

Use of Hepatoprotective Agents in Hepatomegaly Syndrome in Children: An Experience with Liv.52 Syrup

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ABSTRACT

An open clinical trial was conducted during 6 months from February to August 2002 in children diagnosed with hepatomegaly syndrome. The children were given Liv.52 syrup and monitored according to a study protocol, which included physical and clinical parameters (hepato-splenomegaly, weight, waist size, appetite and nausea) and biochemical markers related to principal hepatic functions.

It was observed that Liv.52 syrup was effective and safe treatment for hepatomegaly syndrome. Liv.52 produced following beneficial effects:

- *decrease of liver and spleen size*
- *improvements of clinical symptoms like appetite and relief from nausea*
- *normalizing biochemical markers indicating protective effect on liver cells*
- *increase in synthesis of proteins revealed by increased levels of serum proteins*
- *normalizing gamma-globulin and gamma-glutamic transaminase*

INTRODUCTION

Hepatomegaly syndrome represents an important clinical observation in pediatric pathology. Most of the time, the causative factors are varied in nature. Currently there are several approaches for the management of hepatomegaly syndrome, however specific treatment approach to correct the hepatomegaly and to prevent its subsequent complication are not available.

In order to understand the primary pathology of liver diseases associated with hepatomegaly requires the evaluation of clinical and biochemical markers, which are measured subjectively and objectively.

A hepatomegaly syndrome in children has been described in the literature also as Debre's Syndrome II as well as Baker-Winegard Syndrome al^{1,2}. Debre's Syndrome II is characterized by hypotonia associated with accumulation of fat and glycogen in the liver caused by disorder of carbohydrate and lipid metabolism. This is associated with hepatomegaly. Several other factors causing hepatomegaly are also reported in scientific literature.

The objective of present study was to evaluate efficacy and safety of Liv.52 in children suffering from hepatomegaly syndrome associated with or without viral infection. Liv.52 was administered as syrup dosage form as it is most acceptable and palatable dosage form for pediatric age group.

MATERIAL AND METHODS

Seventy-one children with hepatomegaly syndrome, aged between 2 and 17 years were included in trial. Fifty-one were treated with Liv.52 syrup as they showed the evidence of viral infection, while 20 were considered as a control group and were submitted to other types

of treatments. The duration of the study was six months (February – August 2002). The protocol included administration of Liv.52 syrup for 4 months in following doses:

- 2.5 ml (½ teaspoon), twice daily for children under 12 years of age
- 5 ml (1 teaspoon) twice daily for children above 12 years.

All the children were examined for complete physical and systemic evaluation. They were followed at 2, 4 and 6 months for repeat evaluation. Liv52 treatment was not continued after four months. The criteria of efficacy were considered as improvement of appetite, well-being, gain in the weight and waist size, relief from nausea and reduction in hepatomegaly. This was also combined with improvement in the liver function as determined by biochemical markers of liver functions. The evidence of hepatosplenomegaly was confirmed on clinical examination as well as ultrasonography.

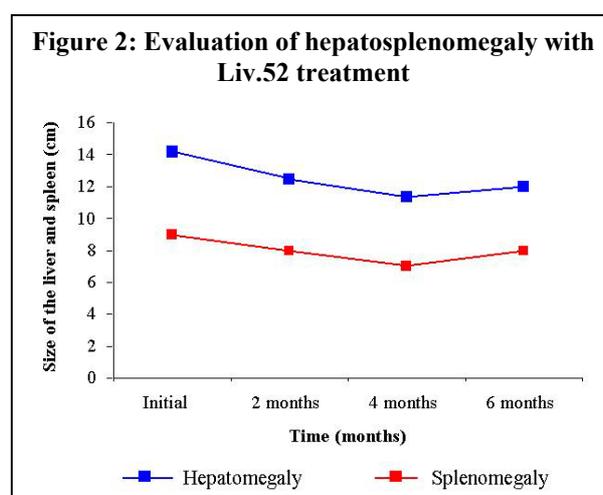
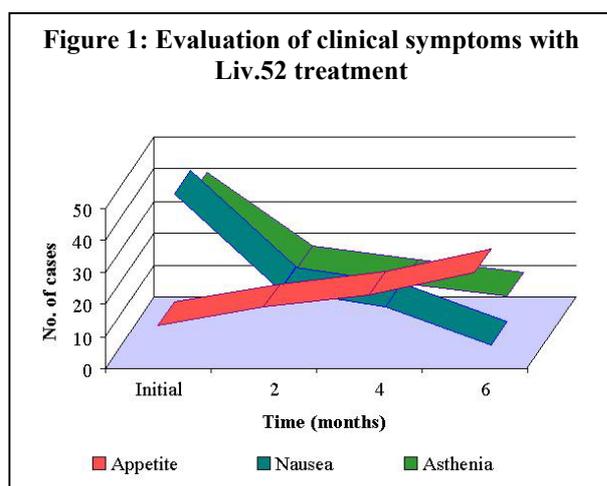
The main biochemical parameters evaluated were asparatate and alanine transaminase (AST and ALT), lactic-dehydrogenase, gamma-glutamic transpeptidase, imunoglobulins, prothrombin index and serum proteins mainly as albumin. Depending on viral markers, patients from the studied group were divided in two sub-groups A and B. The group A showed presence of hepatotropic viral infection while the group B did not.

