Original Article	**Lithium Carbonate-Induced Nephrotoxicity in Albino Rats and the Possible Protective Effect of Vitamin E: Histological and Immunohistochemical Study**
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ABSTRACT

Lithium containing drugs are the drugs of choice for the treatment of bipolar disorder, preventing recurrence and suicide attempts. Recently, lithium may be used to encourage growth of gray matter in the cerebral cortex and to prevent progression of Alzheimer's disease, senile dementia and Parkinson's disease.

The present study was designed to study the toxic effect of lithium on albino rat kidneys and the possible protective effect of vitamin E.

Thirty-two adult male albino rats were used. They were divided into 4 groups of eight rats each (control group, lithium carbonate treated group, lithium carbonate plus vitamin E treated group and vitamin E treated group). In the experimental groups, lithium treated group received daily intraperitoneal injection of 50 mg/kg of lithium carbonate dissolved in 0.9% NaCL divided in 2 doses for 4 weeks. Lithium and vitamin E treated group received lithium carbonate (50 mg/kg) and intraperitoneal injection of vitamin E (50 mg/kg) dissolved in olive oil once daily for 4 weeks.

Blood samples were collected from all groups at the end of the experiment for serum creatinine level measurement. Kidneys were dissected rapidly, fixed in 10% formalin, processed and stained with haematoxylin and eosin, PAS, Masson trichrome stains and with immunohistochemical stains for bax and αsma.

Kidneys of lithium carbonate treated rats showed degenerated renal tubules, distorted glomeruli with loss of apical brush border of the proximal convoluted tubules and high expression of bax and αsma stains. A significant increase in the serum creatinine levels and a significant decrease in the diameter of renal glomeruli were observed 4 weeks after lithium administration.

Addition of vitamin E to lithium resulted in less renal degenerative changes and less expression of bax and αsma stains with a highly significant decrease in serum creatinine levels compared with lithium carbonate treated group.

It was concluded that the harmful effect of lithium on the kidneys should be closely monitored in patients taking lithium containing drugs and it could be attenuated by additional use of vitamin E.

1. INTRODUCTION

lithium carbonate is the drug of choice in treatment of bipolar disorder that affects around 1% of population *(da Rosa et al. 2016)*. Recent reviews added few uses to lithium as protection from cerebrovascular disorders (Lan et al. 2015), dementia *(Gerhard et al. 2015)* and suicide thoughts (Saunders and Hawton, 2013). Lithium level should be observed very frequently on the ground that it has a limited

therapeutic window (Malhi and Tanious, 2011). Despite the fact that lithium is very important drug, many side effects have been reported such as vomiting, diarrhoea, hands tremor, mental confusion, hallucinations, convulsions *(Nciri et al, 2012)* and endocrine manifestations particularly in thyroid and parathyroid functions (Kusalic and Engelsmann, 1999). Renal reaction to lithium included one of three classes, nephrogenic diabetes insipidus, chronic kidney disease and acute lithium intoxication (Grunfeld and Rossier, 2009).

Long-term usage of lithium could affect the functions of the kidney and cerebrum *(Laliberté et al. 2015)*, in the light of fact they are the destinations where lithium has a tendency to accumulate *(Lichtinger et al. 2013)*. Generally, lithium toxicity had been connected to disturbed cellular metabolism *(Rybakowski et al. 2013*; Trepiccione and Christensen, 2010).

Lichtinger et al. (2013) have suggested that the toxic effect of lithium on the cerebrum and kidney is due to its toxic effect on the endothelium of the blood vessels.

Disturbed kidney function in patients taking lithium was reported as early as the 1970s *(McKnight et al. 2012)*. Checking of renal function is a standard care because of the known impact of lithium on the kidney *(Kripalani et al. 2009)*. Lithium could influence tubular function resulting in nephrogenic diabetes insipidus (Gitlin, 1999). Lithium could prompt tubulointerstitial nephritis which is characterized by the presence of cortical and medullary interstitial fibrosis and tubular atrophy *(Markowitz et al, 2000)*. Different reviews suggested that the harmful impacts of lithium are caused by oxidative stress *(Oktem et al, 2005)*.

Vitamin E is considered as the most important and best known antioxidant *(Azzi et al. 2002)*. It acts as a chain-breaking antioxidant that scavenges reactive oxygen species and lipid peroxyl radicals both in vitro and vivo *(Kir et al. 2005)*. It protects the integrity of the membrane by inhibiting lipid peroxidation and augmenting the activity of antioxidant enzymes *(Kadkhodaee et al. 2005)*.

Therefore, this study was designed to investigate the efficacy of vitamin E protection against lithium induced nephrotoxic effect using histological and immunohistological techniques.

2. MATERIALS AND METHODS

2.1. Animals used

Thirty-two adult male albino rats weighing 200-250 gm were used in this study. They were housed three per cage and allowed free access to water and food (standard rodent chow) under normal day-night cycle (12-12).

2.2. Study plan:

After acclimatization for two weeks they were separated and divided randomly into 4 groups:

- **Group I:** control group (No=8) that received intraperitoneal injections of 0.9% NaCl twice daily for 4 weeks.

- **Group II (No=8) lithium-treated group:** they received daily intraperitoneal injections of 50 mg/kg of lithium carbonate dissolved in 0.9% NaCL divided in 2 doses, each of 25 mg/kg for 4 weeks *(Oktem et al.2005)*.

- **Group III (No=8) lithium and vitamin E treated rats:** they received daily intraperitoneal injections of 50 mg/kg of lithium carbonate dissolved in 0.9% NaCL divided in 2 doses, each of 25 mg/kg for 4 weeks and 50 mg/kg of vitamin E dissolved in olive oil (intraperitoneal) once daily for 4 weeks *(Jaarin et al. 2006)*.

- **Group IV (No=8) vitamin E treated group:** received a daily dosage of 50 mg/kg of vitamin E dissolved in olive oil intraperitoneal for 4 weeks.

