Morphometric and Phasic Activity Changes of Urinary Bladder in Hyperthyroid Rats and the Possible Protective Effect of Folic Acid

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Abstract

Background: Hyperthyroidism was one of the most common endocrine disorders. Urinary tract dysfunctions were common symptoms in hyperthyroid patients. Folic acid is affected by Thyroid dysfunction as hyperthyroidism is associated with subclinical deficiency and depletion of folate stores.

Aim of Study: To study the morphometric and the in-vitro contractility changes of the urinary bladder in hyperthyroid rats, and the protective effect of folic acid and its possible mechanisms.

Material and Methods: Forty male albino rats divided into four groups: Control, hyperthyroid, folic and (hyperthyroid + folic) groups. TSH, T_3, T_4, MDA & PGE2 were measured. Rats were then sacrificed. The weight, morphometric changes and phasic activity of the urinary bladder were assayed.

Results: Hyperthyroid group significantly decreased TSH and increased T_3 (Triiodothyronine), T_4 (thyroxine), MDA (malondialdehyde) and PGE2 (prostaglandin E2), bladder weight, wall, and lumen areas with unchanged wall thickness, and increased smooth muscle and urothelium areas with unchanged collagen area and increase the contractile response of the urinary bladder strips to acetylcholine when compared to the control group. Co-administration of folic acid to hyperthyroid rats significantly increased TSH and decreased T_3, T_4, MDA and PGE2, bladder weight, wall, lumen areas, smooth muscle, urothelium areas and the contractile response of the urinary bladder strips to acetylcholine when compared to the hyperthyroid group.

Conclusions: Folic acid protects against enhanced bladder contractility and bladder remodeling in hyperthyroid rats possibly through ameliorating the increased thyroid hormones levels, anti-oxidative, and anti-inflammatory properties.

Key Words: *Folic acid – Hyperthyroidism – Morphometric changes – Phasic activity.*

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Introduction

HYPERTHYROIDISM has been recognized as one of the most common endocrine disorder throughout the world in human [1]. Patients with hyperthyroidism may develop lower urinary tract symptoms in the form of urinary frequency, storage symptoms such as urgency, urge incontinence, nocturia, enuresis, and voiding symptoms such as incomplete emptying and straining [2]. Lower urinary tract dysfunction and urinary frequency were common symptoms in hyperthyroid patients [3]. Goswami et al., [4] reported that 40% of patients with Graves' disease had significant bladder symptoms. Hyperthyroidism is characterized by exaggerated responses to catecholamines and lower urinary tract symptoms in hyperthyroid patients [3]. Researches addressing bladder dysfunction in hyperthyroidism is few and most of them are case reports [4].

Folic acid is one of the water-soluble vitamins of B group that exists in foods like dried beans, lentils, peas, oranges, liver, asparagus, broccoli, spinach and brussels sprouts [5]. Folate is involved in the synthesis of DNA, RNA, and proteins [6]. Folate acts as a natural antioxidant [7,8]. Folic acid is affected by Thyroid dysfunction as hyperthyroidism is associated with subclinical deficiency and depletion of folate stores that increase the demand for folic acid in the hypermetabolic state [9]. The possible protective effect of folic acid administration on hyperthyroidism is not fully understood so, in our research we investigated the effect of hyperthyroidism on the in vitro urinary bladder contractility and morphometric changes in hyperthyroid male albino rats as well as, we tried to investigate the protective effect of folic

acid against these changes and its possible mechanisms.

Material and Methods

Forty Sprague Dawley male rats weighing 150 ± 30 grams were fed with standard laboratory diet and water under normal light/dark cycle and room temperature and housed in the Animal House at the Faculty of Medicine, Menoufia University.

This study was performed from November 2017 to April 2018 and the study protocol was approved by the Ethics Committee of Faculty of Medicine, Menoufia University and the animals were treated in accordance with Guide for the Care and Use of Laboratory animals (8 th edition, National Academies Press).

The animals were acclimatized to these conditions for 7 days before the experiment and classified into four groups of ten animals each.

• *Group 1:* Control group. It is considered euthyroid as T_3, T_4 & TSH are normal, and intraperitoneal (I.P) daily injected by normal saline and administered distilled water by oral gavage for 4 weeks.

• *Group 2:* Hyperthyroid group by I.P daily injection of L-thyroxine (T_4) (0.1 μg/Kg) dissolved in normal saline for 4 weeks [10], and administered distilled water by oral gavage for 4 weeks. L-thyroxine (T_4) was purchased from Sigma Aldrich Company, Germany.

• *Group 3:* Folic acid group, folic acid was dissolved in distilled water and given by oral gavage in a dose of 8mg/Kg for 4 weeks [8] and I.P daily injected by normal saline for 4 weeks. Folic acid was purchased from Nile Company, Pharmaceutical and Chemical Industries, Egypt.

• *Group 4:* Hyperthyroid + folic group by I.P daily injection of L-thyroxine (T_4) (0.1 μg/Kg) dissolved in normal saline for 4 weeks [10] and co-treated with folic acid (8mg/Kg) for 4 weeks [8].

