THE EFFECT OF BISMUTH CHLORIDE ON SOME BLOOD AND BIOCHEMICAL PARAMETERS IN MALE LABORATORY RATS (*RATTUS-RATTUS*)

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ABSTRACT

The present study amid to characterized the potential toxic effects of bismuth chloride through oral administration on blood and biochiemical parameters of laboratory rats.Solutions of bismuth chloride were chronically feed by stomach tube to rats in(2.5mg/kg and 5 mg/kg).Animals were anesthetized after two months and blood samples were obtained,blood and biochemical parameters were appreciated between control and experimental Groups.The investigation of blood parameters included red blood cells count (RBC) hemoglobin concentration,packed cell volume PCV and total white blood cell count(WBC)biochemical parameters included total serum cholesterol(TSCH),alanin aminotransferase (ALT) and aspartate aminotransferase(AST).The results showed significant decrease ($p \leq 0.05$) of R.B.C count ,Hb concentrations PCV value and total W.B.C count in contrast ,there was significant increase($p \leq 0.05$) of the total serum cholesterol(,ALTand AST) activities.

INTRODUCTION

Bismuth,which is located next to lead in the periodic table has very similar physicochemical character to that of lead and because of its low melting point wettability and low thermal conductuctivity it has already been wideldy used as lead substitute in the industridal fieled ,bismuth compounds have been used for more that 300 year for the treatment of skin lesions ,syphilis and various gastrointestinal disorders .recently bismuth compounds such as ranitidine bismuth citrate have been frequently used for treating drug-resistant *Helicobactor pylori* infections in

combination with antibiotics(1) accumulation of high concentration of heavy metals may cause pathological and physiological dysfunction of organs (2).

Bismuth is one of the least toxic of the heavy metals ,however intoxication has occured from its use in medicine(4) Bismuth compounds, in particular colloidal bismuth subcitrate have been actively promoted for the treatment of diarrhea and peptic ulcer disease (5).bismuth chloride has also been used successfully in the treatment of duodenal ulcer disease(6).however therapeutic bismuth compounds are now being marred by episodes of serious adverse reactions(6).as amatter of fact ,the toxic effects of bismuth chloride were dctected in liver and kidney from control and treated animals(7,8).deposits of bismuth were found in lymph nodes ,liver spleen and kidney as well as In macrophage in the gastrointestinal lamina propria at the subcellular level bismuth found exclusively in lysosomes primarily in macrophages and dendritic cells(8). Again ,pathological effects of bismuth compounds were established in humans nephropathy encephalopathy osteoarthropathy gingivitis somatits and colitis(9). The aim of present study was to characterize the potential toxic Effect of bismuth on some blood and biochemical parameters in male rats.

MATERIAL AND METHOD

The experiment was conducted at the animal house of veterinary Medicine college – University of Basra.where 24males white laboratory rats(*Rattus Rattus*) age(8)week old and average body weight between (150 – 200)g were used. The animals were accommodated in the same laboratory condition by keeping them in special cages. The experiment conditions were unified for all animals where the room temperature was set between 20-25C by the use of air conditioner, and the light period was 12 hours daily, by the use of two fluorescent lamps,and the humidity rate was about 50% food and water were provided daily (*ad libitum*). The animals of the experiment was divided randomly into three groups with 8 male rats in aech, as follows:

Group1(control):administered orally 0.9% normal saline (N.S)daily for two mounth.

Group2:administered orally 2.5mg/kg of bismuth chloride daily for two mounth.

Group3:administered orally 5mg/kg of bismuth chloride daily for two mounth.

Stomach tube.also know as gavage was used to instill liquids directly into stomach after 8 week from exposure to doses of bismuth chloride the rats were anaesthetized with chlorophorm, blood sample were collected directly form the heart bythe use of adisposable syringes. The blood sample divided into two parts the first part of blood poured in tube containing(EDTA) anticoagulant to accomplish the blood parameters (RBC,HB,PCVandWBC). While the second part of blood was poured into test tube free from anticoagulant to isolated blood serum to estimated the biochemical parameters (TSCH,ALT and AST).the soures of bismuth chloride was(BDH)England company.

RESULT

It seems as table (1)below illustrates that the treated animals with bismuth chloride (2.5mg/kg)and (5mg/kg)decreases the RBC counts hemoglobin levele ,hematocrit values and WBC significantly ($p \leq 0.05$) after two month of treatment compared with control group

Table ((1))the effect of bismuth chloride on blood parameter of male rats Mean±SD n=8.

Parameters / Group	RBC (cell/mm^3)x10^6	Hb %(gm/dl)	P.C.V (%)	WBC (cell/mm^3)x10^3
Control(0.9%N.S)	9.493 a 0.114±	15.39 0.142± a	49.510 6.871±a	9.567 0.47±a
T1(2.5mg/kg) Bismuth chloride	8.402 0.306±b	14.223 0.179± b	40.787 7.89±b	7.598 0.31±b
T2(5mg/kg) Bismuth chloride	6.405 0.921 ± c	11.876 0.329± c	37.713 10.745±c	6.640 0.34±c
LSD	1.09	1.17	3.07	0.958

The number represent the mean ± standard Deviation . .

The deferent letters refer to significant defferences among groups $p \leq 0.05$

It seems from table(2) that the treated animals with bismuth chloride (2.5 mg/kg) and(5mg/kg)increases the alanine amino transferase ,aspartate amino transferase and total serum cholesterol significantly ($p \leq 0.05$) after2month of the treatment compared with the control group asignificant difference is also abserved between T1andT2.

