Role of dexamethasone in correction of liver functions following oral administration of paraquat in male albino rats

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Abstract : This study was conducted to evaluate the therapeutic potency of dexamethasone (Dx) in the adjustment of liver function tests in experimental paraquat (PQ)- induced oxidative stress in male albino rats. Three groups of rats were subjected to this trial, control, PQ group (50 mg/ kg orally) and PQ with Dx (50 mg/ kg orally, 4 mg/ kg ip. respectively) throughout 15 days. Results revealed that treatment with PQ caused a mortality rate in a ratio of 30%, increased *($p \leq 0.05$)* glucose, cholesterol, bilirubin concentrations and alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase and amylase active ties but the concentrations of both triglycerides and serum proteins were reduced compared with control whereas the treatment of PQ- treated rats with Dx improved the mortality rate and corrected the activity of serum transaminases, alkaline phosphatase enzymes whereas Dx treatment induced an elevation in amylase activity in addition to the elevation of concentrations of total cholesterol, total protein and albumin in comparison with values of PQ- treated rats, Dx did not affect the concentration of glucose. In conclusion, the treatment of PQ- induced toxicity with Dx in rats was efficient in correction of most liver functions tests.

Key words: dexamethasone, paraquat, enzymes, rat

Introduction

Paraquat (PQ) [1,1- dimethyl 4,4- bipiridillium] is widely spread non- selective contact herbicide. However, PQ is highly toxic to human and animals, in Asia and Africa since 1960, mortality in human due to paraquat intoxication was about 300000 case/ year. A ratio of 40- 60% of acute poisoning perish within 24- 72 hours while sub acute cases perishes throughout a few weeks (Eddleston and Phillips, 2004; Roberts *et al.*, 2011). Oral intoxication with PQ is the most common route in mammals resulting in acute inflammation in throat and gut, liver and kidney necrosis in addition to the fibrosis of pneumocytes that is considered the target organ (Goel and Aggarwal, 2007) depending on PQ ability to promote redox reactions and create a heavy pool of reactive oxygen species (ROS) (Yang and Tiffany-castiglioni, 2007) which is the cause of oxidative stress and lipid peroxidation (Gawarammana and Buckley, 2011). Some reports of PQ poisoning observed a cases of hepatotoxicity including degeneration and necrosis of hepatocytes (Dinis- Oloveira *et al*., 2008). Studies which concern PQ poisoning did not touch a successful treatment with an antagonizing mechanism of action, so treatments were limited on using only antioxidants and

hemodialysis (Ayse *et al*., 2010). Dexamethasone (Dx) is well known drug used as immunosuppressant, it is an artificial drug affiliates to the glucocorticoides hormones, it's activity is about 20- 30 folds more than cortisol. Dx used as anti-inflammatory and anti allergic drug as well as the treatment of odema. Studies referred to that Dx has some antioxidant properties based on reduction of malondialdehyed (MDA) and elevation of superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GSH-PX) during treatment with Dx in both plasma and tissues (Ayse *et al*., 2010). Because of the fatal impact of PQ on human and animals, and loss o f respective treatment (Wesseling *et al*., 2001) also there was no studies on the advantages of the use of Dx to treat PQ poisoning (Gawarammana and Buckley, 2011). The present study aimed to evaluate the hazardous effects of PQ on liver function and the effect of Dx in correction of disturbed liver functions indices resulted from the treatment with acute dose of PQ in male albino rats.

Materials and Methods

Animals: Thirty adult albino male rats with age ranged 70-90 days and weight 210 -245 g and they were divided into three groups (10 rats/ group) and kept in rat cages in controlled temperature (22 ±3ºC) and light:dark cycle (12:12 hours). Animals supplied with diet and drinking water *ad libitum*, diet ingredients were got from market and mixed in order to match the nutritional requirements of rats.

Treatments comprised of i) control: treated with distilled water by oral intubation and injected with normal saline (0.9 % NaCl) ip. daily for 15 days, ii) PQ group: Treated with PQ by oral intubation (50 mg/ kg) (Dere and Polat, 2001) daily for 15 days and iii) PQ +Dx group: treated with PQ by oral

intubation (50 mg/ kg) and injected with Dx (4 mg / kg) (Veals *et al*., 1977) ip daily for 15 days.