At the end of the experiment, retro-orbital blood samples were taken and used for estimation of TSH, total T_3, total T_4, MDA & PGE_2 levels. Then, Rats were sacrificed by cervical decapitation, urinary bladders from different groups were dissected, weighed and five bladders in each group were prepared for morphometric study and the other 5 were prepared for recording phasic activity.

Blood sampling:

Fasting blood samples were collected from retro-orbital venous plexus of rats, using a fine heparinized capillary tube. We collect three milliliters of blood in a clean graduated tube and centrifuged at 3000rpm for 15min. The serum was collected in a dry clean tube, and stored at $-80C°$ until the time of analysis. It was used for estimation of TSH, total T_3, total T_4, MDA, and PGE_2.

Measurement of TSH, total T 3, total T4:

TSH, total T_3, and T_4 were measured using a Chemiluminescence Enzyme Immunoassay (CLIA) quantitative method with the immulite 2000 analyzer using kits supplied by Diagnostic Automation, Inc., CA, USA, according to the method described by Rogen et al. [11].

Measurement of serum malondialdehyde (MDA):

The serum was used for measurement of MDA by colorimetric method. Malondialdehyde is an indicator of lipid peroxidation; we used thiobarbituric acid reaction for its measurement as described by Draper et al., [12]. MDA was measured spectrophotometrically using photometer 5010V5+, Germany at 535nm, using commercial kits from (Biodiagnostic Company, Egypt).

Measurement of serum PGE 2:

Serum PGE_2 concentrations were measured using the PGE_2 Enzyme-Linked Immunosorbent Assay (ELISA) Kit, DRG International, Inc., the USA by the method described by Qin et al., [13].

Morphometric study (by image analysis) [14]:

After removal of surrounding adipose tissue, the bladder was transferred into Petri dish containing Krebs' buffer solution aerated with carbogen at pH 7.4 and left to equilibrate for 20 minutes. The bladder was sectioned at the equatorial midline. Samples were fixed in 10% formol saline and prepared for staining with hematoxylin and eosin (H & E) and Masson's trichrome [15]. The whole cross-section of the bladder was captured at 4X magnification, and digital images were saved for analysis. The inner and outer edges of the bladder wall were traced by the image analysis software (ImageJ 1.47v, USA). The area including wall area and lumen area (the area within the outer circumference) and the area including lumen area only (the area within the inner circumference) were measured. Wall area was calculated as the difference between both areas. Images from the Masson's trichrome-stained slides were captured at 10X magnification for determination of urothelium, collagen, and smooth muscles areas. The software can distinguish different regions stained by different colors. Percentage of the pink-stained tissue area (urothelium), cyan-stained tissue area (collagen), and blue-stained tissue area (smooth muscle) were

accurately measured. The images were processed by investigators that were blinded to the groups. This study was done at the Regional Centre for Mycology and Biotechnology, Azhar University, Egypt.

Phasic activity of urinary bladder strips[16]*:*

The bladder was longitudinally incised from the base to the dome and opened up to form a flat sheet. After removal of the base and the dome, the bladder body was cut and 3-4 longitudinal strips measuring 2-4 X 6-12mm were prepared. The strip was suspended in 10ml organ bath containing freshly prepared Krebs' solution bubbled with carbogen gas and left to equilibrate for 60 minutes. The tissue was maintained at 37°C and 1g resting tension throughout the experiment. Phasic activity of the tissue and response to acetylcholine (10-5 ACh) were recorded on a polygraph by using a force transducer (Grass, USA) and physiograph-6 MK III-S (four channels universal coupler, Narco Bio-System, USA). Isometric tension was measured and the change in the maximal amplitude of contractile activity was calculated. Acetylcholine powder was purchased from Fluka Chemika, Switzerland.

Statistical analysis:

SPSS version 16 was used for the analysis of data. The results of the experiments were expressed as the means ± standard error of the mean (S.E). We used one-way analysis of variance (ANOVA) followed by post hoc (Tukey's test) to determine the significance of differences between groups. $p<0.05$ is considered significant [17].

Results

Serum TSH (μU/ml), total T3 (ng/ml) and total T4 (μg/dl):

Table (1): TSH, hyperthyroid group showed significant decrease 0.043 ± 0.015 μU/ml, $p<0.000\ 1$ comparing to control, and folic groups (0.612 ± 0.12 μU/ml and 0.7 ± 0.1 μU/ml, respectively). The hyperthyroid + folic group showed a significant increase of 0.28 μU/ml ± 0.03, $p<0.05$ when compared to hyperthyroid group. T 3, hyperthyroid group showed significant increase 3.93 ± 0.2ng/ml, $p<0.0001$ when compared to control and folic groups (1.49 ± 0.185ng/ml and 1.44 ± 0.09ng/ml, respectively). The hyperthyroid + folic group showed significant decrease 2.57 ± 0.16ng/ml, $p<0.0001$ comparing to hyperthyroid group and significant increase $p<0.0001$ when compared to control and folic groups. T 4, hyperthyroid group showed significant increase 10.42 ± 0.39 μg/dl $p<0.0001$ comparing to control and folic groups

(5.42 ± 0.16 μg/dl and 5.32 ± 0.19 μg/dl respectively). Hyperthyroid + folic group showed significant decrease 7.55 ± 0.37 μg/dl $p<0.0001$ when compared to hyperthyroid group and significant increase $p<0.0001$ when compared to control and folic groups. Folic group showed insignificant change to the control group regarding TSH, T 3, and T4.