2.3. Chemicals Used:

Lithium carbonate (Li2Co3) (Sigma-Aldrich, Egypt) and vitamin E (Pharco pharmaceutical co.) were used in this study. Antibodies against bax and αsma were bought from Abcam, Egypt.

2.4. Processing of the specimens:

At the end of the experiment, rats were sacrificed by intraperitoneal injection of chloral hydrate (300 mg/kg body weight). Then, the rats were fixed by intracardiac perfusion with 10% buffered formalin through the left ventricle and blood samples were obtained by direct left ventricle puncture for serum creatinine measurement. Kidneys were immediately removed and processed for paraffin blocks. Sections (3-5μm thick) were cut and stained with haematoxylin and eosin (Hx and E), periodic

acid schiff (PAS), Masson trichrome and stained immunohistochemically with bax antibodies and anti-αsma (alpha smooth muscle actin) antibodies.

2.5. Immunohistochemistry:

After rehydration of paraffin sections, endogenous peroxidases were blocked with 0.3% H2O2. Antigens retrieval were performed by heating in microwave using sodium citrate buffer (pH6) for 20 min and then blocked with 5% bovine serum albumin in Tris buffered saline. Sections were then incubated overnight at 4 °C with a primary antibody against bax and αsma. The reaction was detected using ABC kit following the manufacture instructions (Abcam, Egypt). Sections were then counterstained with haematoxylin, dried and mounted with a synthetic resin medium *(Chen et al. 2010)*.

2.6. Creatinine level assessment:

At the end of the experiment, serum creatinine was measured for all groups by Creatinine Assay Kit (Young and Friedman, 2001).

2.7. Measurement of the average diameter of glomeruli:

The diameter of the glomeruli was measured in haematoxylin and eosin stained sections at 100 x magnification by using an ocular micrometer calibrated with a stage micrometer. At least 30 glomeruli were randomly chosen for each animal. Two measurements were taken for each glomerulus (at the maximum transverse diameter perpendicular to the pervious one). The average diameter = (Maximum transverse diameter+ Maximum perpendicular diameter) ÷ 2 *(Johara et al. 2014)*.

2.8. Image analysis for immunostained sections:

The percentage of colour density (brown) of the reaction was measured using the colour deconvolution plugin feature of the free software Image J programme to separate colours. Digital images were captured with a digital camera (Olympus SC100) from randomly chosen areas in αSMA and bax immunostained sections. The analysis was done at a magnification of ×400 so that positive cells could be obvious. Three sections per animal were used.

2.9. Statistical analysis:

Data were presented as mean ± SEM, and were analyzed using one way-analysis of variance (ANOVA) followed by Student-t test. *P-values<0.05* was considered significant.

3. RESULTS

3.1. Control group:

The kidney showed normal architecture, formed of outer cortex and inner medulla. Proximal convoluted tubules appeared deeply stained with narrow lumen and with acidophilic granular cytoplasm. Distal convoluted tubules appeared more lightly stained than the proximal tubules and the glomeruli were surrounded by Bowman's capsule formed of two layers separated by Bowman's space (Fig. 1a). The average glomerular diameter was 124.389 ± 3.17μm (Fig. 5d). A strong PAS positive reaction was demonstrated in the basement membrane of renal tubules, brush border of proximal convoluted tubules and parietal layer of Bowman's capsule (Fig. 1b). A little amount of fibrous tissue was present around glomeruli and around blood vessels ((Fig. 1c). Limited autoimmune reaction was detected for bax in the distal tubules (Fig. 1d) and the area fraction was 2.58% (Fig. 5a). Autoimmune reaction for αsma was seen limited to vascular smooth muscle cells (Fig. 1e) and the area fraction was 2.29% (Fig. 5b). Creatinine level was 0.74 ± 0.011 (mg/dl) (Fig. 5c).

3.2. Lithium-treated group:

The architecture of the kidney was distorted. Distorted glomeruli, hyaline casts in the lumen of some tubules, loss of architecture of other tubules with completely degenerated cells were also observed (Fig. 2a). The average glomerular diameter was 116.25 ± 3.03 μm (Fig. 5d). Interruption of the positive PAS reaction in the brush border of proximal convoluted tubules and areas of basement membrane loss of some tubules were observed (Fig. 2b). Increased amount of fibrous tissue around glomeruli and blood vessels was seen (Fig. 2c). In distal convoluted tubules and collecting tubules, bax reaction was increased. Bax reaction was detected in the damaged glomeruli, in dilated proximal tubules and in some interstitial cells (Fig. 2d) and the area fraction was 21.3% (Fig. 5a). Increased αsma expression around glomeruli and in interstitium was observed (Fig. 2e) and the area fraction was 16.04% (Fig. 5b). Creatinine level was 1.56 ± 0.053 (mg/dl) (Fig. 5c).

3.3. Lithium and vitamin E treated group:

Restoration of shape of most of renal tubules and preservation of Bowman's space were noticed. However, some vacuolated tubules were seen

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(Fig. 3a) and the average glomerular diameter was 113.52 ± 2.54 μm (Fig. 5d). Restoration of the positive PAS reaction in the basement membrane of renal tubules, brush border of proximal convoluted tubules and the parietal layer of Bowman's capsule was observed. Local areas of tubular basement membrane loss were seen (Fig. 3b). The amount of the fibrous tissue around glomeruli was decreased compared with that of the lithium treated group. However, an increase in the amount of fibrous tissue in the interstitium was seen (Fig. 3c). An obvious decrease in bax expression (Fig. 3d) and αsma expression (Fig. 3e) were observed compared to the lithium treated group. The area fraction for bax and αsma were 8.16% (Fig. 5a) and 4.62% respectively (Fig. 5b). Creatinine level was 1.037 ± 0.048 (mg/dl) (Fig. 5c).

