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EVALUATION OF THE EFFECT OF LIVER FUNCTION TEST OF BETA & HBE/BETA THALASSAEMIA PATIENTS ON TRANS-RESVERATROL THERAPY

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Abstract:

Recent studies demonstrated that resveratrol has many therapeutic effects on liver disorders. It significantly increased survival after liver transplantation, decreased fat deposition, necrosis, and apoptosis which induced by ischemia in Wistar rats. It provided liver protection against chemical, cholestatic, and alcohol injury. Resveratrol can improve glucose metabolism and lipid profile and decrease liver fibrosis and steatosis. Furthermore, it was able to alter hepatic cell fatty acid composition.

This study we observed the pre-treatment and post-treatment of resveratrol and evaluation of blood CBC parameters in patients with beta and HbE-beta thalassaemia shows three categories of response: Complete Response (52.2%; in patients who can able to maintain at an average Hb level of 6-9 gm/dL without blood transfusion, in this group 12.3% patients are without any previous H/O blood transfusion, others shifted from monthly blood transfusion dependency to a stable transfusion-free condition); Partial Response (18.2%; in patients who remained transfusion dependent but at longer intervals : 2-3 months or more) and Non response (15.9%; in patients who, after more than one year of treatment, remained at the same level of transfusion dependency) and we observed the evaluation of LFT of Beta and Hb E/Beta thalassaemic patients on Trans Resveratrol Therapy.

Key words: *Resveratrol, β-thalassemia, LFT, Blood transfusion, Good responder, Moderate responder, Non responder.*

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INTRODUCTION:

The β-thalassemias are characterized by a very heterogeneous group of inherited mutations causing abnormal expression of globin genes, leading to total absence or quantitative reduction of synthesis of β-globin chains (1–3). This disease is frequent in the Mediterranean area, Middle East, Africa and Asia. More than 200 different mutations have been identified in β-thalassemia patients, including deletions of the β-gene region, stop codons leading to premature termination of a non-functional β-globin chain, mutations suppressing correct maturation of the β-globin RNA precursor, most of all need regular blood transfusions. (1–3,4,5).

Resveratrol (3,4',5-trihydroxystilbene) belongs to a class of poly-phenolic compounds called stilbenes (6) which is effective in response to stress, injury, fungal infection, or ultraviolet (UV) radiation (7)**.** Resveratrol is a fat-soluble compound that occurs in a *trans* and a *cis* configuration in combination to glucose forming glucosides. Resveratrol-3-*O*-beta-glucoside is called piceid (8)**.** Literature study revealed that, Scientists became interested in exploring potential health benefits of resveratrol in 1992 when its presence was first reported in red wine (9)**,** and more recently, reports on the potential for resveratrol to inhibit the development of cancer (10) and extend lifespan (11) in cell culture and animal models have continued to generate scientific interest .From 2005 until the middle of 2010, there have been more than thousands new studies on cells, animals, and humans. Not a single commercially available drug was known to medical science which had the wide range of potential preventative, therapeutic, and quality of life enhancement properties as like as resveratrol. It has been shown to inhibit cancer, kill bacteria, viruses and fungal infections, extend life span in animals, improve energy production in cells, quench free radicals, increase glucose tolerance in diabetics, improve cardiac function, enhance physical and mental fitness and concentration, repair damage of DNA, prevent cell damage from nuclear radiation, and much more. Resveratrol improved health and survival in obese mice,[12] and chronic liver diseases.[13] These findings suggested that resveratrol could therapeutically intervene with liver injury[14] and polyphenol-rich foods may serve as an adjuvant treatment in chronic liver diseases.[15]

Hence, we study that the Evaluation of the effect of Liver Function Test (LFT) of Beta & HbE/Beta thalassaemia patients on Trans-Resveratrol Threrapy.

MATERIALS AND METHODS

Study groups:

Patients with HPLC-screened documented Sickle cell anaemia, S-beta thalassemia, beta thalassaemia, HbE thalassaemia, HbE-beta thalassaemia, HPFH genotypes have been considered in this primary analysis.

Collection of Sample: Sample was collected from OPD of Thalassaemia Foundation, Kolkata. Total 220 patients were evaluated. Among which 140 patients with HbE-beta and 69 patients with Beta and HPFH and 11 patients with other hemoglobinopathies were observed.

Fetal hemoglobin studies

Hb variants' (HbA / HbA2 / HbF & others) levels was estimated by HPLC (High Performance Liquid Chromatography) (Bio-Rad, USA). Estimation of HbF was also done by using HPLC method.

Biochemical Analysis

Liver Function test (LFT) (Bilirubin /Serum Alanine aminotransferase acitivity / Serum Aspartate aminotranseferase activity/ Total Protein Concentration) was performed by Biochemical Analyser [Microlab 300, EMerck].