Serum MDA (nmol/ml):

Hyperthyroid group showed significant increase 34.25 ± 2.07nmol/ml, $p<0.0001$ when compared to the control and folic groups 7.65 ± 0.58nmol/ml and 8.47 ± 0.63nmol/ml, respectively. Hyperthyroid + folic group showed significant decrease 16.32 ± 0.88 nmol/ml, $p<0.0001$ when compared to the hyperthyroid group. The folic group showed insignificant change to the control group Fig. (1).

Serum PGE2 (pg/ml):

Fig. (2): Hyperthyroid group showed significant increase 35600 ± 1758.78pg/ml, $p<0.0001$ when compared to control and folic groups (20320 ± 1200.07pg/ml and 20120 ± 687.15pg/ml, respectively). Hyperthyroid+folic group showed significant decrease 27600 ± 1446.83pg/ml, $p<0.001$ when compared to hyperthyroid group. Hyperthyroid + folic group showed a significant increase, $p<0.01$ when compared to control, and folic groups. Folic group showed insignificant change to control group.

Morphometric analysis of urinary bladder:

The weight of urinary bladder was significantly increased in hyperthyroid group (113 ± 3.2mg) comparing to control and folic groups (73.8 ± 2.9 and 79.7 ± 5.1mg respectively, $p<0.00\ 1$). Treatment with folic acid significantly decreased bladder weight in the hyperthyroid + folic acid group (85.1 ± 8mg) when compared to hyperthyroid group ($p<0.001$) to a level that was significantly higher than control ($p<0.01$). Fig. (3).

Image analysis of H & E section of urinary bladder showed an insignificant change in bladder wall thickness (1.11 ± 0.08, 1.15 ± 0.02, 1.13 ± 0.02, and 1.09 ± 0.01mm respectively) among the studied groups. A significant increase in lumen and wall areas was observed in hyperthyroid group (8.4 ± 0.4 and 14.3 ± 0.4mm^2 respectively) when compared to control (1.6 ± 0.06 and 8.9 ± 0.3mm^2 respectively) and folic groups (2.2 ± 0.6 and 8.9 ± 1mm^2 respectively) ($p<0.001$). In hyperthyroid + folic group, there was a significant decrease in lumen and wall areas (4.7 ± 0.8 and 10 ± 0.9mm^2 respectively) when compared to hyperthyroid group ($p<0.001$) to a level that was still significantly higher than control and folic groups ($p<0.05$) Figs. (4,5).

We measured urothelium, collagen and smooth muscle areas in Masson's trichrome stained sections of the urinary bladder. The hyperthyroid group showed a significant increase in urothelium and smooth muscle areas (1.4 ± 0.1 and $7.9\pm0.4\text{mm}^2$ respectively, $p<0.001$) when compared to control (0.5 ± 0.08 and $4\pm0.4\text{mm}^2$ respectively) and folic groups (0.6 ± 0.16 and $4.6\pm0.8\text{mm}^2$ respectively) which showed insignificant change when compared to each other. A significant decrease in urothelium and smooth muscle areas was observed in the hyperthyroid + folic group (0.8 ± 0.1 and $5.6\pm1\text{mm}^2$ respectively) when compared to the hyperthyroid group to a level that was still significantly higher than control group ($p<0.001$ and $p<0.01$ respectively). There was an insignificant change when collagen area was compared among groups Fig. (6A,B).

Table (1): TSH (µIU/ml), total T3 (ng/ml) and total T4 (µg/dl) in control, hyperthyroid, folic and hyperthyroid + folic groups.

Groups	Control	Hyperthyroid	Folic	Hyperthyroid + folic	ANOVA
Parameters:					
TSH	0.612 ± 0.12	0.043 ± 0.015*#	0.7 ± 0.1	0.28 ± 0.03\$	*#$p<0.0001$, \$$p<0.05$
T3	1.49 ± 0.185	3.93 ± 0.2*	1.44 ± 0.09\$	2.57 ± 0.16*\$#	*\$#$p<0.0001$
T4	5.42 ± 0.16	10.42 ± 0.39*	5.32 ± 0.19\$	7.55 ± 0.37*\$#	*\$#$p<0.0001$

