Original Article

The Possible Protective Role of Quercetin on Nicotine Induced Liver and Kidney Damage of Neonates Albino Rats: Histological and Immunohistochemical Study

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ABSTRACT

Introduction: Nicotine is the most important component of cigarettes and is considered a strong carcinogen. Quercetin (QCT) is potent anticancer and antioxidant agent. Both nicotine and QCT can pass the placenta and appear in breast milk.

Aim of the Work: To study the possible protective role of QCT on nicotine induced liver and kidney structural damage of neonates.

Materials and Methods: Eighteen pregnant female albino rats were divided into 3 groups. The control group was injected subcutaneously (SC) by distilled water. The nicotine group was injected SC by nicotine (6mg/kg/d). Nicotine and QCT group was injected by nicotine and take simultaneously QCT orally (302 mg/kg/day). Twelve male neonates were taken from each group and divided into two subgroups (a and b). Offspring subgroups (1a, 2a, 3a) were sacrificed 2 weeks postnatal and offspring subgroups (1b, 2b, 3b) were sacrificed 4 weeks postnatal. By end of experiment, liver and kidney specimens were processed for histological and immunological studies.

Results: In nicotine group, neonates' liver showed hepatocytes with pyknotic nuclei and vacuolated cytoplasm. Portal area showed more than one bile duct and cellular infiltrates. QCT and nicotine group showed moderate restoration of hepatic architecture especially in subgroup 3a. Transforming growth factor -β immnoexpression was increased in nicotine group indicating liver damage while decreased in nicotine and QCT group, indicating some improvement. Neonates' kidney of nicotine group showed shrunken glomeruli, congestion of peritubular capillaries and homogenous eosinophilic material in tubular lumina. In nicotine and QCT group, there was minimal renal tissue improvement. Immunoexpression of COX-2 was much in kidney tissue of nicotine group indicating kidney damage, while in nicotine and QCT group, it was less expressed.

Conclusion: Maternal QCT administration has a moderate role to protect neonatal liver against damage produced by maternal nicotine injection while this protective role was less in kidney

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Key Words: Kidney, liver, nicotine, offspring, quercetin.

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INTRODUCTION

Smoking is a common risk factor for diseases in civilized countries. This habit is still very public despite educational programs concerning bad effects of tobacco smoking[1]. Tobacco smoking has critical effects during pregnancy and lactation. Tobacco compounds as nicotine reach neonates via breast milk. The amount of nicotine present in breast milk is more than double that nicotine circulating in maternal serum[2]. It is believed that children exposed to tobacco smoke during the gestation and after birth have a higher morbidity and mortality rate up to 5 years of age. The mortality rate among children would be reduced by ten percent if all mothers gave up smoking during pregnancy[3].

Cigarette smoke composed of more than 3600 various compounds, nicotine is the most important one and responsible for many of the tobacco effects[4]. Nicotine; a major tobacco alkaloid; is widely used in the experiments due to its well-studied pharmacological properties. Nicotine is a strong carcinogen that is oxidized into cotinine metabolites mainly in the liver, kidney and lung. In addition, nicotine has an important role in the pathogenesis of tissue injury[5] and increases the oxidative stress[6]. The oxidative stress is responsible for the pathogenesis of several disorders as cardiovascular, hepatic, lung, renal and brain diseases[7].

Quercetin (QCT) is a plant pigment flavonoid which is natural polyphenols vastly found in fruits, vegetables, seeds and stems[8]. QCT is one of the most extensively studied flavonoids that have strong anticancer[9], antioxidant that attain oxygen free radicals uptake, anti-inflammatory and antifibrogenic effect[10]. Isorhamnetin, a methylated QCT, prevent progress of breast cancer cells, attenuate the effect of oxidative stress on HepG2 cancer cells and protect against inflammatory bowel disease[11]. It was proved that QCT has prophylactic and therapeutic effect against Alzheimer's disease[12].

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AIM OF THE WORK

The present work aimed to study the possible protective role of QCT on the nicotine induced liver and kidney structural damage of neonates albino rats.

MATERIALS AND METHODS

Ethical Approval

The study protocol was approved by the Research Ethics Committee (REC) for Human and Animal Research at the Faculty of Medicine, Helwan University, Cairo Egypt, serial: 57- 2020.

Animals

Eighteen pregnant female albino rats were used in this study. The rats were housed in Experimental Animal Research Unit – FMASRI (Faculty of Medicine, Ain Shams Research Institute). The rats were housed in animal cages under the prevailing atmospheric conditions and given tap water.

Chemicals

Nicotine and QCT were purchased from Sigma Chemical Company (St. Louis, MO, USA.) in the form of powder. Nicotine was dissolved in distilled water and was used at 6 mg/kg/day subcutaneously[13]. QCT (302 mg/kg/day) was dissolved in distilled water and given orally[14].

Study Design

Eighteen pregnant female albino rats were divided randomly and equally into 3 groups, each group contained 6 rats. The first control group (Gp1) was injected subcutaneously (SC) by distilled water. The second nicotine group (Gp2) was injected SC by nicotine (6mg/kg/d). The third nicotine and QCT group (Gp3) was injected SC by nicotine (6mg/kg/d) and take QCT (302 mg/kg/day) orally. The pregnant rats received distilled water, nicotine and nicotine and QCT from the beginning of the experiment (first day of conception; detected by vaginal smear) till 4 weeks after delivery. Twelve neonate male rats were taken randomly immediately after delivery from each group and divided randomly into 2 subgroups (a & b), each contained 6 rats. The neonate subgroups (1a, 2a, 3a) were sacrificed 2 weeks after delivery and neonate subgroups (1b, 2b, 3b) were sacrificed 4 weeks after delivery.

