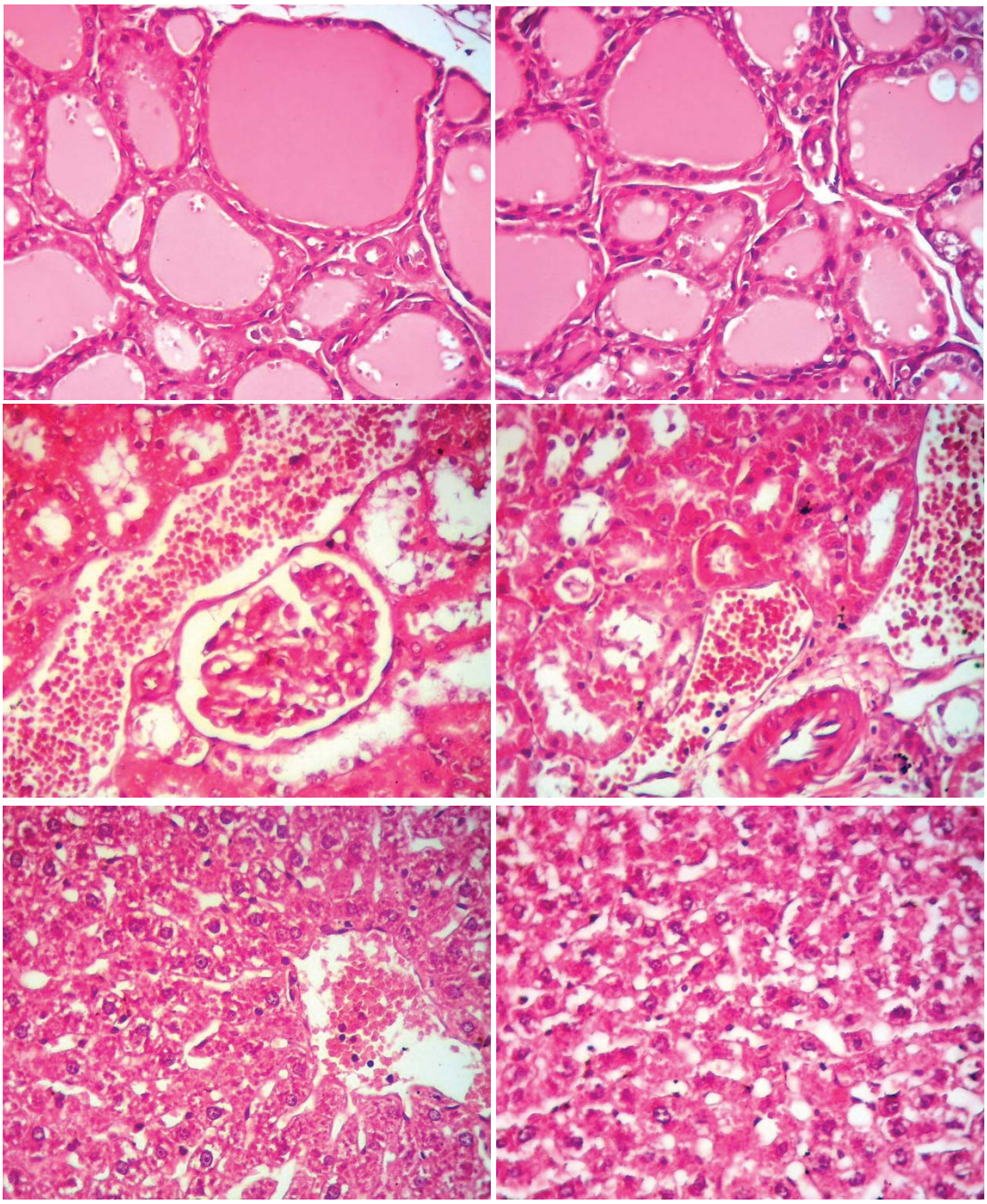

Figure2: show effect of 75mg\kg caffeine on thyroid, kidney and liver in which there is increase dilation of thyroid acini which filled with colloid, renal show vascular congestion and degenerative changes in renal tubules and shrinkage glomeruli, the liver appear central vein congestion and vacuolation of liver cells.

