Protective Effect of Vitamin b_6 On Lead-Induced Hematological Changes in Male Albino Wistar Rats

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Abstract

Background: Lead is a common environmental pollutant capable of causing acute and chronic illness. Lead acetate has been reported to have a higher binding affinity for erythrocytes and also for inducing haemolysis. This study was carried out to investigate the effect of lead acetate on some hematological parameters and the protective effect of Vitamin B_6. **Methods:** Twenty (20) adult male albino Wistar rats, weighing between 180-250g, were randomly assigned into 4 groups with 5 rats per group. Group A rats served as control. Group B rats were administered 50mg/kg body weight of lead acetate; Group C rats were administered 50mg/kg body weight of vitamin B_6; Group D rats were co-administered vitamin B_6 and lead acetate. This experiment lasted for 28 days. At the end of the experimental period, the animals were sacrificed and blood samples were collected, by Cardiac puncture, and transferred into EDTA bottles. The hematological parameters were analyzed were Red blood cell (RBC) count, Hemoglobin concentration (HbC), packed cell volume (PCV), Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin (MCH), Mean Corpuscular Hemoglobin Concentration (MCHC), White Blood Cell (WBC) count, differential white blood cell count (lymphocyte, granulocyte and monocyte) and Platelet count. Statistical analysis was done using graph pad Prism 8.0 software. The results were presented as mean ± SEM and $P<0.05$ was taken to be statistically significant. **Results**. There was a significant reduction in RBC, PCV, Hemoglobin concentration, MCV, MCHC, MCH and a significant increase in WBC, lymphocyte and platelet counts in rats administered with lead acetate only. In rats that were co-administered with lead acetate and vitamin B_6, there was a significant improvement in RBC, PCV, Hemoglobin concentration, MCV, MCHC, MCH and a significant decrease in WBC, lymphocyte and platelet counts when compared with rats that wereadministered with lead acetate only. **Conclusion**: In conclusion, this study has shown that vitamin B_6 protected the blood cells against lead-induced damage. Therefore it could be an effective therapeutic agent against lead-induced hematological changes and its associated complications

Keywords: Lead acetate, Vitamin B_6, hematological parameters

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Introduction

Lead is one of the most prevalent heavy metal contaminants in the environment with widespread industrial and domestic applications (1). While it has some beneficial uses (use in the manufacture of paint, ceramics, pipes and plumbing materials, solders, gasoline, batteries, ammunition and cosmetics), it has been extensively reported to have toxic and deleterious effects on the general health of humans by affecting various organs and body systems (1). Lead can adversely affect kidney function and the nervous, immune,

reproductive, developmental, and cardiovascular systems (2). Humans are exposed to lead through drinking water (3), soil (4) and air released from industrial sources (such as paint, cosmetic and ammunition industries) which utilize Lead as a raw material for production (5, 6, 7). The red blood cell is the principal transport component of lead from the gut to the various other tissues in the body (8). Erythrocytes have a high affinity for lead, binding 99 percent of lead in the bloodstream thus more than 90% of lead in the blood resides on the red blood cells and is transported to various organs and tissues (9). Lead has been reported to have a destabilizing effect on cellular membranes (10, 11), and in red blood cells (RBC). Lead acetate reduces the fluidity of cell membranes and increases the rate of hemolysis of red blood cells. Lead also inhibits hemoglobin synthesis (12) thus affecting the oxygen-carrying capacity of the blood. Lead has also been reported to increase leukocyte count (leukocytosis), monocytosis, eosinopenia, neutrophilia, and thrombocytosis (13). Oxidative stress is considered a possible mechanism involved in lead toxicity (14). Lead induces the production of reactive oxygen species in target organs such as blood, brain, liver and Kidneys (15).

Vitamin B_6 (Pyridoxine) is a water-soluble vitamin which acts as a cofactor in amino acid metabolism (16). Food sources of vitamin B_6 include poultry, fish, potatoes, chickpeas, bananas and fortified cereals and they play an important role in normal brain development and in keeping the nervous system and immune system healthy (17). Vitamin B6 is involved in the formation of red blood cells since pyridoxal phosphate is the rate-limiting substance in making heme, a component of hemoglobin (18). Vitamin B_6 is a potent antioxidant that is reported to be more potent than Vitamins C and E (19). Researchers have reported its crucial role in oxidative stress tolerance and other abiotic stressors (20, 21). Since oxidative stress and free radical generation have been implicated as a mechanism by which lead induces damage and hematological changes, this study was carried out to investigate the protective effect of Vitamin B_6 on lead-induced hematological changes.

