First research

Light and Scanning Electron Microscopic Study of 5-Fluorouracil-Induced Mucosal Injury in the Gastric Fundus and the Possible Protective Role of Omeprazole in Adult Male Albino Rat

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ABSTRACT

Introduction: Administration of chemotherapy in a wide variety of cancers is associated with various side effects, with structural affection of gastrointestinal tract being a major clinical concern and a major cause of cancer treatment-related morbidity.

Aim of the work: This current study was performed to assess the light and scanning electron microscopic changes of 5-fluorouracil (5-FU) induced cytotoxicity on the mucosa of gastric fundus in male albino rats and to assess the possible protective role of omeprazole.

Materials and methods: Forty adult male albino rats were divided into four groups: Group I (control rats), Group II administrated (10 mg/kg) omeprazole orally via gastric tube/ once daily for 5 consecutive days, Group III injected IV with (50 mg/kg) 5-fluorouracil once daily for 5 consecutive days and Group IV received 5-fluorouracil as group III + omeprazole as group II. At the end of the experiment, specimens from gastric fundus mucosa were processed for light and scanning electron microscopic study.

Results: Light microscopic examination in 5-FU group revealed many changes such as, erosion at pits of the mucosa with destructed surface mucous cells with distorted nuclei and intra-luminal exfoliated cells, vacuolated parietal cells with pyknotic and karyolitic nuclei and distorted chief cells with apical migration of their nuclei. Also, the lamina propria showed inflammatory cell infiltration and extravasated RBCs. Specimens from group IV revealed mild mucosal injury in gastric fundus as compared to 5-FU-treated rats.

Scanning electron microscopy examination of 5-FU-treated rats revealed loss of demarcation between mucous cells, many necrotic areas in the mucosa with umbilicated apices. Other specimens showed complete shedding of mucosal surface leaving irregular wide openings of the gastric pits with a shape of honeycomb. Scanning electron specimens in group IV revealed apparent normal fundus mucosal surface. However, mild changes in the mucosal surface were observed in some specimens.

Conclusion: It is concluded that concomitant administration of omeprazole with 5-FU has a protective effect against 5-FU-induced structural changes in the mucosa of stomach fundus.
Second research

Possible Cardioprotective Effect of Nicorandil on Isoproterenol-Induced Myocardial Injury in Adult Male Albino Rats

By

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Abstract

Introduction: Ischemic heart disease is a global health concern and the development of new strategies to protect the heart has attracted significant attention.

Aim of the work: This work aimed to study the possible cardioprotective effect of nicorandil on isoproterenol-induced myocardial injury in adult male albino rats.

Materials and methods: Forty adult male albino rats were divided into four groups: Group I (control rats), Group II received Nicorandil (3 mg/kg) orally/once daily by gastric tube for 7 consecutive days, Group III received (85 mg/kg) isoproterenol in two consecutive subcutaneous injections at an interval of 24 h. and Group IV received Nicorandil (3 mg/kg) orally/once daily by gastric tube for 7 consecutive days followed by (85 mg/kg) isoproterenol in two consecutive subcutaneous injections at an interval of 24 h.

At end of the experiment, specimens from the cardiac muscle were processed for light and electron microscopic study. Immunohistochemical study was carried out using an antibody against vimentin.

Results: Microscopic examination of specimens of isoproterenol-treated animals showed peripheral deeply stained nuclei. The surrounding sarcoplasm was vacuolated with focal lysis of cardiac myocytes, swelling of mitochondria and distortion of the intercalated disc. However, specimens from group IV revealed normal appearance of cardiac myofibrils with localized focal areas of sarcoplasmic vacuolation. All these findings were associated with highly significant increase in vimentin immunoreactions in the perimysial sheaths and in walls of blood vessels of isoproterenol group. This finding was reversed in Nicorandil & isoproterenol group rats to become more or less similar to the control group.

