Liver Transplantation In Saudi Homozygous Familial Hypercholesterolemia Patients

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INTRODUCTION

Patients with homozygous familial hypercholesterolemia (HoFH) suffer from this disorder from birth. They have abnormally high cholesterol levels due to a disease that has an autosomal dominant inheritance of genetic aberrations in the coding region for low density lipoprotein receptors (LDLR) in more than 90% of cases. Other gene defect includes mutations in apolipoprotein B100 (apoB100) and proprotein convertase subtilisin/kexin type 9 (PCSK9).

Persons with two mutant LDL-receptor genes (homozygous familial hypercholesterolemia) produce few or no LDL receptors and therefore remove LDL from plasma at a reduced rate. These patients almost always have severe atherosclerosis in childhood, with death from myocardial infarction often occurring before the age of 20.

Many modalities have been used for the treatment of (HoFH) patients including diet, drugs, LDL apheresis, and portacaval shunts. The effectiveness of these therapeutic regimens has shown limited efficacy in reducing the total cholesterol and LDL cholesterol in plasma and only provide temporary solutions for hypercholesterolemia. The possibility of an improved treatment has been raised by two recent advances: the recognition that up to three fourths of the total LDL receptors in the body are located in the liver, and progress in surgical and immunologic techniques for liver transplantation.

METHODOLOGY

A retrospective study was conducted to review the treatment outcomes of 17 patients who met the criteria for diagnosis of homozygous familial hypercholesterolemia (HoFH) and received liver transplants. The patients who were referred for liver transplantation came from different centers located within the Kingdom of Saudi Arabia to the pediatric endocrine clinic at King Faisal Specialist Hospital. The patients ranged in age from 1 year old to 14 years old and had previously been diagnosed with HoFH. Initially the patients received medical treatment with prescription drug therapy.

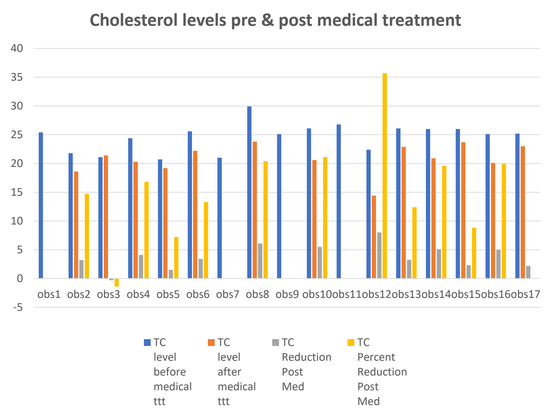
The results of total cholesterol and LDL cholesterol testing were compared from before treatment with prescription medication to the total cholesterol and LDL cholesterol results after the patients had received drug therapy. Subsequently, all seventeen patients had undergone liver transplantation. The patients' total cholesterol and LDL values were evaluated before and after receiving liver transplantation. Statistical data analysis was performed to examine the effectiveness of each treatment on the patients' lipid levels using the t-test.

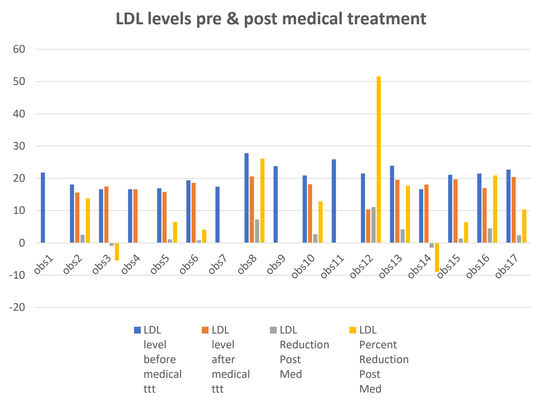
All patients included in this study met at least two of the following criteria: 1) Serum fasting untreated cholesterol level above 13 mmol/L (above 500 mg/dL), 2) Presence of physical signs like xanthomas, corneal arcus or generalized atherosclerosis at early age (1st decade of life),
3) Detection of hypercholesterolemia or clinical features in both parents.

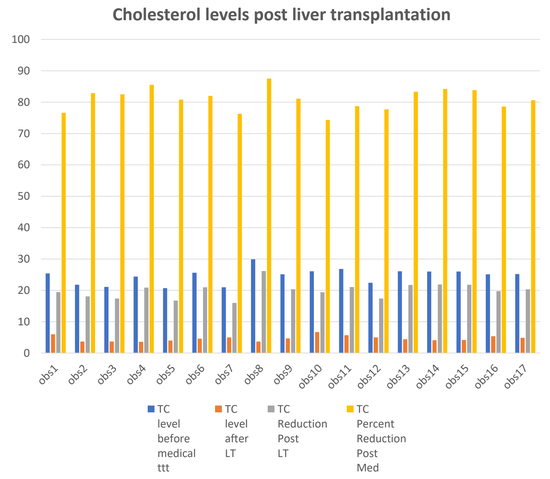
RESULTS

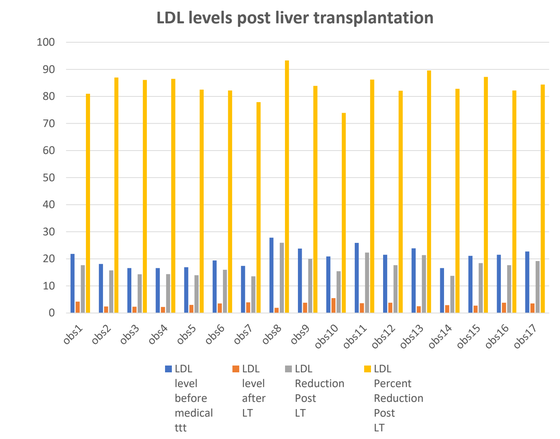
For total cholesterol in our patients the mean decrease between pre and post medical treatment results was 3.79 mmol/l. These results indicated a significant difference with a p value of <0.0001. The average percent reduction in total cholesterol after receiving pharmacological treatment was 15.2%. Whereas LDL cholesterol levels were decreased by an average of 12% after pharmacological treatment. A p value of 0.0146 was significant at the 95% confidence level.

As a comparison following liver transplantation, the patients' total cholesterol had been reduced by 81%, with a mean 19.96 mmol/l decrease in total cholesterol results from pre-operative levels, a p value of <0.0001. LDL cholesterol results were also compared post transplantation in all seventeen patients, the results of the post-transplant LDL evaluations indicated an average reduction in LDL of 17.48 mmol/l, the significance of this difference was confirmed by a p value of <0.0001. The mean percent decrease in LDL cholesterol was 84% after patients had received liver transplantation. Patients results are summarized in following figures.









CONCLUSION

The liver transplantation procedure did help to restore normal lipid metabolism in all 17 pediatric patients. The findings from this study revealed the efficacy of liver transplantation for reducing total cholesterol and LDL cholesterol levels in homozygous familial hypercholesterolemia (HoFH) patients. The medication was effective in lowering the level of total cholesterol circulating in 12 of 13 patients and LDL cholesterol in 11 of 13 patients.

Although liver transplantation is the better treatment for elevated cholesterol, risks, complications, and a shortage of donor organs may present problems. In the present study, the pharmacological treatment was observed to be much less effective than liver transplantation for lowering plasma concentrations of the lipids. More research is needed to develop improved pharmacological treatments for HoFH patients.

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