Values are measured as mean $\pm$ S.E.M.   \$: $p<0.05$ hyperthyroid group.
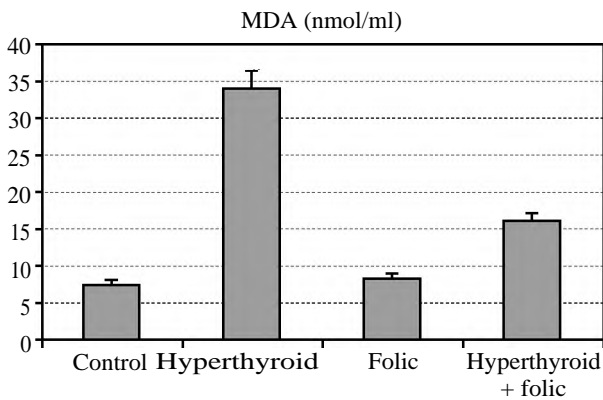*: $p<0.05$ control group.   #: $p<0.05$ folic group.

Fig. (1): MDA (nmol/ml) in control, hyperthyroid, folic and hyperthyroid + folic groups.

Values are measured as mean $\pm$ S.E.M.
*: $p<0.05$ vs. control group.
\$: $p<0.05$ vs. hyperthyroid group.
#: $p<0.05$ vs. folic group.

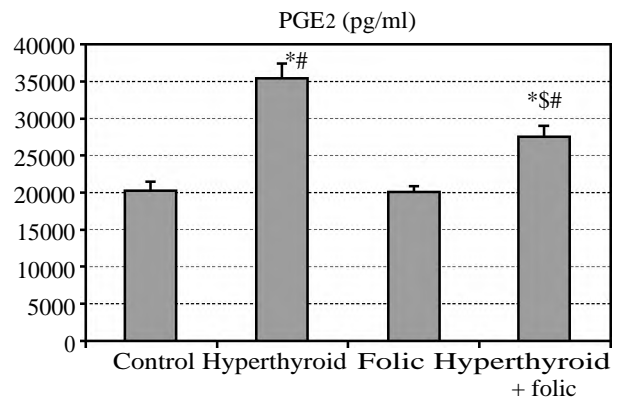
Fig. (2): PGE2 (pg/ml) in control, hyperthyroid, folic and hyperthyroid + folic groups.

Values are measured as mean $\pm$ S.E.M.
*: $p<0.05$ vs. control group.
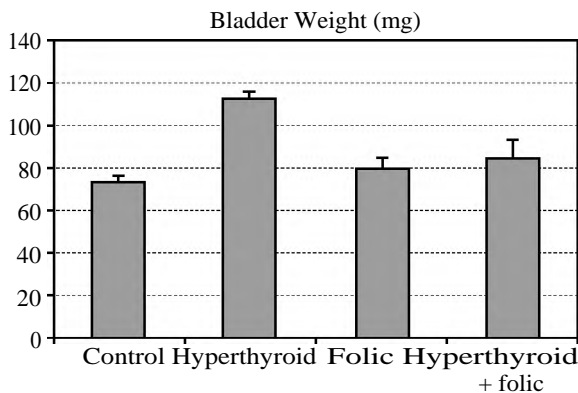\$: $p<0.05$ vs. hyperthyroid group.
#: $p<0.05$ vs. folic group.

Fig. (3): Weight of urinary bladder (mg) in control, hyperthyroid, folic and hyperthyroid + folic groups.

Values are measured as mean $\pm$ S.E.M.
*: $p<0.05$ vs. control group.
\$: $p<0.05$ vs. hyperthyroid group.
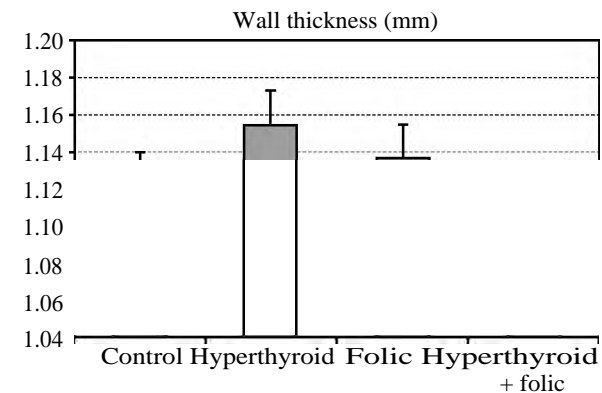#: $p<0.05$ vs. folic group.

Fig. (4): Wall thickness of urinary bladder (mm) in control, hyperthyroid, folic and hyperthyroid + folic groups.

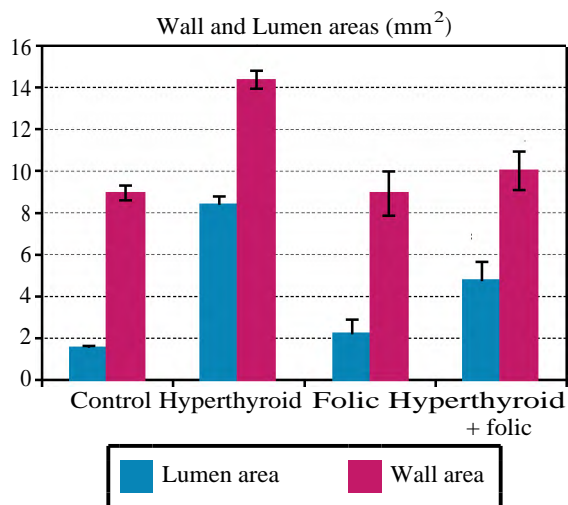Values are measured as mean $\pm$ S.E.M.
$p>0.05$ between groups.