The duration of treatment (15 days) was based on a preliminary study which revealed that 15 days was the more suitable period with minimum mortality rate.

Blood samples: Blood was collected from 12- hour fasting rats through retro- orbital vein using capillary tubes at times, 0, 7 and 15 days. Blood obtained in centrifuge test tubes, permitted for complete coagulation then centrifuged at 1500 rpm for 20 minutes using Wagtech, UK centrifuge, serum aspirated using Pasteur pipettes and preserved at -18º C.

Liver function tests: Transaminases and alkaline phosphatase (ALP) activity were estimated using commercial kits (Bio MERIEUX, France) whereas glucose, total cholesterol (TC), triglycerides (TG), total bilirubin and albumin estimated using kits (Fabricant Biolabo SA, France). Absorbance was detected using spectrophotometer UV/VIS Biotech 2601, UK. Amylase activity was estimated using Reflotron® plus chemistry analyzer, Roche, USA. Total protein (TP) was estimated using Biuret method whereas globulin concentration calculated according to Burtis and Ashwood, (1999).

Statistical analysis

Data were subjected to analysis of variance (Steel and Torrie, 1980), differences were

obtained using two ways- Duncan multiple test (Duncan, 1955) in P≤0.05.

Results

Treatment with Dx overcame the fatal effect of PQ which was seen in PQ– treated group and caused 30% mortality in rats since 5th day of treatment.

Table (1): Effect of PQ with or without Dx on serum glucose

Glucose (mg/ 100 ml)			
Time / Treatment	**Zero**	**7 days**	**15 days**
Control	77.71 ±3.82 ***c***	79.37 ± 2.93 ***c***	77.71 ± 3.82 ***c***
PQ	77.64 ± 5.26 ***c***	108.13 ± 6.58 ***b***	123.73 ± 2.49 ***a***
PQ+ Dx	73.27 ± 6.25 ***c***	103.66 ± 5.71 ***b***	119.34 ± 3.45 ***a***
TC (mg/ 100 ml)			
Time / Treatments	**Zero**	**7 days**	**15 days**
Control	91.78± 1.28 ***d***	90.20± 2.67 ***d***	90.06± 0.72 ***d***
PQ	91.06± 2.34 ***d***	104.65± 1.80 ***c***	140.13± 1.13 ***b***
PQ+ Dx	90.74± 0.55 ***d***	106.27± 1.55 ***c***	202.50± 3.12 ***a***
TG (mg/ 100 ml)			
Control	75.24± 0.80 ***cd***	77.34± 1.30 ***c***	81.32± 0.63 ***bc***
PQ	71.55± 1.56 ***d***	69.12± 0.88 ***d***	71.46± 3.03 ***d***
PQ+ Dx	71.08± 0.95 ***d***	85.88± 0.89 ***b***	93.22± 1.85 ***a***

Values expressed as mean ± SE.

- Different letters in a row or column refers to significance (p≤0.05)
- n = 10

A significant (p≤0.05) elevation in serum glucose in PQ- treated group at 7th day was observed compared to either control or zero value, this value elevated at 15th day however the treatment of PQ- treated group with Dx did not reflect any change in glucose concentration in comparison with PQ- treated group (table 1). An elevation in TC resulted from the treatment with PQ at 7th day compared to both control and zero

day, TC elevated significantly in the same group at 15th day compared to values of zero, 7th day and control. No significance observed in TC of PQ+ Dx- treated group at 7th day compared to PQ– treated group whereas this group showed an elevation in TC concentration at 15th day compared to PQ- treated group to represent the higher TC value among the three groups throughout 15 days (table 1). The concentration of TG started to reduce since the 7th day compared to control as a result of oral intubation with PQ and continued in the same manner till the end of treatment in comparison with control. However, the injection of PQ-treated group with Dx in the PQ+ Dx group led to a gradual elevation of TG since 7th day compared to either control or zero day, this value showed the more significant elevation at 15th day compared to zero, PQ-treated group, control and 7th day values.

Table (2): Effect of PQ with or without Dx on serum proteins and bilirubin.

