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SHORT–TERM EFFECT OF CHLORPROMAZINE AND DIAZEPAM ON BLOOD PLASMA ACETYLCHOLINESTERASE ACTIVITY IN CHICKS

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ABSTRACT

The response of blood plasma acetylcholinestrase to acute administration of chlorpromazine and diazepam was examined in chick. Chlorpromazine in a dose–dependent manner at 25, 50, and 75 mg/Kg, subcutaneously inhibited the activity of Ache in the blood. Chlorpromazine (50, 75 mg /kg) significantly decreased the enzyme activity in the plasma by 14.7 % and 17.6 %, respectively for a period of 60 min, as well as, 14.5 % and 13.1 % for a period of 60 and 120 min, respectively in groups received chlorpromazine 50 mg/kg. Diazepam at 10, 20 and 30 mg/kg subcutaneously did not significantly affect the enzyme activity in comparison with the control group. The result suggests that chlorpromazine changes Ache activity in the blood and possibly in other tissues.

تاثير الكلوربرومازين والدايازيبام فى نشاط خميرة الا ستيل كولين استراز فى بلازما الدم فى افراخ الدجاج

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الخلاصة

تم دراسة تاثير الكلوربرومازين والدايازيبام فى فعالية خميرة الكولين استراز لدم الافراخ (بلازما الدم) حيث ادى حقن الكلوربرومازين (25 , 50 ,75 ملغم/كغم) والدايازيبام (10 , 20 , 30 ملغم /كغم) تحت الجلد الى تثبيط نشاط الخميرة المدكورة . قللت جرعتا الكلوربرومازين (50 , 75 ملغم /كغم) تحت الجلد وبشكل معنوى نشاط خميرة الكولين استراز فى بلازما الدم بواقع 14.7 % و17,6% وبشكل متعاقب خلال فترة 60 دقيقة من زمن الحقن. وكذلك 14,5% و13,1% خلال فترة 60 دقيقة و120 دقيقة وبشكل متعاقب فى المجاميع التى حقنت بالكلوربرومازين50 ملغم / كغم. بينما لم تكن لجرع الدايازيبام وباختلاف فترات زمن الحقن تاثير معنوى فى نشاط الخميرة المذكورة. توحى هدة النتاج بان الكلوربرومازين يغير من نشاط خميرة الاستيل كولين استراز فى الدم ومن المحتمل فى العديد من انسجة الجسم االاخرى.

INTRODUCTION

Acetyl cholinesterase is a microsomal membrane – bound enzyme, found in the tissue of all animals, which hydrolyzed acetylcholine to choline and acetic acid (1-6). Cholinesterase is formed by the liver and determination of the plasma blood levels is a biochemical marker of enzyme function (1, 6, 7). Blood Ache activity is affected by various psychotropic drugs (4, 5, and 6). In vivo and vitro treatment of rat with chlorpromazine resulted in diminished brain and/or blood acetylcholinestrase activity (1, 3, 8, 9). This inhibition appears to be reversible (1, 8). The purpose of the present study was to examine the effect of chlorpromazine and diazepam upon blood plasma cholinesterase activity in chicks.