3.4. Vitamin E-treated group:

kidney histological structure appeared almost similar to the control group (Fig. 4a) and the average glomerular diameter was 126.38 ± 2.77 μm (Fig. 5d). A strong positive PAS reaction in the basement membrane of renal tubules, brush border of proximal convoluted tubules and parietal layer of Bowman's capsule was seen and appeared almost similar to the control group (Fig. 4b). A little amount of fibrous tissue was present around glomeruli and renal tubules was noticed (Fig. 4c). Limited bax (Fig. 4d) and αsma expression (Fig. 4e) were observed and appeared almost similar to those of the control group. The area fraction for bax and αsma were 4.66% (Fig. 5a) and 3.54% respectively (Fig. 5b). Creatinine level was 0.68 ± 0.01 (mg/dl) (Fig. 5c).

3.5. Statistical Results

a. Serum creatinine level:

A highly significant increase in serum creatinine in lithium treated group compared to that of control group *(P<0.001)* was detected. Serum creatinine of rats treated with both lithium and vitamin E was significantly increased compared to that of control group *(P<0.01)*. On the other hand, a highly significant decrease in serum creatinine in rats treated with lithium and vitamin E compared with that of lithium treated group *(P<0.01)* was noticed. Insignificant difference in serum creatinine level of vitamin E

treated group compared control group *(P>0.05)* was observed (Fig. 5c).

b. Diameter of renal glomeruli:

A significant decrease in renal glomerular diameter in lithium treated group compared with that of control group *(P=0.048)* was observed. A highly significant decrease in renal glomerular diameter in lithium and vitamin E treated group compared to that of control group *(P=0.009)* was noticed. However, there was insignificant difference in renal glomerular diameter in vitamin E treated rats when compared to that of control group *(P>0.05)*.

Moreover, insignificant difference in renal glomerular diameter in lithium and vitamin E treated group when compared to that of lithium treated group *(P>0.05)* was noticed. On the other hand, a highly significant decrease in renal glomerular diameter in lithium treated and lithium plus vitamin E treated groups when compared to vitamin E treated group was observed *(P=0.01and 0.002)* respectively (Fig. 5d).
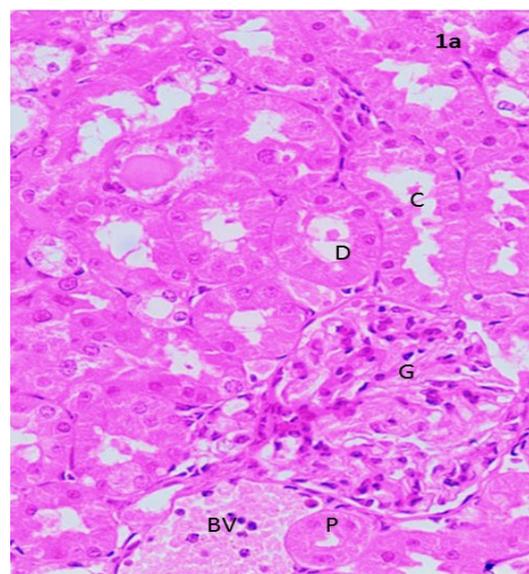

**Fig. (1):** Photomicrographs of kidney of adult rats of control group showing:

(1a) Proximal convoluted tubules (P) which appear with narrow lumen and acidophilic granular cytoplasm. The glomerulus (G) is surrounded by Bowman's capsule having two layers separated by Bowman's space (arrow). Distal convoluted tubules (D) appear more lightly stained than the proximal tubules. Collecting tubules (C) and blood vessel (BV) are also shown (Hx & E x 400).
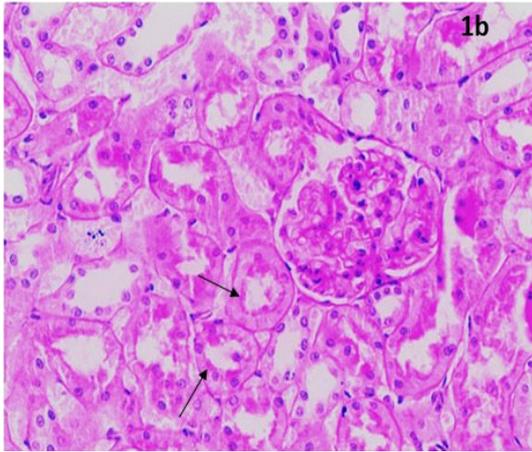
(1b) PAS stained section showing a strong positive reaction in the brush border of proximal convoluted tubules (arrows) (x 400).
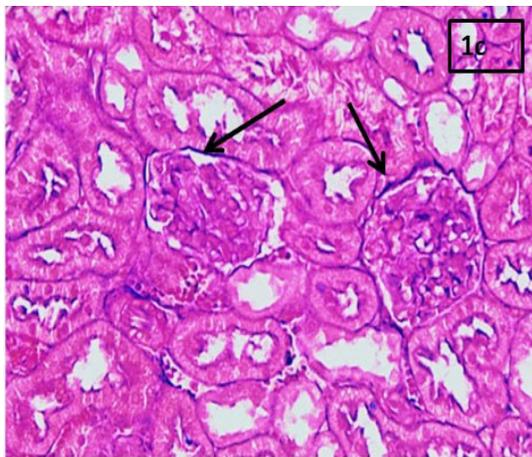
(1c) Masson trichrome stained section showing little amount of fibrous tissue around glomeruli (arrows) (x 400).
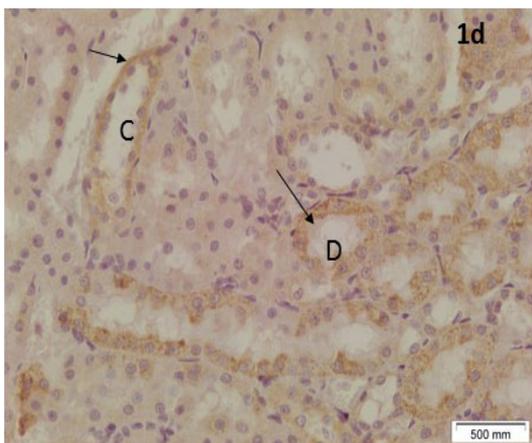
(1d) Section stained with bax antibodies showing limited positive reaction (arrows) in the distal tubules (D) and collecting tubules (C) (x 400)
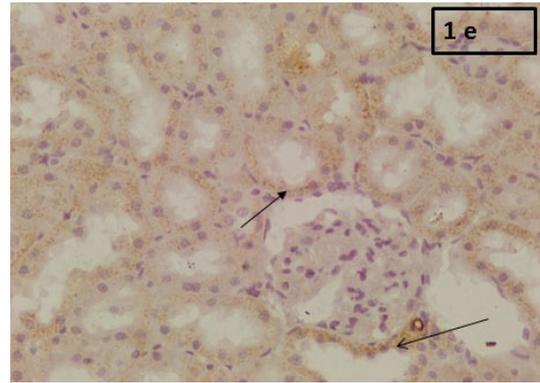
(1e) Section stained with αsma antibodies showing limited positive reaction (arrows) (x 400).
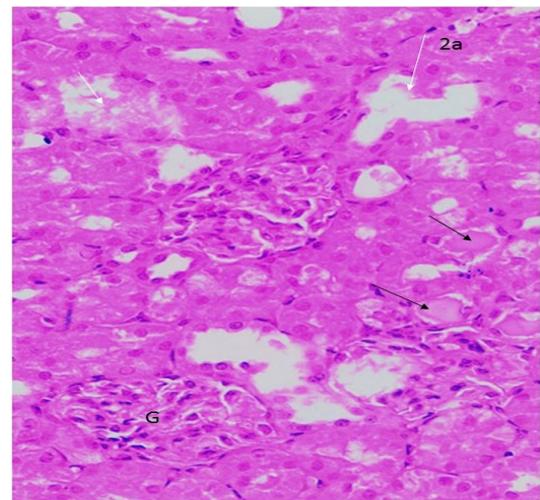