Fig. (5): Wall and lumen areas of the urinary bladder (mm^2) in control, hyperthyroid, folic and hyperthyroid + folic groups.

Values are measured as mean ± S.E.M.
*: $p<0.05$ vs. control group. $: $p<0.05$ vs. hyperthyroid group.
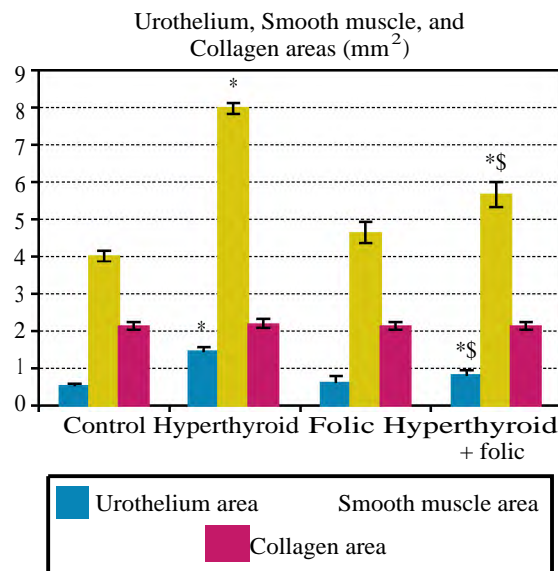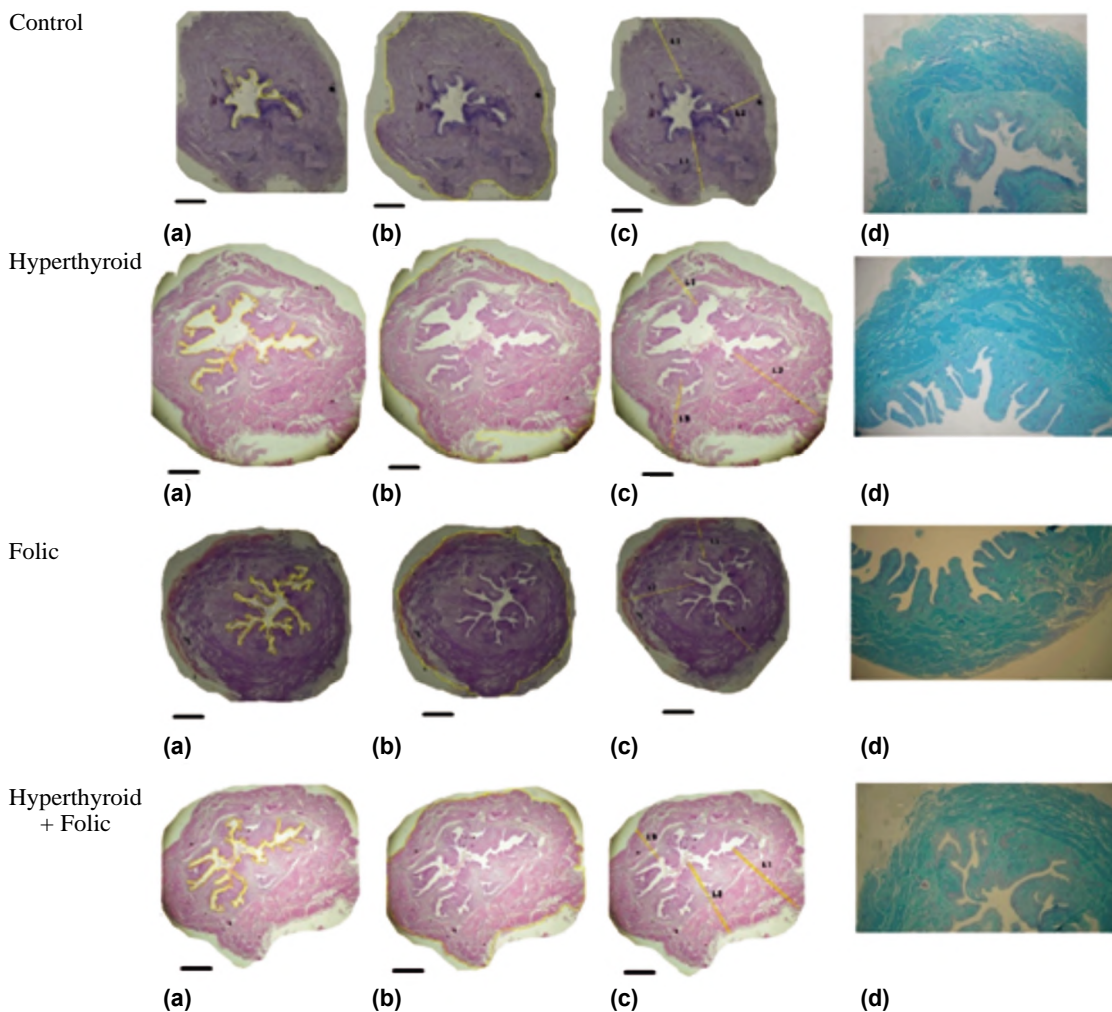#: $p<0.05$ vs. folic group.