Samples Collection

The male neonate rats were euthanized by cervical dislocation under anesthesia[15]. Liver and kidney tissues were gathered. All specimens were fixed in 10% formalin and processed for paraffin blocks formation, sectioned and subjected to the following techniques:

I – Hematoxylin and Eosin staining

All samples were fixed in 10% formalin for twenty-four hours. Paraffin wax tissue blocks were prepared for sectioning at 4 microns thickness by sledge microtome[16].

II – Immunohistochemical staining

Transforming growth factor (TGF-β); Labvision, ThermoFisher, USA mouse monoclonal antibody, catalog no.MA5-16949; the reaction is cytoplasmic and the positive control was the brain tissue. It was used for detection of liver damage[17]. Cyclooxygenase 2 (COX-2); Labvision, Thermoscientific, USA rabbit polyclonal antibody, catalog no. RM9121R7; the reaction is cytoplasmic and nuclear. The positive control was the lung; it was used for detection of kidney inflammation such as glomerulonephritis[18].

Morphometric study

An image analyzer Leica Q win V.3 program installed on a computer in the Histology Department, Faculty of Medicine, Ain Shams University, was used. The computer was connected to a Leica DM2500 microscope (Wetzlar, Germany).

Six sections from six different offspring rats of each subgroup were examined. For each section, six different captured non-overlapping high-power fields (×20) were taken to measure area percentage of immunoexpression (IE) of TGF-β in liver and COX-2 in kidney to indicate the degree of tissue oxidative damage caused by nicotine.

Statistical Study[19]

Quantitative data were summarized as means and standard deviations and compared using Analysis of variance (ANOVA). Any significant ANOVA was followed by Bonferroni post-hoc test to detect which pairs of groups caused the significant difference. *P-values* <0.05 were considered statistically significant. Calculations were made on Statistical package of the social sciences (SPSS) version 18.0 for Windows (IBM Corporation, USA).

RESULTS

Histological and immunohistochemical results

A- Hematoxylin & eosin staining

Liver sections

In control group (Gp1), all sections taken after two and four weeks revealed the same well-known normal histological structure. The central vein is surrounded by cords of hepatocytes which have strongly acidophilic cytoplasm and central pale nuclei. In addition, the hepatic sinusoids appear between the rows of hepatocytes (Figure 1a). The portal area demonstrated portal vein, hepatic artery and bile duct (Figure 1b).

In the nicotine treated group (Gp2): on examination of liver sections, subgroup 2a showed central vein dilatation, some hepatocytes exhibiting pyknotic nuclei and vacuolated cytoplasm (Figure 2). Comparable with subgroup 2a, subgroup 2b showed apparently marked dilated central vein with minimal congestion, most of hepatocytes exhibiting pyknotic nuclei and vacuolated cytoplasm (Figure 3). Other field recruited more than one

bile duct in the portal area and focal cellular infiltrates among homogenous material. Most of the surrounding hepatocytes showed pyknotic nuclei and vacuolated cytoplasm (Figure 4).

In the nicotine & QCT (Gp3) treated group: liver sections of subgroup 3a showed few hepatocytes with pyknotic nuclei and vacuolated cytoplasm (Figure 5), however subgroup 3b showed some hepatocytes exhibiting pyknotic nuclei and vacuolated cytoplasm. In addition, slightly congested and dilated central vein was observed (Figure 6).

Kidney sections

In the control group, sections taken from rats after two weeks presented apparently small (Figure 7a) and after four weeks presented apparently large (Figure 7b) glomeruli surrounded by Bowman′s capsule with normal urinary space in-between and renal tubules (Figures7a,7b).

In the nicotine treated group, renal cortex of rat in subgroup (2a) showed focal scattered shrunken glomeruli with apparently dilated capsular space and few congested glomeruli (Figure 8). Compared to Subgroup (2a), Subgroup (2b) demonstrated some shrunken glomeruli, obvious congestion of peritubular capillaries and homogenous eosinophilic material in tubular lumina (Figure 9).

In the nicotine and QCT treated group, renal cortex of subgroup 3a revealed accidental congested glomeruli & vessels. Apparently normal tubules with few congested peritubular capillaries were observed (Figure 10). Subgroup (3b) showed apparently normal glomeruli and some tubules, but accidental shrunken and fewer congested glomeruli were observed compared to Subgroup 3a (Figure 11).

B- Immunohistochemical staining

TGF-β (IE)

The liver section of control group showed -ve immunoexpression (IE) in the cytoplasm of hepatocytes (Figure 12). In subgroup (2a), there was +ve IE in some hepatocytes (Figure 13). However, subgroup (2b) showed +ve IE in multiple hepatocytes (Figure 14). On other hand, Subgroup (3a) demonstrated +ve IE in accidental hepatocytes (Figure 15). While subgroup (3b), demonstrated +ve IE in few hepatocytes (Figure 16).

COX-2 (IE)

The control group revealed -ve IE among glomeruli and tubular cells (Figure 17). In subgroup (2a), there was +ve IE among some glomeruli and some tubular cells (Figure 18). While subgroup (2b), demonstrated IE among +ve multiple glomeruli and multiple tubular cells (Figure 19). On other hand, Subgroup (3a) showed +ve IE among few glomeruli and few tubular cells (Figure 20) and, subgroup (3b) demonstrated +ve IE among some glomeruli and some tubular cells (Figure 21).