Fig. (2): Photomicrograph of kidney of adult rats of lithium treated group for 4 weeks showing:

(2a) Distorted glomeruli (G), hyaline casts (black arrows) in the lumen of some tubules, loss of architecture of some tubules (white arrows) with completely degenerated cells and ill-defined lumen (Hx & E x 400).
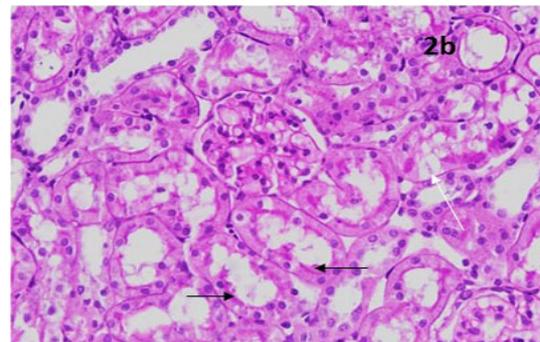

(2b) PAS stained sections showing positive PAS reaction in the interrupted brush border of proximal convoluted tubules (black arrows). There are areas of loss of basement membrane of renal tubules (white arrow) (x 400).
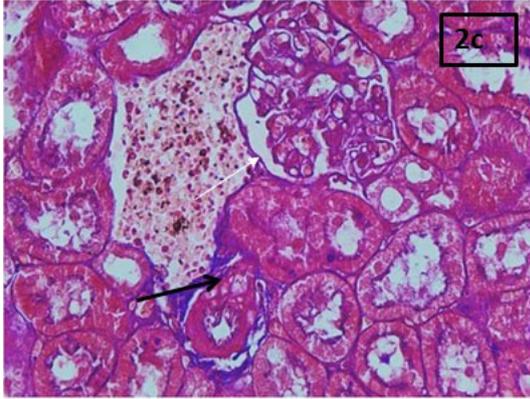
(2c) Masson trichrome stained section showing an increased fibrous tissue around the glomerulus (white arrow) and around the tubules (black arrow) (x400).
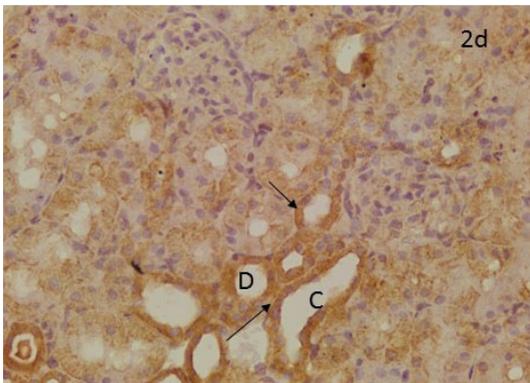
(2d) Section stained with bax antibodies showing increased positive reaction (arrow) in distal convoluted tubules (D) & collecting tubules (C) and in some proximal tubules (P).
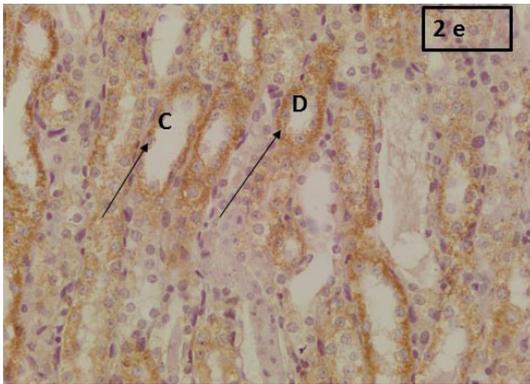
(2e) Section stained with αsma antibodies showing increased expression (arrows) around distal convoluted tubules (D) and collecting tubules (C) (x 400).
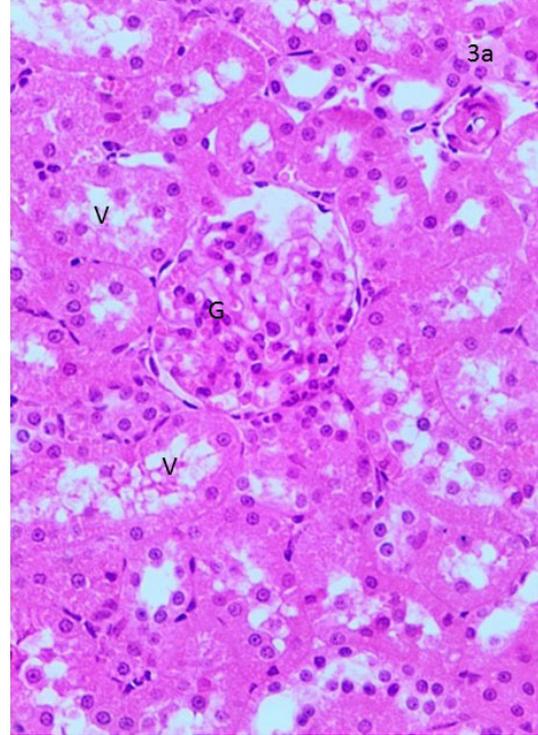

