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RENAL AND LIVER TEST- INDICES UNDER SPONTANEOUS CASES OF PREGNANCY TOXEMIA IN DOES WITH SPECIAL REFERENCE TO THERAPUTIC TRIALS

(With One Table and 2 Figures)

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(Received at 9/5/2005)

مؤشرات اختبارات الكبد والكلى في حالات تسمم الحمل في الماعز مع الاشارة المرجعية الى محاولات العلاج

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الهدف من هذه الدراسة هو دراسة العلاقة بين اضطرابات الكبد والكلى في الماعز المصابة بتسمم الحمل ومدى الاستجابة للعلاج. اشتملت هذه الدراسة على ٣٥ حيوان من الماعز في الاسابيع الاخيرة من الحمل، ١٠ من هذه الحيوانات كانت بحالة صحية ظاهرية جيدة واستخدمت كمجموعة ضابطه. جمعت عينات دم من جميع الحيوانات الخاضعة للدراسة بغرض فصل مصل الدم، استخدم هذا المصل في قياس أنشطة بعض الإنزيمات مثل الأسبارتيت أمينوترانسفيريز، الألانين أمينوترانسفيريز والألكالين فوسفاتيز، وأيضا لتقدير مستوى البولينا والكرياتينين والجلوكوز والدهون الكلية والدهون الثلاثية والكوليستيرول الكلى. أوضحت النتائج ان هناك علاقة تعكس مدي التغير في مؤشرات وظائف كل من الكبد والكلى في حالات تسمم الحمل الماعز المصابة. استخدم نظام علاجي في هذه الحالات وكانت هناك استجابة متفاوتة اعتمدت بالدرجة الأولى على مرحلة الاصابة وضراوتها.

SUMMARY

The goal of the present study was to investigate the relation between the extent of liver and kidney damage in pregnancy toxemic does and the responsiveness of these does to therapeutic treatment. A total of 35 late pregnant does were included in this study from which, ten does were proved healthy and used as a control group. Blood samples were collected for separation of serum from all animals before and after

therapeutic treatment. The following serum biochemical parameters were determined in the collected samples; enzyme activities of aspartate amino tansferase (AST), alanine amino tansferase (ALT), alkaline phosphatase (ALP). Blood urea nitrogen, creatinine, glucose, total lipid, triglycerides and total cholesterol levels were also measured. The results of the study have showed a direct relation between the extent of liver and kidney affection and the response of the pregnancy toxemic does to conventional therapeutic treatment.

Key words: *Pregnancy toxemia, liver function test, kidney function test.*

INTRODUCTION

Pregnancy toxemia is a metabolic disorder characterized by hypoglycemia and hyperketonemia as a result of the incability of the animal to maintain an adequate energy balance. The clinical picture comprises neurological manifestations and weakness (Hay and Baird 1991). In general, the problem develops in the last third of pregnancy, with a greater incidence in animals presenting two or more fetuses, though it can also be observed in poorly or under nourished sheep with only a single fetus (Van Saun 2000). The determining cause of toxemia is an alteration in energy metabolism, as a consequence of an imbalance between glucose offer and demand, thereby giving rise to a negative energy balance. This imbalance is caused by a reduction in energy supply due to poor or inadequate nutrition, deficient food absorption, or an incorrect metabolic use of the food ingested, in addition to the increasing requirements of the fetus in its last prenatal growth phase and the pressure of the gravid uterus upon the digestive organs within the abdominal cavity (Hay and Baird 1991; El-Sebaie *et al.* 1995 and Van Saun 2000). The consumption of low energy levels or poor utilization of the available energy supply gives rise to a gradual reduction in blood glucose levels, with depletion of the liver glycogen reserves and mobilization of the fatty depots for use as an unusual energy source with the subsequent formation of ketone bodies and fatty liver infiltration. (Radostits *et al.* 1994). The present study aimed to investigate the alteration in liver and kidney functions in pregnancy toxemic does prior to and after therapeutic trial and to find the relation between the extent of their damage and the responsiveness to the treatment.

MATERIALS and METHODS

1- **Animals.** A total number of 35 late pregnant does were subjected to the study. The animals were divided into two groups; the first group was the diseased group and composed of 25 does that were admitted to the Veterinary Teaching Hospital (Faculty of Veterinary Medicine, Assiut University) with variable signs of pregnancy toxemia upon clinical and laboratory examination. The second group was the control one and composed of 10 late pregnant animals that were proved healthy after precise clinical and laboratory examinations and were used as a control group.

2- Samples and Adopted methods.

A- Serum samples. Blood samples for separation of serum were collected from the jugular vein in clean and dry centrifuge tubes from all animals before therapeutic trial and from recovered does after treatment (Coles 1986).