Morphometric results

The area % of TGF-β and COX-2 IE determined a significant increase in subgroup 2b (nicotine 4 weeks) compared to all other subgroups. While in subgroup 2a, it was significantly increased compared to subgroup 3a and 3b (nicotine and QCT 2 and 4 weeks). On other hand, in subgroup 3b (nicotine and QCT 4 weeks) a significant increase was found compared to subgroup 3a (nicotine and QCT 2 weeks) (Table 1).

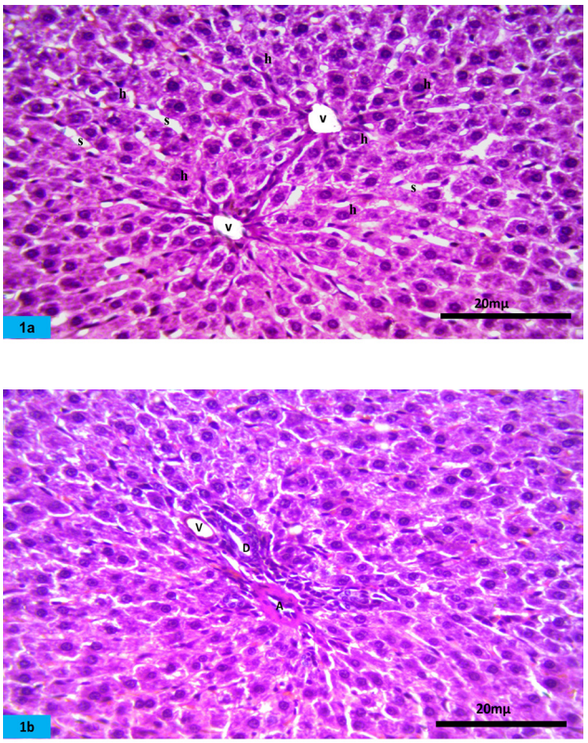

Fig. 1: Liver of a control rat (group1) (H&E, x400). **1a:** Liver of rat in subgroup (1a) showing central vein (v) surrounded by cords of hepatocytes (h) which have strongly acidophilic cytoplasm and central pale nuclei. The hepatic sinusoids (s) appear between the rows of hepatocytes. **1b:** Liver of rat in subgroup (1b) showing portal area exhibiting portal vein (V), hepatic artery (A) and bile duct (D).

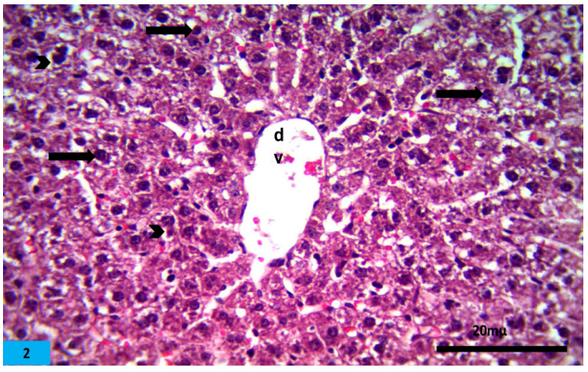

Fig. 2: Liver of rat in subgroup (2a) showing central vein dilatation (dv), some hepatocytes exhibiting dark nuclei (thick arrows), and vacuolated cytoplasm (arrowheads) (H&E, x400).

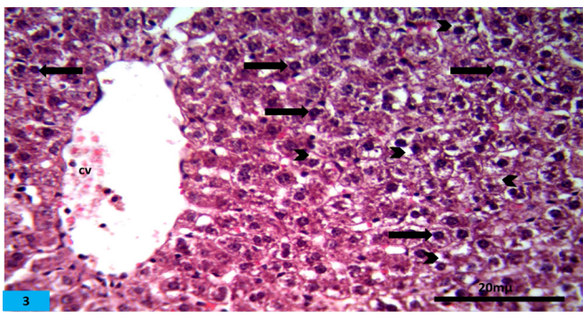

Fig. 3: Liver of rat in subgroup (2b) showing apparently markedly dilated central vein with minimal congestion (cv), and most of hepatocytes exhibiting dark nuclei (thick arrows), as well as vacuolated cytoplasm (arrowheads) (H&E, x400).

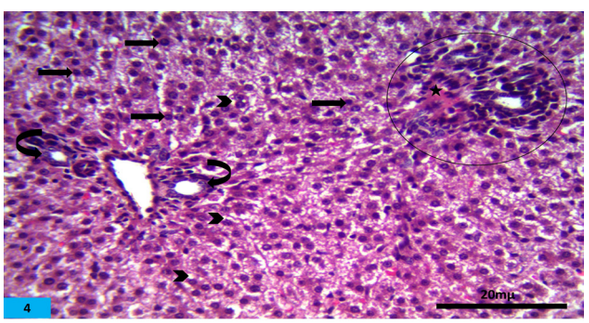

Fig. 4: Liver of rat in subgroup (2b) showing portal area with more than one bile duct (curved arrows) and focal cellular infiltrates (demarcated by circle) among homogenous material (star). Note multiple surrounding hepatocytes with dense nuclei (thick arrows) and vacuolated cytoplasm (arrowheads) (H&E, x400).