Fig. (3): Photomicrographs of kidney of adult rats of lithium plus vitamin E treated group for 4 weeks:

(3a) Section showing restoration of shape of most of glomeruli (G). Some vacuolated tubules (v) are seen (Hx & E x 400).
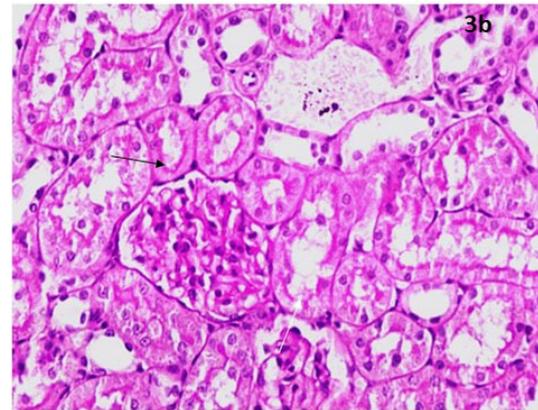
(3b) PAS stained section showing restoration of the strong positive reaction in the brush border of proximal convoluted tubules (black arrow). Local areas of tubular basement membrane loss are still seen (white arrow) (x 400).
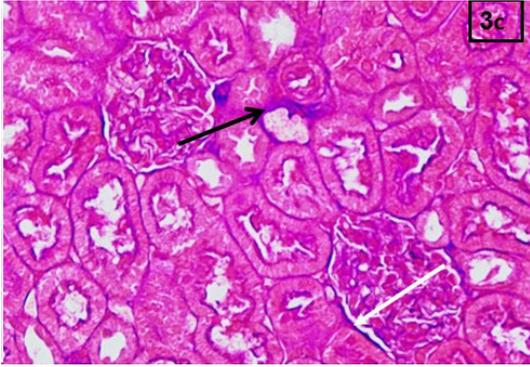
(3c) Masson trichrome stained section showing decreased fibrous tissue around glomeruli (white arrow) as compared with that of lithium treated group. An increase in the amount of fibrous tissue in the interstitium is seen (black arrow).
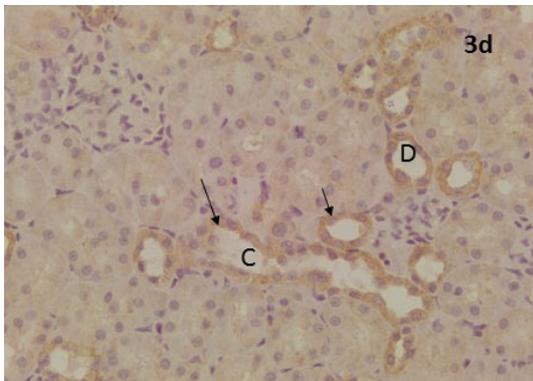
(3d) Section stained with bax antibodies showing decreased positive reaction (arrows) in distal convoluted tubules (D) and collecting tubules (C) (x 400).
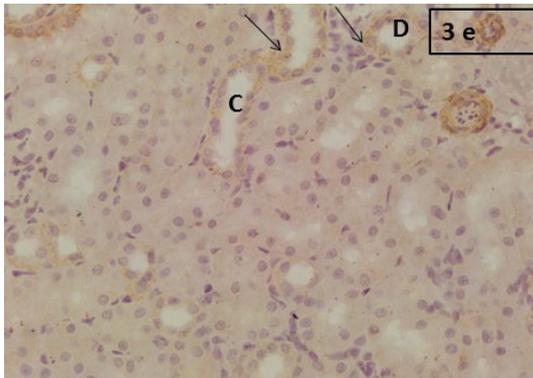
(3e) Section stained with αsma antibodies showing decreased positive reaction (arrows) in distal convoluted tubules (D) and collecting tubules (C) (x 400).
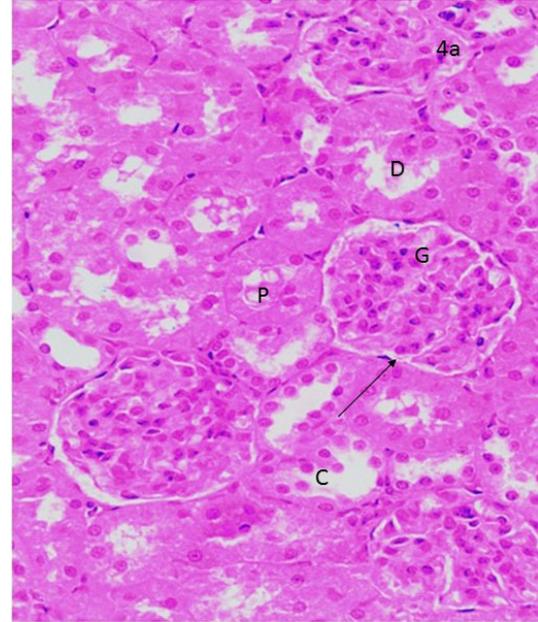