Conclusion: It is concluded that nicornadil pretreatment ameliorated isoproterenol-induced myocardial injury.
Third research

Effect of Interferon, Ribavirin and Combination of both on the Retina of Adult Male Albino Rats: Histological and DNA Electrophoresis Study

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Abstract

Background: Interferon-α is a natural glycoprotein produced and secreted by immune cells in response to viral infections. Interferon has been used clinically to treat numerous viral and malignant diseases.

Aim of the work: To assess the effect of interferon and ribavirin and combination of both on the retina of adult albino rats using light, transmission electron microscopy and DNA electrophoresis.

Materials and methods: Thirty five adult male albino rats were used and divided into four groups: Group I (control group), group II received 7,500 IU of interferon alpha-2b/intra-peritoneal injection/3 times weekly/for 3 weeks, group III received ribavirin 30 mg/kg/orally via gastric tube once daily/for 3 weeks and group IV received both Interferon alpha and ribavirin at the same dose and periods as the previous 2 groups. All the animals were sacrificed and the retina were prepared for histological, DNA electrophoresis and morphometric study.

Results: H&E-stain sections of group II revealed apparent reduction in the thickness of the different retinal layers with disrupted, degenerated in the ganglionic cells and irregular inner limiting membrane. Toluidine blue-stain showed karyolitic irregular nuclei of pigmented epithelium with irregular outer limiting membrane and longitudinal space in between the cells of the outer nuclear layer. The ganglionic cells layer revealed migration of the chromatin at the nuclear membrane with congested blood vessels in the choriocapillaries layer. While in group III it showed vacuolated receptor layer of rods & cones with focal areas of denuded pigmented epithelium and dark stained irregular nuclei of the pigmented epithelium cells. Group IV clarified disorganization of retinal layers with extravasated red blood corpuscles. Electron microscopic results confirmed light microscopic one.

The DNA electrophoresis results revealed an increase in DNA fragmentation in interferon group and ribavirin group. Meanwhile, marked increase in DNA fragmentation was observed in the rats treated with both interferon and ribavirin.

Conclusion: it could be concluded that usage of ribavirin with interferon accentuated its effects and results in more damage to the retina.
Forth research

Effect of Anti-epileptic Drugs on the Thyroid Gland in Adult Albino Rats: Hormonal Assay, Histological and Morphometric Study

By

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ABSTRACT

**Background:** Normal thyroid hormone blood levels are essential for growth and development of tissues and maintenance of organ function. Antiepileptic drugs may induce disturbances in thyroid hormonal level.

**Aim of the work:** This work was done to evaluate effects of anti-epileptic drugs on the thyroid gland of adult male albino rats using hormonal assay, histological and morphometric study.

**Material & Methods:** Thirty adult male albino rats were used and divided into control and experimental groups. The latter group was equally subdivided into two subgroups (IIA & IIB). Rats of subgroups IIA &IIB were given 200 mg/kg/day valproate sodium &100 mg /kg/ day phenytoin for five weeks via gastric tube respectively. After five weeks, blood samples of all rats were taken for hormonal assay, then all rats were sacrificed and specimens of thyroid glands were extracted and processed for histological and morphometric studies.

**Results:** In subgroup IIA (valproate- treated group), hormonal assay clarified mild significant decrease in serum T3 & T4 with decrease in free thyroxine (FT4) and increased of thyroid stimulating hormone (TSH). Mild thyroid follicles changes were revealed with mild interstitial exudate and amalgamated highly stained colloid in some follicular lumen. Morphometric study showed increased follicular epithelial height and decreased dimensions of follicles.

While in subgroup IIB (phenytoin-treated group), hormonal assay showed moderate significant decrease in serum T3&T4 with decreased of (FT4) and non significant changes in TSH level. Also, revealed signs of thyroid follicles destruction as, disrupted follicles with desquamated follicular cells in their lumen and severe interstitial exudate. Highly vacuolated cytoplasm in the follicular cells and amalgamated scanty colloid in the follicular lumen were seen. Morphometric study demonstrated decreased follicular epithelial height and dimensions of follicles.

