THE EFFECTS OF LOW AND HIGH DOSE OF URANYL NITRATE ON HORMONAL ANALYSIS AND SOME BLOOD PARAMETERS IN RATS [+]

تأثيرات الجرع الواطئة والعالية لنترات اليورانيل في التحليلات الهورمونية وبعض معايير الدم في الجرذان

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Abstract :

In this study the effects of low dose (75 mg/ kg/ bw) and high dose (100 mg/ kg/ bw) of uranyl nitrate (UN) on hormonal analysis and some blood parameters were investigated. Sixty male mature Sprague–Dawlley rats were divided into three equal groups.

1. **Control group A (adminstrated normal Saline)**
2. **Low dose group B (administrated 75 mg /kg/ bw of uranyl nitrate)**
3. **High dose group C (administrated 100 mg /kg/ bw of uranyl nitrate).**

The route of administration was oral intubations for 53 days. The results have recorded the following:

1. **Low and high dose of uranyl nitrate treatment cause a significant (P<0.05) increament of alkaline and acid phosphatase enzyme in blood stream**
2. **Low and high dose of uranyl nitrate treatment cause a significant (P<0.05) increament of testosterone hormone.**
3. **Low dose of uranyl nitrate treatment cause a significant (P<0.05) elevation of total white blood cells (WBCs) count, while high dose of uranyl nitrate treatment cause a significant (P<0.05) decrement of total WBCs count**
4. **Low dose of uranyl nitrate treatment cause a significant (P<0.05) increament of Lymphocyte percentage, while a significant (P<0.05) decrement was found in nentrophil percentage**
5. **Low dose of uranyl nitrate treatment cause a significant (P<0.05) decreament of neutrophil percentage, while high dose of uranyl nitrate treatment restore the neutrophil percentage in blood.**

From this study we conclude that uranyl nitrate treatment caused a marked effect on some enzymes concentrations, hormonal level in blood stream and on total and differential count of WBCs.

المستخلص :

تم في هذه الدراسة البحث عن تأثيرات الجرعة الواطئة (٧٥ ملغم / كغم / وزن الجسم) والجرعة العالية (١٠٠ ملغم / كغم / وزن الجسم) من نترات اليورانيل في التحليلات الهورمونية وبعض معايير الدم. استخدم ستون جرذا ابيض ناضج قسموا إلى ثلاثة مجاميع متساوية وهي

١. مجموعة السيطرة (ا) :(أعطيت الماء المقطر).

٢. مجموعة الجرعة الواطئة (ب) : أعطيت (٧٥ ملغم / كغم / وزن الجسم من نترات اليورانيل) .

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٣. مجموعة الجرعة العالية (ج) : أعطيت (١٠٠ ملغم / كغم / وزن الجسم من نترات اليورانيل).

جرعت الحيوانات عن طريق الفم ولمدة ٥٣ يوما و سجلت النتائج التالية

1. ان الجرعة الواطئة والعالية من نترات اليورانيل أدت الى حصول زيادة معنوية ($P<0.05$) في انزيم الفوسفاتيز القاعدي والحامضي في مجرى الدم

٢.ان المعاملة بالجرع الواطئة والعالية لنترات اليورانيل أدت إلى حصول زيادة معنوية ($P<0.05$) في هورمون التستوستيرون (الشحمون الخصوي)

٣. ان المعاملة بالجرعة الواطئة لنترات اليورانيل أدت إلى حصول زيادة معنوية ($P<0.05$) في العد الكلي لخلايا الدم البيض بينما ادت المعاملة بالجرعة العالية من نترات اليورانيل إلى انخفاض معنوي ($P<0.05$) في العد الكلي لخلايا الدم البيض

٤. ان المعاملة بالجرعة الواطئة من نترات اليورانيل أدت إلى حصول زيادة معنوية ($P<0.05$) في النسبة المئوية للخلايا اللمفية بينما أدت هذه الجرعة الواطئة إلى حصول انخفاض معنوي ($P<0.05$) في النسبة المئوية للخلايا العدلة

٥. ان المعاملة بالجرعة الواطئة لنترات اليورانيل أدت إلى حصول انخفاض معنوي ($P<0.05$) في النسبة المئوية للخلايا العدله بينما أدت المعاملة بالجرعة العالية من نترات اليورانيل إلى استعادة النسبة المئوية للخلايا العدلة إلى الحد الطبيعي . من هذه الدراسة نستنتج إن المعاملة بنترات اليورانيل لها تأثيرات ملحوظة في تركيز بعض الانزيمات وفي مستوى الهورمونات في مجرى الدم وفي عدد خلايا الدم البيض والنسبة المئوية لهم .

Introduction:

Uranyl nitrate (UN) is one of the uranium salts, which is most commonly associated with oxygen as the uranyl ion [1].