RESULTS

The study group included children upto 20 years. The study revealed 2% of children less than 1-year age, 37% in 2 to 5 years, 20% in 6 to 10 years, 33% in 11 to 15 years and 8% in 16 to 20 years of age. In this group, 78% were boys, while 22% were girls. 65% were coming from urban environment. Children and their parents subjectively appreciated administration of Liv.52 syrup. Children were evaluating this product by taste while parents were evaluating it by positive change of appetite.

The children treated with Liv.52 syrup showed improvements in asthenia (as indicated by weight gain). In addition, they showed significant improvement in appetite, dynamic daily activities and relief from nausea (Figure. 1).

There was a decrease in liver and spleen size during the first 4 months of the treatment with Liv.52 syrup. However, marginal increase was observed following discontinuation of Liv.52 treatment (Figure 2).



The group treated with Liv.52 syrup showed significant decrease in AST and ALT values - emphasized in the subgroup A associated with viral hepatic infections (Figure 3). LDH level were also improved after the treatment with Liv.52 syrup (Figures 4 and 5). Although, the

Figure 3: Alanine and aspartase transaminase (ALT and AST) with Liv.52 treatment

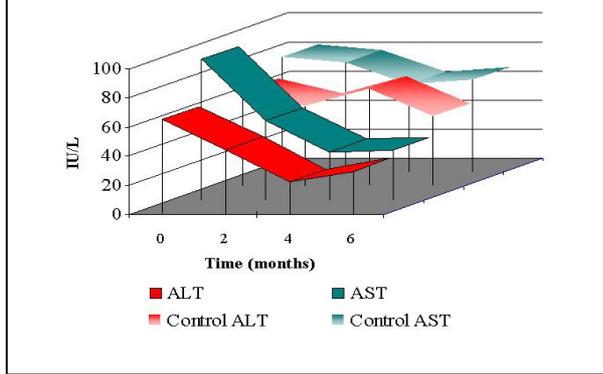
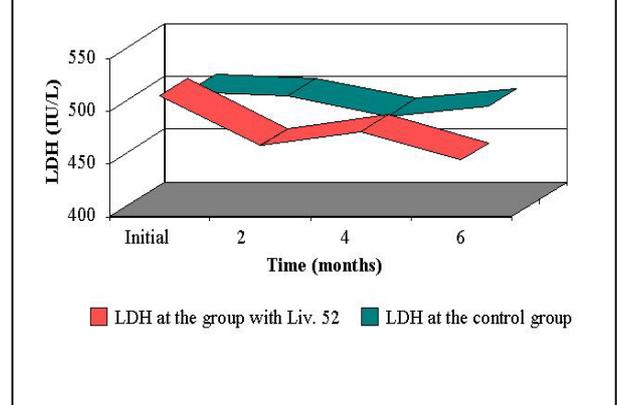


Figure 4: Lactic dehydrogenase (LDH) with



transaminases showed marginal rise following the discontinuation of Liv.52 syrup treatment, LDH levels maintained the fall even after the treatment was discontinued.

Figure 5: Lactic dehydrogenase (LDH) following viral infection

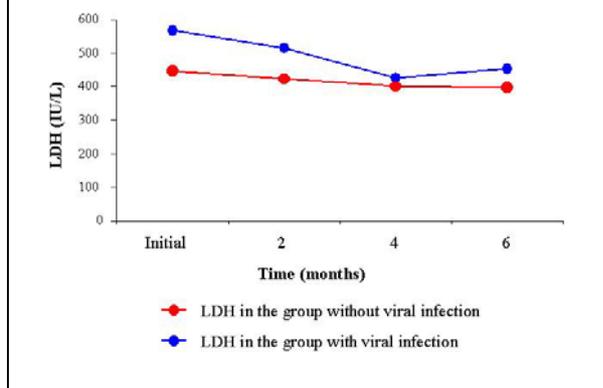
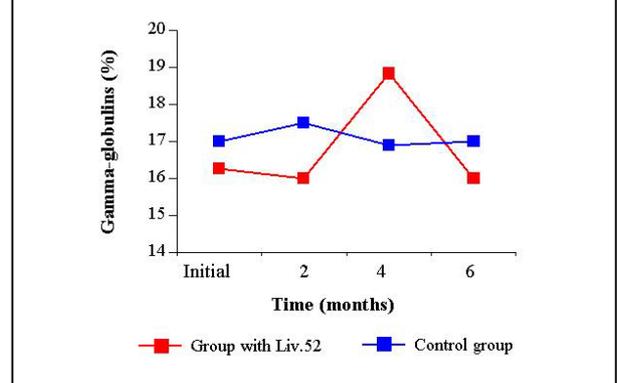