Materials and method

Chemicals

Lead acetate [$Pb(C_2H_3O_2)_2$] manufactured by Lobachem [Loba Chemie Pvt. Ltd. (India)] and Vitamin B6 (pyridoxine hydrochloride; 99.5% purity) manufactured by JHD corporation (Ontario, California, USA) were purchased from Pyrex chemicals, in Benin City, Edo State, Nigeria.

Experimental animals: Twenty (20) adult male albino Wistar rats, weighing between 180-250g, were used for this study. The animals were purchased and cared for in the animal house of the Department of Anatomy, School of Basic Medical Sciences, College of Medical Sciences, University of Benin, Benin City. They were kept in clean cages in a well-ventilated environment. They had access to clean water and sufficient feed *ad libitum*, in line with the National Research Council Guide for the Care of laboratory animals [22]. They were allowed to acclimatize for two weeks with free access to food and water before the commencement of the experiment.

Experimental design: Twenty (20) adult male albino Wistar rats weighing between 180 - 250g, were randomly divided into four groups with 5 rats per group. Group A rats served as control. Group B rats were administered 50mg/kg body weight of lead acetate; Group C rats were administered 50mg/kg body weight of vitamin B_6; Group D animals were co-administered with vitamin B_6 and lead acetate. All administrations were done orally using an orogastric tube. The experimental period lasted for 28 days.

Collection of samples: At the end of the experimental period, the rats were observed for general physical characteristics, and were weighed. The rats were sacrificed using chloroform anesthesia and blood samples were collected by Cardiac puncture

and transferred into EDTA bottles for hematological analysis.

Haematological analysis: Blood analysis was carried out using an automatic hematological assay analyzer at the laboratory of Accident and Emergency (A & E), University of Benin Teaching Hospital, Benin City. Hematological parameters analyzed include the Red blood cell (RBC) count, Hemoglobin concentration (HbC), packed cell volume (PCV), Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin (MCH), Mean Corpuscular Hemoglobin Concentration (MCHC), White Blood Cell (WBC) count, differential white blood cell count (lymphocyte, granulocyte and monocyte) and Platelet count.

Statistical analysis

Statistical analyses were carried out using the GraphPad Prism software version 8.0. One-way Analysis of variance (ANOVA) was used to assess the significant differences among multiple groups under various treatments. Results were expressed as Mean ± SEM and P values less than or equal to 0.05 or 0.01 ($P \leq 0.05$ or $P \leq 0.01$) were taken to be statistically significant.

Results

Effect of Vitamin B_6 and Lead on body weight changes of male albino Wistar Rats

Table 1 shows the effects of Vitamin B_6 and lead acetate on the body weight of male Wistar rats. There was a significant difference ($P<0.05$) between the initial and final weight of rats administered lead acetate only. When the final weights were compared, a significant reduction ($P<0.05$) in the final body weight of rats administered lead acetate only was observed when compared with those of the control. In rats that were co-administered vitamin B_6 and lead acetate, a significant improvement ($P<0.05$) in the final body weight was observed when compared with those that were administered lead acetate only.

Effect of Vitamin B_6 and lead acetate on red blood cell count, packed cell volume, hemoglobin concentration and some erythrocyte indices in Wistar rats.

There was a significant reduction ($P<0.05$) in the total red blood cell count (RBC), packed cell volume and haemoglobin concentration in rats that were administered lead acetate only when compared with those of the control (Table 2). In rats that were co-administered vitamin B_6 and lead acetate, there was a significant improvement ($P<0.05$) in the total red blood cell count (RBC), packed cell volume and haemoglobin concentration when compared with rats administered lead acetate only (see table 2). The mean cell volume (MCV), mean haemoglobin concentration (MCH) and mean cell haemoglobin concentration (MCHC) were also significantly reduced ($P<0.05$) in rats administered lead acetate only when compared with those of the control rats. In the co-administration protocol, vitamin B_6 was able to significantly improve ($P<0.05$) the mean cell volume (MCV), mean haemoglobin concentration (MCH) and mean cell haemoglobin concentration (MCHC) when compared with rats administered lead acetate only (see table 2).

Effect of Vitamin B_6 and Lead acetate on leukocyte count, lymphocyte, granulocyte, monocyte and platelet count in Wistar Rats

The White blood Cell counts of rats administered lead acetate only were significantly increased when compared with those of the control ($P<0.05$). In rats co-treated with Vitamin B_6 and lead acetate, there was a significant reduction ($P<0.05$) in the leukocyte count when compared with those that were administered lead acetate only (Table 3). There was also a significant increase ($P<0.05$) in lymphocyte count in rats administered lead acetate only when compared with those of the control. However, in the co-treatment group, there was a significant reduction in the lymphocyte count when compared with

those administered lead acetate only (Table 3). There was no significant (P>0.05) difference in the granulocyte and monocyte counts of rats administered lead acetate only compared with those of the control (Table 3). The Platelet count of rats administered lead acetate only was significantly (P<0.05) increased when compared with rats in the control group. In rats that were co-treated with Vitamin B_6 and lead acetate, a significant reduction (P<0.05) in the platelet count was observed in these rats when compared with those administered lead acetate only (Table 3).