Fig. (6A):

Fig. (6B): Image analysis of H & E-stained (a-c) and Masson's trichrome (d)-stained equatorial sections of urinary bladders demonstrating measurement of areas within inner (a) and outer (b) circumferences and measurement of thickness (c) of the bladder wall at positions L1, L2, and L3 in control, hyperthyroid, folic, and hyperthyroid + folic groups. Scale bars, 1mm.

Contractility of the urinary bladder:

The response of urinary bladder contractility to acetylcholine was significantly increased in hyperthyroid group (1.8 ± 0.1g tension) when compared to control (0.4 ± 0.1g tension) and folic (0.6 ± 0.1g tension) groups ($p<0.001$). Hyperthyroid + folic group showed a significant decrease in bladder contractility (0.9 ± 0.3g tension) in response to acetylcholine when compared to hyperthyroid group ($p<0.001$) to a level that was still significantly higher than control ($p<0.01$) Fig. (7A,B).
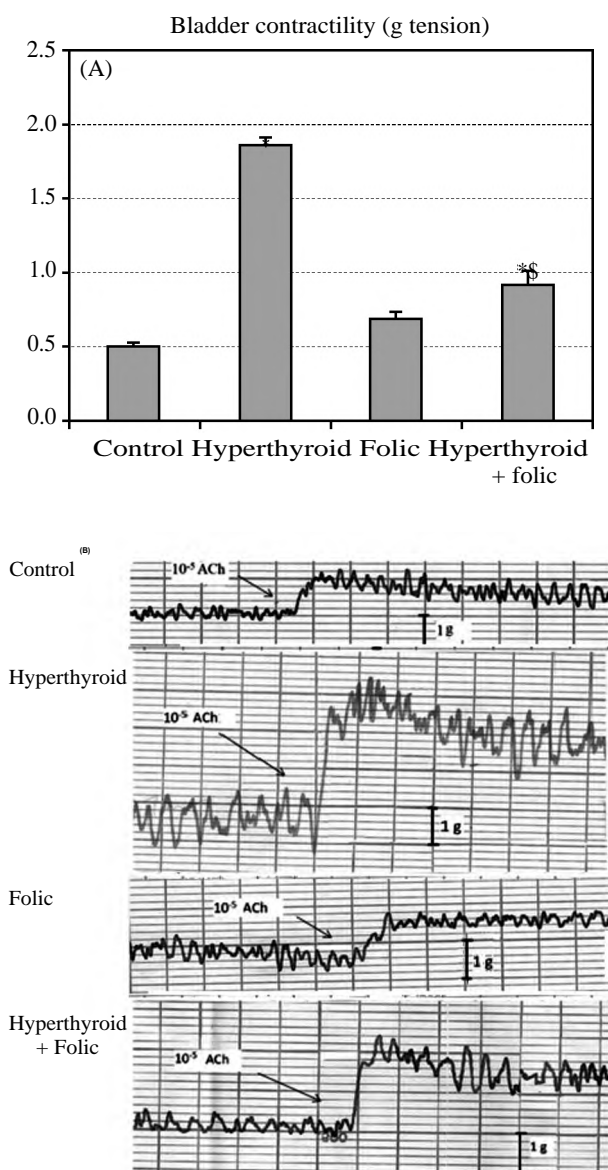

Fig. (7): (A, B) Contractility of the urinary bladder in response to acetylcholine (g tension) in control, hyperthyroid, folic and hyperthyroid+folic groups. (7A): Values are measured as mean $\pm$ S.E.M. *: $p<0.05$ vs. control group. \$: $p<0.05$ vs. hyperthyroid group. #: $p<0.05$ vs folic group. (7B): Effect of ACh (10-5M) on the contractile responses of bladder strips of rats of control, hyperthyroid, folic, and hyperthyroid + folic groups.

Discussion

Our result revealed a disturbing correlation between TSH and thyroid hormones induced by hyperthyroidism and amelioration of these hormones after folic acid treatment. This disturbed correlation between TSH and thyroid hormones due to the negative feedback mechanism caused by increase T_3 and T_4 on TSH hormone that lowers serum level of TSH [18]. Folic acid co-treatment significantly decrease T_3 and T_4 and increase TSH when compared to hyperthyroid group, these results were in agreement with Mohamed et al., [8] who recorded that co-treatment of folic acid with hyperthyroidism has an ameliorating effect on thyroid hormones in experimental induced hyperthyroid rats. Beltagy et al., [19] reported that treatment of hyperthyroid rats with folic acid and or ascorbic acid reduce T_3 and T_4 levels near to normal especially post-treated rats and TSH was decreased but still below normal level in treated rats.

