INFLUENCES OF THIAMINE AND/OR ASCORBIC ACID ON LEAD INTOXICATION

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Abstract — The effects of thiamine, ascorbic acid and their combination on workers who are continuously exposed to lead has been investigated. In this study 60 persons in a Battery industry was selected and divided into four equal groups. Group I received placebo, group II thiamine (300 mg), group III ascorbic acid (250 mg) and group IV thiamine (300 mg) plus ascorbic acid (250 mg) three times a day (Orally). At beginning of the study and after one month of above drug regimen; blood, urine and a questionnaire about their clinical signs were examined. There were no significant differences between blood and urine lead level in all groups after treatment. Zinc protoporphyrin (zpp) level showed a significant reduction in ascorbic acid treated group (group III) as compared to pretreatment. Clinical manifestation improved in the group that received both vitamins (group IV). However, from a clinical stand point, it appears the usage of these vitamins may have a beneficial effects in lead occupational exposure.

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INTRODUCTION

Lead toxicity has been known for thousands of years and is one the oldest recognized chemical toxin (1,2). Despite this, the use of this metal has increased dramatically over the last 50 years (2). Lead poisoning not only can be seen in the factory workers who use this element in industry but also is a most commonly environmental pollutants and general population especially in big cities is exposed to it continously (3).

Lead is distributed in body like calcium by blood and it is known as an antagonist of calcium (1). Its deposition occurs in various tissues but the long-term deposition and accumulation of lead is in the bones (1). So a three-compartment models include blood, soft tissues and bones can be suppose for lead distribution (4).

Although there has been many success in decreasing blood lead level of general pupulation but still lead intoxication is a current problem (2). However the treatment of this poisoning can be carry out by chelating agents that remove lead from extracellular site through competing with thiol enzymes (5). These agents have numerous side effect and toxicity (5). In the recent years vitamins as a natural compounds have been considered which may act as a chelating agent in body without any toxic properties (10, 17).

This study was investigated to find the effects of thiamine and ascorbic acid in a battery industry worker who exposed to high level of lead.

MATERIALS AND METHODS

The aim of this study was throughly explained to 92 persons who work in foundry section in Niro battery industry (Tehran, Iran) and asked them to come to clinic for some laboratory test and a special questionnaire was prepared for them to fill them out.

Their weight was measured in clinic and then 5 ml of blood was taken for lead and zpp determination in citrated tube. Urine sample was collected in an acid washed tubes for lead determination. Placebo, ascorbic acid and thiamine were given by Osveh and Hakim pharmaceutical company (Tehran, Iran).

The workers were randomly divided into four equal groups as follows: Control group (N=23), in order to eliminate any psychological effects of using vitamins in clinical presentation, the persons in control group took placebo three times daily by their meals. Thiamine group (N=23), the workers of this group received thiamine tablets that contain 300 mg and asked them to take three times daily by their meals. Ascorbic acid group (N=23), this group received chewable tablets which contain 250 mg ascorbic acid and took each tablets three times daily after their meals. Thiamine - ascorbic group (N=23), this workers took thiamine tablets and ascorbic acid chewable tablets as described in groups II and III.

After one month of treatment, the workers were asked to come to clinic again to repeat the blood, zpp, urine examination and questionnaire about clinical manifestation to compare it with pretreatment results. Zpp was measured flurometerically using AVIA Haematofluorometer (Models zpp meter 205, USA) at 595nm and expressed as ug of zpp/g of hemoglobin. Determination of lead in blood after digestion of samples by nitric acid was estimated by flame atomic

absorption spectrophotometer (Phillips P.U. 9090, Cambridge, England) at 217nm and expressed as ug of Pb/dl of blood sample. Lead was laso estimated in urine by using above instruments at 283.3nm according to NIOSH method (6,7) and expressed as ug of Pb/1 of urine sample.

Statistical Analysis

The data from the first - stage (before treatment) were analyzed by analysis of variance followed by Duncan Multiple Test to show homogeneousity of groups (8). For comparison between two stage, differences between two group were evaluated by using the student t-Test for equal variance (8). Fisher's Exact Test was used for showing the improvement of clinical signs as compared to placebo (8). All differences were considered significant at $p<0.05$.

RESULTS

This study was done in male only with the average age of 32 years old. The results of 60 persons (15 workers in each group) due to some confunding factors, were only calculated by statistical calculation. These confunding factors were included changes in their working conditions or did not take the drugs more than 15 doses (of 90 total doses).

1. Measuring weight showed that those who were taking vitamins for one month have an increase in weight and there was no significant increase in wieght of control group. There was significant difference in thiamine group ($p<0.01$), ascorbic acid group ($p<0.05$) and thiamine / ascorbic groups ($p<0.05$) when compared to pretreatment weight (Table 1).

2. Zpp was significantly decreased in ascorbic acid group ($p<0.05$) and did not changes in other groups (Table 1).

3. There was no significnat differences in blood and urine lead level of all groups when compared to pretreatment results (Table 1).

4. Many of clinical manifestation in vitamins groups improved; especially sleepiness, halitosis, weakness, termor, numbness, foot and joint pain and headache. Numbness was improved only by thiamine, and other signs were improved when both vitamins were taken in combination (Table 2).

Table 1. The effects of thiamine and/or ascorbic acid on bdoy weight, zpp, blood and urine lead levels in battery workers.