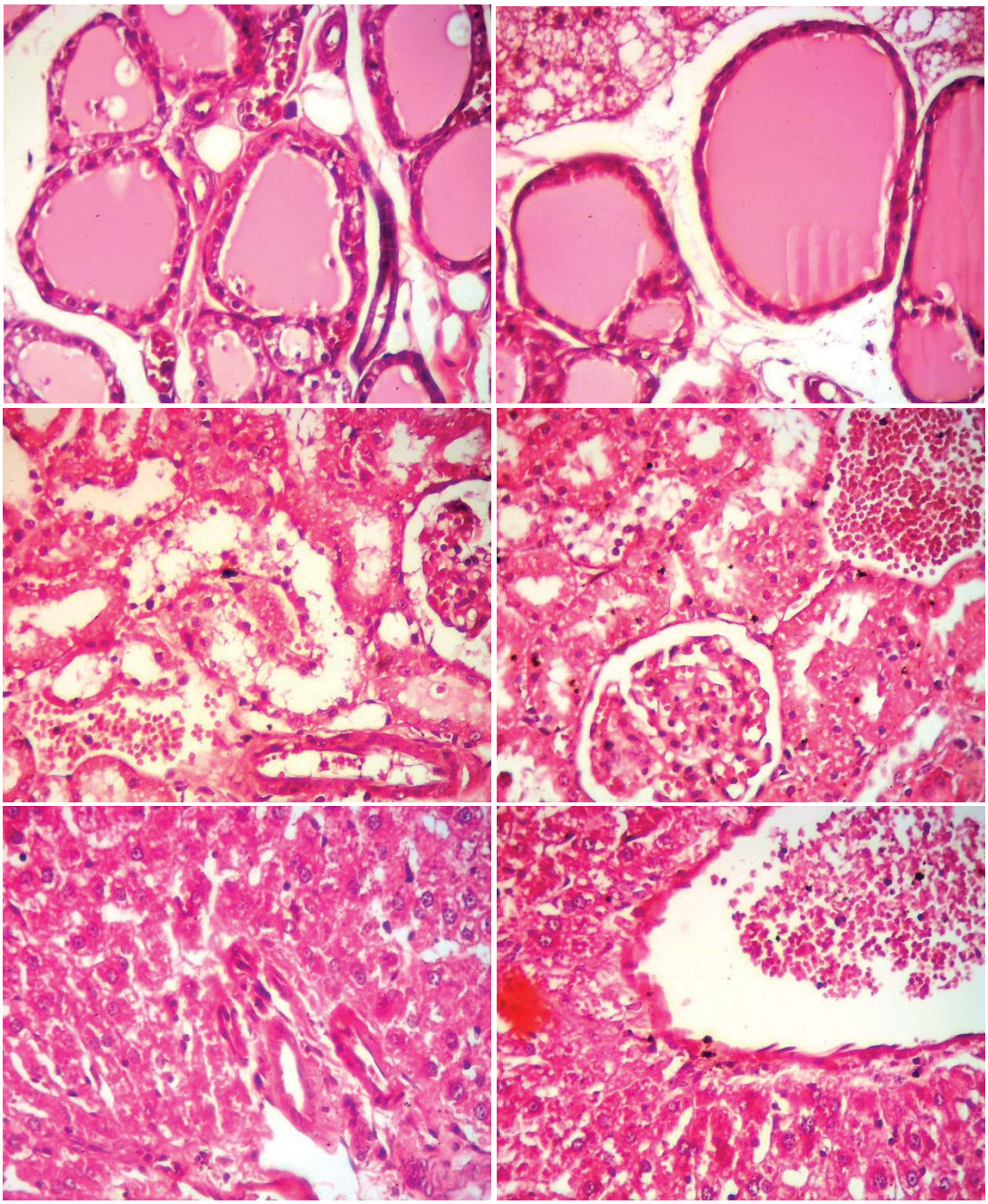

Figure3: show effect of 150mg\kg caffeine on thyroid, kidney and liver in which thyroid follicles increased with more flattened epithelium, kidney show degenerative changes in renal tubules and glomeruli with congestion of vessels, some hepatocytes appear necrosed, other with vacuolative changes and congestion.

Discussion

This study denote that caffeine causes significant reduction in thyroid function in all treated groups compared to control group with main reduction in T3, however, non-significant variations in TSH, T4 levels were detected. This result opposes with results of other studies which state that thyroid hormones are increased by use of caffeine[7,8,9]. Another researcher states that consumption of caffeine in high doses cause significant increase in T3 and T4 with non-significant change in TSH level[10] and clarified that may be due to caffeine inhibition of c-AMP breakdown by blocking the activity of phosphodiesterase enzyme resulting an elevated

c-AMP level which is necessary for proliferation and secretion of thyroid follicles[11,12,13].

Other researchers findings consistent with our result made by Spindle et al pointed that caffeine ingestion decreases the serum level of TSH in a dose-dependent manner followed by lowered T3 and T4 levels, this is because caffeine lowers TSH concentration by releasing hypothalamic somatostatin. A study pointed that administration of anti-somatostatin antiserum to rats block the inhibition effect of caffeine on TSH[9,4,14]. Daily administration of caffeine for short time (7 days) cause a decrease in TSH level and it is secretion, while high dose affect secretion of hormones[4,15]. Ezzat and his colleague found that administration of caffeine daily cause fatty hepatocytes change and several liver lesions in rabbits after treatment for 1month, this in agreement with present study[16]. The histopathological results revealed lack of inflammation in the liver tissue which confirm the studies displaying that after its digestion. Caffeine is metabolized to a compound called para-xanthine which may induce slowing of the growth of scar tissue involved in fibrosis. Para-xanthine may help to defend against cancer of liver, alcoholic fatty liver diseases and hepatitis[17,18]. One of the important results of the present study is the marked vascular congestion of the liver and kidneys due to caffeine which is can be attributed to caffeine's effect on endothelial cells.

It also antagonize the effect of adenosine which affect blood vessels wall that are responsible for vasoconstriction and eventually resulting in vasodilation[19,20]. Histopathological sections of the kidneys showed renal tubular degeneration in all treated groups and this result is consistent with other studies in which treatment of male albino Wistar rats with caffeinated coffee gave rise to renal tubular degeneration, loss of epithelial lining and vascular degeneration as compared to control group[21,22]. The liver sections showed degeneration and vacuolation of hepatocytes with necrosis as the dose increase and this outcome is in agreement with other researches which mentioned that caffeinated drinks, soft and energy drinks have adverse effects on morphology as well as histology of hepatocyte of adult albino rats[23,22].

Conclusion

Caffeine overuse may induce many adverse effects in different organs like the liver, kidneys and thyroid function.

Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both MOH and MOHSER in Iraq

Conflict of Interest: None

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