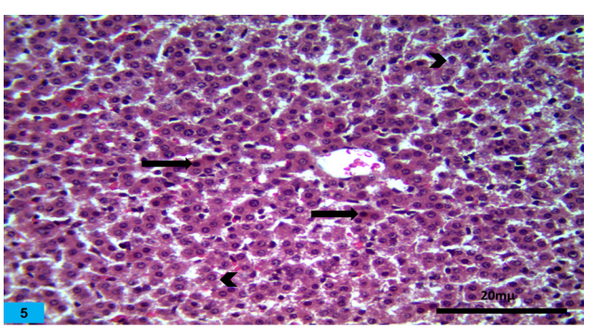

Fig. 5: Liver of rat in subgroup (3a) showing few hepatocytes with dark nuclei (thick arrows) and vacuolated cytoplasm (arrowheads) (H&E, x400).

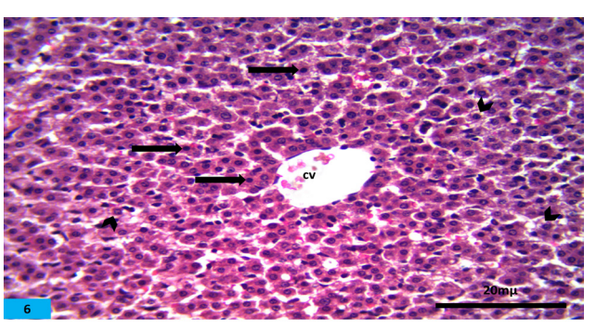

Fig. 6: Liver of rat in subgroup (3b) showing some hepatocytes exhibiting dark nuclei (thick arrows) and vacuolated cytoplasm (arrowheads). Central vein is slightly congested (cv) and dilated (H&E, x400).

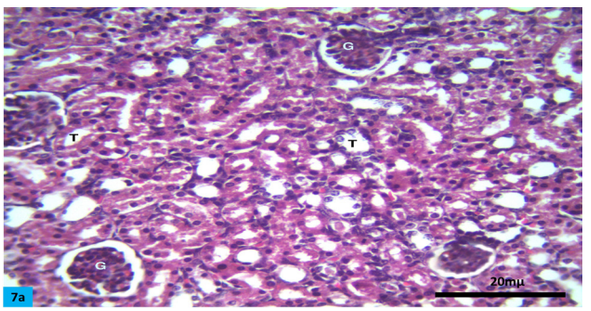

Fig. 7a: The renal cortex of control group (2 weeks) presented apparently small glomeruli (G) surrounded by Bowman′s capsule with normal urinary space in-between and renal tubules (T) (H&E, x400).

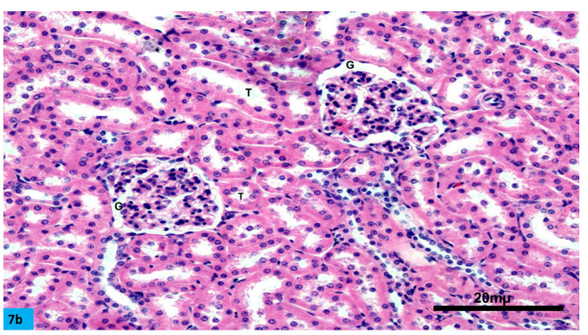

Fig. 7b: The renal cortex of control group (4 weeks) presented apparently large glomeruli (G) surrounded by Bowman′s capsule with normal urinary space in-between and renal tubules (T) (H&E, x400).

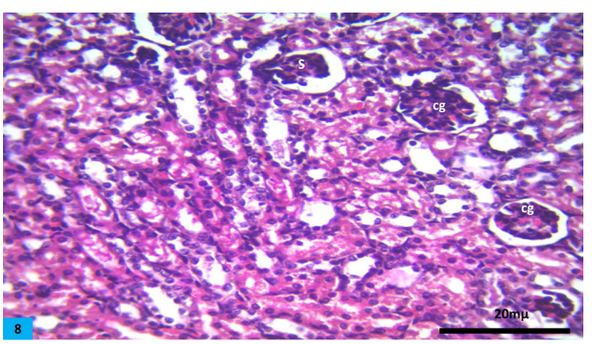

Fig. 8: The renal cortex of rat in subgroup (2a) showing a shrunken glomerulus (S) and some congested glomeruli (cg). (H&E, x400).

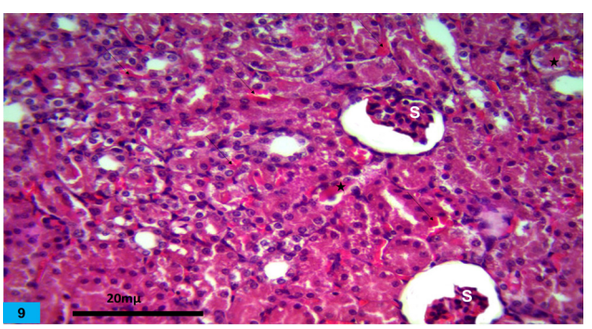

Fig. 9: The renal cortex of rat in subgroup (2b) showing two shrunken glomeruli (S), obvious congestion of peritubular capillaries (thin arrows) and homogenous eosinophilic material in tubular lumina (stars) (H&E, x400).

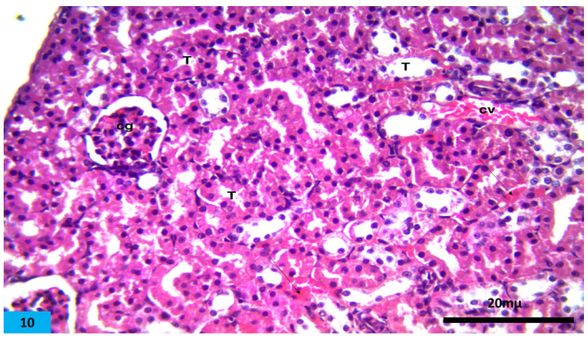

Fig. 10: The renal cortex of rat in subgroup (3a) showing congested glomerulus (cg), congested vessel (cv), apparently normal tubules (T) and few congested peritubular capillaries (thin arrows) (H&E, x400).