MATERIALS AND METHODS

Eighty chicks, 4– 6 weeks old weighing 120-150 g were used. They were housed under standard condition of temperature (27 C) and humidity, and had free access to food (Commercial chick ration, Nebrase Co., Mosul, Iraq) and water. The birds were divided into four groups of 20 chicks each. In a dose–response experiment, the chicks (5/ group) were injected with chlorpromazine (May and Beaker Co., England) at; 0 (saline–control), 25, 50 and 75 mg/kg, and diazepam (Arab Pharmaceutical Manufacturing Co., Jordan) at 0 (saline–control), 10, 20 and 30 mg/kg. The control group received physiological saline at 1 ml /kg. The volume of injection of chlorpromazine and diazepam was 1 ml /kg body weight. The chicks were killed 60 min after drug injection. In a time – response experiment, the birds in each group (N = 5) were injected with chlorpromazine at 50 mg / kg and diazepam at 30 mg/kg, and they were killed 30, 60 and 120 min after drug administration. The chicks were sacrificed after ether anaesthesia and blood was rapidly collected, blood samples were derange by using washed heparin zed syringe (Braun, Germany) and separated plasma from blood cell by centrifugations in (3000 rpm) for 10 min. Samples of blood plasma stored in - 20 C until the time of estimation the enzyme activity (7 – 10 Day). 0.2 ml from plasma samples was used for cholinesterase activity measurement using acetylthiocholine iodide (7.5 %) (Fluka, Switzerland) as a substrate (10). All assays were done in duplicate. The statistical significance of the differences between mean values was analyzed by analysis of variance following by Tukey multiple comparison tests (11). The level of significance was $P < 0.05$.

RESULTS

The mean values for enzymatic activity obtained from all groups are shown in table 1 and 2. In dose - response experiment, chlorpromazine at 50 and 75 mg/kg significantly inhibited cholinesterase activity in plasma by 14.7 % and 17.6 % respectively 60 min after injection in comparison with control group (Table 1). In the time–response experiment ,the percentage of inhibition was 14.5% and 13.1 % after 60 and 120 min, respectively in groups received chlorpromazine at 50 mg /kg (Table 2). Diazepam with different doses and at different times did not significantly affect the activity of acetylcholinestrase when compared with the respective control values.

Table 1: Plasma cholinesterase activity in chicks treated with chlorpromazine and diazepam.

Treatment	Δ PH/ 30 min	% inhibition
Saline (control)	0.68 ± 0.01	
Chlorpromazine (25mg/ kg)	0.65 ± 0.02	4.4 %
Chlorpromazine (50mg/ kg)	0.58 ± 0.02 *	14.7 %
Chlorpromazine (75mg/ kg)	0.56 ± 0.01*	17.6 %
Saline (control)	0.66 ± 0.02	
Diazepam(10mg/ kg)	0.64 ± 0.02	3.1 %
Diazepam(20mg/ kg)	0.63 ± 0.01	4.5 %
Diazepam(30mg/ kg)	0.61 ± 0.02	6.5 %

*P < 0.05 VS saline control group. The value are mean ± SE of 5 chicks/groups.

Table 2: Plasma cholinesterase activity in chicks treated with chlorpromazine and diazepam at 50 and 30 mg/kg respectively.

Treatment	Post treatment time (min)	Δ PH/ 30 min	% inhibition
Saline (control)		0.69 ± 0.02	
Chlorpromazine	30	0.67 ± 0.03	2.9 %
Chlorpromazine	60	0.59 ± 0.01*	14.5 %
Chlorpromazine	120	0.60 ± 0.02*	13.1 %
Saline (control)		0.63 ± 0.02	
Diazepam	30	0.62 ± 0.01	1.6 %
Diazepam	60	0.60 ± 0.03	4.7 %
Diazepam	120	0.62 ± 0.01	1.7 %

*P < 0.05 VS saline control group. The value are mean ± SE of 5 chicks/ groups

DISCUSSION

In study concerning acetylcholinestrase activity in blood and different tissues is of primary importance (1, 4-6, 9). In this study, the activity of blood cholinesterase following acute administration of chlorpromazine and diazepam was investigated by assaying blood plasma cholinesterase. The result showed that , short – term administration of chlorpromazine resulted in inhibition of plasma cholinesterase activity .The inhibitory effect of chlorpromazine may be due to competitive inhibition at the anionic site of Ache (4, 5, 6, 12) . On the other hand , many reports suggest that such inhibition is due to a decrease in the internal micro viscosity of phospholipids leading to changes in the fluidity of microsomal membrane of the cell (1, 2, 4-8). The non-significant decrease of cholinesterase

activity by diazepam is in accordance with other studies in which diazepam did not affect Ache activity (13).

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