It was reported that thyroid hormones have a role in the regulation of antioxidant systems. Both hyperthyroidism and hypothyroidism have a relation to oxidative stress and increase free radicals and decrease antioxidant [20]. Our result showed an increased level of MDA as an indicator of increased lipid peroxidation and oxidative stress in hyperthyroid group. Folic acid co-treatment significantly decreased MDA when compared to hyperthyroid group. This result may be due to the ameliorating effect of folic acid on thyroid hormones and its antioxidant effect. This result was in agreement with Joshi et al., [7] who concluded that folic acid is an effective scavenger for free radical. It protects bio-constituents from free radical damage by competition that lead to oxidative stress. It inhibits also lipid peroxidation. It is an antioxidant as it scavenges and repairs the thiyl radicals.

Prostaglandin E_2 is an important lipid inflammatory mediator [21]. Hyperthyroid group showed a significant increase in PGE_2 when compared to control group. Thyroid hormones increase the expression of inflammatory cytokines involved in the genesis of osteoclast-like Interleukin 6 (IL_6), IL_8 and PGE_2 [22]. Franzone et al., [23] reported that hyperthyroidism induces a significant increase of in vitro production of PGE_2 from added arachidonic acid. Folic acid and/or folic acid co-treatment decreased PGE_2 as folic acid has a role in protection against inflammation and has an antioxidant effect. Our result was in agreement with Liang et al., [21] who reported that folic acid attenuated CoCl2-induced (hypoxia-induced) PGE_2 production via increasing nitric oxide and decreasing hypoxia-

inducible factor 1-alpha (HIF-1 α) expression and cyclooxygenase-2 (COX-2) and altered endothelial nitric oxide synthase (eNOS) signaling.

Using digital image analysis, our study showed significant structural bladder changes (hypertrophy and chamber dilation) in the form of increased bladder weight, bladder wall, and lumen areas with unchanged wall thickness, and increased smooth muscle and urothelium areas with unchanged collagen area in the hyperthyroid group when compared to control. All these changes were reversed in the folic acid hyperthyroid-treated group. A previous urodynamic study reported that increased pelvic floor activity and detrusor overactivity that was associated with normal or changed bladder capacity in patients with Graves' disease [4,24].

Oxidative stress-induced a significant increase in bladder weight, muscle hypertrophy, and increased collagen area in a rat model of obstructive bladder syndrome [25]. Increased oxidative stress is implicated in hypertrophy and remodeling of several other tissues such as cardiac and vascular remodeling [26,27]. Pitre et al., [28] observed increased bladder weight in transgenic mice that selectively overexpress a pro-oxidant gene and reported that oxidative stress is a causative factor for increased bladder weight. ROS enhances the activity of several hypertrophy signaling kinases and transcription factors such as protein kinase C, mitogen-activated protein kinase, tyrosine kinase Src and nuclear transcription factors. ROS also activated cardiac fibroblast proliferation which led to fibrosis and matrix remodeling and induced DNA and mitochondrial damage that enhanced activation of proapoptotic signaling kinases [29]. We observed remodeling of the urinary bladder in hyperthyroid rats which were represented as increased urinary bladder weight, wall and lumen areas, with an insignificant change in wall thickness, that was associated with increased urothelium and smooth muscle areas and insignificant change in the collagen area comparing to control. ROS impair bioactivity of NO which has antihypertrophic and antifibrotic effects [24]. The primary source of increased bladder mass was the smooth muscle layer. A significant increase in urothelium layer was also observed. Another study showed that there were focal areas in the urothelium widely separated, shrunken, and denuded with frequent mast cells in the connective tissue beneath the urothelium. Collagen fibers and residues of degenerated nerve fibers were seen between myocytes [30]. We observed an insignificant change in the collagen area. Thus as a percentage of total tissue area change, a decrease in relative collagen was

detected. This decreases the extracellular support and in the presence of smooth muscle hypertrophy would change the passive bladder function (bladder compliance) and decrease contractile efficiency leading to increased post voiding pressure and impaired bladder emptying [31].

Oxidative stress may also explain, in part, the increase in the contractile response of the urinary bladder strips to muscarinic agonist, acetylcholine. ROS modulate the contractile responses of tissues to various agents due to modulation of the signal transduction system [32]. Oxidative stress induces long-term NO deficiency, NO is a mediator of relaxation of the lower urinary tract in rats, NO deficiency led to supersensitivity of detrusor smooth muscle to muscarinic agonists via increasing receptor affinity and reduction of B3-adrenoceptor-mediated detrusor smooth muscle relaxation causing detrusor overactivity [33].

