Effects Of Isofluperdone Acetate Administration On Blood Picture And Some Biochemical Parameters In Albino Rats

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ABSTRACT

Fifteen rats (4-6 month old)were used to study some adverse effects of isofloperdone acetate on the haemogram and some biochemical parameters in rats.The rats were divided into three equal group.G(1) was left without treatment as control .G(2and3) were itramuscularly injected by 0.4 and 0.8 mg/kg B.Wt. isofloperdone acetate as therapeutic and double therapeutic doses respectively for5successive days.Blood samples were taken after 5,10 and 20days post last injection for determination of hemogram and some biochemical changes.

The intramuscular injection of isofloperdone acetate at both doses induced a significant decrease in the haemoglobin concentration, peacked cell volume, erythrocytic count, total protein, globulins and soduim which remained low after 10 days from drug administration. On the other hand it induced an elevation in the total leucocytic count, albumin AST, ALT, potassium, calcium and inorganic phosphorus for 5,10 and 20 days post interamuscular injection.

It could be concluded that the interamuscular injection isofloperdone acetate in both doses induced several haematological and biochemical changes in rats and remaind 10 days post injection.

INTRODUCTION

The intiinflammatory drugs occupy a particular place in among the modern clinical therapeutics. The most widly used anti-inflammatory drugs are the steroids and non steroid.The anti-inflammatory drugs have analgesic, antipyretic and antiprostaglandine effects.

The steroidal anti-inflammatory drugs are the most important and often life saving class of potent anti-inflammatory agent in the treatment of several pathological conditions *(1).*The steroidal anti-inflammatory also used in the treatment of adrenal hormone deficiency *(2),* ketosis and shock *(3),* anaphylactic shock and some allergic reactions *(4).* In acute infectious diseases combination of corticosteroid and antibiotic therapy may be indicated *(5).*The isofloperdone acetate is one of the most important common synthetic glucocorticoids used in Egypt. Isofluperdone acetate is one of the steroidal anti-inflammatory drugs which acts on leukocytes and inhibits the action of phospholipase A2 *(6).* Isofluperdone acetate could be used for treatment of ketosis in cow *(7)* and chronic respiratory diseases or aseptic laminitis *(8).*

The present study was carried out to investigate the effect of the parenteral administration of isoflo- perdone acetate on the hematological picture and some serum biochemical parameters of the rats.

MATERIAL AND METHODS

1)Drugs:-

The iosfluperdone acetate (Predef 2X)^{R} a sterile solution Upjohn Puurs Belgium Co. USA available as 50 ml vial.

2)Animals:-

Fifteen rats(4-6 months old)were housed under hygienic condition, maintained at temperature of 25-30 ° C fed commercial pellets and watered *ad-libitum* during the experimental period .

3)Experimental design:-

The rats were randomly divided into three equal groups, each of 5 rats.G(1)was left without treatment as control.G(2)and(3)were daily injected for 5 successive days intramuscularly with 0.4 and 0.8mg isofloperdone acetate /kg B.Wt.. respectively as therapeutic and double therapeutic doses (recommended dose according to the manufacturing company) Five rats from the each groups were sacrificed after 5,10 and 20days post treatment. Blood samples were obtained from each of the three groups.

4)Sampling:-

Two blood samples were collected from each rat on the 5th, 10th, and 20th days

after the injection of both doses. The first sample was collected in heparenized tube for the haematological study and the second sample was collected in centrifuge tube to obtain clear serum for clinico-biochemical study.

A)Haematological studies:-

Blood picture(total erythrocytic count (R.B.Cs.),, packed cell volume percent (pcv%), haemoglobin percent (Hb%), and total leukocytic count (T.L.C.) were determined according to techniques described by *(9).*

B)Clinico- biochemical studies:-

Sera of rats were analysed for the determination of the total Proteins *(10)and* abumin *(11)* Globulins was calculated as the determination of the total Proteins *(10)and* the difference between total protein and albumin. Serum transaminases **(AST-ALT)** were determined coloremetrically according to *(12).* Serum sodium and potassium c *(13),* calcium *(14)* and inorganic phosphorus *(15)* were determined.

5)Statistical analysis:-

The obtained data were tabulated and statistically analysed according to *(16).*

RESULTS

1) Haematological studies:-

The effects of isofloperdone acetate on haematological picture are shown in table(1) the results obtained showed that the therapeutic and double therapeutic dose of isofloperdone acetate induce significant decrease in erythrocytic count haemoglobin concentration and packed cell volum at 5,10 days post injection but induced significant increase in total leucocytie count at same peroid.

