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Full Length Research Paper

Effects of lead on Epidermal wound Contraction and serum biochemistry in West African dwarf goats

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Lead contamination through wound could either be environmental and or systemic sources that impair wound healing in animals. The haematological, biochemical changes including thewound healing effects of topical lead poisoning were therefore investigated using ten adult West African dwarf (WAD) goats, randomly divided into two groups of five animals each. The first group served as the control and the second group was treated with lead chloride solution. Wound contraction was compared between the two groups, haematology and serum biochemistry were analysed at each stage of the healing process. The results revealed a delay in wound contraction in the lead treated group. Erythrocyte sedimentation rate, haemoglobin concentration, packed cell volume, albumin, neutrophil count in the lead treated group decreased significantly (P<0.05).Heart rate and temperature increased significantly (P<0.05, P<0.01) in the treated group. This study concluded that epidermal lead exposure impaired wound healing.

Keywords: Lead, wound contraction, haematology, biochemistry, West African dwarf goats.

INTRODUCTION

Lead is a common cause of poisoning in domestic animals throughout the world. It is a heavy, low melting, bluish-gray metal that is ubiquitous in human environment but rarely found naturally as a metal (Siddiqui and Rajurkar, 2008). It is usually found combined with two or more other elements to form lead compounds. Environmental lead (Pb) continues to pose a dangerous and health risk to both humans and animals (Brownie *et al*., 2009). Lead toxicity is one of the most common poisoning in farm animals (Radostits *et al*., 2000), and as one of the most hazardous and cumulative environmental pollutants that affect all biological systems through exposure from air, water and food sources (Patra and Swarup, 2000). Lead has been recognized as toxic to wildlife for over a century; and even sub lethal levels may cause immunological and neurological problems, biochemical and behavioral changes and physiological disorders that may affect immune response and reproduction (Pain *et al*., 2009).On a molecular level, proposed mechanisms for toxicity involve fundamental biochemical processes which include lead's ability to inhibit or mimic the actions of calcium (which can affect calcium-dependent or related processes) and to interact with proteins including those with sulfhydryl, amine, phosphate and carboxyl groups (ATSDR, 2005).Lead has been reported to impact a variety of health outcomes including, but not restricted to; neurodevelopment (Bellinger, 2008), cardiovascular disease (Navas-Acien *et al*., 2007), neurodegenerative diseases and cognitive decline (Weisskopf *et al*., 2004), immune system impairment (Dietert and Piepenbrink 2006), renal system function (Weaver *et al*., 2009), and adverse birth outcomes (Andrews *et al*., 1994).

Wound healing is a complex and dynamic process where by cellular structures and tissue layers are

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reconstructed consisting of four continuous, overlapping, and precisely programmed phases. These phases and their biophysiological functions must occur in the proper sequence, at a specific time, and continue for a specific duration at an optimal intensity (Mathieu *et al*., 2006). There are many factors that can affect wound healing which interfere with one or more phases in this process, thus causing improper or impaired tissue repair. Goat is an integral part of a traditional crop livestock production (Seyoum, 2002) and is referred to as poor man's cow because they provide milk in enough quantity for household consumption (Odunsi *et al*., 2005). Goats are also used in ceremonial feasting and payment of social dues (Okunlola, 2000).Goat production contributes to local handcraft industries where its fiber and skins are used extensively. Despite several animal studies on the toxicity of lead, there remains a dearth of information on its effect on wound healing in goats. Therefore, this study was designed to investigate the lead exposure through wound on haematological indices, wound contraction, serum biochemical indices, temperature, respiratory rate and heart rate in West African dwarf goat.

MATERIALS AND METHODS

Experimental animals: Ten apparently healthy West African dwarf (WAD) goats (age 1-3 years; body weight 15-20 kg) were used for the experiment. After the wound creation, the animals were randomly divided into two groups of five goats each i.e. the control and the experimental group. The wound of the experimental group was dressed daily with 0.035ppm solution of lead chloride. Blood lead at this level caused clinical symptoms of excessive perspiration at rest and headache (Elegbede *et al*., 2012). The control group was also dressed daily with 0.9% normal saline. The wounds were covered with moist saline dressing to safe guard it and the experiment lasted for nine days when control animal wound healed completely.