Fig. (4): Photomicrograph of kidney of adult rats of vitamin E treated group for 4 weeks showing:

(4a) Section showing normal kidney histological structure. The shape of proximal convoluted tubules (P), collecting tubules (C), renal glomeruli (G) and Bowman's space (arrow) is normal (Hx & E x 400).
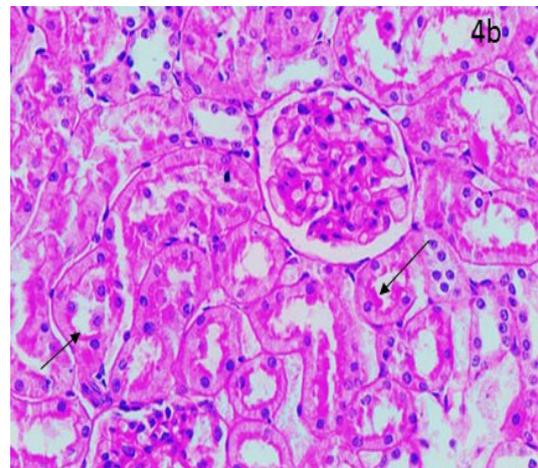
(4b) PAS stained section showing positive reaction in the brush border of proximal convoluted tubules (arrows) (x 400).
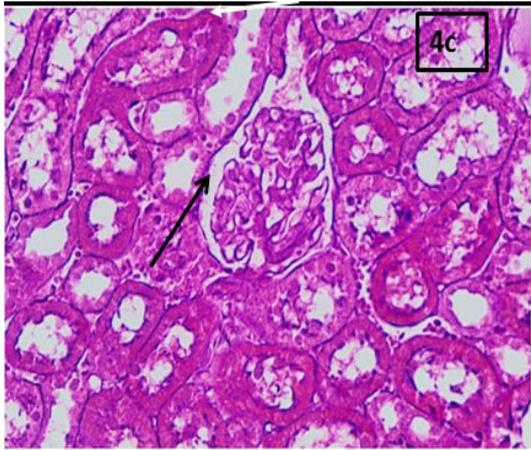
(4C) Masson trichrome stained section showing little amount of fibrous tissue around glomeruli (black arrow) & around renal tubules (white arrow) (400).
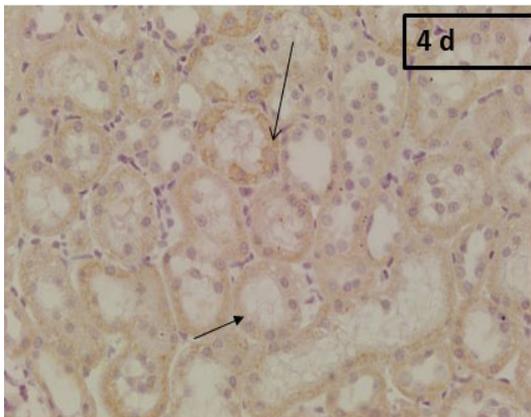
(4d) Section stained with bax antibodies showing limited positive reaction (arrows) (x400).
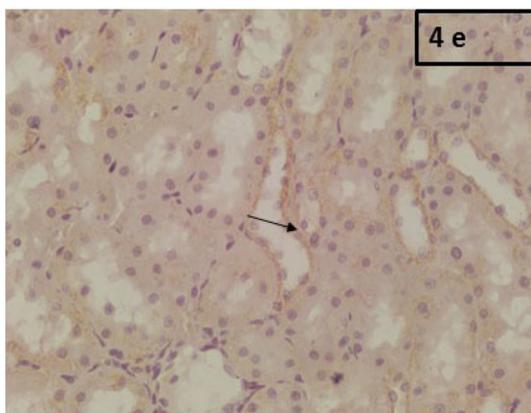
(4e) Section stained with αsma antibodies showing limited positive reaction (arrow) (x 400).
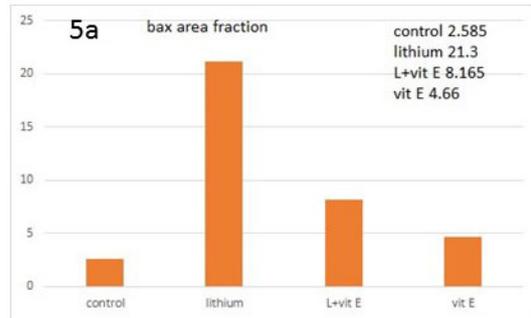
Fig. (5) Charts showing comparison:

**(5a)** A chart of mean area fraction of bax expression of kidney sections of different groups. Significant increased expression in lithium treated group (21.3%) and significant decrease expression in lithium and vitamin E treated group (8.16%) are seen.
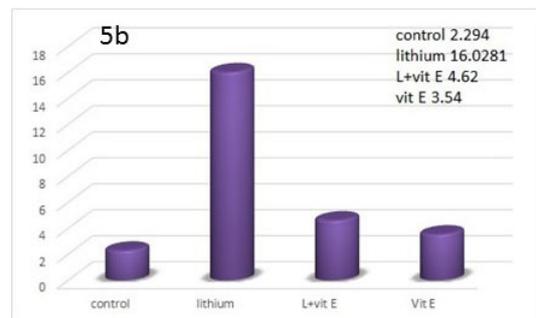
(5b) A chart of mean area fraction of αsma expression in kidney sections of different groups showing significantly increased expression in lithium treated group (16.09%) and significantly decreased expression in lithium and vitamin E treated group (4.62%).
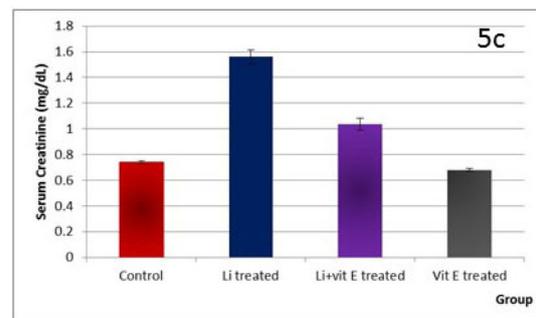
(5c) A chart of the means of serum creatinine of different groups. There is insignificant difference between vitamin E treated group and that of control group. On the other hand, there is a highly significant increase in serum creatinine in lithium treated group compared to that of control group. There is a highly significant decrease in group treated with lithium and vitamin E compared with lithium treated group.

