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EFFECT OF SOME ANTIDIABETIC DRUGS ON BIOCHEMICAL PARAMETERS IN EXPERIMENTALLY INDUCED EPILEPTIC RATS

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ABSTRACT

The present study was conducted to evaluate the effect of glibenclamide and metformin on some biochemical parameters in rats induced epilepsy. Male Wister was induced epilepsy by injection of pentylenetetrazole (PTZ) at a dose 100 mg/kg of body weight, the rats randomly divided into 3 groups (10-12 rat/group). The group 1: leaved without treatment and served as control group; Group 2: was treated with glibenclamide 5 mg/kg.b.w.; Group 3: was treated with metformin 150 mg/kg.b.w. All treatments were once daily for 1 week, blood samples were collected at 3, 24 hours, and week after induced of epilepsy. The results show that treated with PTZ leads to significant decrease in glucose level in all times after treatment, and significantly decreased level of cholesterol after 3 hours, and a week after treatment, while level of albumin was significantly decreased after a week of treatment, also PTZ treatment increased level of aspartate aminotransferase (AST) in all times after treatment, while level of alanine aminotransferase (ALT) was significantly increased after 3 hours, then significantly decreased after a week of treatment. PTZ treatment doesn't show any effect on levels of total protein, and globulin. Treatment with glibenclamide leads to significant increase level of glucose in all times after treatment, also level of cholesterol was significantly increased at 3, 24 hours after treatment with glibenclamide. Level of (AST) was significantly decreased in all times after treatment with glibenclamide, but level of (ALT) was increased only after a week of treatment, glibenclamide don't cause any effect on levels total protein, albumin, and globulin. Treatment with metformin leads to significantly decreased level of glucose after 3, 24 hours of treatment, with significant increase after a week of treatment, while level of cholesterol was significantly increased after 3 hours, and significantly decreased after 24 hours of treatment. Levels of total protein and globulin were increased significantly after 3 hours only, level of albumin significant decrease after 24 hours treatment, also metformin lead to significantly decreased level of (AST) after 3 hours, and significantly increased after a week of treatment, while (ALT) level significantly increased after 24 hour, and week of treatment. These results indicate that glibenclamide and metformin have good roles in control of epilepsy-induced by PTZ in rats through several significant changes of biochemical parameters.

Key words: *Epilepsy, Glibenclamide, Metformin, Biochemical changes, PTZ*

INTRODUCTION

Epilepsy is a disorder of the brain characterized by an enduring predisposion to generate epileptic seizures and by the neurobiologic, cognitive, psychological and social consequences of the condition (Fisher *et al*., 2005). And cause abnormal electrical firing patterns of neurons, and epilepsy is one of the most common and challenging neurologic disorder (Jarrar and Buchhalter, 2003). WHO in 2009 indicate that one seizure does not signal epilepsy (up to 10% of people worldwide have one seizure during their life-time), also epilepsy is one of the world oldest recognized condition, fear, misunderstanding, discrimination and social stigma have surrounded epilepsy for centuries (WHO, 2009). The most carefully indicated that about 1 adult in 200 suffer from recurrent epilepsy (WHO, 2009). The one of the aims of epilepsy is the investigation and treatment of pathological and biochemical changes (Bauer *et al*., 2002).

Metformin (sold as Glucophage) is an oral antidiabetic drug in the biguanide class. It is the first-line drug of choice for the treatment of type 2

diabetes, in particular, in overweight and obese people and those with normal kidney function. (American Diabetes Association, 2009). Metformin has first synthesized and found to reduce blood sugar in 1920s (Bailey, 2004). Its use in gestational diabetes has been limited by safety concerns; it is also used in the treatment of polycystic ovary syndrome (Lord *et al*., 2003). Metformin works by suppressing glucose production by the liver (Bailey, 2004), and it is the only antidiabetic drug that has been conclusively shown to prevent the cardiovascular complications of diabetes. It helps reduce LDL cholesterol and triglyceride levels, and is not associated with weight gain, as of 2010, metformin is one of only two oral antidiabetics in the World Health Organization Model List of Essential Medicines (the other being glibenclamide). Metformin is used for non-alcoholic fatty liver disease (NAFLD) (Marchesini *et al*., 2001) and premature puberty, (Ibáñez *et al*., 2006).

