Title:

Study on Lead detoxifying potential of Vitamin C in adult population.

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Lead detoxifying effect of Vitamin C in adult population
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Abstract:

Lead is one of the most toxic metals known to humans. Lead toxicity, especially chronic toxicity has been labeled as a major health problem globally, Pakistan being no exception. Lead toxicity is implicated in severe adverse effects to the central nervous, cardiovascular, hematologic, renal and reproductive systems. Data from Pakistan show that 70 percent of children as well as adults in urban population of Karachi have blood lead levels above the limits set by international standards (< 10µg/dL for children and <20µg/dL for adults). Currently, there are no satisfactory drugs for chronic Lead toxicity. Intravenous CaNa2EDTA and Penicillamine are available but mainly used for emergency situations like acute Lead poisoning and do not address chronic poisoning. On the other hand, Vitamin C is an inexpensive, safe and readily available chelating agent, which could be explored for its possible Lead detoxifying potential. An earlier pilot scale study assessing the role of Vitamin C in reducing body Lead levels of children in Karachi showed that treatment with Vitamin C reduced Lead levels in hair while increased urinary excretion. However, such studies with direct measurement of Lead in blood are expected to give more meaningful outcome and also provide an impetus for expanding the study to adult Lead exposed populations on a larger sample size under controlled conditions. The current investigation aims to study the effects of Vitamin C supplementation in different doses in reducing body Lead levels by assessing whole blood samples. A total of approximately 300 adult subjects of either sex will be recruited and randomly divided into 3 groups. One group shall serve as control with no treatment. The other two groups will receive 500mg and 1000mg Vitamin C respectively for one month. Blood samples will be

collected once before treatment (baseline) and then after 15 days and another after 30 days of treatment. Lead in urine will also be determined for a limited number of samples to assess the possible mode of Lead excretion. Blood levels of Vitamin C and hemoglobin will be determined in a selected set of samples to assess their relationship with the baseline values of Lead. Lead estimation will be carried out in all samples on flameless Zeeman Atomic Absorption Spectrophotometer. The study is likely to have a direct impact on public health.

Introduction:

Lead has been mined for 6,000 years, and the history of lead poisoning is nearly 2,500 years old. After undergoing periods of sporadic reporting, 'Lead poisoning' was rediscovered in the 19th century, a period in which it reached epidemic dimensions owing to rapid industrialization. Epidemiological studies from around the world depict the serious threat faced due to Lead toxicity. At the local scenario, data collected from various cities of Pakistan through studies on adult Lead levels show them to be above the limits set by international standards (Manser et al., 1990; Shah et al., 2004). A more recent study in Karachi on children aged 36-60months showed that about 80% of the children ad blood Lead concentrations of more than 10µg/dL, with an overall mean of 15.6µg/dL (Rahbar et al., 2002). A study conducted on a Lead factory workers showed that fume exposed workers have significantly higher blood Lead levels (Khan et al., 1995).

In nature, Lead exists as a bluish gray metallic element, present in small amounts in the earth's crust mostly as PbS called galena. Lead's presence in air, food, water, soil, leaded petrol, paints, ceramic glazes, pesticides, batteries etc renders it to be one of the most ubiquitous toxic elements. The major routes for absorption of Lead into the body are through inhalation and through ingestion. Children are more prone to ingested Lead where as adults are affected by inhaled Lead. Tetraethyl Lead added in petrol, as an antiknock agent, can be absorbed via skin.

The detrimental relationship of Lead to health is a firmly established fact. Medical literature obviously raises the issue in succinct detail but a quick search

on the internet or even a perusal of the local newspapers will highlight the importance of this problem sufficiently. Once Lead enters the body, it is excreted out with difficulty. It deposits in the bone, hair and nails and exerts its harmful effects over a long course of time, especially on the brain. The adverse effects of Lead toxicity are manifold. Children are more prone to the behavioral and intellectual adverse effects such as hyperactivity, aggressiveness, and reduced attention spans and so on. In adults, weakness of memory is a common symptom compounded by more serious adverse effects such as anemia, encephalopathy, neuropathy, and hypertension and in higher doses; it may bring about convulsions, coma and even death.

The currently available antidotes for Lead poisoning like calcium disodium ethylenediamine tetraacetic acid (CaNa2 EDTA), D-pencillamine, dimercaprol (BAL) do provide an emergency treatment to overt toxicity but are not free from side effects and inconvenience of administration. This is compounded with the fact that very little is known about the therapeutic effects on lead poisoning of the orally available chelator, 2,3-meso-dimercaptosuccinic acid (Succimer). There is an immediate need for a safer, easily available and easily affordable alternative. This especially holds true for a third world country like Pakistan where the occupationally Lead exposed workers in particular have no awareness or access to proper health facilities.

