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RESEARCH ARTICLE

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

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ABSTRACT

Resveratrol (3,5,4′-trihydroxystilbene), a natural polyphenolic compound found in grapes and red wine, is reported to have beneficial effects on cardiovascular diseases, including renal diseases. These beneficial effects are thought to be due to this compound's antioxidative properties: resveratrol is known to be a robust scavenger of reactive oxygen species (ROS). In addition to scavenging ROS, resveratrol may have numerous protective effects against age-related disorders, including renal diseases, through the activation of SIRT1. SIRT1, an NAD^+-dependent deacetylase, was identified as one of the molecules through which calorie restriction extends the lifespan or delays age-related diseases, and this protein may regulate multiple cellular functions, including apoptosis, mitochondrial biogenesis, inflammation, glucose/lipid metabolism, autophagy, and adaptations to cellular stress, through the deacetylation of target proteins. This study we observed the pre-treatment and post-treatment of resveratrol and evaluation of blood CBC parameters in patients with beta and E-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 RFT of Beta and Hb E/Beta thalassaemic patients on Trans Resveratrol Therapy.

INTRODUCTION

β-thalassemias (β-thal) are common inherited red cell disorders characterized by absent or reduced synthesis of β-globin chains. Despite extensive knowledge of the molecular defects causing β-thalassemia, less is known about the mechanisms responsible for the associated ineffective erythropoiesis and reduced red cell survival (De Franceschi *et al.,* 2011; Rund *et al.,* 2005; de Franceschi *et al.,* 2004; De Franceschi *et al.,* 2007; Olivieri *et al.,* 1994; Ginzburg and Rivella, 2011; Liu *et al.,* 2013). Increased levels of reactive oxygen species (ROS) have been reported to contribute to the anemia of β-thalassemia, although the effects of ROS have not been fully defined (De Franceschi *et al.,* 2011; Rund *et al.,* 2005; de Franceschi *et al.,* 2004; De Franceschi *et al.,* 2007; Olivieri *et al.,* 1994; Ginzburg and Rivella, 2011; Liu *et al.,* 2013; Fibach and Rachmilewitz, 2008). Exogenous anti-oxidant molecules might represent complementary therapeutic strategies to counteract the toxic effects of ROS in β-thalassemia. However, few of them have been shown to beneficially affect *in vivo* β-thalassemic red cell features and/or thalassemic ineffective erythropoiesis *in vivo*. (de Franceschi *et al.,* 2004; De Franceschi *et al.,* 2007; Olivieri *et al.,* 1994; Ginzburg and Rivella, 2011; Liu *et al.,* 2013; Fibach and Rachmilewitz, 2008) Resveratrol (3,5,4′-trihydroxystilbene), a natural polyphenolic compound found in grapes and red wine, is reported to have beneficial effects on cardiovascular diseases, including renal diseases. These beneficial effects are thought to be due to this compound's antioxidative properties: resveratrol is known to be a robust scavenger of reactive oxygen species (ROS). In addition to scavenging ROS, resveratrol may have numerous protective effects against age-related disorders, including renal diseases, through the activation of SIRT1. SIRT1, an NAD^+-dependent deacetylase, was identified as one of the molecules through which calorie restriction extends the lifespan or delays age-related diseases, and this protein may regulate multiple cellular functions, including apoptosis, mitochondrial biogenesis, inflammation, glucose/lipid metabolism, autophagy, and adaptations to

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cellular stress, through the deacetylation of target proteins. Resveratrol can ameliorate several types of renal injury, such as diabetic nephropathy, drug-induced injury, aldosterone-induced injury, ischemia-reperfusion injury, sepsis-related injury, and unilateral ureteral obstruction, in animal models through its antioxidant effect or SIRT1 activation. Therefore, resveratrol may be a useful supplemental treatment for preventing renal injury. Hence, we study that the Evaluation of the effect of Renal Function Test 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 222 patients were evaluated. Among which 142 patients with Hb-E-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: Renal Function test (Creatinine /Urea / Uric Acid Concentration) was performed by Biochemical Analyser [Microlab 300, EMerck].

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). The pre-treatment and post-treatment of renal function test analysis of 222 patients with Trans-resveratrol therapy revealed that there was significant response in RFT parameters against control. The pre and post treatment values were clearly depicted in [Table-2] and (Table 3).