TP (g/ 100 ml)			
Time / Treatments	**Zero**	**7 days**	**15 days**
Control	8.93± 0.07 ***c***	8.89± 0.16 ***c***	8.79± 0.06 ***c***
PQ	8.98± 0.08 ***c***	9.47± 0.06 ***b***	7.02± 0.03 ***d***
PQ+ Dx	8.90± 0.11 ***c***	7.72± 0.14 ***cd***	12.51± 0.59 ***a***
Albumin (g/ 100 ml)			
Control	5.21± 0.08 ***b***	5.16± 0.08 ***b***	5.08± 0.15 ***b***
PQ	5.23± 0.11 ***b***	4.46± 0.06 ***c***	4.39± 0.13 ***c***
PQ+ Dx	5.17± 0.12 ***b***	5.06± 0.07 ***b***	7.63± 0.06 ***a***
Globulin (g/ 100 ml)			
Control	3.72± 0.02 ***c***	3.73± 0.03 ***c***	3.71± 0.05 ***c***
PQ	3.75± 0.03 ***c***	5.01± 0.04 ***a***	2.63± 0.36 ***d***
PQ+ Dx	3.73± 0.01 ***c***	2.66± 0.03 ***d***	4.88± 0.05 ***b***

Total bilirubin (mg/ 100 ml)			
Time / Treatments	**Zero**	**7 days**	**15 days**
Control	0.21± 0.001 ***b***	0.20± 0.011 ***b***	0.21± 0.007 ***b***
PQ	0.020± 0.006 ***b***	0.31± 0.008 ***a***	0.31± 0.009 ***a***
PQ+ Dx	0.20± 0.008 ***b***	0.20± 0.005 ***b***	0.19± 0.004 ***b***

- Values expressed as mean ± SE.
- Different letters in a row or column refers to significance ($p \leq 0.05$)
- n = 10

An elevating effect of PQ to TP and globulin ($p \leq 0.05$) observed compared to either control, zero day or PQ+ Dx groups after 7 days of treatment. However TP in turned to drop after 15 days significantly ($p \leq 0.05$) in relation to both control and zero values whereas the concentration of TP in the PQ+ Dx group revealed a statistical elevation to be the higher value in comparison with control and PQ- treated groups. On the other hand, albumin reduced at 7^{th} day of treatment in the PQ- treated group compared to control and zero values to keep on same level throughout the next 7 days yet the treatment with both PQ and Dx did not show any significant altrations at the 7^{th} day of treatment however this value elevated over the other two groups at 15^{th} day in the same manner of TP mentioned above, also the concentration of serum globulin observed in the current study was parallel to that of TP (Table 2). The treatment with PQ revealed an elevation ($p \leq 0.05$) in total bilirubin concentration since 7^{th} day till the end of experiment relative to either control or zero values, in the same time, injecting PQ-treated rats with Dx was efficient to correct bilirubin level to be around the value of control in both 7^{th} and 15^{th} days (Table 2).

Table (3): Effect of PQ with or without Dx on serum enzymes.

ALT (U/ L)			
Time / Treatments	**Zero**	**7 days**	**15 days**
Control	20.60± 0.81 ***d***	21.80± 1.65 ***d***	23.20± 1.46 ***d***
PQ	20.80± 1.65 ***d***	44.0± 0.63 ***b***	58.60± 0.92 ***a***
PQ+ Dx	22.60± 1.50 ***d***	25.80± 0.73 ***c***	45.40± 1.40 ***b***
AST (U/ L)			
Control	48.49± 1.77 ***ab***	46.91± 3.53 ***a-c***	40.56± 1.66 ***c***
PQ	42.02± 1.58 ***bc***	48.77± 1.18 ***ab***	50.24± 2.99 ***a***
PQ+ Dx	45.39± 1.54 ***a-c***	41.64± 2.78 ***bc***	40.24± 2.99 ***c***
ALP (U/ L)			
Control	113.20± 7.44 ***dc***	114.60± 5.35 ***dc***	113.0± 5.80 ***dc***
PQ	113.20± 3.71 ***dc***	171.0± 16.12 ***a***	173.40± 4.44 ***a***
PQ+ Dx	111.0± 7.54 ***d***	118.0± 12.60 ***c***	151.60± 9.55 ***b***
Amylase (U/ L)			
Control	955± 17.96 ***c***	930± 12.31 ***c***	952± 8.02 ***c***
PQ	958± 13.49 ***c***	1037± 17.32 ***b***	1049± 29.04 ***b***
PQ+ Dx	938± 8.68 ***c***	653± 16.22 ***d***	1168± 29.09 ***a***

