Comparative Effects Of Chelating Agents With And Without Antioxidants On Liver Parameters In Lead-Exposed Rats.

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Abstract

Background and Aim: Lead exposure raises serious health issues,and its effects on the human body are devastating. Especially with regard to liver function because of its roles in metabolism and detoxification. This work investigates on liver biomarkers in lead-exposed rats the relative effects of chelating agent with and without antioxidants.

Material and methodology

Adult Wistar rats were utilised and divided into 4 groups: The groups included were a control group, a lead-exposed group, a chelation therapy group and group was given both chelation therapy and antioxidants. Biochemical investigation of liver parameters. To evaluate liver function, biochemical markers—ALT, AST, Total protein, Total bilirubin

Results

Lead exposure clearly raised liver enzymes. therefore, suggesting hepatic damage. Chelating drugs helped to lower lead load but only somewhat improved liver capacity. But chelators along with antioxidants together produces a noticeable effect on liver parameters.

Conclusion

The results of the study showcases that antioxidant supplementation might provide a synergistic support to chelation therapy for the management of Pb-induced liver damage

Keywords: Antioxidant, Alanine aminotransferase (ALT), Aspartate aminotransferase (AST), Chelationtherapy, meso-DimercaptoSuccinicAcid(DMSA),Lead toxicity, Liver function biomarkers,Vitamin c

Introduction

Extremely poisonous heavy metal lead (Pb) presents major public health and environmental hazards. Lead accumulates in important organs, including the liver, kidneys, and nervous system [1] after being present in polluted air, water, food, and occupational risks. “As the main site of xenobious metabolism and detoxification, the liver is quite vulnerable to lead-induced toxicity, which disturbs enzymatic activities, raises oxidative stress, and causes hepatocellular damage [2]. Chronic lead exposure is been related to liver malfunction marked by raised blood indicators including alanine aminotransferase (ALT), aspartate aminotransferase (AST), Total Protein (TP), Total bilirubin (TB).

Moreover, lead affects important metabolic pathways and disturbs normal liver homeostasis, therefore influencing the physiological and biochemical effects of lead poisoning outside direct hepatocellular damage [3]. Lead exposure also affects the lipid metabolism, which elevates lipid peroxidation and damages hepatocyte membranes structurally, therefore aggravating hepatic malfunction [4]. Together, these causes a cascade of pathogenic processes including inflammation, death, and fibrosis, which, treatable or not, can lead to chronic liver damage.

Since liver is so important for systemic detoxification, knowing how chelation treatment interacts with antioxidant supplements helps one create successful treatment plans. This work aims to close current knowledge gaps by methodically assessing liver function indicators in lead-exposed rats undergoing various treatment approaches. This study focuses on determining whether an integrated therapy approach offers superior hepatoprotective effects by comparing biochemical markers such as ALT, AST, total bilirubin, and total protein. The results might have important effect on improving therapeutic treatments for lead poisoning and creating more successful hepatoprotective policies [5]

The treatment approaches for reducing liver damage are researched even if lead's well-documented toxicity and negative consequences on hepatic health call for attention. Although chelation treatment is generally agreed upon as the primary treatment for heavy metal intoxication, its efficacy in restoring hepatic damage is sometimes questioned because its inability to directly address oxidative stress [6]. Further research on the possible advantages of combining antioxidant therapy with chelation treatment would help to ascertain whether such a mix can offer more efficient liver protection and functional restoration. This work intends to give a more complete knowledge of how diverse treatment options affect liver function and recovery in lead-exposed rats by including a thorough investigation of many indicators

Materials and Methods

Experimental animals

Twenty-four adult Wistar rats, weighing 180-220 gm, were utilised in this study. The rats were kept under standerized conditions with a 12-hour light/dark cycle and had continuous access to food and water. All experimental techniques were adhered to ethical guidelines for animal research and were approved by the Institutional Animal Ethics Committee of Krishna Institute of Medical Sciences (approval number: 2017/7/17).

Lead exposure and treatment protocols

For groups exposed to lead, lead acetate was administered in drinking water for four weeks. After this exposure period, different treatment protocols were followed. The chelation therapy group received DMSA (25mg/kg body weight) administered intraperitoneally once daily for one week. The combination therapy group underwent the same lead acetate exposure, followed by chelation therapy with DMSA (25 mg/kg body weight) and antioxidant supplementation with Vitamin C (500 mg/kg body weight), administered orally once daily for one week.

Sample collection

When the course of treatment period was over, the rats were anesthetized and sacrificed by euthanasia using isoflurane inhalation, as per methods selected based on previous animal experiment studies. Blood collection was done through cardiac puncture, and tissues were obtained for analysis. All facilities required for the procedure were available at Krishna Institute of Medical Sciences, Karad. The blood samples were processed promptly in the biochemistry lab under the proper guidance of experts using semi-automated machinery, and all samples were stored at -80°C for further analysis.

Biochemical assays

Liver function was assessed by measuring serum levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), and total bilirubin. Total Protein. Using standard enzymatic assay kits. These biomarkers were selected as they provide an indication of hepatocellular integrity.

Statistical Analysis

All data were presented as mean ± standard deviation (SD). Statistical analysis was done using one-way analysis of variance (ANOVA) followed by Tukey's post-hoc test to determine significant differences between groups. A p-value of less than 0.05 was considered statistically significant.