Factors	Control		Thiamine		Ascorbic acid		Thiamine / ascorbic	
Measured	before	after	before	after	before	after	before	after
Weight (kg)	70.3 ± 2.2	71.2 ± 9.4	73.1 ± 1.8	74.6 ± 1.9**	70.0 ± 2.8	71.1 ± 2.6*	70.3 ± 2.4	71.2 ± 2.3*
Zpp (μg Hb)	4.7 ± 1.1	4.5 ± 1.0	3.5 ± 0.6	3.2 ± 0.7	5.3 ± 1.4	4.4 ± 1.1*	3.8 ± 0.9	3.7 ± 0.9
Blood Pb (μg Hb)	63.3 ± 3.4	64.8 ± 3.1	57.9 ± 6.2	65.5 ± 3.6	59.6 ± 4.9	66.5 ± 4.4	50.9 ± 5.7	58.7 ± 3.0
Urine Pb (μg/1)	236.1 ± 25.3	205.2 ± 21.2	246.6 ± 30.7	216.9 ± 19.3	237.2 ± 25.5	191.1 ± 18.1	196.3 ± 21.9	184.9 ± 18.6

Data are presented as mean ± SEM of 15 workers and significancy were determined using student t-test.
* Significant at $p<0.01$ ** Significant at $p<0.05$

Table 2. Improvement of clinical manifestation after thiamine and/or ascorbic acid treatment

Clinical Signs	Control (%)[a]	Thiamine (%)	Ascorbic acid (%)	Thiamine-Ascorbic (%)
Anorexia	44	83	50	82
Sleepiness	33	58	50	82*
Libido	10	20	19	50
Concentration	10	38	55	42
Memory	22	33	30	46
Learning	55	25	36	36
Nervousness	46	54	63	84
Sharpness	66	50	85	72
Depression	37	50	55	60
Night mare	NC	37	10	84
Metal taste	40	84	100	60
Halitosis	NC	38	28	100*
Nausea	NC	50	40	80
Weakness	20	83**	75**	86**
Tremor	NC	28	12	100*
Staggering	NC	50	34	60
Numbness	23	77*	40	50
Handache	40	78	50	100
Foot pain	12	66*	63	66*
Joint pain	NC	54**	55*	85*
Lowback pain	25	63	NC	57
Constipation	NC	50	100	72
Abdonimal pain	100	66	NC	50
Headache	20	50	50	100*

[a]Data are presented as percent improvement in clinical signs after the treatment. Raw data were campared to control and significancy were determined by Fisher's exact test.
* Significant at $p<0.01$ ** Significant at $p<0.05$ NC Not Changed

DISCUSSION

The importance of thiamine deficiency and changing in ascorbic acid metabolism has been previously reported in lead intoxication (9,10). Thiamine pyrophosphate is an essential cofactor for many enzyme activities. Coppock et al (1991) reported lead decreases mitochondrial oxidative decarboxylation which catalyzed by thiamine - dependent pyruvate dehydrogenase which also can changes the availability of thiamine or phosphorylated thiamine to thiamine-dependent enzymatic organelle systems (11). Moreover, others showed thiamine changes the whole body retention of lead (12). Dalley et al. (1990) reported that ascorbic acid may increase the renal clearance and also decrease the absorption of lead (13). The mechanism by which thiamine and ascorbic acid can alter lead's kinetic in body is not yet known well.

Blood lead level in all groups of this study did not alter significantly. This result is in agreement with others which showed thiamine's effects in cattle's lead poisoning (14). However, thiamine also showed to decreased blood lead in calves, fish and goats respectively (5, 14, 15). Moreover, ascorbic acid in combination with DMSA (2,3-dimercaptosuccinic acid) decreases blood lead level significantly in rats (9).

Thiamine and ascorbic acid did not alter the lead level in urine significantly in all groups. Kim et al. (1991) also showed similar results when thiamine administered (12). But others reported thiamine increases lead excretion via urine in sheep (16). Moreover, an increase in lead excretion were reported in rats when treated with DMSA and ascorbic acid and also when both thiamine and ascorbic acid used in combination with MFA (α-mercapto-ß-(2-furyl acrylic acid) and DMSA (9,10).

The mean of zpp level in ascorbic acid group in this study decreased significantly but in other groups did not. Reduction of zpp level was reported when combination of thiamine and ascorbic acid used in rats (17). In our study this combination had no effect on zpp level in human subject. This discrepancy may be because the later used rodents whereas ours were human subject. Others also observed the supplemention of DMSA and ascorbic acid caused higher decreases of zpp level in rat as compared to DMSA alone (10).

Many of clinical presentation which usually are seen in plumbism, in treated groups improved except numbness which improved in thiamine group. Others like sleepiness, halitosis, weakness, tremor, foot and joint pain and headache improved when both vitamins were taken. Some of these behaviour observation findings was reported previously in animals (5, 11, 15).

There is three possible reason about the mode of action of thiamine and ascorbic acid in lead poisoning, included the modification of thiamine and ascorbic acid deficiency, alteration in cell permeability which facilitate the removal of the intracellular lead (9,10) and the formation of complex between lead and thiamine or ascrobic acid or one of their metabolites which can facilitate the excretion of lead from body (5,12,14,16,19).

Blood zpp level may indicate the accumulation of lead in soft tissue, therefore significant reduction in blood zpp level in ascorbic acid group in this study may show the reduction of lead accumulation in soft tissues (3). Moreover, iron may compete with lead for absorption, tissue accumulation and intracellular binding, one can speculate that administration of ascorbic acid may increase iron absorption from gastrointestinal tract and absorbed iron compete with lead intracellular accumulation, therefore it may decrease lead toxicity (1, 20). However use of these vitamins from a clinical stand point suggest a beneficial effects but using them without chelator therapy to alter lead levels in blood and urine needs further investigations.

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