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Research article

A clinical study to evaluate the liver regeneration effect of L-arginine

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ABSTRACT

The liver is important for protein synthesis, detoxification, and amino acid metabolism. Nitric oxide (NO) is a key mediator in hepatocyte proliferation during liver regeneration. It is an oxidative metabolite of L-arginine produced by enzymes called nitric oxide synthase. The aim of this study is to evaluate the effect of L-arginine on the liver functions of patients with liver disorders and to explore the role of L-arginine in the pathogenesis of the liver. The biochemical tests of the liver like ALT, AST, and ALP were done in the groups. The treatment with L-arginine as a test drug showed a significant decrease in the levels of biochemical markers to the near-normal levels. The study concluded that the treatment with formulations containing L-arginine helped in regaining the normal hepatic architecture.

INTRODUCTION

Nitric oxide (NO) regulates blood pressure, apoptosis, and mitogenesis in organ and tissue (Yao et al., 2007; Mei and Thevananther, 2011; Cacanyiova et al., 2012; Chen et al., 2012). It is enzymatically synthesized by use L-arginine by nitric oxide synthase (NOS) inducible (i)NOS and endothelial (e)NOS. NO has been reported to reduce organ injury and enhance liver regeneration by experimentally modulating hepatic macrohaemodynamics (Cantré et al., 2008).

Recently, there have been studies assessing whether delivery of a specific amino acid can improve patient outcome, as some amino acids are precursors of many important biologic compounds essential for the normal functioning of the human organism (Lawson et al., 2011). Furthermore, these supplements can be taken orally to provide effective clinical availability. There has been no research describing whether or not L-arginine enhances liver regeneration.

MATERIALS AND METHOD

General

L-Arginine was purchased from NOW foods, USA. The diagnostic kits for the estimation of ALT, AST and ALP were purchased from Bioassay, China.

Patients' studies

A total of 20 patients were selected for the study who were suffering from diseases of high liver enzymes in the center of the digestive system in Al-Sader Teaching Hospital in AL-Najaf Province, Iraq from April 2019 to November 2019. The patients with heart failure, kidney failure and low blood pressure were excluded, and personal approvals for ten of the patients were taken to provide them with experimental treatment and clinical follow-up after taking the food supplement for 10 days.

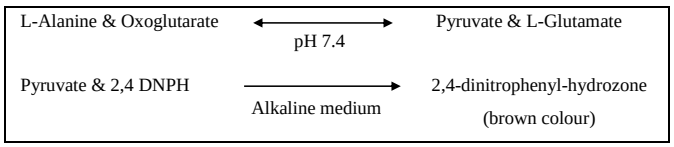
The patients were distributed in two groups (10 patients in each group). Group 1 (control group) patients received a normal diet and Group 2 (protection group) received L-arginine 1000 mg prepared formulation orally for 10 days.

Biochemical studies

The blood was obtained from all patients. The blood samples were allowed to clot for 45 min at room temperature. Serum was separated by centrifugation at 2500 rpm at 30°C for 15 min and utilized for the estimation of various biochemical parameters (Bergmeyer et al., 1978; King, 1965). The estimation of biochemical parameters was done using a calorimetric method by auto biochemistry analyzer (AU240, China).

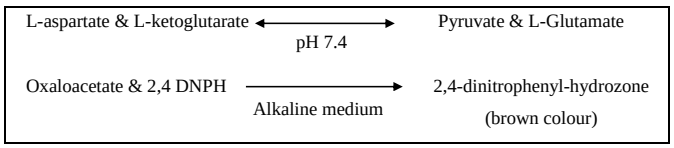
Serum Alanine Transaminase (ALT)

The ALT catalyzes the transfer of amino group from L-Alamine to L-Katogthta rate with the formation of pyruvate and glutamate. The pyruvate so formed is allowed to react with 2,4-dinitrophenyl hydrasine (2,4 DWPH) to produce 2,4-dinitrophenyl-hydrazone derivative which is brown coloured in alkaline medium. The absorbance of this hydrazone derivative is correlated to SALT activity by plotting a calibration curve using pyruvate (Retiman and Frenkel, 1957; Burtis et al., 2008).



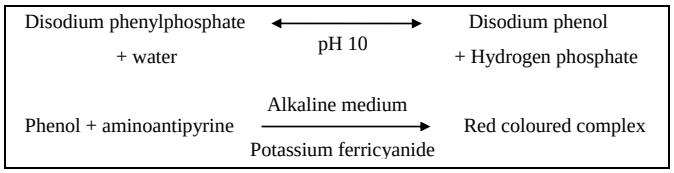
Serum Aspartate Transaminase (AST)

SAST catalyzes the transfer of amino group from L-aspartate to L-ketoglutarate with the formation of oxaloacetate and glutamate. The oxaloacetate so formed, is allowed to react with 2,4, DNPH to form 2,4-dinitrophenyl-hydrazone derivative which is brown coloured in alkaline medium. The absorbance of this hydrazone derivative is correlated to SAST activity by plotting a calibration curve using pyruvate standard (Retiman and Frenkel, 1957; Burtis et al., 2008).