Ascorbic Acid or Vitamin C is as old as Lead. It is one of the most extensively studied water soluble vitamins with a very good safety profile. An antioxidant molecule, Vitamin C alone and in combination with thiamine was found to increase urinary elimination of Lead as wellas reducing hepatic and renal Lead

burden and reversing lead-induced inhibition of the activity of ä-aminolevulinic acid dehydratase (ALAD). This beneficial role of Vitamin C was attributed to its ability to complex with Lead (Dhawan et al., 1988). In the current study, it is hoped that this Vitamin proves of good benefit to the population in general and to occupationally exposed workers in particular in bringing down the very high Lead levels.

Statement of the Problem:

The use of Vitamin C as an antidotal measure in Lead detoxification is a rather old concept. Over half a century ago, two case series of occupational lead exposure reported significant clinical improvement among workers after daily administration of Vitamin C (Holmes et al., 1939). However, this useful concept remained rather dormant until environmental exposure to Lead pollution gained attention in recent years. An earlier conducted study showed marked reductions in blood Lead levels after administration of Vitamin C in psychiatric patients (Sohler et al., 1977). A survey conducted in U.S.A suggested that high serum levels of ascorbic acid were independently associated with a decreased prevalence of elevated blood Lead levels (Simon and Hudes, 1999). A more recent study on laboratory animals showed Vitamin C effective in prevention of lead-induced neuromyopathy (Hasan et al., 2003). However, there is hardly a clinically controlled study on the curative potential of Vitamin C on Lead detoxification particularly in this part of the world. A recently conducted pilot scale study on school children in Karachi showed that a 500mg Vitamin C supplementation for four weeks to school children reduced Lead levels in hair while the urinary excretion of Lead increased (Gilani et al., 2003). However, such studies with direct measurement of Lead in blood are expected to give a more meaningful outcome. Hence, there was a need to extend the study further to include larger number of subjects of different age groups as well as those who are occupationally exposed to Lead. This would include Lead batteries factory workers, traffic policemen, and possibly painters to name only a few.

Objective of study:

1. Determine baseline Lead, Vitamin C and hemoglobin levels in the blood of adult urban population of Karachi and assess the relationship of Lead and vitamin C as well as of Lead and hemoglobin levels in blood

2. Assess the impact of one month supplementation of 500 and 1000 mg vitamin C on blood Lead levels. A significant drop in body lead is expected.

3. To assess the effect of vitamin C supplementation on urinary Lead excretion. Increased urinary Lead levels are expected.

Method of study:

The study participants will be adults (18 years and above) selected on volunteer basis preferably from occupationally Lead exposed populations. Proposal for the study will be sent to the Ethical Review Committee of the Aga Khan University for ethical review and approval. Around 300 subjects will be recruited in this study. After informing about the purpose of the study, participants will be asked to sign a consent form to express their willingness to participate. A questionnaire will then be filled for each participant. Besides general information, the questionnaire will also ask questions related to work place as well as other relevant health data. The study participants will be then randomized into three groups consisting of two treatment groups and one no treatment (control) group. Out of two treatment groups (who will be treated with vitamin C), up to 50 individuals from each group will be randomly selected to be recruited for extended duration study. Those 50 subjects from both treatment groups will receive vitamin C (500mg and 1000mg per day, respectively) for an additional period of one month. The purpose of the extended duration study is to see if there is further improvement in the detoxification of body lead levels by vitamin C. One control group in this study will not receive any treatment but the Lead levels in blood will be assessed after one month to see if there is any significant change in the body Lead levels over a period of time.

Whole blood samples (10ml) will be collected from the participants in heparinized blood collecting tubes. These samples will be analyzed and will serve as baseline Lead and Vitamin C levels. Hemoglobin levels prior and after

treatment will also be investigated to see relationship if any between blood Lead and hemoglobin levels. Urine samples for baseline and post treatment Lead levels will also be collected from a selected number of volunteers. This is intended to see the possible route of elimination of Lead. It is expected that Lead forms a water soluble complex with Vitamin C (Lead Ascorbate) which is easily excreted through kidneys (urine). Two of the groups will be supplemented with Vitamin C chewable tablets to be purchased for the Aga Khan Hospital Pharmacy. Group I shall receive one tablet (500mg) of Vitamin C daily. Group II shall receive two tablets (1000mg) of Vitamin C daily. The supplementation will continue for one month. Though each participant in the treated!

group will act its own control, a separate control group receiving no Vitamin C will also be recruited. Blood samples will then be collected after fifteen days of treatment. A final collection will be done at the end of the one month Vitamin C treatment protocol. Results on the Lead content will be compared with the control in each group, as well as within the groups with and without Vitamin C supplementation.

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