- Values expressed as mean ± SE.
- Different letters in a row or column refers to significance ($p \leq 0.05$).
- n = 10

As considered with serum enzymes, the treatment with PQ caused an increase in the activities of ALT and ALP since 7th day till the end of experiment compared to either control or zero values with a statistical elevation ($p \leq 0.05$) of the value of 15th day

compared with that of 7th day. In the same time, the activity of both ALT and ALP elevated in the group exposed to PQ+ Dx at the 7th day relative to zero day and at 15th day relative to both control group or zero time however both values of this group still significantly ($p \leq 0.05$) less than that of PQ-treated group (Table 3). AST elevated only at 15th day as a result of treatment with PQ compared to control and zero time but the treatment of PQ- intoxicated rats with Dx was successful to correct the elevated activity AST to be statistically less than the value of PQ- treated group and around those of control and zero time. Amylase activity elevated in the PQ- treated group at 7th day compared to control and zero time to keep on same manner till the end of experiment while amylase activity observed in the group treated with both PQ and Dx declined at 7th day significantly ($p \leq 0.05$) beyond those of control and zero time however this value inturned to elevate to represent the higher activity compared with control throughout the duration of experiment (Table 3).

Discussion

The mortality- limiting impact of Dx may be due to the anti- inflammatory effect particularly on target organ, lung which considered the main cause of death (Ayse *et al.,* 2010). One of the results of PQ treatment and subsequent oxidative stress is hyperglycemia (Gawaramanna and Buckley, 2011). PQ might be metabolized through enzymatic systems leading to formation of PQ^{+} which rapidly in turns to PQ^{2+} elaborating superoxide anion $O2^{-}$. Oxygen acts as an electron receiver, the process responsible for formation of hydroxyl radical (OH^{-}). In this stage, nitric oxide NO^{-} binds with $O2^{-}$ resulting in peroxynitrite $ONOO^{-}$ (Ahmad *et al.,* 2008). The state of oxidative stress plays a role in the creation of insulin resistance (Kimura *et al.,* 2010) which can be explained as a result of the inhibitory action of ROS on the gene of insulin receptors in addition to the destructive action of ROS on molecules that promotes insulin secretion (Kimura *et al.,* 2007). Also there will be an impeding in glucose entry to the cells (Mahadev *et al.,* 2001). The adverse effect of Dx on serum glucose was more pronounced in the cases of hyperglycemia irrespectively to the reasons, this effect of Dx may limit insulin secretion (Cecil *et al.,* 1997) also Dx exerts a negative effect on phosphatidyle inositol 3-kinase (Weinstein *et al.,* 1995), it may be attributed to the administration of Dx in repetitive doses throughout the period the trial. Results related to TC can be explained as a result of PQ– induced oxidative stress and subsequent LDL oxidation, apo- proteins in LDL oxidized leading to incompatibility of LDL to there receptors on the cells (Stevinkel *et al.,* 2004) on the other hand, Dx- induced hypercholesterolemia might be related to the interference of Dx with monocytes function in removing excess cholesterol as well as to the inhibition of cholesteryl esters hydrolysis and nitric oxide synthase (Severino *et al.,* 2002). Related to TG, the high consumption of it will be an alternative source of energy in the states of stress (Akinloye *et al.,* 2011). Regarding to the effect of Dx on TG, the elevation is due to the action of Dx in promoting TG- rich VLDL formation on one aspect and inhibiting lipoprotein lipase on the other aspect (Plonne *et al.,* 2001). As considered with serum proteins, the decline might be attributed to the PQ- induced depletion of blood proteins and defective