DISCUSSION

Resveratrol, which is present in red wine, has been postulated to explain the protective effects on the cardiovascular system observed in the French Paradox, and the effects of this compound are exerted through several mechanisms, including antioxidant effects. SIRT1, an NAD^+-dependent deacetylase, has been identified as one of the molecules through which calorie restriction (CR) extends the lifespan and delays age-related diseases (Catalgol *et al.,* 2012; Fontana *et al.,* 2010; Cohen *et al.,* 2004). The activation of SIRT1 exerts cytoprotective effects through multiple mechanisms, such antioxidative, and anti-inflammation effects and the regulation of mitochondrial biogenesis, autophagy, and metabolism in response to the cellular energy and redox status (Guarente, 2011). Resveratrol has been shown to be aSIRT1 activator (Kitada and Kum, 2013), and numerous previous studies have shown that the administration of resveratrol can prevent many

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		Female=24 (%)	Female = 5 (%)	Female = 5 (%)
GROUP-I	88 (%)	Male = 46 (%)	Male = 7 (%)	Male = 1 (%)
(withdrawal of BT)		Female = 9 (%)	Female = 2 (%)	Female = 0 (%)
GROUP-II (No H/O BT)	27 (%)	Male = 12 (%)	Male = 4 (%)	Male = 0 (%)
NON RESPONSE	35 (%)	Female = 2 (%)	Female = 5 (%)	Female = 0 (%)
GROUP-III		Male = 6 (%)	Male = 22 (%)	Male = 0 (%)
PARTIAL RESPONSE	40 (%)	Female = 9 (%)	Female = 9 (%)	Female = 0 (%)
GROUP-IV		Male = 11 (%)	Male = 10 (%)	Male = 1 (%)
CONTROL GROUP	32 (%)	Female = 9 (%)	Female = 2 (%)	Female = 2 (%)
(without HU)		Male = 14 (%)	Male = 3 (%)	Male = 2 (%)

Table 2. Evaluation of the effect of Renal Function Test of Beta thalassaemia patients on Trans-Resveratrol Therapy

RFT Parameter	Control	Pre-treatment	Post-treatment
Creatinine (mg/dl)	0.7±0.3	4.6±1.23	1.8±0.90*
Urea(mg/dl)	6.8±3.20	18.36±1.30	12.36±2.3*
Uric Acid (mg/dl)	5.36±2.36	16.23±1.20	9.36±2.36*

*Standard deviation was done in all the result, *Significant at P<0.05 against Control

Table 3. Evaluation of the effect of Renal Function Test of Hb E/Beta thalassaemia patients on Trans-Resveratrol Therapy

RFT Parameter	Control	Pre-treatment	Post-treatment
Creatinine (mg/dl)	0.7±0.3	3.6±1.23	1.8±0.90*
Urea(mg/dl)	6.8±3.20	12.36±1.30	10.36±2.3*
Uric Acid (mg/dl)	5.36±2.36	13.23±1.20	8.36±2.36*

*Standard deviation was done in all the result, *Significant at P<0.05 against Control.

RESULTS

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

diseases, such as diabetes, neurodegenerative disorders, cognitive disorders, cancer, kidney diseases, and cardiovascular disease through SIRT1 activation (Guarente, 2011; Kitada and Kum, 2013; Kitada *et al.,* 2013). Thus, resveratrol exerts its cytoprotective effects through at least two

mechanisms, antioxidant activity and SIRT1 activation. In this present study, pre-treatment and post-treatment of resveratrol and evaluation of blood CBC parameters in patients with beta and E-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 RFT of Beta and E/Beta thalassaemic patients on Trans Resveratrol Therapy.

Conclusion

Resveratrol can exert protective effects against both acute and chronic kidney injuries through its antioxidant effects and ability to activate SIRT1. Therefore, resveratrol should be a useful additional treatment for preventing renal injury. However, it remains unclear whether resveratrol has beneficial effects on kidney diseases in humans and other animal models of renal diseases. In addition, a number of recent studies indicate that many of the protective effects of resveratrol could be mediated by SIRT1-independent mechanisms. Among them, the activation of mammalian target of rapamycin (mTOR) signaling pathway is involved in the pathogenesis for several kidney diseases, such as diabetic nephropathy (Inoki *et al.,* 2011; Gödel *et al.,* 2011; Sakaguchi *et al.,* 2006) and the autosomal dominant polycystic kidney disease (Lieberthal and Levine, 2012). Liu et al. reported that RSV increases the association between mTOR and the DEP-domain-containing and mTOR-interactive protein (DEPTOR), an identified negative regulator of mTOR (Liu *et al.,* 2010). Therefore, resveratrol is expected to protect the kidney by the inhibition of mTOR pathway. Further studies are necessary to verify the beneficial effects of this compound in humans and other animals of kidney diseases and to clarify the detailed mechanism for the renal protective effect of resveratrol. In our present study in post treatment value of Trans Resveratrol therapy the Renal function parameters (Creatinine, Urea, Uric acid) level of Beta and E/Beta thalassaemic patients were near about the control individuals. In thalassaemic patients excess iron can damage the kidney which we were estimate the Renal Function Test. Now we might be concluded that resveratrol can protect the kidney injury.

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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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