B- Biochemical study. The following serum biochemical parameters were determined in studied cases; enzyme activities of aspartate amino tansferase (AST U/l), alanine amino tansferase (ALT U/l), alkaline phosphatase (ALP U/l), blood urea nitrogen (BUN) (mmol/L), creatinine (μmol/L), glucose (mmol/L), total lipids (g/L), triglycerides (mmol/L), and total cholesterol (mmol/L) levels. Blood serum levels of AST, ALT, ALP, urea, creatinine, glucose, total lipids, triglycerides and total cholesterol were determined using test kits supplied by Boehringer Mannheim GmbH Diagnostica and by means of Digital VIS/Ultraviolet Spectrophotometer (CE 292, series 2, Cecil instruments, Cambridge England, Series No. 52.232.).

C- Conventional treatment of diseases does. Treatment of diseased cases were done using Dextrose 5 % (I.V. injection for 3 successive days), 10 gram sodium bicarbonate orally, 50 cc Cofacalcium (composed of calcium gluconate, magnesium and dextrose) (Tradimpex-Egypt), injected I.M., and 250 cc Ringer solution daily for 3 successive days.

D- Statistical analysis. Statistical analysis was done by using window program (SPSSWin. 1997), depending on one way ANOVA for analysis of data.

RESULTS

Clinical Findings. A total of 25 cases of pregnancy toxemic does were admitted to the Veterinary Teaching Hospital with variable degrees of affection upon clinical examination. Pregnancy is assured by trans-

abdominal ultrasonic examination carried out by the staff members of the Gynecology department. According to the severity of the clinical signs, diseased animals were subdivided into two groups. The first group comprises 20 cases of moderately affected animals that showed signs ranged from dullness, depression, inappetance, star gazing to sternum recumbency of some cases (Fig.1). This group have showed clinical improvement after the therapeutic trial and marked as the responsive group. The second group comprises 5 cases of severely affected animals with clinical sings of marked drowsiness, apparent blindness and lateral recumbency with deviation of the head (Fig. 2). All animals of this group did not respond to the therapeutic trial and died and hence marked as the non-responsive group.

Laboratory Findings of Biochemical Study.

The results of the study as shown in Table 1 have showed a significant increase ($P<0.01$) in both liver enzymes activities; AST, ALT, and ALP and kidney parameters (urea and creatinine) in the disease group as compared to the control group. In addition, the non-responsive animals have showed marked significant increase ($P<0.01$) in the liver and kidney functions as compared to the responsive diseased group. All selected liver and kidney parameters have showed significant improvement after treatment in the responsive group.

With regard to carbohydrate metabolism, there was a significant decrease ($P<0.01$) in the glucose level in the diseased group as compared to the control one. However, in the non-responsive group, although there was a significant reduction in the glucose, but the reduction was less marked than that of the responsive group (Table 1).

With regard to lipid metabolism, there was a significant increase ($P<0.01$) in the level of total lipids in the diseased group as compared to the control one. However, total cholesterol and triglycerides levels were significantly decreased ($P<0.01$) in the diseased group (Table 1). All studied carbohydrate and lipid parameters have showed significant improvement after treatment in the responsive group. Ketone bodies were detected in urine of diseased animals by sodium nitroprusside test.

DISCUSSION

Based on the severity of clinical signs, laboratory findings, and response to treatment, diseased animals were subdivided after treatment into responsive group and non-responsive one, which died after treatment.

It was obvious from the results of the current study that the alteration of the liver and kidney function parameters of the non-responsive group of diseased does were significantly higher than that of the responsive ones, which was in accordance with the clinical picture manifested by severe clinical signs and treatment failure with the subsequent death of severely affected animals.

Regarding the liver function parameters, the results have showed a significant ($P<0.01$) increase in all liver enzymes, which is in accordance with the fact that in the event of energy deficiency, the body uses its fatty tissue reserves as a source of energy. Thereby leading to important lipolysis, which in turn increases the presence of circulating free fatty acids that reach the liver and induce fatty infiltration with subsequent liver degeneration (Brus 1989; Radostits *et al.* 1994 and El-Sebaie *et al.* 1995). Although the AST and ALP enzymes are specific for liver affection, the changes of the ALT enzyme reflected its action as a muscle affection specific enzyme rather than being a liver specific enzyme. This was attributed to the muscle wasting due to use of proteins in glyconeogenesis to produce glucose with the subsequent elevation of the ALT level (Sargison *et al.* 1994). Although hypoglycemia is expected during pregnancy toxemia, it is not a constant finding, since temporary normal or even elevated blood glucose levels can be recorded as a consequence of endogenous corticosteroid release with subsequent stimulation of glyconeogenesis (formation of glucose from fat and protein) (Latimer *et al.* 2003) or as a result of fetal death and reduction on the demand for glucose (El-Sebaie 1992 and Radostits *et al.* 1994). This was manifested in the present study in the non-responsive severely affected group, which showed elevated glucose level as compared to the less severely affected group that responded to the treatment.