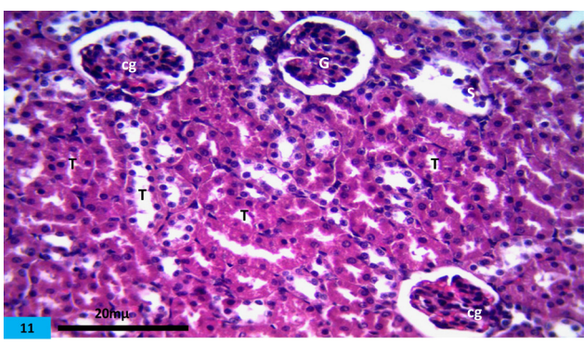

Fig. 11: The renal cortex of rat in subgroup (3b) showing apparently normal glomerulus (G) and some tubules (T), shrunken glomerulus (S) and two congested glomeruli (cg) (H&E, x400).

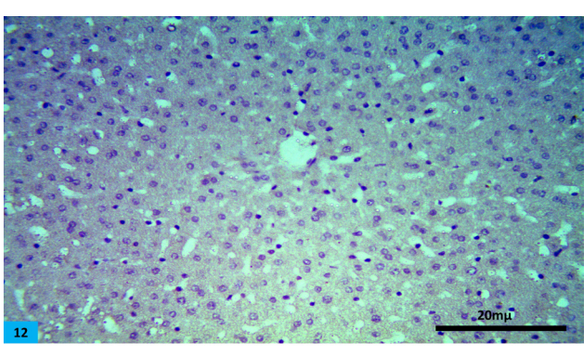

Fig. 12: Immunostaining of control group showing -ve cytoplasmic immunoexpression in hepatocytes (TGF-β, x400).

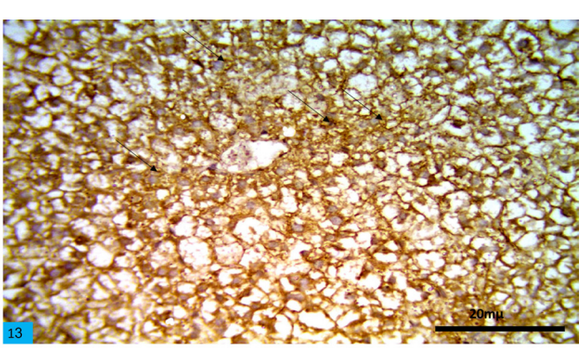

Fig. 13: Immunostaining of subgroup (2a) showing +ve cytoplasmic immunoexpression in some hepatocytes (arrows) (TGF-β, x400).

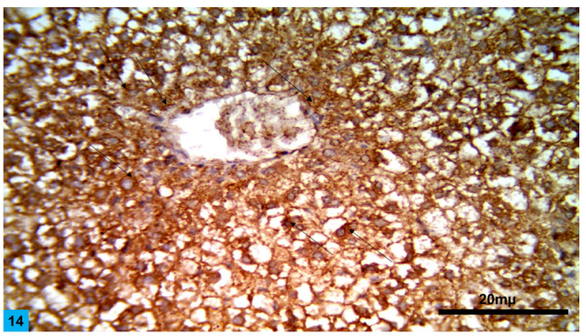

Fig. 14: Immunostaining of subgroup (2b) showing +ve cytoplasmic immunoexpression in multiple hepatocytes (arrows) (TGF-β, x400).

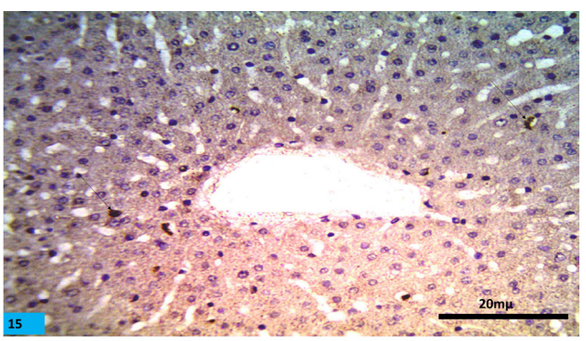

Fig. 15: Immunostaining of subgroup (3a) showing +ve cytoplasmic immunoexpression in accidental hepatocytes (arrows) (TGF-β, x400).

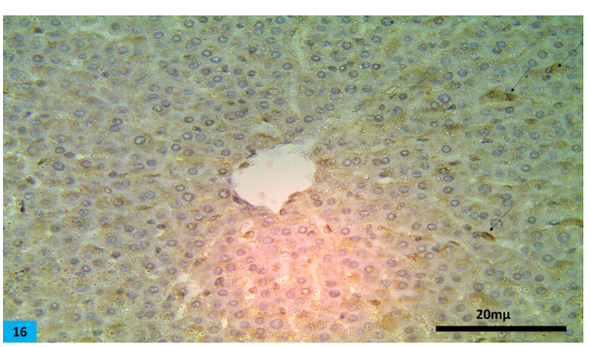

Fig. 16: Immunostaining of subgroup (3b) showing +ve cytoplasmic immunoexpression in few hepatocytes (arrows) (TGF-β, x400).