Prostaglandin E2 is the most common prostaglandin in the mammalian tissue, it is important for myoblasts proliferation and differentiation. In the urinary bladder, PGE2 is released from urothelium, smooth muscle cells, and neurons and patients suffering from overactive bladder syndrome have high serum levels of PGE2. A previous study reported that female overactive bladder syndrome patients treated with anticholinergics had no significant change in the elevated urine PGE2 level [34]. PGE2 is an important modulator of oxidative stress. It regulates mitochondrial function which is the major sites for the production of ROS and enhanced PGE2 increases mitochondria biogenesis which increase ROS production [35]. Increasing data is supporting the involvement of PGE2 in detrusor overactivity. Prostaglandins were known to alter the motor activity of the urinary bladder; installation of PGE2 in the bladder of normal conscious rats led to increased frequency of micturition and basal intravesical pressure and was negatively correlated to the maximum cystometric capacity. PGE2 was observed to facilitate afferent nerve activity, and enhance the micturition reflex [36]. It was also thought to be co-released with acetylcholine and cause muscle excitation, inhibit acetylcholine esterase, enhance bladder myogenic activity, or modulate firing at afferent nerves to trigger micturition at lower bladder volumes [37].

Folic acid co-treatment decreased the enhanced bladder contractility and bladder remodeling in hyperthyroid rats due to ameliorated thyroid hormone levels, decreased the levels of MDA and PGE2, although folic acid level did not measure

in our study, our result supported the decrease in its level in hyperthyroid rats because it reversed the changes occurred. Folic acid levels have been reported controversially in hyperthyroidism patients, Fein and Rivlin [38] reported that hypothyroidism, hyperthyroidism, and thyroiditis were associated with megaloblastic anemias, which are typically sustained by vitamin B12 and folate deficiencies. Lippi et al., [39] reported that biochemical hypothyroidism or hyperthyroidism, reflected by TSH baseline levels, are not associated with increased folic acid and vitamin B 12 deficiencies, regardless of the use of thyroid medication. Ozkan et al., [40] reported conflicting results between animal models and patients. They found that rat models of hyperthyroidism and hypothyroidism cannot represent human hyper or hypothyroidism as folic acid level in hyperthyroid group insignificantly increase than control and hypothyroid groups.

Conclusion:

Folic acid protects against enhanced bladder contractility and bladder remodeling in hyperthyroid rats possibly through ameliorating the increased thyroid hormones levels, anti-oxidative and anti-inflammatory properties.

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التغيـر المرفومترى والنشاط الطورى للمثانة البـولية
فى الفئران المصابة بفرط نشاط الغدة الدرقيـة
والتأثيـر الوقائى المحتمل لحمض الفوليك

خلفية البحث: يعتبر فرط نشاط الغدة الدرقية من آمراض الغدد الصماء الأكثر شيوعاً حيث يصحبها إختلالاً فى وظائف المسالك البولية حيث يتأثر حمض الفوليك بضعف الغدة الدرقية ويرتبط فرط نشاط الغدة الدرقية بالنقص تحت الإكلينيكى ونضوب مخازن حمض الفوليك.

الهدف من البحث: دراسة التغيرات الموفومترية والإنقباضية للمثانة البولية والتأثير الوقائى لحمض الفوليك وآلياته الممكنة.

مواد وطرق البحث: إستخدم فى هذا البحث آربعون من ذكور الفئران مقسمة إلى آربع مجموعات: مجموعات التحكم ومجموعة فرط نشاط الغدة ومجموعة الفوليك ومجموعة (فرط نشاط الغدة الدرقية + الفوليك). تم قياس هرمونات الغدة الدرقية (السيروكسين وتراى آيودوسيرونين وسيرويد ستميولاتيد هرمون) والمالوندالدهيد وبروستاجلاندين آى ٢. ثم تم التضحية بالفئران وتم قياس الوزن والتغيرات المورفومترية والنشاط الإنقباضى للمثانة البولية.

النتائج: زادت هرمونات الغدة الدرقية والمالوندالدهيد والبروستاجلاندين آى ٢ ووزن المثانة وجدارها، والتجويف مع زيادة سماكة الجدار والعضلات الملساء مع عدم تغيير فى منطقة الكولاجين وزيادة إستجابة المثانة البولية للاستيل كولين فى مجموعة فرط نشاط الغدة الدرقية بالمقارنة مع مجموعة التحكم. آدى تناول حمض الفوليك مع الفئران المصابة بفرط نشاط الغدة الدرقية إلى تقليل هرمونات الغدة الدرقية والمالوندالدهيد والبروستاجلاندين آى ٢ ووزن المثانة وجدارها ومناطق التجويف والعضلات الملساء ومناطق اليوروسيليم وإستجابة المثانة البولية للآسيتيل كولين عند مقارنته ب مجموعة فرط نشاط الغدة الدرقية.

الخلاصة: يحمى حمض الفوليك من إنقباضات المثانة المفرطة والغير المرفومترى لها وذلك خلال تحسين مستويات هرمونات الغدة الدرقية المتزايدة وخصائصه المضادة للآكسدة وللإلتهابات.