**Conclusion:** Study clarified less damaging effects of valproat sodium versus that of phenytoin on the thyroid gland and its hormones. So, use of these drugs should be justified in clinical situation under direct medical supervision.
Fifth research

Effect of Aromatase Inhibitors on the Endometrium and Ovary with their Possible Role on Ovulation in Adult Albino Rats: A Histological, Immunohistochemical, Morphometric and Hormonal Assay

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ABSTRACT

Introduction: Aromatase inhibitors act by inhibiting estrogen synthesis and depletion of its concentrations in the circulation.

Aim of the work: To study the effect of exemestane and letrozole, on the endometrium and ovary with their possible role on ovulation in adult albino rats.

Material and Methods: Thirty adult female albino rats were used and divided into control and experimental group. In subgroup IIA each rat was given 1mg/kg/daily exemestane and in subgroup IIB each rat was given 5 mg/kg/daily letrozole via gastric tube for 5 consecutive ovarian cycles in both control and experimental groups. Specimens from their ovaries and endometrium were taken and prepared for hematoxylene and eosin stain and immunohistochemical for VEGF study. Morphometric study of endometrial thickness and surface area percentage of immunoreaction in the endometrium was evaluated. Hormonal assay of luteinizing hormone and Follicular stimulating hormone was determined.

Results: Significant decrease in endometrial thickness in exemestane-treated group. Letrozole-treated group revealed significant thickened endometrium. Exemestane-treated group showed marked disturbed ovarian architecture in the form of thickened germinal epithelial cell layer and multiple corpora lutea with atretic follicle. Letrozole-treated group revealed ovarian cortex with multiple stages of follicular development. The VEGF immune-reaction of letrozole-treated group showed significant highly positive cytoplasmic reaction. Significant decrease in LH level in exemestane group and significant increase in the letrozole group were detected.

Conclusion: It is concluded that letrozole improved the endometrial thickness and may give a hand in ovulation induction. In contrary, exemestane led to disruption of the endometrium and ovary. Therefore, not all AIs could help in ovulation.
Sixth research

Histological Changes of the Albino Rat Cerebellar Cortex under the Effect of Different Doses of Tramadol Administration

By

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Abstract

Background: Tramadol hydrochloride is centrally acting synthetic analgesic used to treat moderate to severe pain with wide range applications.

Aim of the work: This study was designed to investigate the effect of tramadol on the histology of the cerebellar cortex in adult albino rats.

Materials and methods: Thirty adult male albino rats weighed about 200 grams were used and divided into control and experimental groups. The latter group was subdivided into two subgroups (IIa&IIb). Rats of subgroup IIa &IIb were injected intraperitoneally with 0.7 mg &1.8 mg as single daily dose of tramadol solution for 2 weeks respectively. Rats were sacrificed after 2 weeks and decapitated. The cerebellum was removed and subjected to histological, immunohistochemical and morphometric studies.

Results: Histological study of subgroup IIa revealed mild Purkinje cells distortion with destructed mitochondria and cisternea of rER . Meanwhile, subgroup IIb showed Purkinje cells arranged in multilayer cells with obvious damaging criteria as small nucleus with indented membrane. Granular layer contained small cells most of which lost their nuclei where as others showed condensed chromatin with thin rim of cytoplasm.
Results of inducible Nitric Oxide Synthase (iNOS) reaction revealed moderate positive cytoplasmic reaction of granular and Purkinje cells in subgroup IIa. However, subgroup IIb showed highly positive cytoplasmic reaction.
Morphological study of the cerebellar layers thickness revealed significant decrease in thickness of Purkinje and granular layers with significant increase in the thickness of molecular layer in both experimental subgroups. As regards Purkinje cell count it revealed significant decrease in its number in both experimental subgroups.