Glibenclamide also known as glyburide, it is an antidiabetic drug , and was the 2nd generation of a medications known as sulfonylureas, It was developed in 1966 (Marble, 1971). It is used in the treatment of type 2 diabetes. As of 2011, it is one of only two oral antidiabetics in the World Health Organization Model List of Essential Medicines (the other being metformin). (WHO Expert Committee, 2011), additionally, recent research shows that glibenclamide improves outcome in animal stroke models by preventing brain swelling (Simard *et al*., 2006), and enhancing neuroprotection (Serrano-Martín *et al*., 2006). A retrospective study showed that in type 2 diabetic patients already taking glyburide, NIH stroke scale scores on were improved on discharge compared to diabetic patients not taking glyburide. (Meloni and Meloni, 1996).

The aims of present are to investigate the effects of oral antidiabetic drugs; metformin and glibenclamide on some biochemical parameters in rats induced epilepsy by pentylenetetrazole (PTZ).

MATERIALS and METHODS

Animals

The study was performed on male Wister albino rats, with mean body weight about (160-250 gm.) and average age of (2-2.5 months). The animals were housed in groups of (12 per cage), in a room with a controlled light/dark cycle (12 hrs light /12 hrs dark) at (22 ± 2°C) and were allowed free access to diet and tap water during the entire experimental period.

Induction of epilepsy in rats

PTZ (Sigma, Germany) was dissolved in saline at 100mg/ml and administered to all three groups of rats subcutaneously (S.C.) under the loose skin behind the neck in a single dose (100 mg/kg B.W. in a volume of 0.1 ml/100 gm. B.W.) (Khosla and Pandhi, 2001). Approximately 6-28 min. after PTZ injection, most of the animals entered status epilepticus.

Experimental design

Rats were divided into 3 groups: group1; were served as control, Group 2; were treated with glibenclamide (Medochmic LTD-Cyprus) at a dose of 5 mg tablet (5 mg /kg of body weight) (Mahomed and Ojewole, 2003), Group 3; were treated with metformin at dose 800 mg tablet (150 mg/kg of body weight) (Majithiya and Balaraman, 2006). Glibenclamide and metformin were given as a suspension orally by gavages needle. All treatment was once daily and lasted for one week.

Samples collection and biochemical analysis

Blood samples were collected from the retro-ocular vein (Fox *et al*., 1984) into clear dry centrifuge tubes after 3 hrs, 24 hrs, and 1 week, allowed clotting; serum was separated after centrifugation at 3000 rpm for 15 minute. Serum glucose, total cholesterol, total protein, albumin, AST, ALT levels was enzymatically measured using standard enzymatic assay kit (Biolabo reagents, France) and globulin level was estimated mathematically by subtracting albumin from total protein (Gill *et al*., 2000).

Globulin concentration (gm/100ml) = Total protein – Albumin

Statistical analysis: All data analyzed by one way analysis of variance, the specific group differences were determined using Duncan multiple range test; the accepted level of significance was $P< 0.05$ (Bruning and Kintz, 1977).

RESULTS

Table (1) show that treatment with PTZ leads significantly to decrease the serum glucose level after 3, 24 hours and week, also the table show when treatment with glibenclamide lead to significant increase of serum glucose level after 3, 24 hours and week when compare with control group. But when rats treated with metformin lead to decrease serum glucose level after 3, 24 hours, while increases after a week and return near to normal.

Treatment with PTZ leads to significant decrease of serum TC level after 3 hours, and week, while glibenclamide, and metformin treatment leads to significant increase after 3, 24 hours, without effect after week (Table 2).

PTZ treatment don't have any significant effect on serum TP level, but glibenclamide lead to significant decrease after 24 hours only, while metformin significant increase serum TP level after 3 hours only (Table 3).

Table (4) indicate that treatment with PTZ leads to significant decrease the serum albumin after week without any significant effect on other times, glibenclamide don't cause any significant effect on serum albumin level, while metformin treatment lead to decrease serum albumin after 24 hours only.

(Table 5) show that treatment with PTZ doesn't have any effect on serum globulin level. Glibenclamide treatment leads to decrease serum globulin level only after 3 hours when compare with zero time, also metformin treatment leads to decrease serum globulin level only after 3 hours but when compare with control group.