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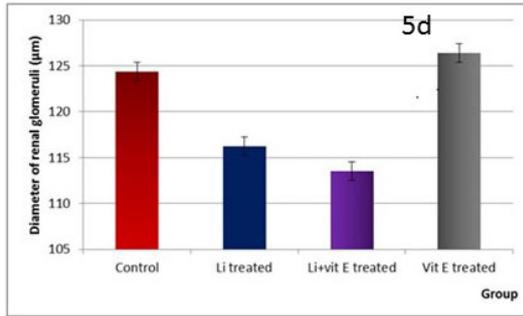
(5d) A chart of of the renal glomerular diameter of different groups. There is a significant decrease in lithium treated group compared to the control group. There is a highly significant decrease in lithium and vitamin E treated group when compared to control group. Insignificant difference in vitamin E treated group compared to that of control group.

4. DISCUSSION

Lithium remains the "gold-standard" treatment for bipolar disorder and as an essential medication for resistant depression *(Yatham et al. 2013)*. Great attention was focused on the clinical usage of this drug due to its several side effects, especially the nephrotoxicity *(Oktem et al. 2005)*.

Histopathological examination of kidneys of lithium treated rats for 4 weeks showed clear distortion in the renal morphology as vacuolation, degeneration of renal tubules, hyaline casts in the lumen of collecting ducts and loss of the PAS positive brush border of the proximal convoluted tubules.

These histopathological changes were in concurrence with the results of previous investigators, Kanfer and Blondiaux (2000) and Sharma and Iqbal (2005), who reported tubulointerstitial nephropathy after lithium treatment in human and rats. They reported that glomerulosclerosis and congestion of renal vessels were direct toxic effects of lithium on the renal tissue.

Similarly, *Trepiccione et al. (2014)* reported that rat medullary collecting tubules are the first part to be affected after lithium treatment. This would explain the results of the present study in which the expression of the immune stain (bax and αsma) appeared primarily evident in collecting tubules.

Therien and Blostein (2000) suggested that vacuolation of renal tubules might be due to the disturbance of the sodium pump which results in hydropic degeneration. Additionally, it is expected to develop expansion of the mitochondrial inter-membrane space and the external mitochondrial layer *(Higgins et al. 2003)*.

Alwin and Arthur (2009) postulated that invasion of interstitial inflammatory cellular infiltration in the renal cortex could be an immunologic mechanism or due to renal ischemia induced by of nephrotoxic materials. Moreover, *Oliveira et al. (2010)* have reported that renal blood vessels damage is due to direct toxic impact of lithium on the renal blood vessels prompting their dilatation and congestion.

Recently, *Haleem et al. (2015)* clarified that interruption or complete loss of the apical brush border may be due to attachment of antibodies to the antigenic segment of the brush border of the proximal convoluted tubules. In addition, lithium carbonate caused the appearance of the red hyaline casts. The hyaline casts were parts of the protein reabsorption and degradation pathway (Markowitz, 2000).

Previous investigators have reported that lithium administration is known to affect the physiological functions of the nephron. Nephrogenic diabetes insipidus was the most common side effect of lithium. The lining cells of the collecting duct became partially insensitive to the actions of vasopressin and aldosterone, which affect the ability of the cell to increase water permeability (Grunfeld and Rossier, 2009; *Oliveira et al. 2010; Prense et al. 2003*). Studies on the cerebral cortex and kidney proposed that dangerous impact of lithium was due to oxidative stress and lipid peroxidation *(Efrati et al. 2004)*. Moreover, Grunfeld and Rossier (2009) showed that metabolic acidosis is a result of tubular affection by lithium treatment and it was thought to be due to decreased proton secretion in the collecting duct.

In the present study, Masson trichrome stained sections demonstrated a little increase in the fibrous tissue around glomeruli and blood vessels after 4 weeks of lithium treatment. No marked interstitial fibrosis when compared with the results of Kanfer and Blondiaux (2000). This could be due to the difference in the length of the experiment.

In the present study, marked and highly significant increase in serum creatinine levels after lithium treatment was observed compared with the control group. This finding is in good agreement with that of *Arreola-Mendoza et al. (2009)* who found that serum creatinine level was increased after toxic injuries to the renal tubules and loss of functional integrity of the kidney.

The present study exhibited a significant and critical decrease in renal glomerular diameter in lithium carbonate treated rats compared to that of the control group. This was also recorded by *Min et al. (2003)* who demonstrated shrinkage of the glomeruli and the capillary network. They claimed that this shrinkage was due to glomerulosclerosis caused by lithium toxicity. On the other hand, hypertrophy of the renal glomeruli as a compensatory growth with an increase in the number of glomerular capillaries were detected by *Skyum et al. (2004)*.

The biochemical and histopathological results of the present study demonstrated that daily administration of lithium for 4 weeks prompted nephrotoxicity. These changes may suggest addition of an antioxidant with lithium carbonate to decease its destructive impacts on the kidney.

In the present study, the results showed that the combined treatment of lithium carbonate and vitamin E caused a partial improvement of the histopathological and biochemical changes in the renal tissue.