protein synthesis in the endoplasmic reticulum in addition to excessive loss of proteins through partially damaged renal system (Jee *et al.,* 2005). Dx injection elevated serum proteins which is in agreement with Simmons *et al.,* (2005) who referred to the impact of Dx in correction of proteolysis. Bilirubin elevated as a net result of ROS and consequence liver fibrosis and proliferation of bile duct endothelium, these effects disturb resistance of sinusoids leading to cholestasis and hyperbilirubinemia (Tuchweber *et al*., 1996). Zhang *et al*., (2011) proposed that either the immunosuppressive activity of Dx, inhibition of ROS and cytokines, improvement of lysosomal membrane or inhibition of proteases induced by Dx may be responsible for bilirubin improvement, another trial demonstrated that Dx has a pronounced antioxidant activity through inhibiting NO formation (DeVera *et al*., 1997) also Dx inhibit antifibrotic mediators secreted from Kuffer cells and sinusoidal epithelium in liver (Melgert *et al*., 2001). As considered with liver enzymes, Akinloye *et al.,* (2011) reported that elevated activity of ALT, ALP and AST refers to hepatotoxicity resulted from ROS activity (Dinis- Oloveira *et al*., 2008). The observations of current study related to incrased amylase activity can be explained as a result of pancreatic dysfunction. The results of Dx treatment on serum enzymes might be related to the anti-inflammatory properties and limiting of vasoactive substances (Ki *et al*., 2005) and aggregation of stimulated macrophages and α- tumor necrotic factor (Ayse *et al*., 2010). Dropping of amylase might be due to secretion of amylase inhibiting factor accompanying hyperlipidemia. Furthermore, Kandil *et al*., (2006) illustrated the reason of amylase decline as that Dx can elevates pancreatitis associated protein II & III mRNA leading to decline in amylase activity however the detrimental effects of PQ might be overcame on the therapeutic potency of Dx in addition to that long term treatment with Dx stimulated the secretory function of pancreatic cells and enlarging secretory granules in rough endoplasmic reticulum raising the level of amylase biosynthesis in pancreas, so Dx might be a useful agent at least in partial correction of liver enzymes which they are a vital determinant in the metabolism and homeostasis of body systems. The conclusion related to the outcomes of present study, authors suppose that the use of Dx in treating PQ intoxication is effective in some extent especially in the emergency with some considerations related to the time of administration and doses which may need a further studies in order to adjust the effective dose with minimal side effects in different species.

References

Ahmad, I., Kumar, A., Shukla, S., Prasad Pandey, H. and Singh, C. 2008. The involvement of nitric oxide in maneb- and paraquat-induced oxidative stress in rat polymorphonuclear leukocytes. Free Radic. Res., **42**(10),849-862.

Akinloye, O. A., Adamson, I., Ademuyiwa, O. and Arowolo, T. A. (2011). Supplementation of vitamins C, E and its combination on paraquat-intoxicated rats: effects on some biochemical and markers of oxide-

tive stress parameters. Journal of Applied Pharmaceutical Science, 10(06), 85-91.

Ayse, Er., Feray, A. G. C., Altan, K. U.,, Bunyamin T, Muammer, E. and Enver, Y., 2010. Effects of enrofloxacin, flunixin and dexamethasone on indicators of oxidative and organ damage in lipopolysaccharide-induced endotoxemia. Journal of Animal and Veterinary Advances., 9 (10), 1495-1500.

Burtis, C.A. and Ashwood, E.R. (1999). "Tietz Textbook of Clinical Chemistry". 3d ed., W.B. Saunders., New York.

Cecil, L., Patric, G. and Jean-Claude, H. (1997). Direct glucocorticoid inhibition of insulin secretion. J. Clin. Invest., 3, 414-423.

De Vera, M. E., Taylor, B. S., Wang, Q., Shapiro, R. A., Billiar, T.R. and Geller, D. A. (1997). Dexamethasone suppresses iNOS gene expression by upregulating I-kappa B alpha and inhibiting NF-kappa B. Am. J. Physiol. 273, 1290-1296

Dere, E. and Polat, F. (2001). The effect of paraquat on the activity of some enzymes in different tissues of mice (Mus musculus - Swiss albino). Turk. J. Biol., 25, 323-332.