Wound creation: The operation site (lateral to the thoracic vertebrae and lying to the proximal body of the rib)was clipped, washed with soap and water and shaved. Ethanol (70%) was applied as an antiseptic for the shaved region before the wound creation and the animal was placed on the operation table on left lateral recumbency. Infiltration anaesthesia was performed using 2% lignocaine hydrochloride at the back of the animals i.e. the dorsum in the thoracic and lumbar region of each of the animals. The dimension of the epidermal wound created was $1cm^2$. The progressive changes in the wound contraction were monitored grossly by placing clean and sterile veniercaliper on the wound margins. The length and breadth were also measured to determine the wound surface area. This method was according to previous work (Olaifa *et al*., 2016).This experiment was carried out in accordance with the ethical committee of the university of Ibadan ethical rules on animal experiment with approval number UI-ACUREC/App/2016/019. Hematology and serum biochemical studies Blood was collected on days 0, 3, 6 and 9 through the jugular vein, into an anti-coagulant free sample bottle and allowed to coagulate at room temperature (27 0C) with the bottle slanted to obtain the serum.

The serum total protein was determined by the Biuret method (Reinhold, 1953), while albumin value was obtained by bromocresol green method (Doumas and Biggs, 1971). Globulin was obtained from the difference of total protein and albumin. Serum urea and Creatinine levels was determined using photoelectric colorimeter (Coles, 1989). Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) activities were measured using a colorimetric method (Reitman and Frankel 1957). The blood samples collected for haematology were evaluated for packed cell volume (PCV) through the haematocrit method (Jain and Schalm, 1986). Haemoglobin concentration was evaluated using the cyanomethaemoglobin method (Schalm *et al*., 1975). Red blood cell count was determined by the haematocytometry method (Jain and Schalm, 1986). Total white blood cell (WBC) counts and differential leucocyte counts were made according to Coles (1989). Haematometric indices including Mean Corpuscular Volume (MCV) and Mean Corpuscular Haemoglobin (MCH) were determined from the values obtained from red blood cell count, haemoglobin level and PCV values (Duncan *et al*., 1994).

Data analysis

Data collected were subjected to statistical analysis using the student's t-test, values of $P<0.05$ were considered statistical significant and were presented as Mean ± standard error of mean.

RESULTS

WAD goats subjected to lead chloride administration through the wound revealed marked delayed in wound contraction (Table 1), marked decrease in PCV, Hb, ESR, albumin (Table 2 and 3) and a significant increase in heart rate and temperature. Creatinine, BUN, globulin, glucose, and total protein did not show any significant changes.

DISCUSSION

Wound healing is a complex and dynamic process, with the wound environment changing with the shifting healt

Table 1: Wound Contraction rate (cm2) of control and lead chloride treated goats.

Day	Control	Lead-treated
0	100.00±0.00	100.00±0.00
3	59.53±2.66	68.35±3.18
6	0.00±0.00	23.74±8.98*
9	0.00±0.00	12.95±8.72

***** *P<0.05, values are Mean ± SEM*

Table 2: Effect of wound lead poisoning on Hematological indices

Haematological indices	Day	Control	Lead-treated
ESR	0	2.80±0.58	1.80±0.37
	3	2.60±0.81	2.40±0.51
	6	2.00±0.32	1.00±0.00*
	9	1.60±0.24	1.80±0.37
Hb (g/l)	0	13.10±1.67	13.12±1.29
	3	11.04±1.24	10.22±0.94
	6	10.60±1.13	7.72±0.56
	9	10.32±1.64	7.02±1.04*
PCV (%)	0	40.60±4.18	43.60±4.70
	3	34.00±3.26	30.80±2.84
	6	32.00±3.42	24.60±1.86
	9	31.20±4.90	21.20±3.18*
RBC(x10^{12}/l)	0	10.77±0.59	11.54±1.03
	3	13.79±1.56	17.03±1.74
	6	20.10±1.62	19.97±1.55
	9	15.97±2.08	21.39±3.08
MCH (pg)	0	11.80±1.07	13.20±2.54
	3	6.80±0.58	6.20±0.66
	6	3.40±0.51	5.00±0.45
	9	3.40±0.51	5.00±0.45
MCV (fl)	0	40.40±4.18	34.80±2.42
	3	22.00±1.55	19.60±1.78
	6	12.00±1.58	15.60±1.69
	9	12.00±1.58	15.60±1.69
WBC(x10^{9}/l)	0	8.32±1.25	9.48±0.49
	3	7.20±0.75	10.12±0.77
	6	12.96±1.25	12.40±2.11
	9	10.88±1.30	13.96±3.72
Neutrophils (x10^{9}/l)	0	36.40±2.71	30.00±2.66
	3	38.20±1.28	42.20±1.46
	6	38.80±1.39	42.60±2.50

Table 2 cont.