Serum ALT level were increased after 3, 24 hours, and week when rats treated by PTZ. Also this table indicates that serum level of ALT are decreased after treatment by glibenclamide after 3, 24 hours, and week, while treatment by metformin leads to decrease serum ALT level after 3 hours, but this level increases after week of treatment (Table 6).

Table (7) show that serum level of AST were increased after 3 hours, and week, while glibenclamide treatment leads to increase serum AST level after week only, but the group that treated by metformin causes increase level of serum AST after 24 hours and week.

Table 1: Effect of glibenclamide, metformin on serum glucose level (mmol/L) in PTZ treated rats.

Groups	Zero Time	After inducing epilepsy		
		3 hrs.	24 hrs.	1 week
Control	**F**	**CDE**	**BC**	**CD**
	4.23 ± 0.09	3.44 ± 0.22	2.86 ± 0.18	3.24 ± 0.23
Glibenclamide	**F**	**F**	**DFE**	**F**
5 mg /kg**.b.w**	4.47 ± 0.22	4.6 ± 0.23	3.97 ± 0.19	4.31 ± 0.08
Metformin	**EF**	**A**	**AB**	**F**
150 mg/kg.b.w	4.05 ± 0.16	1.96 ± 0.42	2.42 ± 0.41	4.64 ± 0.17

No. of mice (12-14) in each group
Data is the mean ± SEM
Different letters indicate significant differences between groups horizontally and vertically at $P < 0.05$

Table 2: Effect of glibenclamide, metformin on serum cholesterol level (mg/dl) in PTZ treated rats.

Groups	Zero Time	After inducing epilepsy		
		3 hrs.	24 hrs.	1 week
Control	**CD**	**AB**	**CD**	**AB**
	86.56 ± 6.02	64.01 ± 9.86	88.56 ± 9.3	58.91 ± 6.03
Glibenclamide	**CDE**	**EF**	**F**	**BC**
5 mg /kg.b.w	93.81 ± 6.28	104.49 ± 5.77	124.14 ± 2.99	77 ± 4.52
Metformin	**DE**	**EF**	**AB**	**A**
150 mg/kg.b.w	101.14 ± 4.36	109.29 ± 4	59.36 ± 1.9	56.41 ± 5.4

No. of rats (12-14) in each group
Data is the mean ± SEM
Different letters indicate significant differences between groups horizontally and vertically at $P < 0.05$

Table 3: Effect of glibenclamide, metformin on serum total protein level (g/dL) in PTZ treated rats.

Groups	Zero Time	After inducing epilepsy		
		3 hrs.	24 hrs.	1 week
Control	**CDE** 5.99 ± 0.30	**ABC** 4.91 ± 0.47	**CDE** 5.71 ± 0.25	**BCD** 5.1 ± 0.44
Glibenclamide 5 mg /kg.b.w	**CDE** 5.71 ± 0.29	**A** 3.92 ± 0.18	**AB** 4.32 ± 0.16	**BCD** 5.34 ± 0.22
Metformin 150 mg/kg.b.w	**BCD** 5.24 ± 0.42	**E** 6.67 ± 0.13	**DE** 6.22 ± 0.6	**CDE** 6.04 ± 0.49

No. of rats (12-14) in each group
Data is the mean ± SEM
Different letters indicate significant differences between groups horizontally and vertically at $P < 0.05$

Table 4: Effect of glibenclamide, metformin on serum albumin level (g/dL) in PTZ treated rats.

Groups	Zero Time	After inducing epilepsy		
		3 hrs.	24 hrs.	1 week
Control	**D** 3.55 ± 0.26	**D** 3.44 ± 0.11	**D** 3.39 ± 0.20	**AB** 2.71 ± 0.19
Glibenclamide 5 mg /kg.b.w	**D** 3.66 ± 0.09	**BCD** 3.21 ± 0.15	**A-D** 3.09 ± 0.1	**A-D** 3.11 ± 0.22
Metformin 150 mg/kg.b.w	**A-D** 3.03 ± 0.11	**CD** 3.30 ± 0.18	**A** 2.6 ± 0.23	**ABC** 2.79 ± 0.12

No. of rats (12-14) in each group
Data is the mean ± SEM
Different letters indicate significant differences between groups horizontally and vertically at $P < 0.05$

Table 5: Effect of glibenclamide, metformin on serum globulin level (g/dL) in PTZ treated rats.