Histopathological examination of kidneys revealed that combined treatment with lithium and vitamin E lead to restoration of the shape of majority of renal tubules, preservation of Bowman's space and decrease in the amount of fibrous tissue around the glomeruli. Vitamin E diminished the histological damage caused by lithium, but it did not totally prevent the renal affection.

After vitamin E administration with lithium, the present study showed a highly significant decrease in the serum creatinine level compared with that of the lithium treated group indicating an improvement in the renal function. Moreover, there was insignificant difference in renal glomerular diameter when compared to that of lithium treated group.

The present results are in agreement with those of *Khan et al. (2010)* who reported ameliorating effect of vitamin E in potassium dichromate induced nephrotoxicicty in rats. In addition, *Kadkhodaee et al. (2005)* demonstrated that vitamin E had an ameliorating effect on the kidney damage induced by drugs such as gentamicin, cisplatin, sodium chromate and vancomycin. The ameliorating effect of vitamin E could be attributed to its antioxidant properties as reported by Herrera and Barbas (2001).

Packer et al. (2001) reported that vitamin E protects the cell membrane from oxidation by reacting with lipid radicals produced in the lipid peroxidation chain reaction. Moreover, Halliwell and Gutteridge (2002) and *Sukru et al. (2008)* suggested that vitamin E averted oxidative damage, probably through its capacity to scavenge lipid peroxide radicals before they attack the membrane lipids.

The anti-oxidant activity of vitamin E played a key role in its nephroprotective effect as demonstrated by *Bjelakovic et al. (2008)* who found that daily treatment with vitamin E resulted in significant reduction in lymphocytic infiltration in the renal tissue. This is in agreement with the histopathological findings in the present study.

Apoptosis occurs in response to multiple stimuli and gives protection against cancer (Rao and White, 1997) but tissue response to stimuli depends on the balance kept between cellular apoptosis and proliferation (Savill, 1994). Uncontrolled apoptosis leads to loss of kidney functional tissue which could progress to renal insufficiency. Increase expression of bax directs cells to enter into apoptosis (Savill, 1999).

Progression of kidney disease depends on the interaction between kidney cells and cytokines (Eddy, 1996). Cytokines induce cells proliferation so they increase expression of αsma and production of collagen *(Howie et al. 1995 and Zhang et al. 1995)*. The increased expression of αsma could reflect the kidney damage progression. Expression of αsma is normally detected in vascular smooth muscle cells but other cells such as interstitial fibroblasts, mesangial and tubular cells could express αsma protein in reaction to glomerular diseases *(Geleilete et al. 2001)*.

In conclusion, it is recommended that patients with chronic lithium usage should take anti-oxidant as vitamin E as a protection from the toxic effect of lithium that may cause many side effects particularly renal damage and renal failure.

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التأثير السمي لكربونات الليثيوم على كليه الفئران البيضاء والتأثير الوقائي المحتمل لفيتامينه: دراسه هستولوجيه وهستوكيميائيه

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ملخص البحث

ان الأدوية التي تحتوي على الليثيوم هي العقاقير المفضلة لعلاج الاضطراب الثنائي القطب، ومنع تكرار ومحاولات الانتحار و في الآونة الأخيرة، يستخدم الليثيوم لتشجيع نمو المادة الرمادية في القشرة الدماغية، ومنع تطور مرض الزهايمر، خرف الشيخوخة ومرض باركنسون.

ولقد صممت هذه الدراسة لمعرفة تأثير سمية الليثيوم على كلى الفئران البيضاء والتأثير الوقائي المحتمل لفيتامين ه

استخدم في هذه الدراسة اثنان وثلاثون من ذكور الجرذان البيضاء البالغة. تم تقسيمهم إلى 4 مجموعات من ثمانية فئران كل (المجموعة القياسية، المجموعة التي تلقت العلاج بكربونات الليثيوم ، المجموعة التي تلقت العلاج بكربونات الليثيوم و فيتامين ه و المجموعة التي تلقت العلاج بفيتامين ه) تلقت مجموعة الليثيوم حقن في البريتون يوميا بجرعة 50 ملغ / كغ من كربونات الليثيوم مذاب في 0.9% كلوريد الصوديوم مقسمه على جرعتين لمدة 4 أسابيع. مجموعة الليثيوم وفيتامين E وتلقت حقن كربونات الليثيوم وحقن فيتامين ه 50ملغ / كلغ مذاب في زيت الزيتون مرة واحدة يوميا لمدة 4 أسابيع.

تم جمع عينات دم من جميع المجموعات في نهاية التجربة لقياس مستوى الكرياتينين. تم تشريح الكلى ومعالجتها للصباغة بالهيماتوكسلين والايوسين ، البي اي اس، ماسون ثلاثي الألوان والصبغة المناعية للباكس و الفا سموث مس اكتين

وأظهرت كلى المجموعه التي عولجت كربونات الليثيوم تشوه الحويصلات الكلوية و الأنابيب الكلويه الملتويه و تسلل خلايا وحيدة النواة، وزيادة مستوى صبغات الباكس و الفا سموث مس اكتين. وقد لوحظت زيادة كبيرة في مستويات الكرياتينين في الدم وانخفاض ملحوظ في قطر الحويصلات الكلوية.

أدت إضافة فيتامين ه إلى الليثيوم لتقليل التغيرات السمية في الكلى مع انخفاض كبير جدا في مستويات الكرياتينين في مصل الدم مقارنة مع المجموعة التي تلقت العلاج بكربونات الليثيوم.

استنتج البحث الى أنه يجب مراقبته التأثيرات الضارة لليثيوم على الكلى عن كثب في المرضى الذين يتناولون عقاقير تحتوي على الليثيوم ومن الافضل اضافة فيتامين ه مع الليثيوم

الكلمات الدلالية: الليثيوم فيتامين ه باكس الفا سموث مسل اكتين