	9	36.40±2.62	32.80±3.28*
Lymphocyte (x10^9/l)	0	63.40±2.54	70.00±2.66
	3	61.20±1.46	57.20±1.59
	6	60.40±1.40	56.80±2.31
	9	62.40±2.66	65.80±3.10
Platelets (x10^9/l)	0	14.00±1.26	13.60±1.33
	3	10.00±1.41	11.00±1.48
	6	8.40±1.17	11.20±1.36
	9	7.60±1.44	10.60±1.54

**P < 0.05, values are Mean ± SEM*

Table 3: Effect of wound lead poisoning on serum biochemical parameters

Biochemical Parameters	Days	Control	Lead-treated
Albumin (mg/dl)	0	1.14±0.04	1.46±0.21
	3	1.12±0.06	1.28±0.19
	6	1.24±0.07	1.12±0.04*
	9	1.06±0.04	1.34±0.22
ALT	0	42.20±3.20	42.40±9.19
	3	38.60±2.89	40.00±8.06
	6	37.60±2.32	37.80±7.44
	9	29.80±7.89	40.00±12.08
AST	0	10.00±0.63	10.80±1.96
	3	8.00±0.63	8.60±1.94
	6	6.60±0.60	10.20±1.28*
	9	5.00±1.41	9.00±3.00
BUN	0	1.07±0.03	1.25±0.25
	3	1.02±0.02	1.26±0.24
	6	1.02±0.02	1.29±0.21
	9	1.06±0.04	1.50±0.31
Creatinine	0	1.18±0.08	1.26±0.24
	3	1.10±0.04	1.22±0.22
	6	1.10±0.03	1.26±0.19
	9	1.06±0.04	1.30±0.19
Globulin (mg/dl)	0	2.54±0.28	2.34±0.26
	3	2.26±0.28	2.04±0.35
	6	1.92±0.20	2.34±0.14
	9	2.06±0.15	2.36±0.32

Table 3 Cont.

Glucose (mg/dl)	0	51.20±3.01	53.20±5.07
	3	47.80±3.35	46.60±5.88
	6	43.40±3.89	44.60±5.53
	9	35.80±7.28	44.20±9.22
Total Protein (mg/dl)	0	3.68±0.29	3.82±0.43
	3	3.38±0.32	3.34±0.50
	6	3.16±0.26	3.46±0.18
	9	3.12±0.18	3.70±0.49

P < 0.05*, *values are Mean ± SEM

status of an individual. Among the heavy metals, lead still remains the major toxic pollutant of the environment which occurs through air, food, dust and water. Lead intoxication through wound could be an environmental and local factor that impairs wound healing in animals.

The result of this study shows a significant delay in wound healing of the lead-treated goats. Exposure to lead has been shown to increase production of reactive oxygen species (ROS) and consequently induce lipid peroxidation and alteration of antioxidant defense systems in mice (Demirezen and Kadiriye, 2006), rats (Haleagrahara *et al*., 2011)and goat (Mousa *et al*., 2002)resulting in oxidative stress (Xienia *et al*., 2000).The pathophysiology of stress results in the deregulation of the immune system, mediated primarily through the hypothalamic-pituitary adrenal (HPA) and sympathetic-adrenal medullary axes or sympathetic nervous system (Boyapati and Wang, 2007). Studies in both humans and animals have demonstrated that stress causes a substantial delay in wound healing (Broadbent *et al*., 2003; Lisa *et al*., 2006). The hypothalamic-pituitary-adrenal and the sympathetic- adrenal medullary axes regulate the release of pituitary and adrenal hormones. These hormones include the adrenocorticotrophic hormones, cortisol, and catecholamines (epinephrine and norepinephrine). Stress up-regulates glucocorticoids (GCs) and reduces the levels of the proinflammatory cytokines IL-1β, IL-6, and TNF-α at the wound site. Stress also reduces the expression of IL-1α and IL-8 at wound sites—both chemo attractants that are necessary for the initial inflammatory phase of wound healing (Boyapati and Wang, 2007).