Groups	Zero Time	After inducing epilepsy		
		3 hrs.	24 hrs.	1 week
Control	**BCD** 2.44 ± 0.5	**AB** 1.53 ± 0.42	**BCD** 3.31 ± 0.23	**BCD** 2.39 ± 0.51
Glibenclamide 5 mg /kg.b.w	**BCD** 2.25 ± 0.23	**A** 0.69 ± 0.19	**AB** 1.23 ± 0.08	**ABC** 2.03 ± 0.49
Metformin 150 mg/kg.b.w	**ABC** 2.03 ± 0.42	**CD** 3.36 ± 0.3	**D** 3.62 ± 0.81	**CD** 3.26 ± 0.53

No. of rats (12-14) in each group
Data is the mean ± SEM
Different letters indicate significant differences between groups horizontally and vertically at $P < 0.05$

Table 6: Effect of glibenclamide, metformin on serum AST level (IU/L) in PTZ treated rats.

Groups	Zero Time	After inducing epilepsy		
		3 hrs.	24 hrs.	1 week
Control	**AB** 5.74 ± 0.25	**E** 13.32 ± 1.02	**DE** 12.28 ± 0.44	**CD** 9.96 ± 1.27
Glibenclamide 5 mg /kg**.b.w**	**A** 5.42 ± 0.29	**BC** 8.12 ± 0.4	**BC** 8.06 ± 0.53	**AB** 6.84 ± 0.41
Metformin 150 mg/kg.b.w	**AB** 6.44 ± 0.36	**ABC** 7.9 ± 1.01	**DE** 12.30 ± 1.19	**F** 21.28 ± 1.16

No. of rats (12-14) in each group
Data is the mean ± SEM
Different letters indicate significant differences between groups horizontally and vertically at $P < 0.05$

Table 7: Effect of glibenclamide, metformin on serum ALT level (IU/L) in PTZ treated rats.

Groups	Zero Time	After inducing epilepsy		
		3 hrs.	24 hrs.	1 week
Control	**BC** 242 ± 14.95	**DE** 317 ± 25.06	**AB** 224 ± 5.5	**A** 185 ± 4.4
Glibenclamide 5 mg /kg.b.w	**CD** 286 ± 6.1	**CD** 281 ± 17.71	**BC** 248 ± 19.6	**E** 339 ± 9.01
Metformin 150 mg/kg.b.w	**CD** 277 ± 7.6	**CD** 281 ± 19.25	**CD** 280 ± 5.61	**BC** 252 ± 20.82

No. of rats (12-14) in each group
Data is the mean ± SEM
Different letters indicate significant differences between groups horizontally and vertically at $P < 0.05$

DISCUSSION

Pentylenetetrazole PTZ has been used widely to produce the animal model of chemically induced seizure, because this model is highly sensitivity for comparing different chemical under standardized conditions (Shafaroodi *et al*., 2004).

This study indicates that epilepsy which induced by PTZ in rats caused significant decrease after 3, 24 hours, and after week, this result are agreement with (Yuzo *et al*., 1998), which indicate that spontaneous epileptic rats showed decrease in serum glucose level are due to the frequent occurrence of tonic convulsion and wild jumping associated with low body weight. Our results were disagree with (Ali *et al*., 2012; Schwechter *et al*., 2003), they found that in adult rats susceptibility to clonic and tonic, clonic induced seizures was positively correlated with blood glucose concentration, as the increase glucose concentration was associated with proconvulsant effects. Also this result is disagreement with result of (Ali, 2010) who observed a significant increase in the serum glucose level after 3 hours, 24 hours of epilepsy.

In the present study serum TG was decreased after 3 hours, and after week of induction epilepsy by PTZ, this result were agreement with (Yuzo *et al*., 1998) who found that serum TG levels decreased significantly in spontaneous epileptic rats. (Ali, 2010) observed that TG level decreased significantly after 3 hours and week from inducing epilepsy in male rats.