Conclusion: Results of this study provided evidence that tramadol intake has neurotoxic effect on cerebellar structure in an ascending manner according to the administered dose. So, The Ministry of Health must direct their efforts to control dealing of this drug among teenagers and correct misconceptions about this medication.
Seventh research
Effect of Nandrolone Decanoate Drug on the Testis in Adult Male Albino Rats
(Light and Electron microscopic study)

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ABSTRACT

**Background**: Anabolic-androgenic steroid (AAS) compounds are widely abused with the goal of improving athletic ability and appearance. It was found that these compounds have side effects on both humans and animals.

**Aim of the work**: The present study was performed to evaluate the effects of nandrolone decanoate (ND) drug on the testis of adult male albino rats.

**Material and Methods**: Forty adult male rats were used and divided into: Control group I (10 animals), subdivided into control subgroup IA which received no medication & control subgroup IB which was injected by peanut oil intramuscularly/week for 10 weeks. Experimental group II (30 animals): subdivided into experimental subgroup IIA [injected by nandrolone decanoate drug (10mg/kg) intramuscularly/week for 10 weeks] and experimental subgroup IIB [received the same dose of drug for the same period then left without injection for 8 weeks]. At the end of the experiment the testes specimens were removed and processed for light and electron microscopic study.

**Results**: In experimental subgroup IIA, microscopic examination of the testes revealed that most of the seminiferous tubules were atrophied with depleted and disorganized germinal epithelial lining. There was detachment of spermatogonia from the basement membrane and the surrounding germ cells with atrophy in some germ cells leaving empty spaces. Sertoli and Leydig cells were also affected. In experimental subgroup IIB, there was some sort of self recovery.

**Conclusion**: Administration of ND drug at high doses provoked negative action on the histology of the testis; hence impairment of their functions could be predicted. After stoppage of drug administration, there was some sort of self recovery.
Eighth research

Effect of Leflunomide on the Lung of Adult Albino Rats and Role of Pentoxifylline Co-administration: A Histological and Morphometric Study

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ABSTRACT

Background: Leflunomide is an immunosuppressive compound that is effective in the treatment of autoimmune disease and rheumatoid arthritis. It has anti-inflammatory and anti-proliferative properties. Pentoxifylline is used to treat vascular and cerebrovascular disorders.

Aim of the work: This work aimed to study the structural changes in the lung of adult albino rats after administration of leflunomide alone and in combination with pentoxifylline using histological and morphometric study.

Materials and methods: In this study forty adult albino rats were used. They were divided into two groups, control and experimental. The latter group was subdivided into three equal subgroups. Each rat in subgroup IIA received 50 mg/kg/day pentoxifylline. In subgroup IIB, each rat received 2.5 mg/kg/day leflunomide. In subgroup IIC, each rat received co-administration of 50 mg/kg/day pentoxifylline and 2.5 mg/kg/day leflunomide. All animals were sacrificed at the end of the experiment, after eight weeks. Specimens from the lung was taken and prepared for light and transmission electron microscopes and morphometric study for thickness of the inter-alveolar septa.

Results: H&E stained sections of subgroup IIB revealed a marked alternation in lung histological structure as; many alveoli appeared collapsed with thickened inter-alveolar septa. Cellular infiltration of interstitial tissue and the inter-alveolar septa with mononuclear cells and extravasated RBCs in the alveolar lumen could be detected. On the other hand, examination lung section of subgroup IIC revealed that most of the changes which were observed in the previous group decreased but did not disappear completely. Electron microscopic results of subgroup IIB revealed degeneration of type II pneumocytes as; destructed mitochondria with damaging of their cristae, lamellar bodies appeared to be deprived from their secretory surfactant material with many nuclear changes. There was interstitium inflammatory cells infiltration. While in subgroup IIC, most of the observed changes in leflunomide treated group were decreased. There was a highly statistically significant increase in the mean thickness of the inter-alveolar septa in leflunomide treated rats compared to
control rats. Meanwhile, a non-statistically significant increase was noticed in subgroup IIC.

**Conclusion:** It can be concluded that administration of leflunomide could induce structural alterations in the lung and pentoxifylline can ameliorate this alterations. So, long-term administration of leflunomide must be used with caution or with pentoxifylline as a prophylactic therapy against possible lung destruction.