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**STUDY THE EFFECT OF PHENYLBUTAZONE ON SOME BIOCHEMICAL
PARAMETERS IN HORSES**

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ABSTRACT

Non steroidal anti inflammatory drugs (NSAIDs) are commonly used to manage the pain and inflammation. Phenylbutazone currently used in veterinary medicine as a pain killer and it is readily absorbed from the gastrointestinal tract with peak plasma concentrations occurring about 2 hours after ingestion. It is also readily absorbed when administered rectally. Phenylbutazone is widely distributed throughout body fluids and tissues; it diffuses into the synovial fluid, crosses the placenta, and small amounts enter the CNS and breast milk. It is 98% bound to plasma proteins. Phenylbutazone is considered valuable in the training of sore horses to maintain fitness in those with early joint or ligament problems. The use of a NSAID such as Phenylbutazone enables a horse to continue training or return to training in a shorter period of time. So, the aim of present study is effect of phenylbutazone on some biomedical parameters of horses. According to this propose 10 adult horses weigh 220 ± 5 Kg selected that having the equal conditions in regard to their age, nutrition and management. Before injection, three consecutive day blood samples were taken from the horses and the values obtained were considered as a control group. It should be noted that the control group received same volume of drug saline injections. First of all, phenylbutazone as much as 4 mg/kg was injected intravenously for 3 days and up to 1 week after injection, blood samples were taken every day of horses. For measuring biochemical parameters, each time 10 ml of blood was taken from the jugular vein of horses.

Blood samples for biochemical tests in tubes without anticoagulant were dumped. After the blood clot and then centrifuged at 3000 rpm for 15 min, the serum separated and kept frozen. As the results Albumin, globulin, glucose, urea nitrogen, creatinine, calcium and AST activities in the days before and after injection of of phenylbutazone have significant differences ($p<0.05$) (table1). So after the Injection of Phenylbutazone amount of albumin, glucose, urea nitrogen, calcium, and serum AST activity was significantly reduced and creatinine levels and serum globulin significantly increased ($p<0.05$). As a result, phenylbutazone has side effects on blood biochemical parameters in horses.

Keywords: Phenylbutazone, Biochemical Parameters, Horses

INTRODUCTION

Non steroidal anti inflammatory drugs (NSAIDs) are commonly used to manage the pain and inflammation. The term non steroidal distinguishes these drugs from steroids, which, among a broad range of other effects, have a similar eicosanoid-depressing, anti-inflammatory action. As analgesics, NSAIDs are unusual in that they are non-narcotic and thus are used as a non-addictive alternative to narcotics. NSAIDs inhibit the activity of both cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2), and thereby, the synthesis of prostaglandins and thromboxanes. It is thought that inhibiting COX-2 leads to the anti-inflammatory, analgesic and antipyretic effects and that those NSAIDs also inhibiting COX-1, particularly aspirin, may cause gastrointestinal bleeding and ulcers [1]. The

widespread use of NSAIDs has meant that the adverse effects of these drugs have become increasingly prevalent. Use of NSAIDs increases risk of having a range of gastrointestinal (GI) problems [2]. Phenylbutazone currently used in veterinary medicine as a pain killer and it is readily absorbed from the gastrointestinal tract with peak plasma concentrations occurring about 2 hours after ingestion. It is also readily absorbed when administered rectally. Phenylbutazone is widely distributed throughout body fluids and tissues; it diffuses into the synovial fluid, crosses the placenta, and small amounts enter the CNS and breast milk. It is 98% bound to plasma proteins. It is extensively metabolized in the liver by oxidation and by conjugation with glucuronic acid [3]. It was introduced into veterinary medical practice in the 1950s and still remains

one of the more commonly used non-steroidal anti-inflammatory drugs in the horse [4]. Phenylbutazone is considered valuable in the training of sore horses to maintain fitness in those with early joint or ligament problems. The use of a NSAID such as phenylbutazone enables a horse to continue training or return to training in a shorter period of time. On the other hand a major drawback to the use of phenylbutazone is the veterinarians' inability to evaluate the degree of lameness with this medications present in the horse's system [5]. It was also the opinion of many veterinarians that phenylbutazone would allow a horse to compete with mild chronic arthritic changes, but did not possess sufficient anti-inflammatory activity to allow a horse with a serious injury to compete. Toxicity of phenylbutazone in the horse and ponies has been reviewed and several factors may predispose towards phenylbutazone toxicity in the horse, including breed and age, but high dose is considered to be particularly important [6]. Clinical experience suggests that phenylbutazone can be administered to horses in modest doses for a prolonged period of time without detectable side-effects [4]. So, the aim of present study is effect of phenylbutazone on some biomedical parameters of horses.