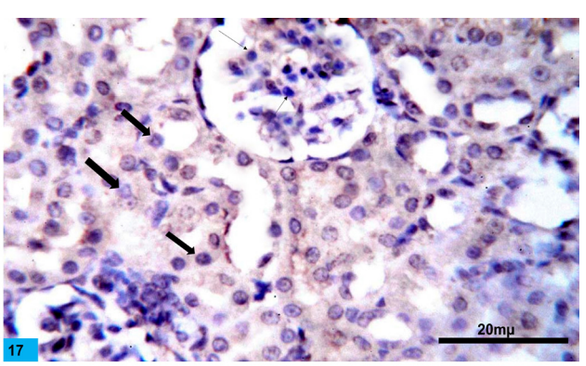

Fig. 17: Immunostaining of control group showing -ve immunoexpression among glomeruli (thin arrows) and tubular cells (thick arrows) (COX-2, X400).

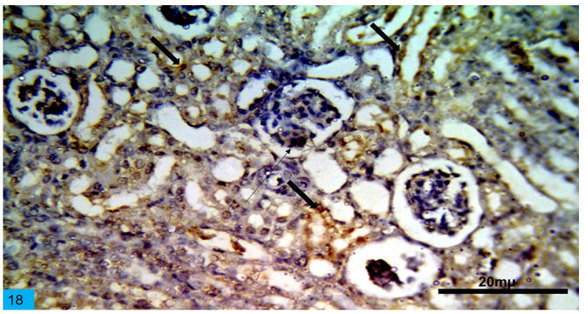

Fig. 18: Immunostaining of subgroup (2a) showing +ve immunoexpression among glomeruli (thin arrows) and some tubular cells (thick arrows) (COX-2, x400).

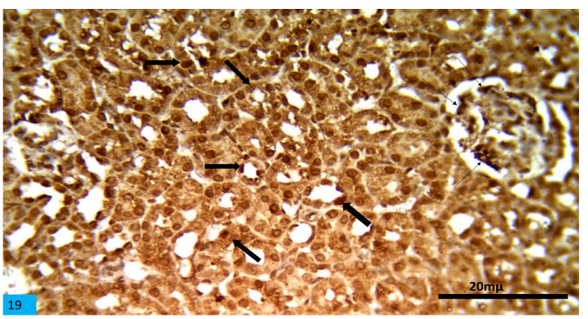

Fig. 19: Immunostaining of subgroup (2b) showing +ve immunoexpression among glomeruli (thin arrows) and multiple tubular cells (thick arrows) (COX-2, x400).

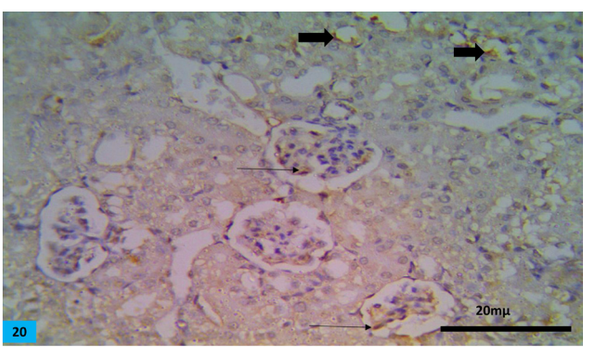

Fig. 20: Immunostaining of subgroup (3a) showing +ve immunoexpression among glomeruli (thin arrows) and few tubular cells (thick arrows). (COX-2, x400).

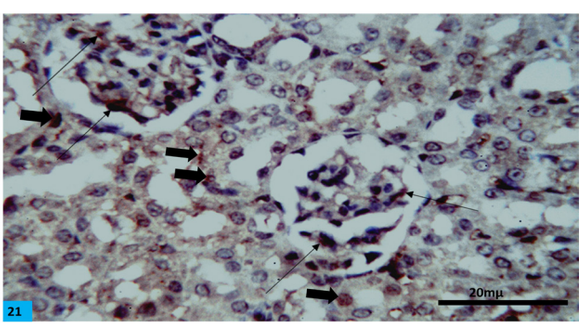

Fig. 21: Immunostaining of group (3b) showing +ve immunoexpression among glomeruli (thin arrows) and some tubular cells (thick arrows) (COX-2, x400).

Table 1: Area % of TGF-β (in liver) and COX-2 (in renal cortex) (IE) (± SD)

Groups and subgroups	Area % TGF-β (IE)	Area % COX-2 (IE)
Control 2 weeks (1a)	0	0
Nicotine 2 weeks (2a)	5.333 ± 1.583 #	4.719 ± 0.798 #
Nicotine and QCT 2 weeks (3a)	0.715 ± 0.138	0.781 ± 0.066
Control 4 weeks (1b)	0	0
Nicotine 4 weeks (2b)	7.992 ± 1.33 *	10.765 ± 1.752 *
Nicotine and QCT 4 weeks (3b)	1.297 ± 0.155 ^	2.280 ± 0.094 ^

P significant increase <0.05
(*) Significant compared to all other subgroups.
(#) Significant compared to subgroups 3a and 3b
(^) Significant compared to subgroups 3a

DISCUSSION

In the present study, morphological changes in the liver and kidney of neonate rats were found under the effect of the maternal nicotine administration histologically and immunohistochemically. These changes were confirmed by morphometry. On the other hand, the regression of previous changes was noticed under the effect of QCT administration.