2)Clinico- biochemical studies :-

The isofluperdone acetate induced significant decrease in total proteins, globulines and a significant increase in albumin at 5, 10 day post injection (Table 2). The results illustrated in table (3) clarified that iosfluperdone acetate injection increased transaminases (AST and ALT), potassium calcium and phosphorusbut decreased sodium.

Table (1): Effects of Isofloperdone acetate (0.4 and 0.8mg / kg b. wt.)on hemogram after intramuscular injection for 5 succesive days. (Mean + S. E)

Time of sampling / Parameter	Units	Control group	5 Days		10Days		20 Days	
			Therap. dose	D.therap. dose	Therap. dose	D.therap. dose	Therap. dose	D.therap. dose
RBCs	10^6/cm.m	7.25±0.24	6.02±0.42*	5.84±0,22**	6.64±0.13*	6,41±0.25*	6.94±0.69	6.82±0.84
HB	g m %	14.52±0.41	10.14±1.72*	9.26±1.13**	11.24±1.36*	11.03±1.21*	13.49±1.83	14.76±1.69
PCV	%	48.57±1.46	43.63±1.05*	42.49±1.42*	45.42±0.33*	44.31±0.54*	47.79±1.09	47.54±1.32
WBCs	10^3/cmm	14.92±1.21	18.09±0.63*	19.73±0.52**	17.74±0.42*	18.96±0.61*	15.13±0.93	15.42±0.84

*** Significant at P < 0.05 ** Significant at P < 0.01**

Table (2): Effects of Isofloperdone acetate (0.4 and 0.8mg / kg b. wt.)on proteinogram after intramuscular injection for 5 succesive days. (Mean + S. E)

Time of sampling / Parameter	Units	Control group	5 Days		10Days		20Days	
			Therap. dose	D.Therap. dose	Therap. dose	D.therap. dose	Therap. dose	D.therap. dose
T.protein	mg/dl	8.03±.0.31	6.72±0.34*	5.53±0.63**	6.98±0.19*	6,47±0.43*	8.05±0.95	7.94±0.63
Albumin	mg/dl	3.70±0.13	4.22±0.14*	4.51±0.29*	4.34±0.40	4.60±0.36*	3.91±0.26	4.02±0.72
Globulin	mg/dl	4.33±0.61	2.50±0.34*	1.02±0.31**	2.64±0.07*	1.87±0.45**	4.14±0.43	3.92±0.63

*** Significant at P < 0.05 ** Significant at P < 0.01**

Table (3): Effects of Isofloperdone acetate (0.4 and 0.8mg / kg b. wt.)on some biochemical parameters after intramuscular injection for 5 succesive days. (Mean + S. E)

Time of sampling / Parameter	Units	Control group	5 Days		10Days		20 Days	
			Therap. dose	D.therap. dose	Therap. dose	D.therap. dose	Therap. dose	D.therap . dose
AST	U/L	79.12±2.35	87.37±1.94*	93.95±2.16**	85.73±1.57*	87.49±2.54*	83.52±1.98	84.49±1.89
ALT	U/L	43.262±2.74	55.92±3.87*	59.84±2.86**	51.96±2.72*	54.78±2.65*	48.12±3.56	51.62±3.89
Sodium	mEq/L	12.30±0.32	8.83±1.42*	7.83±1.04**	10.41±0.57*	9.62±0.82*	11.95±0.86	11.34±0.69
Potasium	mEq/L	2.48±0.21	3.53±0.14**	3.82±0.24**	3.04±0.21	3.51±0.32*	2.64±0.34	2.82±0.34
Calcium	mg%	10.65±0.72	12.83±0.45*	13.12±0.61*	12.15±0.32	12.75±0.42*	11.19±0.64	11.63±0.49
phosphorus	mg%	4.97±0.21	5.84±0.30*	6.09±0.23*	5.38±0.13	5.78±0.24*	5.03±0.42	5.22±0.63

*** Significant at P < 0.05** **** Significant at P < 0.01**

DISCUSSION

The anti-inflammatory drugs are widely used in the veterinary practice to provide symptomatic relief of the acute and chronic inflammatory conditions,the anti-inflammatary drugs are steroid and non steroid *(16).*