MATERIALS AND METHODS

This research was conducted upon 10 adult horses weighs 220 ± 5 Kg having the equal conditions in regard to their age, nutrition and management. First, all horses were examined clinically to ensure their health. Two weeks before to start of the study, an anti-parasitic drug albendazole 15 mg/kg were given. Before getting blood, stool test was done and no parasites were seen in horses. Before injection, three consecutive day blood samples were taken from the horses and the values obtained were considered as a control group. It should be noted that the control group received same volume of drug saline injections. First of all, phenylbutazone as much as 4 mg/kg was injected intravenously for 3 days and up to 1 week after injection, blood samples were taken every day of horses. For measuring biochemical parameters, each time 10 ml of blood was taken from the jugular vein of horses. Blood samples for biochemical tests in tubes without anticoagulant were dumped. After the blood clot and then centrifuged at 3000 rpm for 15 min, the serum separated and kept frozen. Measuring total protein by biuret method, albumin by bromocresol green method, glucose by the enzyme glucose oxidase method, blood urea by nitrogen di-acetyl

monoxime method, creatinine by Jaffe method, calcium clozole fetalein method, phosphorus by Goldenberg and Fernandez and AST by modified Reitman Frankel method was done [7]. For statistical analysis of the results and determine the difference between the control group and the days after administration of the test, analysis of variance (Anova) was used. To realize the significant difference between the means Duncan test ($p < 0.05$) was used.

RESULTS

Phenylbutazone Drug Efficacy results are presented in **Table 1**. Albumin, globulin, glucose, urea nitrogen, creatinine, calcium and AST activities in the days before and after injection of of phenylbutazone have significant differences ($p < 0.05$) (table1). So after the Injection of Phenylbutazone amount of albumin, glucose, urea nitrogen, calcium, and serum AST activity was significantly reduced and creatinine levels and serum globulin significantly increased ($p < 0.05$).

Table 1: Biochemical Parameters of Blood Serum Levels After Injection of Phenylbutazone

Parameters	Protein g/dl	Albumin g/dl	Globulin g/dl	Glucose g/dl	Urea g/dl	Creatinine g/dl	Calcium g/dl	Phosphorus g/dl	AST U/L
Control group	5.8±0.1	3.8±0.1	2.0±0.1	72.9±5.6	8.3±0.6	2.4±0.0	11.0±0.3	6.7±0.4	181.0±14.4
1 day after injection	5.5±0.2	3.3±0.2	2.0±0.3	57.2±3.5	5.6±1.2	4.9±0.4	9.5±0.4	7.2±0.4	69.4±11.9
2 days after injection	6.0±0.2	3.4±0.0	2.4±0.1	57.7±4.4	4.4±0.9	3.4±0.3	9.5±0.5	6.4±0.8	55.6±12.9
3 days after injection	5.5±0.2	3.3±0.0	2.3±0.1	66.3±2.6	7.9±1.8	2.4±0.3	8.9±0.3	6.4±0.5	77.4±13.8
4 days after injection	5.6±0.2	3.2±0.1	2.5±0.2	66.7±1.4	4.8±0.4	2.2±0.3	8.8±0.3	7.4±0.7	47.3±0.4
5 days after injection	5.4±0.4	3.3±0.3	2.0±0.2	65.8±2.8	7.8±1.7	2.2±0.3	9.2±0.4	6.6±0.6	64.5±23.4
6 days after injection	5.7±0.5	2.7±0.1	2.8±0.4	51.2±6.9	11.5±3.4	2.0±0.1	11.6±0.5	7.7±0.4	142.4±6.8
7 days after injection	5.6±0.3	3.5±0.3	2.4±0.2	64.2±3.2	7.4±1.3	2.3±0.2	11.3±0.4	6.8±0.7	154±11.2

DISCUSSION

After injection of phenylbutazone, significant decrease in serum glucose, urea nitrogen, calcium, AST and globulin levels and significant increase in serum globulin and creatinine occurred. In this study, possibly of

decreased albumin after injection of Phenylbutazone because of ulcers and albumin excretion is through the digestive system [8]. Also increase of globulin serum after administration of phenylbutazone can result from the body's reaction of horse [9]. In

current research, decrease body metabolism due to decrease of Glucose concentration of phenylbutazone is in effect [7, 9]. Reduced levels of blood urea nitrogen after injection of phenylbutazone in the horse possibly due to effects on the liver and reduce the production of urea in the urea cycle. Increased serum creatinine can be due to decrease glomerular filtration and have adverse effect of drug-induced on kidneys [9]. Also reduce calcium levels after administration phenylbutazone, probably due to ulcers and an increased excretion of calcium from the gut [10]. Decrease serum AST in the horse after the injection of phenylbutazone is probably due to the decrease in overall body metabolism but cannot be justified; detailed and specific idea in this field gave [9]. As a result, phenylbutazone has side effects on blood biochemical parameters in horses.

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