Furthermore, GCs influence immune cells by suppressing differentiation and proliferation, regulating gene transcription, and reducing expression of cell adhesion molecules that are involved in immune cell trafficking (Sternberg, 2006).The result indicated a significant reduction ($P<0.05$) in haemoglobin (Hb), packed cell volume (PCV) and erythrocyte sedimentation rate (ESR) in lead-treated goat compared to the control group. This haematological alteration might be due to effect of lead on activity of α aminolevulinic acid dehydratase (ALAD), key enzyme of heme synthesis. Moreover lead also inhibit the conversion of coproporphyrinogen III to protoporphyrin IX leading to reduction in haemoglobin production, shortened life span of erythrocytes and interacts with some reactions where calcium is their secondary mediator (Klassen, 2001). This corroborates earlier studies (Mugahi *et al*., 2003; Sujatha *et al*., 2011) and show microcytic hypochromic anemia (Suradkar *et al*., 2009; Alwaleedi, 2015). Progressive destruction of RBCs due to binding of lead with RBCs, leading to increase fragility and destruction and generation of reactive oxygen results from interference of lead in heme synthesis through inhibition of 5-aminolevulinic acid dehydratase activity resulting in increased production of 5-aminolevulinic acid (Moore,
1986; Adonaylo and Oteiza, 1999).; could be another reason for decrease haematological values (Rous, 2000).Platelets count revealed considerable insignificant increase in lead-treated animals compared to the control. This may be due to thrombocytopenia and thrombocytosis after chronic lead intoxication (Sudakova *et al*., 1983; Mugahi *et al*., 2003; Abdulkareem, 2010); while the insignificant increase in the white blood cell may be due to lead induced inflammation (Yagminas *et al*., 1990, Alwaleedi, 2015).Significant increase in ALT and AST which are biomarkers for liver toxicity was observed in this study ($P<0.05$), might be due to increased cell membrane permeability, increased cellular basal metabolic rate or cell membrane damage of hepatocytes caused by lead acetate. These results agree with previous studies reported an elevation in AST and ALT levels after treatment with lead due to acute hepatitis, jaundice, and liver cirrhosis in mice, human and rat(Mehta *et al*., 2002; Patil *et al*., 2007; Shalan *et al*., 2005, Alwaleedi, 2015), also in sheep (Badiei *et al*., 2009). The significant decrease in albumin at the reparatory phase

might be due to binding of lead to albumin (Stone and Soares, 1976), disturbance in the protein metabolism in the liver consequent to accumulation of lead leads to liver injury(Sharaf *et al*., 2008). Patil *et al*., 2007,Dongre *et al*., 2010 and Kshirsagar *et al*., 2015 also reported a decrease in the synthesis of albumin and other protein as a result of increased blood lead level. However, creatinine, BUN, globulin and glucose did not show any significant change which might be due to the homeostasis processes set in by the body in response to wound lead contamination. The result also showed a significant ($P<0.05$) increased in heart rate of lead-treated animals as compared to the control group. This agrees with Park *et al*.,(2008) that reported that people with long-term exposure to higher levels of lead may be more sensitive to cardiac autonomic dysfunction and heart rate variability. Also, Lead exposure effects like increasing the generation of reactive oxygen species by depletion of glutathione and protein-bound sulfhydryl groups, leading to oxidative stress (Gurer and Ercal, 2000); induces iron-dependent lipid peroxidation in liposomal membranes (Adonaylo, 1999); down-regulating of nitric oxide generation (Vaziri, 2002); inhibiting the intracellular calcium messenger system and altering calcium homeostasis because of its mimicry of the calcium ion (Sandhir and Gill, 1994). All these effects are associated with sympathetic excitation and vagal withdrawal (Ding *et al*., 2000; Dursun *et al*., 2005).

In conclusion, epidermal wound lead contamination markedly delayed wound contraction and healing, reduced haematological parametersandhepato-toxicity. Therefore, lead contamination in animals either orally in food and water or epidermally should be avoided.

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