It has been reported that nicotine passes the placenta, concentrates in fetal blood, amniotic fluid and breast milk of the pregnant smoker[20,21]. Nicotine disrupts the mitochondrial respiratory chain producing metabolism that increases free radicals and reacts with DNA and membrane proteins[22,23]. This agrees with other researcher who reported that there was increased oxidative damage specifically to mitochondrial proteins in the pancreas of nicotine exposed neonates[24]. A previous study indicated that subcutaneous injection of nicotine causes iron deposition in the liver and kidney leads to organs toxicity and increase in hydroxyl radicals[25].

In nicotine group, liver tissue of two-weeks-old offspring showed central vein dilatation, some hepatocytes exhibiting pyknotic nuclei, others demonstrated vacuolated cytoplasm. While four-weeks-old offspring rats recruited obviously dilated central vein with minimal congestion. More than one bile duct in the portal area and focal periportal cellular infiltrates among homogenous material were seen. Multiple hepatocytes exhibiting pyknotic nuclei and vacuolated cytoplasm were observed in the lobule. The previous findings denoted inflammatory changes that progressed into degenerative changes that more obvious in prolonged duration subgroup. These results match with Menshawy *et al*,[25] who stated that nicotine administration causes degeneration of the hepatocytes and expansion of portal tracts associated with inflammatory cells. Also, they proved that injection of nicotine causes iron overload, cholestasis, cellular proliferation and appearance of more than one duct in portal area.

Backhle *et al*,[26] clarified that the dilatation of the blood vessels might be related to increased levels of

prostaglandin formation that induces smooth muscle relaxation and vasodilatation. Other study revealed that vascular congestion results from degenerating hepatocytes that obstruct the surrounding sinusoids. It was added that the progressive morphological changes in the liver of rats that were given 0.5mg/kg nicotine for longer duration were observed[27]. It was postulated that the toxicity of injected nicotine causes lymphocytic infiltration at the periphery of the lobules as a defense mechanism[28].

Concerning the kidney, the present results of two weeks-old neonate rats of nicotine group demonstrated accidental shrunken glomeruli and few congested glomeruli. Four-week-old offspring's renal cortex showed some shrunken glomeruli, obvious congestion of peritubular capillaries and homogenous eosinophilic material in tubular lumina. The previous findings denoted inflammatory changes that progressed into degenerative changes. In accordance, maternal nicotine administration during gestation influences the development of the fetal kidney that may lead to kidney diseases during puberty[29]. The glomerular and tubular changes were similar to results of Salahshoor *et al*,[30]. Zarzeckia *et al*,[31] found that there were mark ed abnormalities of glomerular volume and mesangial cells in experimental offspring rats.

The previous results match with another study which concluded that intrauterine nicotine exposure alters morphology and glomerular mass in the offspring rats[32]. It was added that renal tubular cells damage may be due to involvement of the renin–angiotensin mechanism in the pathogenesis of this damage[33]. It was clarified that in the developing kidney, angiotensin II (ANG II) plays a role in renal development. It was also proved that increased neonatal nicotine exposure reduced renal ANG II receptors expression and induced apoptosis of renal cells[34]. It was added that during foetal life, large levels of circulating renin and ANG II ensure sufficient perfusion and boost the foetal kidney's growth. Reduced systemic blood pressure causes decreased renal perfusion, renal ischemia, and defective renal tubule formation[35].

Treatment by natural flavonoids, can moderate lipid peroxidation and consequently diminish nitrite oxide and oxidative stress[36]. In the present study, liver of two-week old neonate rats of QCT & nicotine treated group showed few hepatocytes with dark nuclei and vacuolated cytoplasm denoting restoration of architecture of hepatic cords. The liver tissue of 4-weeks old offspring rats demonstrated some hepatocytes with pyknotic nuclei and vacuolated cytoplasm, expressing less obvious restoration in prolonged duration subgroup. In addition, slightly congested and dilated central vein was observed. Concomitantly, Peres *et al*[36] stated that QCT minimizes liver oxidative injury, proliferation of bile ducts in rats with biliary obstruction. It was added that QCT treatment had a useful effect on liver regenerative ability of the remnant liver tissue post hepatectomy, probably due to its potent antioxidative, antiapoptotic and proliferative properties[37].

Other investigators stated that hepatotoxicity is caused by the production of reactive oxygen species (ROS). The stimulation of Kupffer cells, as well as the release of cytokines and free radicals, amplifies this process, resulting in centrilobular apoptosis[38]. Quercetin inhibits the iNOS/NF-B pathway[39], which consequently protects against oxidative stress and reduces ROS generation and mitochondrial damage in hepatocytes[40]. On other hand, it was stated that QCT reduces progressive changes[17].

In the present study, renal cortex of two weeks-old neonate rats of nicotine and QCT treated group showed apparently normal tubules but accidental congested glomeruli, vessels and few peritubular capillaries indicating some improvement. The renal cortex of four weeks-old neonates recruited accidental shrunken and congested glomeruli indicating less improvement. This is in accordance with a study which reported that the glomeruli are very sensitive to oxidative stress[41]. So, QCT administration causes no apparent improvement in renal tissue in animal models on prolonged exposure of pregnant rats to nicotine. In contrary to our results, it was proved that QCT decreased doxorubicin-induced kidney damage in experimental rats[42].

In subgroup 2a (two weeks-old neonates of nicotine group) +ve cytoplasmic TGF-β IE was found in some hepatocytes indicating significant damage compared to control and QCT treated subgroups. While in subgroup 2b recruited +ve IE in multiple hepatocytes indicating significant damage comparable with all other subgroups. It was reported that TGF-β is a key regulator in chronic liver disease. It plays a role in all stages of histopathological progressive changes ending in disease from early liver injury to inflammation, degeneration and finally to cirrhosis and hepatocellular carcinoma[43].