The effect of AEDs therapy on cerebral blood flow is considered and poses an important question as variation in blood flow and glucose metabolism in the brain may have subsequent effects on neuronal functioning and cognitive performance. Several AEDs have been investigated, including CBZ, PHT, PB and VAP and vigabatrin, all reduced cerebral metabolic rate for glucose and / or decreased cerebral blood flow (Hosking *et al*., 2003).

The importance of glucose balance was identified to demonstrate that hyperglycemia exacerbated ischemia-induced brain damage, whereas fasting induced hypoglycemia protect against neurotoxicity (stafstrom, 2003). The reduction of extracellular glucose could ameliorate seizure activity by decreasing neuronal excitability, and abnormal glucose levels, whether too high or too low can cause seizures (Schwechter *et al*., 2003).

Glibenclamide treatment leads to significant increase glucose level after 3 hours, 24 hours, and week of induced epilepsy when compare with control group. This may be due do to glibenclamide have an action like insulin, so increase the glucose translation and increase metabolism (Tayek, 1995), also glibenclamide acts by stimulation of the surviving β-cells to release more insulin (Chakrabarti and Rajagopalan, 2002), or glibenclamide acts by insulin secretogogne activity (Abdel-Zaher *et al*., 2005). Glibenclamide stimulate insulin release by inhibiting carnitine palmitoyltransferase 1 activity which switches fatty acid metabolism from β-oxidation to protein kinase c-dependent insulin exocytosis (Akira *et al*., 2007). This action of glibenclamide is similar to action of VPA drugs used for treatment of epilepsy, VPA-induced hyperinsulinemia and insulin resistance: also VPA treatment is related to increase in insulin concurrent with decrease in glucose level (Demir and Aysun, 2000).

Metformin treatment leads to decrease serum glucose level after 3 hours and increase its level after weeks. The hypoglycemic action may be due to that metformin stimulates the insulin induced component of glucose uptake into skeletal muscle and adipocytes. The stimulatory effect of the metformin is additive to that of insulin, metformin increase glucose-analogue transport independently of and additive to insulin, suggesting an insulin-independent action. (Amira *et al*., 1990). Or may metformin improve sensitivity to the action of insulin by inhibition of hepatic gluconeogenesis (Kirpichnikov *et al*., 2002). Also metformin alleviates hypoglycemia by inhibiting hepatic glucose production and improving peripherals insulin sensitivity. (Guthrie, 1979). Or may metformin reduce blood glucose level by inhibiting hepatic glucose production and reducing insulin resistance particularly in liver and skeletal muscle (Giannarelli *et al*., 2003). (Greene *et al*., 2001), refer that the reduction in plasma glucose level had antiepileptogenic effect. And the treatment of epileptic patients with VAP monotherapy caused a reduction in fasting plasma glucose concentration (Pylvänen *et al*., 2006).

Metformin is an attempt to minimize dietary starch and sugar, (Roopra and Researcher from ASBMD) identified a small molecule in neurons that senses how much energy is available on hand, glucose normally turns on this sensor, so metformin could suppress over-active never cells by removing their ability to turn sugar into excess energy (ASBMB, 2008).

The pathogenetic mechanism underlying the change in glucose level in the treated epileptic patients remains unknown. AEDs such as VAP does not induce insulin secretion but might interfere with the insulin metabolism in the liver, resulting in higher insulin concentrations in the peripheral circulation (Pylvänen *et al*., 2006) which finally decreased the level of glucose in epileptic patients.
Changes in plasma glucose levels could predict seizure susceptibility, that is, blood glucose levels determine seizure susceptibility in mice and emphasize the importance of blood glucose as a predictor of epileptogenesis in epilepsy model of mice (Greene *et al*., 2001).

CBZ lead to increase of glucose level, and this effect may be due to activation of glycogenolysis on liver and muscle, or/ and inhibition of insulin secretion from β-cells in pancrease (Kortelainen and Hirvonen, 1989). CBZ acts by blocking sodium channels and inhibiting persistent sodium currents, thus inhibiting firing in the brain (Bryan and Waxman, 2005).

In present study glibenclamide treatment leads to increase serum cholesterol level after 3 hours and decrease its level after 24 hours. There are some evidence that glibenclamide also sensitive β-cells to glucose that they limit glucose production in the liver that they decrease lipolysis, breakdown, and release of fatty acids by adipose tissues and decrease clearance of insulin by the liver (Kunte *et al*., 2007).