RESULT:

We were able to classify ***three categories*** of response: a ***Complete Response*** (52.2%) in patients who can able to maintain at an average Hb level of 6-9 gm/dL without blood transfusion, in this group 12.3% patients are without any previous H/O blood transfusion, others shifted from monthly blood transfusion dependency to a stable transfusion-free condition; a ***Partial Response*** (18.2%) in patients who remained transfusion dependent but at longer intervals (2-3 months or more), and ***Non response***(15.9%)in patients who, after more than one year of treatment, remained at the same level of transfusion dependency. **[Table 1]**

We were evaluate the effect of Trans-Resveratrol by liver function test (LFT) (Bilirubin, AST, ALT and Total Protein) value against control were clearly depicted in [**Table 2]**.

Table 1 : Distribution of patients in different categories of response

Groups of different categories	n (%)	HbE-beta (n=142)	Beta/HPFH (n=69)	Haemoglobino-pathies (HbE, Sickle etc) (n=11)
COMPLETE RESPONSE **GROUP-I** **(withdrawal of BT)** **GROUP-II** **(No H/O BT)**	**88 (%)** **27 (%)**	Female=24 (%) Male = 46 (%) Female = 9 (%) Male = 12 (%)	Female = 5 (%) Male = 7 (%) Female = 2 (%) Male = 4 (%)	Female = 5 (%) Male = 1 (%) Female = 0 (%) Male = 0 (%)
NON RESPONSE **GROUP-III**	**35 (%)**	Female = 2 (%) Male = 6 (%)	Female = 5 (%) Male = 22 (%)	Female = 0 (%) Male = 0 (%)
PARTIAL RESPONSE **GROUP-IV**	**40 (%)**	Female = 9 (%) Male = 11 (%)	Female = 9 (%) Male = 10 (%)	Female = 0 (%) Male = 1 (%)
CONTROL GROUP **(without HU)**	**32 (%)**	Female = 9 (%) Male = 14 (%)	Female = 2 (%) Male = 3 (%)	Female = 2 (%) Male = 2 (%)

Table 2: Evaluation of the effect of Liver Function Test of Beta & HbE/Beta thalassaemia patients on Trans-Resveratrol Threrapy.

Type of Thalassaemia	Bilirubin (mg/dl)	AST (U/l)	ALT (U/l)	Total Protein (g/dl)
Beta	2.07±2.5	20.0±3.6	30.5±3.5	2.3±0.5
E/Beta	2.25±2.3	22.6±2.3	28+-6.3	2.3±1.0
Control	1.50±0.5	<30	<40	5.8±8.6

*** Standard deviation was done in all the result**

DISCUSSION:

Resveratrol improved health and survival in obese mice,[12] and chronic liver diseases.[13] These findings suggested that resveratrol could therapeutically intervene with liver injury[14] and polyphenol-rich foods may serve as an adjuvant treatment in chronic liver diseases.[15]

The mechanisms underlying the beneficial effects of resveratrol are not totally elucidated, but have been related mainly to its antioxidant activity that has been demonstrated to protect tissues such as liver, kidney, and brain against a variety of damage caused by oxidative stress.[16]

In this present study, pre-treatment and post-treatment of resveratrol and evaluation of blood CBC parameters in patients with beta and HbE-beta thalassaemia shows three categories of response: Complete Response (52.2%; in patients who can able to maintain at an average Hb level of 6-9 gm/dL without blood transfusion, in this group 12.3% patients are without any previous H/O blood transfusion, others shifted from monthly blood transfusion dependency to a stable transfusion-free condition); Partial Response (18.2%; in patients who remained transfusion dependent but at longer intervals : 2-3 months or more) and Non response (15.9%; in patients who, after more than one year of treatment, remained at the same level of transfusion dependency) and we observed the evaluation of LFT of Beta and HbE/Beta thalassaemic patients on Trans Resveratrol Therapy.

CONCLUSION:

Resveratrol can play a pivotal role in prevention and treatment of liver disorders. Previous studies confirmed its antioxidative properties in different models of hepatitis resulting in reducing of hepatic fibrosis; on the other hand, Resveratrol could reduce hepatic steatosis through modulating the insulin resistance and lipid profile in animals. These high quality preclinical studies propose the potential therapeutic implication of Resveratrol in liver disorders especially those with hepatic steatosis. Additional carefully designed, mechanistic based, laboratory, and clinical studies need to be undertaken to provide scientific evidence for the efficacy of it in treatment of liver disorders especially those with hepatic steatosis and fibrosis.

In our present study we concluded that in Trans Resveratrol therapy the Blirubin level of Beta and HbE/Beta thalassaemic patients is slightly high from the control individuals because The Bilirubin concentration is dependent on Haemoglobin concentration. The AST and ALT level is lie between the control individuals. The other parameter

Total protein which is slightly low from the control individuals.

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Data Sharing Statement: We cannot share any unpublished data with other laboratory or person.

Patients Consent Statement: The signed consent from all the patients were taken before test was performed and kept them as official documents. In case of any unusual condition it will be presented in front of the concerned person.

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