A significant reduction of the erythrocytic count haemoglobin and packed cell volume occurred after 5and10 days post injection of isofluperdone acetate (0.4 and 0.8 mg /kg b.wt.) for 5 successive days. These effects were pronounced with the double therapeutic dose. The present observation may be attributed to deleterious effect of drug on bone marrow resulted in bone marrow dysfunctions (1). Similar observations on the erythrocytic count hemoglobin percentag and packed cell volume were previously recorded in horse *(17)camal, (18)*and goat (19). Also isofluperdone acetate at the same dose induced significant increase in total leukocytic count at the same periods. This result was parallel with those of *(20).* Who found that the administration of dexamethasone to camels at dose (20 mg/kg b. wt.) I.M. or I.V. for 4 days developed an increase in total leukocytic count. The same result is found by *(2)* who reported administration of isofluperdone acetate increase in the leukocytic count in sheep. These results may be attributed to an increase in the polymorphonuclear leucocytes *(22).*

The intramuscular injection of isofluperdone acetate (0.4 and 0.8 mg/ kg b.wt) induced significant decrease in total protein, globuline but albumine increased.These results agreed with those obtained by *(23)* who reported that administratin of therapeutic dose of depomodrol and kenacorte A to the rabbits resulted significant decrease in serum total protein levels *(24)* reported a significant decrease in total protein in rabbits given the therapeutic dose isofluperdone acetate. These results may be attributed to the immunosupressive effect of glucocorticoids *(25).* Our reaults were confermed by *(19)* who reported that dexamethasone induced significant decrease in total proteins, globulin and increase in albumin. Glucocorticoids inhibit proteins synthesis through decrease synthesis of messenger R.N.A. in fibroblast, DNA synthesis is impaired directly by corticosteroids *(27).* Another explanation for the decrease in total protein confirmed by *(28).* Glucocorticoids exert its catabolic effects on muscle protein homeostasis and inhibit protein synthesis.

The significant increase in the liver enszmes(AST-ALT)of rats treated with isofloperdone acetate reflected the degree of tissue damage. These results are comparable with the finding of *(26)* who mentioned that hepatopathy was induced in dogs, cats or rabbits by single or multiple doses of glucocorticoids.Moreover, *(29)* stated that dexamethasone administration increased serum transaminases (AST and ALT) in rabbits.

The effects of isofloperdone acetate on serum minerals were pronounced and mainfested by reduction in serum sodium and elevation in potassium, calcium and inorganic phosphorus. The same results reported by *(29)* in rabbits. The increases in the serum calcium and inorganic phosphorus in lambs after

treatment with dexamethasone were comparable with the results obtained previously by *(21)* and *(30)* in sheep and horse respectively.

It could be concluded that isofluperdone actate induced several hematological and biochemical changes in rats which become normal after 20 days from isofluperdone acetate withdrawal.

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تأثير خلات الايزوفلوبريدون على صورة الدم وبعض الوظائف البيوكيميائية فى الفئران

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كان الغرض من هذا البحث هو دراسة تأثيرات الجلوكوكورتيكويد المخلق (خلات الايزوفلوبريدون على صورة الدم وبعض الوظائف البيوكيميائية فى الفئران.

فى هذة الدراسة تم استخدام ١٥ فار أعمارها من ٤-٦ أشهر تم تقسيم هذه الفئران إلى ثلاث مجموعات متساوية كلا منها تضم ٥فئران. الأولى ضابطة والثانية والثالثة حقنت بالجرعة العلاجية وضعف العلاجية من عقار خلات الايزوفلوبريدون لمده خمس أيام متتالية فى العضل على التوالي بعد نهاية الحقن بـ ٥ ، ١٠ , ٢٠ يوم تم أخذ عينتين دم من كل فار الأولى على هيبارين وذلك لدراسة تأثير العقارين على صورة الدم والأخرى لفصل المصل وذلك لقياس بعض الوظائف البيوكيميائية.

تشير النتائج أن خلات الايزوفلوبريدون بالجرعة العلاجية وضعف العلاجية اديتا الى حدوث نقص معنوى فى عدد كرات الدم الحمراء تركيز الهيموجلوبين ، حجم خلايا الدم المرصوصة ،البروتين الكلى، الجلوبيولين و الصوديوم وهذا النقص استمر لمدة ١٠ أيام بعد إيقاف الحقن كما حدثت زيادة معنوية فى العدد الكلى للكرات الدم البيضاء, الزلال الترانس أمينيزس (**AST – ALT**), البوتاسيوم ، الكالسيوم والفسفور لمدة ١٠ يوم بعد إيقاف الحقن.

نستخلص من هذه الدراسة أن خلات الايزوفلوبريدون أحدث تأثيرات عكسية على صورة الدم ، بعض القياسات البيوكيميائية و كانت الجرعة العلاجية أقل فى أحداث التأثيرات العكسية .