Table 1: Effect of co-administration of vitamin B_6 and lead on body weight changes of male albino Wistar rats

Groupings	Initial Mean body weight (g)	Final Mean body weight (g)
Control	183.00 ± 6.04	189.00 ± 5.70
Lead acetate only	190.00±12.41	175.00 ±13.45†^{a*}
Vit. B_6 only	185.00 ± 9.75	190.00 ± 3.54
Vit. B_6 + Lead acetate	189.00 ±6.04	184.00 ± 3.54^{b*}

Values are represented as Mean ± SEM; n=5/group. † indicates a significant difference (P< 0.05) between the initial and final weight within the group. a indicates a significant difference (P< 0.05) when compared to the control. b* indicates a significant difference (P< 0.05) when compared to the lead acetate-only group.*

Table 2: Effect of co-administration of vitamin B_6 and lead on Packed Cell Volume, Red Blood Cell count and Hemoglobin concentration and erythrocyte indices in Wistar rats

Parameters	Control	Lead acetate only	Vit. B_6 only	Vit. B_6 + Lead acetate
Packed Cell Volume (%)	34.76 ± 0.45	30.22±0.57 ^{a*}	39.38 ± 1.20	36.28 ± 1.14^{b*}
Heamoglobin (Hb)	14.50 ± 0.08	10.74 ±0.16^{a*}	14.30 ± 0.46	13.72 ± 0.37^{b*}
RBC count (x 10^6/µl)	6.54 ± 0.01	5.73 ±0.16^{a*}	7.25 ± 0.24	7.28 ± 0.09^{b*}
Mean Corpuscular Volume (fl/cell)	53.40 ± 0.54	49.74±0.69 ^{a*}	54.26 ± 0.26	52.64 ±0.93^{b*}
Mean Corpuscular Hemoglobin (pg/dl)	18.48 ± 0.09	16.00±0.30 ^{a*}	19.7 ± 0.07	18.7 ± 0.38^{b*}
Mean Corpuscular Hemoglobin Concentration (g/dl)	35.18 ± 0.57	30.9 ±0.59 ^{a*}	36.26 ± 0.13	35.10 ± 0.58^{b*}

Values are represented as Mean ± SEM; n=5/group. a indicates a significant difference (P< 0.05) when compared to the control. b* indicates a significant difference (P< 0.05) when compared to the lead acetate-only group.*

Table 3: Effect of co-administration of Vitamin B_6 and lead on White Blood cell count and other leucocyte indices in male albino Wistar rats

Parameters	Control	Lead acetate only	Vit. B_6 Only	Vit. B_6 + Lead acetate
White blood Cell Count (x 10^3/µl)	5.24 ± 0.29	10.72 ± 0.48[a*]	6.54 ± 0.30	7.30 ± 0.46[b*]
Lymphocyte Count (x 10^3/µl)	2.64 ± 0.13	6.80 ± 0.81[a*]	4.04 ± 0.307	3.58 ± 0.14[b*]
Granulocyte Count (x 10^3/µl l)	2.52 ± 0.14	2.78 ± 0.47	3.12 ± 0.57	2.72 ± 0.47
Monocyte count (x 10^3/µl l)	1.02 ± 0.06	1.34 ± 0.19	1.22 ± 0.18	1.18 ± 0.20
Platelet count (x 10^3/µl)	292.40 ± 13.64	489.2 ±38.25[a*]	195.6 ± 23.11	457.6 ± 38.25[b*]

Values are represented as Mean ± SEM; n=5/group. a indicates a significant difference (P< 0.05) when compared to the control. b* indicates a significant difference (P< 0.05) when compared to the lead acetate-only group.*

Discussion

Lead is a heavy metal with a lot of deleterious effects on various organ systems in humans. Lead acetate has been reported to directly affect the blood content of red blood cells and the rise of white blood cells, as it affects the size and shape of these cells (23). Lead acetate affects the percentage of hemoglobin in the blood as it leads to a decrease in its ratio and many other blood variables (24). Lead-induced oxidative stress in blood and other soft tissues has been postulated to be one of the possible mechanisms of lead-induced toxic effects (25). Based on this observation, it was presumed that antioxidants could be an alternative method for chelation therapy (26). This study was carried out to investigate the protective effect of vitamin B_6 on lead-induced hematological changes.