Uranyl nitrate is a radioactive isotop of uranium since uranium have salts like uranyl nitrate, uranium chloride, uranium dioxide and uranium ethanoate [2].

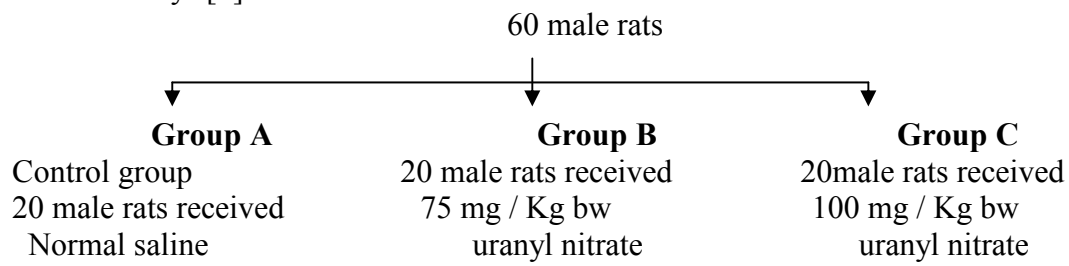
Fisenne and Perry [3] suggest that the uranium can be rapidly appear in the blood stream following ingestion, where it is associated primarily with red blood cells. Because of its high affinity for phosphate, carboxyl and hydroxyl groups, uranyl compounds readily combines with proteins and nucleotides to form stable complexes [3,4]. The amount of soluble uranium accumulated internally is proportional to the intake from ingestion or inhalation [5]. It has been estimated that the total body accumulation of uranium in human is 40 g, with approximately 40% of this have been present in the muscles, 20% in the skeleton and 10 %, 4%, 1% and 0.3% in blood, lung, liver and kidneys respectively [5].

Several investigations have shown a marked effect of uranyl nitrate on numerous organs such as kidney lung and precipitate in the bone skeleton [6,7]. Since there is no information on the effect of the uranyl nitrate (which is one of the uranium salts) on the hormonal concentration in serum and on some blood parameters in rat have not been taken by consideration, this study was designed to put the light on the effects of uranyl nitrate on the following

1) Alkaline and acid phosphatase enzymes
2) Hormonal analysis of testosterone, Lutinizing hormone (LH), Follicle Stimulating Hormone (FSH).
3) Total white blood cells count
4) Differential white blood cells count.

Materials and Methods:

The healthy mature (60) fertile rats were used in this study. The male rats were randomly divided into three groups of 20 rats each. Two groups (B and C) recieved doses of 75 mg/ kg and 100 mg/ kg body weight of uraryl nitrate, which considered as low dose and high dose respectively [8] . The adminstration was done orally via stomach tube five times a week for 53 days [9].



During period of the experiment, the body weight for all groups was measured five times a week (before the adminstration of the dose). Blood were collected from scarified rats by heart puncture, and serum collection was done by centrifugation on 1500 rpm for the detection of enzyme and hormone.

Results and discussion :

1. Body weight changes:

The results of the present study showed that the oral administration of two doses (low and high doses) of uranyl nitrate were affected the body weight of male rats in both groups B and C respectively. the body weight showed significant decrease at $P<0.05$ in group B , this reduction was significant at $P<0.01$ in group C as compared with the body weight of group A which is the control group (Table -1).

Table 1: Body weight (gm) of groups of rats administrated uranyl nitrate for 53 days

Animal group	Administrated dose (mg/ kg bw)	Mean of bw gm ± SE at zero time	Mean of bw gm ± SE after 53 days
Control A	**0**	**230±0.02**	**327±0.05**
Group B	**75**	**224±0.01**	**273±0.07***
Group C	**100**	**235±0.01**	**207±0.09****

Number of rats is 20 / each group
***Significant at P<0.05**
**** Significant at P<0.01**
Means ± SE (Standard Error)

The signs of uranyl nitrate effects were revealed as significant reduction in body weight, arch back due to abdominal pain and hemorrhage in the eye and nose, these results were in agreement with previous results of [10] who suggested that these signs were the most common signs of uranium toxicity.

2. Biochemical analysis

1.2

Enzymes

The biochemical result have shown a significant decreament ($P<0.01$) in both alkaline and acid phosphatase concentration in serum of animals treated with uranyle nitrate compared with their concentration in the serum of control animal group which refer to the kidney insufficient , specially in group (C) (Table 2)

These changes might reflect degenerative changes of renal corpuscles and tubules. Since renal damage confirm with the function of these enzymes (alkaline and acid phosphatase) that were decreased significantly in both groups. Similar result was found by [6,7].