In subgroup 3a QCT therapy revealed +ve TGF-β IE in accidental hepatocytes, indicating obvious improvement. While, in subgroup 3b +ve IE in few hepatocytes indicating less obvious improvement compared to subgroup 3a.

Concerning the kidney, subgroup 2a showed +ve COX-2 IE among some glomeruli and some tubular cells indicating significant renal cortex damage compared to control and QCT treated subgroups. While in subgroup 2b, + ve IE was found among multiple glomeruli and multiple tubular cells indicating significant renal cortex inflammation ending in damage compared to all other subgroups. It was proved that COX-2 expression increased in experimental rats and cultured human mesangial cells in response to nicotine induced acute nephritis[44]. The effect of COX-2 inhibitors was evaluated on nicotine induced renal cytotoxicity model and the results were prostaglandins inhibition and renal injury improvement[45].

In subgroup 3a, +ve COX-2 IE was seen among few glomeruli and few tubular cells indicating some improvement. While in subgroup 3b, +ve IE was found among some glomeruli and some tubular cells indicating less obvious improvement comparable to subgroup 3a.

Recently, it was documented that QCT ameliorates renal function, reduces oxidative stress factors and kidney inflammation in a rat model of chronic kidney disease[46].

The more noticeable improvement in the liver induced damage by nicotine than the renal tissue was supported by Fan *et al*,[47]. The researchers referred wonderful regenerative ability to hepatic oval cells that re-enter into the cell cycle in response to surgical liver resection[47].

CONCLUSION

Maternal nicotine administration during pregnancy and lactation proved deleterious effects on liver and kidney of neonates. This study indicated that the concomitant administration of nicotine and quercetin ameliorated the liver and renal structural damage. However, the hepatic improvement was better than renal. The regression of changes in response to QCT was less noticeable with longer duration.

RECOMMENDATIONS

Other studies can perform more investigations using QCT as an adjuvant to regenerative therapy. Using QCT can be valuable for protection in passive smokers.

CONFLICT OF INTERESTS

There are no conflicts of interest.

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الملخص العربى

الدور الوقائي المحتمل للكرسيتين على كبد وكلى نسل الجرذان البيضاء مع تعرض الأمهات للنيكوتين: دراسة هستولوجيه ومناعيه

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الخلفية: النيكوتين هو أهم مكون للسجائر ويعتبر مادة مسرطنة قوية ويمتلك الكيرستين دور قوى كعامل مضاد للسرطان والأكسده وكليهما يعبر المشيمه ويظهر فى لبن الأم.

الهدف من العمل: تقييم التأثيرالمحتمل للكرسيتين على كبد وكلى نسل الجرذان البيضاء مع تعرض الأمهات للنيكوتين أثناء الحمل والرضاعة.

المواد والطرق: تم تقسيم ثمانيه عشر من اناث الجرذان البيضاء الحوامل إلى المجموعة الضابطة والتى تلقت الماء المقطر عن طريق الحقن تحت الجلد، ومجموعة النيكوتين: تلقت النيكوتين (٦ ملج / كجم / يوم) عن طريق الحقن تحت الجلد. ومجموعة النيكوتين والكرسيتين: تلقت النيكوتين (٦ ملج / كجم / يوم) عن طريق الحقن تحت الجلد والكرسيتين بالفم (٣٠٢ ملج / كجم / يوم) في نفس الوقت، تم أخذ اثنى عشر مولود ذكر من كل مجموعه وتقسيمهم الى مجموعتين فرعيتين (أ و ب). تم التضحية بمجموعات النسل الفرعية (١ أ ، ٢ أ ، ٣ أ) بعد أسبوعين من الولادة وتم التضحية بالمجموعات الفرعية للنسل (١ ب ، ٢ ب ، ٣ ب) بعد ٤ أسابيع من الولادة.وتمت معالجة عينات الكبد والكلى من المواليد من أجل الفحص المجهري الضوئي باستخدام صبغة الهيماتوكسيلين والإيوسين والصبغات المناعية ضد عامل النمو المتحول بيتا و كوكس- ٢.

النتائج: أظهرت مجموعة النيكوتين اتساع فى الوريد المركزى و تغلظ في أنوية الخلايا الكبديه التى أظهرت فراغات فى السيتوبلازم. وأظهرت المنطقه البابيه أكثر من انبوبه مراريه وتسلل خلوى. أما مجموعة النيكوتين والكرسيتين فقد أظهرت بعض التحسن خصوصا مع المجموعه الثالثه (أ). وقد زادت الصبغه المناعية ضد عامل النمو المتحول بيتا مع مجموعة النيكوتين مما يؤكد حدوث التلف وقلت مع مجموعة النيكوتين والكرسيتين مما يعنى بعض التحسن. أظهرت الكلى فى مجموعة النيكوتين انكماش فى كبيبات الكلى واحتقان فى الأوعيه الدمويه المحيطه بها. وقد ظهر بعض التحسن البسيط فى مجموعة النيكوتين والكرسيتين وتأكد ذلك بالصبغه المناعية (كوكس- ٢).

الخلاصة: تناول الامهات للكيرستين يمكن أن يحسن بعض التغيرات التي يسببها النيكوتين لكبد وكلى نسل الجرذان البيضاء ولكن التحسن فى الكلى يكون أقل من الكبد.