Serum level of cholesterol were significant increase after 3 hours when compare with control, and significantly decreased after 24 hours, when rats treated with metformin this results may be due to intrinsic, i.e, glucose lowering independent effect on plasma cholesterol. (Wulffele´ *et al*., 2004).

Combination therapy of either PHT and PB or PHT and CBZ stimulates the hepatic synthesis of cholesterol and increases the formation and pool size of bile acids, which in turn raise the level of intestinal absorption of cholesterol by facilitating micelle formation. An increase in serum cholesterol may be regarded as an adverse effect of long-term anticonvulsant treatment as it increases the risk of coronary heart disease. Therefore, the serum cholesterol level should be regularly monitored in patients receiving such therapy (Kumer *et al*., 2004).

Glibenclamide treatment leads to decrease serum TP after 24 hours, and don't lead any significant change on serum albumin level, and only decrease serum globulin level after 3 hours of treatment. This

improvement could be attributed to increase protein synthesis, increasing incorporation of certain amino acids as a result of increasing insulin secretion, increase of hepatic uptake of glucogenic amino acids. Stimulation amino acids incorporation into protein and decrease proteolysis by activating the enzyme that catalyzing amino acids transamination. Also good correlation between protein synthesis and insulin level has been recorded by (Nahla *et al*., 2006).

Metformin increase significantly levels of serum TP, and globulin after 3 hours, while level of albumin decreased after 24 hours when compare to the control group. This result may be due to that metformin increase sensitivity of amino acids transport across the cell membrane, which increases the available amino acids for protein synthesis (Carla Ribeiro *et al*., 2012).

The changes in protein levels in the treated epileptic patients showed fine structural changes in hepatocytes suggesting a varying degree of drug-induced changes (Dastur and Dave, 1987). Treatment of epileptic dogs with PB are decreased TP and albumin are likely to reflect hepatotoxic effects of PB and are not a normal consequence of therapy (Chauvet *et al*., 1995).

Our result shows that glibenclamide treatment lead to improvement of serum transaminases activity AST, and ALT. Our result are agree with (Zeinab *et al*., 2011) May be this improvement due to the good hepatoprotective and antioxidant activity of glibenclamide, since antioxidants are known to reduce the development chemically induced liver damage (Hui-Yin and Gow-Chin, 2007).

Our result indicate that metformin decrease significantly serum ALT after 3 hours while serum AST elevated after 24 hours, and weeks. This effect may be to that improvements of insulin sensitivity occur with improvement in the liver function (Uygun *et al*., 2004). (Elizabeth and Harris, 2005) Suggest the improved glycemic control and improvement in insulin resistance can reduce elevation of transaminases. This result is similar to result of CBZ (Hadiza Aliyu *et al*., 2013), who observed the increase in albumin concentration may be as a result of over production of cortisol by the adrenal glands (Kaslow, 2012).

Increased serum AST level due to treatment with AEDs may not be derived from the liver only; other tissues possessing these enzymes (like heart, skeletal muscle, intestine, bone and kidney) may contribute to their increased serum activities (Yazar *et al*., 2002). Damage occurring in these tissues caused by drugs can cause elevation of serum AST activity (Rosenthal, 1997). The changes observed in ALT activity may reflect hepatocellular toxicity and damage rather than liver enzyme induction (Raza *et al*., 2006). Sufficient information in the literature indicated that VAP was metabolized to unsaturated toxic products in the body and may cause hepatotoxicity (Raza *et al*., 2006).

Diphenylhydantoin, a PHE derivative was reported to cause a more frequent and higher increase in alanine aminotransferase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase (ALP) than CBZ [Schmidt, 2011].

(Hadiza Aliyu *et al*., 2013) reported that there was an increase in ALT activity in the CBZ and CBZ+PHE-treated groups. This finding disagrees with the report of (McNamara, 2006), who observed moderate elevation of ALT activity with PHE therapy. These changes were transient and may be due in part to induced synthesis of the enzymes. Transient elevation of ALT activity with CBZ therapy may be due to hepatocellular damage (Ekaidem and Akpanabiatu, 2006).

PHE cause more damage to the (liver, cardiac and skeletal muscle, kidney, brain and blood cells) where the enzyme AST is found ((Hadiza Aliyu *et al*., 2013).