Table((2))the effect of bismuth chloride on biochemical parameters of male rats(Means±SD) n=8

Parameters / groups	ALT(IU)	AST(IU)	TSCH(mg/dl
Control 0.9%N.S)) ((	37.18 1.01±c	80.07 1.188±c	138.08 5.75±c
T1(2.5mg/kg) Bismuth chloride	41.68 1.29±b	85.50 1.89±b	146.28 1.42±b
T2(5mg/kg) Bismuth chloride	45.71 3.72±a	90.81 1.53±a	154.81 2.57±a
LSD	9.02	5.31	8.20

The number represent the mean ± standard Deviation .

The deferent letters refer to significant differences among groups $p \leq 0,05$

DISCUSSION

In the present study hematological changes in this parameters (RBC, Hb , and PCV) occur because one of basic mechanisms of the toxic action of heavy metal on mammals is erythrocyte destruction [13] a major compartment was established for bismuth associated with the membrane in RBC .Erythrocyte life span was shortened because increased mechanical of fragility of the cell membrane [14] .It is was also recorded that bismuth chloride forms instable complexes with GSH[19].Glutathione is a tripeptide containing cystein that has a reactive SH group with reductive potency , therefore GSH plays a vital role in the protection of cell against oxidative stress . It can act as no enzymatic antioxidant by direct interaction of the SH group with reactive oxygen species as a factor or a coenzyme[28]. Glutathione is a major

component of RBC [16]. The decreased in cellular glutathione content can effect the physiological response to cell [17] Oxidative stress developed when the level of antioxidant as glutathione are lowered and the production of reactive oxygen species (ROS) exceeds [18] . as a result of ROS activity irreversible modification of biological fundamental macromolecules have been described [19] . In conclusion oxidative stress can disrupt normal physiological pathway and causes erythrocyte destruction . The fall of hematocrit(Ht) it is also a reason for the decreased erythrocyte numbers [20] . The low value of Ht in experimental rats might be due to low rate of RBC . The similarity between the pharmacological and toxic behavior of lead and bismuth has been pointed in literature [9] . The decreased of heme synthesis was due to the inhibition of SH- containing enzyme by lead [14 , 21] . Similarity some effect of bismuth are medated via the blocked of SH – groups [16] . Bismuth chloride might also cause oxidative stress in blood , as a matter oxidative stress leads to the oxidative of protein SH groups [19] . We found that one of the effect bismuth chloride toxicity was the production of erythrocyte with lower MCV and MCHC . MCV and MCHC are closely related to an adequate supply of Fe to hemoglobin [13], [[22]. It is established that the target site of bismuth in protein and enzymes are both Fe sites and Zn sites [23].Bismuth also binds to serum transferrin, transferrin are functional in iron transport to cell from blood [24].The chronic toxic action of the metals probably depresses the proliferative activity of the stem cells [3].The WBC of experimental animals used in this study was significantly low .It is recorded that changes in surface markers of stem cell were remarkable in mice exposed to heavy metal [12].The alteration of blood parameters of mammals is in agreement with the increasing of heavy metal dose [26],[27]. The higher value of alanine aminotransferase ,aspartataminotransferase and total serum cholesterol may be related to the toxic effect of bismuth in the liver and other organs. However when bismuth is absorbed as fat-soluble or a water-soloble organic compound , it has been reported that it leads to kidney , liver and central nervous system toxicity . Kidney damage was observed in rats receiving a single intramuscular injection (0.03 – 1.5 g/kg) of 13 different bismuth compounds such as bismuth triglycollate [5]. In our previous paper we have investigated the influence of bismuth chloride on rats in abiochemical experiments . The dose independent changes of bismuth chloride in serum enzymes of Sprague Dawley rats were observed a 3 day Experiment because the exposure to bismuth

chloride lead to inflammation and nicrosis hepatic cells of liver and them increases in liver inzymrs [10,11].

تأثير كلوريد البزموث على بعض المعايير الدمية والكيموحيوية في ذكور الجرذان المختبريه *Rattus-Rattus*

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الخلاصة:-

إن الهدف من الدراسة الحالية هو لمعرفة التاثير السام لكلوريد البزموث على بعض المعايير الدمية والكيموحيوية في الجرذان المختبرية اذ تم إعطاء محلول كلوريد البزموث فمويا بواسطة انبوب التجريع بتركيزيين مختلفين ((2،5ملغرام/كغم من وزن الجسم و5ملغرام/كغم من وزن الجسم)) من كلوريد البزموث ولمدة شهرين متتاليين 0بعد انتهاء فترة التجربة خدرت الحيوانات وجمع ت عينات الدم لاجراء الاختبارات الدمية والمتضمنة العدد الكلي لكريات الدم الحمر وتركيز نسبة الهيموغلوبين وحجم خلايا الدم المرصوص والعدد الكلي لخلايا الدم البيض والاختبارات الكيموحيوية والمتضمنة قياس تركيز الكولسترول الكلي بالمصل وقياس تركيز أنزيمات الكبد (AST&ALT) 0

اظهرت النتائج انخفا ض معنوي ($P\leq0.05$)في عدد كريات الدم الحمر وتركيز خضاب الدم وحجم خلايا الدم المضغوط والعدد الكلي لخلايا الدم البيض بينما كان هناك زيادة معنوية ($P\leq0.05$)في مستوى الكولسترول الكلي بالمصل وكذلك في فعاليات الانزيمات الكبديةAST&ALT0

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