In this present study, there was a significant reduction in the final body weight of rats administered lead acetate (P<0.05) when compared with those of the control and a significant improvement in the final body weights of rats co-administered vitamin B_6 and lead acetate when compared to those administered lead acetate only. This reduction in body weight by lead acetate had been reported in earlier studies (27, 28, 29, 30). The mechanism of lead acetate-induced weight loss is attributed to its ability to impede the absorption and metabolism of nutrients essential for health (31, 32). This minimal reduction of the final body weight of rats co-treated with vitamin B6 and lead acetate compared with those administered lead acetate only may be a result of enhanced absorption of food nutrients and increased metabolic rate induced by vitamin B_6 (33)

The hematological system is an important target for lead acetate. In this study, a significant reduction in RBC, PCV and haemoglobin concentration was observed in rats administered lead acetate only. Several studies have also reported a lead-induced reduction in RBC, Hb and PCV (34, 35, 36, 37). Lead acetate has been reported to cause oxidative damage RBC membrane which reduces the number of red blood cells leading to anaemia (38, 39). The decrease in Hb concentration has been attributed to the ability of lead to inhibit the body's ability to make hemoglobin by interfering with several enzymes (aminolaevulinic acid dehydratase and ferro chelatase activity) involved in heme biosynthesis (40). The decrease in haemoglobin concentration by lead has also been attributed to the ability of lead to convert coproporphyrinogen III to protoporphyrin IX (41, 42). In rats co-treated with Vitamin B_6 and lead acetate, there was a significant increase in RBC, PCV and Hb concentration compared to those administered lead acetate only. The increase in RBC, PCV and Hb concentration can be attributed to the fact that vitamin B6 plays an important role in the formation of red blood cells and heme (a component of

hemoglobin) (17). Vitamin B_6 is transformed within the body to pyridoxal phosphate which is the rate-limiting substance in the biosynthesis of heme (18). The increase can also be attributed to the antioxidant nature of vitamin B6 (43). Vitamin B_6 scavenges free radicals generated by lead acetate and as such prevents lead-induced oxidative damage to the RBC membrane

A significant reduction in MCV, MCH and MCHC was also observed in rats administered lead acetate when compared with those of the control. The implication of this finding is that lead acetate induced microcytic and hypochromic anemia. Similar findings have also been reported by (44, 45). The decrease in MCV, MCH and MCHC by lead acetate can be attributed to the effects of lead in cell metabolism and alteration of the enzymes involved in the biosynthesis of heme (13). However, in rats that were co-treated with Vitamin B_6 and lead acetate, vitamin B_6 was able to revert the decrease in MCV, MCH and MCHC seen in rats administered lead acetate only. The improvement of MCV, MCH and MCHC by vitamin B6 can also be linked to its role in heme synthesis (46) and its role as a critical co-factor that regulates cell metabolism and overall cellular physiology (47).

Total white blood cell count and Lymphocyte count were significantly increased (P<0.05) in rats administered lead acetate when compared with those of the control. The WBC plays An important role in the body's defense and immune system. The increase in these cells clearly indicates of the toxic effect of lead acetate on the immune system (23). Similar findings have been reported by (23, 48). This increase in the white blood cell count and lymphocyte has earlier been reported to indicate hypersensitivity of leucocytes to lead acetate and the changes may be as a result of immunological reactions to produce antibodies to cope with the stress induced by lead acetate (49). Lead poisoning has also been reported to cause neuroinflammation (50, 51) which could also explain the significant increase in the white blood cell count and lymphocyte count observed in this study. Although a slight increase was observed in the granulocyte and monocyte count, this was however not statistically significant. However, in rats that were co-administered vitamin b6 and lead acetate, there was a significant reduction in the total white blood cell count and lymphocyte count when compared with those administered lead acetate only. Vitamin B6 is considered necessary to maintain a normal immune response, most especially the anti-inflammatory immune response (52). This could be responsible for the significant reduction in the white blood cell and lymphocyte count seen in the co-treatment protocol as compared to those administered lead acetate only

In this study, the platelet count was significantly increased in rats administered lead acetate only. Similar findings have also been reported (53, 54) The increase in the platelet count in rats exposed to lead acetate has been reported to be due to the impairment of clotting function through endothelial tissue injury and nitric oxide synthesis caused by lead acetate (lead-induced thrombocythemia) (49). However, in rats co-administered Vitamin b6 and lead acetate, vitamin b6 was able to significantly reduce the platelet count as against those administered lead acetate only. Vitamin B_6 has been reported to inhibit platelet aggregation (55) and thus could be responsible for the reduction in platelet count observed in the co-treatment protocol as against those treated with lead acetate only.

Conclusion

In conclusion, this study has shown that vitamin B_6 protected the blood cells against lead-induced damage. Therefore it could be an effective therapeutic managing agent against lead-induced hematological changes and associated complications.

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