Figure 6: Gamma globulins with Liv.52 treatment



The group treated with Liv.52 also stimulated the synthesis of gamaglobulins (Figure 6). Liv.52 also improved protein synthesis as indicated by increase proteins with 4 months treatment. The serum protein level remained at the normal level in the following two months during which the treatment with Liv.52 was discontinued (Figure 7).

Gammaglutamic transaminase (GTT) were significantly decreased with Liv.52 treatment and remained at normal after discontinuation of drug (Figure 8). However, there was no significant alteration in prothrombin index with Liv.52 treatment in children with or without viral infection.

Figure 7: Serum proteins with Liv.52 treatment

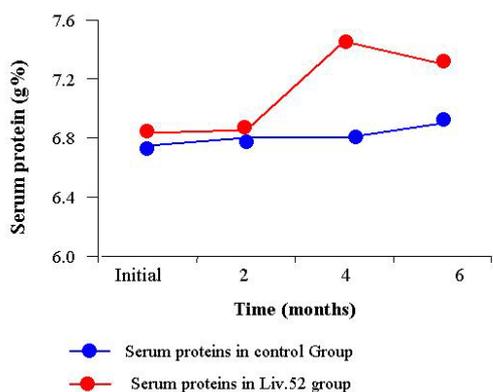
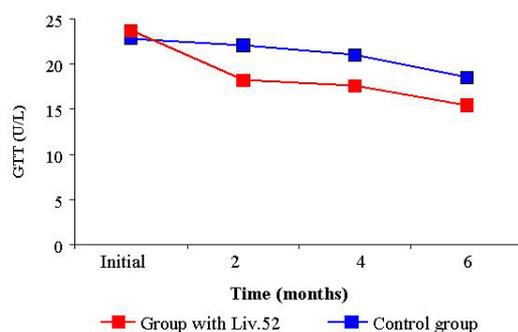


Figure 8: Gamma glutamictransaminase (GTT) with Liv.52 treatment



DISCUSSION

In this study, improvement in clinical signs and biochemical parameters with Liv.52 treatment confirms the role of Liv.52 in hepatomegaly syndrome in children. This study also confirms the hepatoprotective role of Liv.52 as revealed by decreased in ALT, AST and LDH, the biochemical markers of hepatocyte necrosis. Although, the pathophysiology of chronic hepatomegaly syndrome is not definitely known in children, Liv.52 may correct the carbohydrate and lipid abnormality seen in children with hepatomegaly syndrome. The corrections of the metabolic abnormality could be due to anti-oxidant mechanism of Liv.52. Moreover, *Terminalia arjuna* the constituent of Liv.52 also possess the property of reducing cholesterol levels demonstrated in experimental and clinical models. Various researchers and investigators in experimental and clinical models have confirmed the anti-oxidant property of Liv.52. The reversal of hepatomegaly along with the normalization of liver functions observed in our study confirms the hepatoprotective and anti-oxidant mechanism of action of Liv.52 in children presenting with hepatosplenomegaly syndrome.

Recknagel and Ghoshal demonstrated that during CCl_4 toxicity, free radicals are generated in or near the lipoidal centres of endoplasmic reticulum of hepatic parenchymal cells, this initiates autocatalytic peroxidative breakdown of microsomal lipids. The changes in the lipoidal elements of endoplasmic reticulum results in the morphological alterations of endoplasmic reticulum; loss of drug metabolising activity and loss of glucose-6-phosphatase activity. Liv.52 offers protection while reducing these enzymes³.

Thus, it is likely that the potent antiperoxidative agents protect the liver by preventing CCl_3 -induced peroxidative disintegration of membranes produced by drugs and chemicals. The protective effects of Liv.52 in reducing lipid peroxidation in hepatotoxic conditions have been shown earlier and are attributed to the action of Liv.52 in reducing tocopherol levels⁴.

CONCLUSIONS

Thus, in this study, Liv.52 found to be effective and safe hepatoprotective agent in children with hepatomegaly syndrome. Liv.52 also revealed significant inhibition of mesenchymal inflammation and edema on ultrasound examination. Liv.52 can be considered as an adjuvant in the management of hepatosplenomegaly syndrome.

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