Dinis-Oloveira, R. J., Duarte, J. A., Sanchez-Navarro, A., Remiao, F., Bastos, M. L. and Carvalho, F. 2008. Paraquat poisoning mechanisms of lung toxicity: Clinical features and treatment. Crit. Rev. Toxicol., 38, 13-17.

Duncan, D.B. (1955). Multiple range and multiple "F" test. Biometric., 11, 1-42.

Eddleston, M.F. and Phillips, M.R., (2004). Self poisoning with pesticides. BMJ., 328(7430),42-44.

Gawarammana, I.B. and Buckley, N.A. (2011). Medical management of paraquat ingestion.. *British Journal of Clinical Pharmacology., "Accepted article" 10(1111).

Goel, A. and Aggarwal, P. (2007). Pesticide poisoning, Review Article. The National medical Journal of India, 20(4), 152-158.

Jee, L.H., Masroor, F. and Kang, J. (2005). Responses of Cypermethrin induced stress in haematological parameters of Korean rockfish, Sebastes schegeli. Aquac. Res., 36, 898-905.

Kandil, E., Lin, Y-Y., Bluth, M.H., Zhang, H., Levi, G. and Zenilman, M.E. (2006). Dexamethasone mediates protection against acute Pancreatitis via upregulation of pancreatitis-associated proteins. World J. Gastroenterol., 12(42), 6806-6811.

Ki S.H., Choi, D.W., Kim, C.W. and Kim, S.G. (2005). Lack of therapeutic improvement of liver fibrosis in rats by dexamethasone in spite of ascites amelioration. Chem. Biol. Interact., 152, 37-47.

Kimura, K., Katsumata, Y., Ozawa, T., Tawara, S., Igarashi, K., Cho, Y., Shibata, N., Hakuno, F., Takahashi, SI. and Takenaka, A. (2010). Effect of paraquat-induced oxidative stress on insulin regulation of insulin-like growth factor-binding protein-1 gene

expression. J. Clin. Biochem. Nutr., 46(2), 157–167.

Kimura, K., Tawara, S., Igarashi, K. and Takenaka, A. (2007). Effect of various radical generators on insulin-dependent regulation of hepatic gene expression. Biosci. Biotechnol. Biochem., 71,16–22.

Mahadev, K., Zilbering, A., Zhu, L. and Goldstein, B.J. (2001). Insulin-stimulated hydrogen peroxide reversibly inhibits protein-tyrosine phosphatase 1B in vivo and enhances the early insulin action cascade. J. Biol. Chem., 276, 21938–21942.

Melgert, B.N., Olinga, P., Van Der Laan, J.M., Weert, B., Cho, J., Schuppan, D., Groothuis, G.M., Meijer, D.K. and Poelstra, K., (2001). Targeting dexamethasone to Kupffer cells: effects on liver inflammation and fibrosis in rats. Hepatology, 34, 719-728.

Plonne, D., Schulze, H.P., Kahlert, U., Meltke, K., Seidolt, H., Bennett, A.J., Cartright, I.J., Higgins, J.A., Till, U. and Dargel, R. (2001). Postnatal development of hepatocellular apolipoprotein B assembly and secretion in the rat. J. Lipid Res., 42, 1865-1878.

Roberts, D.M., Wilks, M.F., Roberts, M.S., Swaminathan, R., Mohamed, F., Dawson, A., and Buckley, N.A.. (2011): Changes in the concentrations of creatinine, cystatin C and NGAL in patients with acute paraquat self-poisoning. Toxicol. Lett., 202, 69–74.

Severino, C., Brizzi, P., Solinas, A., Secchi, G., Maioli, M. and Tonolo, G. (2002). Low dose dexamethasone in the rat: a model to study insulin resistance. Am. J. Physiol. Endocrinol. Metab., 283, 367-373.

Simmons, C.P., Thwaites, G.E., Quyen, N.T., Chau, T.T., Mai, P.P. and Dung, N.T. (2005). The clinical adjunctive dexamethasone in tuberculosis meningitis is not associated with measurable attenuation of peripheral or local immune responses. The journal of Immunology, 175, 579-590.

Steel, R.G.D. and Torrie, J.H. (1980). "Principles and Procedures of Statistic". 2nd ed., Mc- Graw Hill Book Company., New York.