Results

TABLE 1: Value of Liver Parameters in treatment groups

	CNT	LEG	CTG	COM	F	P
AST	53.3 ± 2.2	74.15 ± 2.1***	72.8 ± 3.0***	71.04 ± 1.28***	32.45	0.0001
ALT	19.97 ± 0.9	37.13 ± 1.2***	32.94 ± 1.1***	28.10 ± 1.2***	276.38	0.0001
TB	0.4 ± 0.04	0.5 ± 0.06***	0.5 ± 0.06	0.49 ± 0.07	8.16	0.0001
TP	6.8 ± 0.3	6.2 ± 0.1***	6.6 ± 0.1**	6.56 ± 0.09*	12.22	0.0001

All values are expressed in the mean ± SD.
* Significant difference with the control group, * ≤ 0.05, ** ≤ 0.01, ***≤ 0.001
SD: standard deviation, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, TP: Total protein, TB:Total bilirubin: probability value, F: statistical factor,

Aspartate aminotransferase

The exposure protocol resulted in significant increase in AST (74.15±2.1) levels in comparison to control (p≤ 0.05, 53.3± 2.2).(Table 1) reflecting severe hepatic damage due to lead hepatoxicity. The AST levels significantly elevate due to enzyme leakage from injured hepatic cells. Chelation therapy reduced the elevated enzymes to (72.83 ±3.0) indicating a partial recovery. However, combination therapy further decreased Enzymes levels to bringing them closer to control levels. The substantial reduction was seen in with combination therapy underscores its efficacy in restoring the enzymes when compared to chelation therapy alone.

Alanine aminotransferase

Our results indicate significant decrease in ALT (37.13±1.2) levels when compared to control group (19.97±0.9)

which can be due to cellular degeneration or destruction in the liver. Chelation therapy reduced the elevated enzymes partially (32.94±1.1) when compared to combination therapy group (28.10±1.2). Compared to AST combination therapy worked well in restoration ALT levels nearer to control group.

Total Bilirubin

The result showed slight elevation in total bilirubin levels in lead exposed group (0.5±0.06) when compared to control group (0.4±0.04). Chelation group (0.5±0.06) had no effect on the elevated levels but combination group (0.49±0.07) showed partial effect with values closer to control group.

Total Protein

TP levels were considerably lower in lead exposed group (6.2±0.1) in comparison to the control group(6.8±0.3). reduced level explains the impairment in synthetic function of liver. Combination therapy group was able to recover the values to (6.56±0.09) closer to control when compared to chelating therapy group (6.6±0.1).

Liver dysfunction due to lead toxicity can affect protein synthesis, leading to decreased levels of total protein. The lead-exposed group showed a notable reduction in total protein levels compared to the control, indicating impaired hepatic synthetic function. Treatment with chelators and its combination of chelators and antioxidants significantly restored protein levels closer to control.

The levels of liver function biomarkers (ALT, AST,) were elevated in the lead-exposed relative to the control group, indicating hepatocellular damage. Chelating agents treatment alone reduced these markers to some extent, but the combination of chelators with antioxidants showed a more pronounced improvement in SGPT and SGOT bringing the values closer to control levels and substantial restoration in Total Bilirubin.

Discussion

lead exposure is well known for its hepatotoxic consequences7. The present work investigated how well chelating agents by themselves and in combination with antioxidants reduce lead-induced liver damage. The findings indicate that lead poisoning seriously affects liver function indicators (ALT, AST, Total Protein and Total bilirubin). Consistent with past results, the substantial rise in ALT, AST, levels in lead-exposed rats points to hepatocellular injury and cholestasis8. Although chelation treatment by itself helped to lower these indicators, the most noticeable change was seen when antioxidants were added.

The rise in the Total bilirubin levels in lead exposed group can be explained due to excessive heme destruction. Increased levels of AST and ALT levels in lead exposed mainly due to the leakage of these enzymes from the liver cytosol into the blood flow. Cell necrosis can be the reason for the release of the enzymes in the blood stream9.The hepatocyte degeneration, vacuolization, and inflammatory infiltration defined the lead-exposed group. Although chelation treatment by itself reduced tissue damage, the group receiving both chelators and antioxidants showed most notable results. This strengthens the conclusion that lead-induced hepatotoxicity is mostly attributes to oxidative stress and inflammation; thus, a combined treatment aiming at these pathways offers better hepatoprotection10.

All things considered, antioxidants greatly increase the effectiveness of chelators even if they by themselves somewhat lower lead load and minimise toxicity. The results imply that these therapies used together not only restore antioxidant balance but also lower inflammation, maintain mitochondrial integrity, and enhance liver performance. The possible therapeutic advantage of including antioxidants into chelation treatment for controlling lead-induced hepatotoxicity is underlined in this work. Deeper understanding of optimising treatment options for lead poisoning will result from further research on several antioxidant combinations and long-term effects.

Conclusion

The present work emphasises the important hepatotoxic consequences of lead exposure, which disturbs liver function by oxidative stress led by tissue damage, inflammation, and mitochondrial malfunction. Although chelation treatment by itself gave some degree of protection by helping lead excretion, its efficacy was much boosted when paired with antioxidants

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