Serum Alkaline Phosphatase (ALP)

SALP hydrolyzes phenylphosphate into phenol and disodium hydrogen phosphate at PH 10.0. The phenol so formed acts with 4-Aminoantipyrine in the alkaline medium in presence of oxidizing agent potassium ferricyanide to form a red-coloured complex whose absorbance is proportionate to the enzyme activity (Kind and King, 1954; Varley, 1975).



Statistical analysis

The data of the present study were articulated as (Mean ± Standard Errors), the statistical analysis (Descriptive statistics, Correlation coefficients, P-value) were calculated by using Graphpad prism. The comparisons between the two groups were analyzed by the t-test and the comparisons among many groups were analyzed by (SPSS-24).

RESULTS

Biochemical studies

Estimation of transaminase

(A) Control group

The SALT activity in group 1 (patients with liver dysfunction) was recorded to be 271.85± 2.87 IU/L

(B) Test group

SALT activity after administration of L-arginine at 1000 mg for 10 days was found to be 80.94± 5.45** for group 2 (protection group) (Table 1).

Serum Glutamate Oxaloacetate Transaminase

(A) Control group

The SAST activity in group1 (patients with liver dysfunction) was recorded to be 445.21 ± 5.22 IU/L.

(B) Test group

SAST activity after administration of L-arginine 1000 mg for 10 days was found to be 380.32± 4.81*IU/L respectively for group 2 (protection group), (Table 1).

Serum Alkaline Phosphate (ALP)

(A) Control group

The mean (SALP) of group 1 (patients with liver dysfunction) was recorded to be 496.26 ± 7.32 IU/L.

(B) Test group

After administration of L-arginine 1000 mg for 10 days was found to be 311.12 ± 4.16** IU/L for group 2 (protection group) (Table 1).

Table 1. Effect of L-arginine on serum parameters for patients with liver dysfunction

Groups		**SALT (IU/L)**	**SAST (IU/L)**	**SALP (IU/L)**
Group 1	**Controls**	**271.85± 2.87**	**445.21 ± 5.22**	**496.26 ± 7.32**
Group 2	**L-arginine (1000 mg/day)**	**80.94± 5.45****	**380.32± 4.81***	**311.12 ± 4.16****

Data are expressed as mean ± S.E.M from 20 patients and analyze by T-test. *P<0.05, **P<0.01 as compared to normal group.

DISCUSSION

Hepatoprotective activity of L-arginine was assessed by measuring serum marker enzymes, and alkaline phosphate. Enhanced levels of serum marker enzymes and alkaline phosphate are an indication of liver damage.

In the present study, significant hepatic damage was observed in group 1 as evidenced by the elevated levels of serum markers. The alteration in levels reflects the structural integrity of hepatocytes, the results agreement the study of Singh et al. (2019). An enhanced Serum AST level is usually associated with increased levels of serum ALT and conversion of amino acids to keto acids is effected by an enhanced level of these enzymes. The treatment with formulations containing L-arginine equivalent to 1000 mg per day; significantly lowered the level of SALT and SAST and it indicates that formulations are able to protect the cell membrane integrity of the liver. The synthesis of SALP gets increased due to enhanced biliary pressure. Both formulations containing L-arginine equivalent to 1000 mg per day significantly reduced the levels of SALP compare to the positive control group. Improvement in the hepatic secretion mechanisms clearly indicates the effective control of SALP and bilirubin levels by L-arginine formulations. Treatment with formulations containing L-arginine equivalent to 1000 mg per day helped in regaining the normal hepatic architecture. Reduction in the levels of ALT and AST reflects the stabilization of the plasma membrane and the repair of hepatic tissue.

Kurokawa et al. (Aguiar et al., 2011) evaluated the effect of L-arginine on liver regeneration process through the liver weight of 70% hepatectomized. When compared to liver function between control and arginine groups of this study, the result stating the benefits of supplementation of L-arginine was observed. There was a significant difference ($p < 0.05$) elevation of alkaline phosphatase in the supplemented group. As it increases when there is proliferation or cell renewal, it can be inferred benefits of L-arginine, which deserves further clarification.

The liver when damaged by disease or surgical procedures has a great capacity for growth by compensatory hypertrophy and hyperplasia of the remaining wolves. The number of mitotic cells in the organ increases approximately 600 times, 24 hours after partial hepatectomy in rats 67% (Tannuri et al., 2007).

CONCLUSION

The liver dysfunction enhanced the SALT, SAST, and ALP levels. Treatment with L-arginine as test drugs shows a significant decrease in the levels of biochemical markers to the near normal levels as compared with the control group while treatment with formulations containing L-arginine helped in regaining the normal hepatic architecture.

CONFLICTS OF INTEREST

The author declares no conflicts of interest.

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