Stevinkel, P.; Diczfalusg, U.; Lindholm, B. and Heimburger, O. (2004). Phospholipid plasmalogen, asurrogate marker of oxidative stress, is associated with increased cardiovascular mortality. Nephrol. Dial. Tranplant., 19(4), 972-976.

Tuchweber, B., Desmouliere, A., Bochaton-Piallat, M.L., Rubbia-Brandt, L. and Gabbiani, G. (1996). Proliferation and phenotypic modulation of portal fibroblasts in the early stages of cholestatic fibrosis in the rat. Lab. Invest., 74, 265-278

Veals, J.W., Korduba, C.A. and Symchowicz, S. (1977). Effect of dexamethasone on monoamine oxidase inhibition by iproniazid in rat brain. European Journal of Pharmacology, 41(3), 291-299.

Weinstein, S.P., Paquin, T., Pristker, A. and Harber, R.S. (1995). Glucocorticoide induced insulin resistance: dexamethasone inhibits the activation of glucose transport in rat skeletal muscle by both insulin and non insulin related stimuli. Diabetes, 44, 441-445.

Wesseling, C., De Joode, B. VW., Ruepert, C., Leon, C., Monge, P., Hermosillo, H. and Partanen, T.J. (2001). Paraquat in developing countries. Int. J. Occup. Environ. Health., 7, 275–286.

Yang, W. and Tiffany-Castiglioni, E. (2007). The bipyridyl herbicide paraquat induces proteasome dysfunction in human neuroblastoma SH-SY5Y cells. J. Toxicol. Environ. Health., 70(21),1849-1857.

Zhang, X-Q., You, L.J., Ping, J., Liu, Y.Y., Peng, J., Zhang, H.Y., Xu, B.Y. and Mao, Q. (2011). Efficacy of short-term dexamethasone therapy in acute-on-chronic pre-liver failure. Hepatology Researchs. 41(1), 46-53.

دور الديكساميثازون في علاج وظائف الكبد المضطربة جرّاء المعاملة بالباراكوات في ذكور الجرذان البيضاء

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2. كلية الطب البيطري، جامعة الموصل العراق

المستخلص

اجريت الدراسة الحالية لتقويم تأثير الديكساميثازون في تصحيح بعض معايير وظائف الكبد المضطربة جرّاء التسمم التجريبي بالباراكوات والمحدث في ذكور الجرذان البيضاء. شملت التجربة استخدام ثلاث مجاميع من ذكور الجرذان هي على التوالي، السيطرة، مجموعة الباراكوات (50 ملغم/ كغم عن طريق الفم)، مجموعة الباراكوات مع الديكساميثازون (50 ملغم/ كغم عن طريق الفم و 4 ملغم/ كغم في غشاء الخلب) اذ دامت فترة المعاملة 15 يوما. بينت نتائج التحليل الإحصائي أن المعاملة بالباراكوات قد أدت إلى نسبة هلاك بلغت 30% فضلا عن زيادة معنوية في تراكيز الجلوكوز، الكوليستيرول والبيليروبين إضافة الى ارتفاع فعالية الإنزيمات الناقلة للأمين، الفوسفاتاز القاعدي والأمايليز مع انخفاض تراكيز الجليسيريدات الثلاثية وبروتينات مصل الدم معنويا *($p\leq0.05$)* عن مجموعة السيطرة بينما أدت معاملة الجرذان المعرضة للباراكوات بالديكساميثازون إلى الحد من نسبة الهلاك فضلا عن خفض فعالية الإنزيمات الناقلة للأمين، الفوسفاتاز القاعدي وتركيز كل من الجليسيريدات الثلاثية والبيليروبين الكلّي في مصل الدم (*$p\leq0.05$*) بينما ارتفعت فعالية الأمايليز وتراكيز كل من الكوليستيرول الكلي، البروتين الكلّي، الألبومين والغلوبيولين في حين لم يظهر الجلوكوز أي تغير مقارنة بالمجموعة المعاملة بالباراكوات لوحده. يستنتج من الدراسة الحالية أن الديكساميثازون يمكن أن يحد من اضطراب مؤشرات وظائف الكبد الناتج عن المعاملة بالباراكوات.