Regarding the kidney function parameters, the results indicate severe kidney affection, which was manifested by the significant ($P<0.01$) increase of the urea and creatinine. The kidney dysfunction is attributed to the acidosis. The acidosis is due to the shift of the ketogenic group (Acetic acid and butyric acid) from the entrance into tricarboxylic acid cycle for energy production and lipogenesis to the entrance into ketogenesis under the effect of glucose deficiency and oxalacetate insufficiency, with the subsequent production of excessive amounts of ketone bodies (Brus 1989; Radostits *et al.* 1994 and Pastor *et al.* 2001)

Regarding the lipogram picture, the results revealed significant increase ($P<0.01$) of total lipids and reduction of triglycerides and total cholesterol levels in the diseased animals as compared to health control

group. The increase of the total lipids level is due to the mobilization of free fatty acid from fat depots to be used as source of energy through increased lipolysis and glyconeogenesis in a trial to compensate the reduction of the glucose level. (Brus 1989 and Henze *et al.* 1998). On the other hand, the reduction of the triglycerides and total cholesterol levels is attributed to the reduction of glucose level that participate in the formation of glycerol and triglycerides. In addition, the liver infiltration with large amount of free fatty acid with the subsequent development of fatty liver have resulted in the inability of the liver to re-esterify fatty acids into triglycerides (Hay and Baird 1991; Radostits *et al.* 1994 and Latimer *et al.* 2003).

It is concluded that there is a direct relation between the extent to which liver and kidney get damaged and the therapeutic treatment responsiveness with the subsequent correction of carbohydrate and lipid parameters in affected pregnancy toxemic does.

Table 1: Alteration of liver and kidney function parameters prior to and after therapeutic treatment of pregnancy toxemic does. Mean values $(\bar{X} \pm SD)$

Parameters	Control group (10)	Diseased group (25)		
		Responsive group (20)		Non-responsive group (5)
		Before treatment	After treatment	Before treatment
AST (U/L)	44.70 ± 1.34	75.10 ± 3.29**	51.67 ± 1.38**	145.20± 22.33**
ALT (U/L)	22.00 ± 0.81	44.40 ± 1.98**	24.00 ± 2.05**	57.60 ± 1.14**
ALP (U/L)	42.4 ±1.77	61.84 ± 1.69**	46.15 ± 1.59 **	77.00 ± 1.58**
Urea (mmol/L)	7.89 ± 0.54	11.62 ± 0.85**	9.73 ± 0.62**	14.49 ± 0.41**
Creatinine (µmol/L)	106.08 ± 12.37	217.46 ±20.33**	147.63 ± 10.61**	279.34± 23.87**
Glucose (mmol/L)	2.50 ± 0.08	1.13 ± 0.26**	2.19 ± 0.16**	1.93 ± 0.12**
Cholesterol (mmol/L)	1.86 ± 0.07	1.40 ± 0.06**	1.62 ± 0.06**	1.29 ± 0.10**
Triglyceride (mmol/L)	0.59 ± 0.01	0.38 ± 0.03**	0.50 ± 0.03**	0.39 ± 0.02**
Total Lipid (g/L)	3.22 ± 0.05	4.16 ± 0.07**	3.52 ± 0.08**	4.48 ± 0.11**

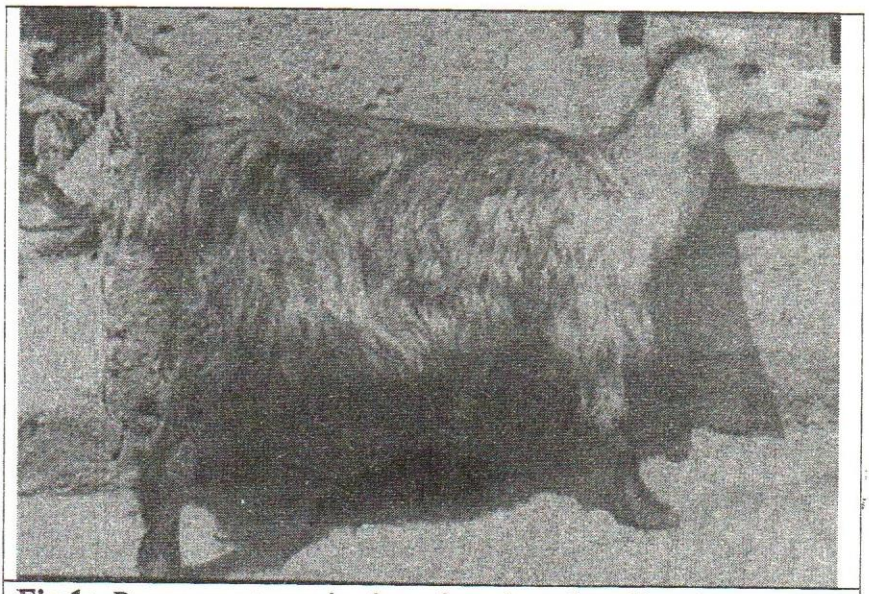

Fig.1: Pregnancy toxemic doe of moderately affected responsive group. The animal shows depression, inappetance, and star gazing.

Fig.2: Pregnancy toxemic doe of severely affected non-responsive group. The animal shows marked drowsiness, apparent blindness and lateral recumbency with lateral deviation of the head.

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