In conclusion, the results of the present investigation indicate that glibenclamide and metformin have good roles in control of epilepsy-induced by PTZ in rats through several significant changes of biochemical parameters.

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تأثير بعض ادوية علاج السكري على بعض المعايير الكيموحيوية في الجرذان المستحدث بها الصرع بواسطة البنتلين تترازول

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تم تصميم تجارب هذه الدراسة لأختبار تأثير الدؤنيل والميتفورمين على بعض القيم الكيموحيوية في الجرذان المُستحدث بها الصرع. اسُتخدمت ذكور جرذان من نوع Wister التي اسُتحدث بها الصرع عن طريق حقنها بمادة Pentylenetetrazole (PTZ) بجرعة ١٠٠ ملغم/كغم من وزن الجسم. ثم قُسمت الجرذان عشوائياً الى ثلاث مجاميع (١٠-١٢ جرذان/مجموعة)،المجموعة الأولى: تُركت دون معاملة وعُدت مجموعة سيطرة، المجوعة الثانية: أعُطيت دواء الداؤنيل ٥ ملغم/كغم من وزن الجسم عن طريق الفم، المجموعة الثالثة: أعُطيت الميتفورمين ١٥٠ ملغم/كغم من وزن الجسم عن طريق الفم. كل المعاملات كانت لمرة واحدة باليوم ولمدة أسبوع، وتم جمع عينات الدم بعد ٣، ٢٤ساعة ، وأسبوع من استحداث الصرع. أظهرت النتائج أن حقن مادة PTZ أدى الى أنخفاض معنوي في تركيز الكلوكوز في جميع الأوقات بعد المعاملة، كذلك انخفض تركيز الكولسترول معنوياً بعد ٣ ساعة وأسبوع من المعاملة، بينما أنخفض معنوياً تركيز الألبومين بعد أسبوع من المعاملة، أيضاً المعاملة بالPTZ أدت الى ارتفع معنوي في تركيز أنزيم الاسبارتيت ناقلة الأمين في جميع الأوقات من المعاملة، بينما تركيز أنزيم الألنين ناقلة الأمين ارتفع معنوياً بعد ٣ ساعة، ثم أنخفض معنوياً بعد أسبوع من المعاملة، ولم يكن لمادة PTZ أي تأثير معنوي على تراكيز البروتين الكلي والكلوبيولين. أما المعاملة بدواء الداؤنيل فقد أظهرت النتائج حدوث زيادة معنوية في تركيز الكلوكوز في كل الأوقات بعد المعاملة، اما تركيز الكولسترول فقد أنخفض معنوياً بعد ٣، ٢٤، ساعة من المعاملة، كما أدى الداؤنيل الى انخفاض معنوي في تركيز أنزيم الاسبارتيت ناقلة الأمين بعد ٣، ٢٤ ساعة وأسبوع من المعاملة، أما أنزيم الألنين ناقلة الأمين فقد ارتفع تركيزه معنوياً بعد أسبوع من المعاملة، ولم يكن للداؤنيل أي تأثير معنوي على تراكيز البروتين الكلي والالبومين والكلوبيولين. أعطاء دواء الميتفورمين أدى ألى حصول أنخفاض معنوي بعد ٣، ٢٤ ساعة من المعاملة مع زيادة معنوية بعد أسبوع من المعاملة، بينما تركيز الكولسترول ارتفع معنوياً بعد ٣ ساعة، وأنخفض معنوياً بعد ٢٤ ساعة من المعاملة، أما تراكيز البروتين الكلي والكلوبيولين فقد ارتفعت معنوياً بعد ٣ ساعة من المعاملة، كذلك أدى أعطاء الميتفورمين الى خفض معنوي لتركيز أنزيم الاسبارتيت ناقلة الأمين بعد ٣ ساعة، وارتفع معنوياً بعد أسبوع من المعاملة، فيما ارتفع تركيز أنزيم الألنين ناقلة الأمين بعد ٢٤ ساعة وأسبوع من المعاملة. تشير نتائج الدراسة الحالية إلى أن هناك دوراً جيداً لكل من الداؤنيل والميتفورمين في السيطرة على الصرع المستحدث بال PTZ من خلال أحداث تغيرات في بعض المعايير الكيموحيوية.