Table 2 : Alkaline and acid phosphatase in control and two treated groups (ng /100ml)

Enzymes / Group	Alk. Pho. ng/ 100ml	Acid Pho. ng/100ml
Control Group Group A	134±0.03	13.1±0.1
Group B 75 mg/kg bw	63*±0.03	13±0.01
Group C 100 mg/kg.b.w	26**±0.04	3.5**±0.09

Number of rats = 20 / each group
*** Significant at P<0.05**
**** Significant at P<0.01**
Means ±SE [Standard Error]

2.2. Hormonal analysis

The hormonal analysis showed an increment in testosterone hormone in both group (B and C). This increment was significantly at $P>0.01$, (Table 3).

Table 3: The LH, FSH, Testosterone Hormone in control and two treated groups (ng/100ml)

Hormones / Groups	Lutinizing hormone ng/100ml	Follicular Stimulating Hormone ng/100ml	Testosterone hormone ng/100 ml
Group A Control	0.3±0.01	48.4± 0.03	0.2 ± 0.02
Group B 75mg/ kg .bw	0.3±0.02	11.25 ± 0.2**	0.75± 0.05**
Group C 100mg /kg .bw	0.35±0.01	2.8 ± 0.1*	3.25 ± 0.06 **

Number of rats = 20 / each group
*** Significant at P<0.05**
**** Significant at P<0.01**
Mean ± SE [Standard Error]

The hormonal assay showed that the level of testosterone hormone was significantly increased as compare with its level in control group. It is well known that the process of spermatogenesis is androgen dependent, thus the disturbance in androgen biosynthesis especially testosterone considerably affected spermatogenesis [11]. The Present results were revealed that this increament found in the systemic circulation. The concentration of testosterone hormone within the testes is very much greater than in the systemic circulations therefore, sampling plasma levels of testosterone dose not provide a measurment for the testicular testosterone level. This result and hypothesis are in agreement with [9] who

indicated that the circulating plasma testosterone dose not provide a measurement of testicular testosterone because the level of the steroid in testicular interstitial fluid can be up to 100-fold higher than in the plasma. On the other hand, the reason of non-affective of testosterone can be explained as uranyl nitrate action as androgen receptor blockade which prevent the testosterone binding to make its activity on its target organs.

Table (4): The effect of low and high dose of uranyl nitrate on total WBCs count and differential count in all animal groups.

Studied Groups	Mean of total WBC/mm^3±SD	Mean of Differential WBCs Count ± SD				
		Neutrophil	Lymphocyte	Monocyte	Eosinophil	Basophil
Control	5100.0±355.90	52.50±2.04	40.50±2.64	5.75±0.50	1.25±0.50	0.00±0.00
Low dose	19637.5±1507.41	41.50±3.87	52.75±3.86	4.25±1.5	1.5±0.57	0.00±0.00
High dose	2025.0±396.86	57.0±1.41	36.75±1.25	5.00±1.63	1.25±0.50	0.00±0.00

Table (4) showed a significant ($P<0.01$) increment in total WBCs count of animal group treated with low dose of uranyl nitrate. This increment reflects a sign of inflammatory response which result from alteration of many tissue organ due to the effect of uranyl nitrate. The latter produce chemotactic factors that stimulate bone marrow to increase WBCs Production then elevate their level in blood [12]. While a significant ($P<0.01$) increment in total WBCs count of animal group treated with high dose of uranyl nitrate was found. This decline might be due to a marked destruction of WBCs or due to the inhibition of bone marrow production of WBCs.

The increment of lymphocyte percentage of animal group treated with low dose of uranyl intrate could be explained that the lymphocyte considered as a target cell for uranyl nitrate effect which lead to the activation of lymphocytes proliferation. This result is in agreement with [13], who suggested that treatment of mice with radiation from radon^{-222} cause increment of lymphocyte in lymphatic organ and blood, while decrement in lymphocyte percentage was found in animal group treated with high dose of uranyl nitrate. This decrement might occur due to chromosomal abbreation in lymphocyte affected with uranyl nitrate which cause different lymphocyte structural alteration [13].

Table (4) also showed a decline in neutrophils' percentage in animal group treated with low dose of uranyl nitrate; this decrement might reflect a sensitive characteristic feature of neutrophils to uranyl nitrate effect that will cause a destruction of neutrophils. This result confirms the result of [14] who found a decrement in neutrophils' percentage in mine workers in Namibia. But neutrophils restore their percentage in animal group treated with high dose of uranyl nitrate.

From this study the following were concluded:

1. Uranyl nitrate treatment effect on the concentration of alkaline and acid phasphatase in blood stream which might reflect a degenerative changes of renal corpuscles and tubules
2. Uranyl nitrate causes elevation of testosterone hormone in blood stream
3. Low and high doses of uranyl nitrate have a marked effect on total and differential count of WBCs.

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