



THE EFFECT OF TRANS-RESVERATROL THERAPY ON BODY WEIGHT AND BODY HEIGHT IN DIFFERENT AGES OF MALE AND FEMALE THALASSAEMIC PATIENTS

Anirban Roy Chowdhury^{1*}, Sudipa Chakravarty² and Amit Chakravarty³

¹Department of Biotechnology, Institute of Genetic Engineering. 30 Thakurhat Road. Kolkata- 700128, West Bengal, India.

²Department of Genetics, Institute of Genetic Engineering. 30 Thakurhat Road. Kolkata- 700128, West Bengal, India.

³Department of Genetics, Institute of Genetic Engineering. 30 Thakurhat Road. Kolkata-700128, West Bengal, India.

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*Corresponding Author

Anirban Roy Chowdhury

Department of
Biotechnology, Institute of
Genetic Engineering. 30
Thakurhat Road. Kolkata-
700128, West Bengal, India.

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, and enhance of body weight. Resveratrol can help to accumulate the fat deposition into the adipose tissue. 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. In this study we observed the blood CBC parameters of beta and E-beta thalassaemic patients with pre-treatment and post-treatment of trans-resveratrol therapy. We categories the drug response into three groups: 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) the other study we evaluate the effect of trans-resveratrol in body weight and body height in different ages of male and female thalassaemic patients.

KEYWORDS: Resveratrol, β -thalassemia, Blood transfusion, Good responder, Moderate responder, Non responder. Body height and Body weight.

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.^[1-7]

Resveratrol (3,5,4'-trihydroxystilbene), a natural polyphenolic compound found in grapes and red wine, is reported to have beneficial effects on cardiovascular diseases, and enhance of body weight. Resveratrol can help to accumulate the fat deposition into the adipose tissue. 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. In this study we observed the blood CBC parameters of beta and E-beta thalassaemic patients with pre-treatment and post-treatment of trans-resveratrol therapy. We categorized the drug response into three groups: 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 the other study we were evaluated the body weight and body height in different ages of male and female thalassaemic patients with trans-resveratrol therapy.

MATERIALS AND METHODS

Study groups

Patients with HPLC-screened documented Sickle cell anaemia, S-beta thalassaemia, 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.

Body height and Body weight study

We were evaluated total 222 thalassaemic male and female patients (age between 5-18 years) for the height and weight study.

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]

The Body weight and Body height evaluation of total 222 male and female thalassaemic patients with pre and post-treatment of trans- resveratrol therapy were clearly depicted in [Chart-2],[Chart-3],[Chart-4] and [Chart-5].

Table 1: Distribution of patients in different categories of response.

Groups of different categories	n (%)	HbE-beta (n=142)	Beta/HPFH (n=69)	Haemoglobinopathies (HbE, Sickle etc) (n=11)
Complete response Group-i (withdrawal of bt)	88 (%)	Female=24 (%) Male = 46 (%)	Female = 5 (%) Male = 7 (%)	Female = 5 (%) Male = 1 (%)
Group-ii (no h/o bt)	27 (%)	Female = 9 (%) Male = 12 (%)	Female = 2 (%) Male = 4 (%)	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 (%)

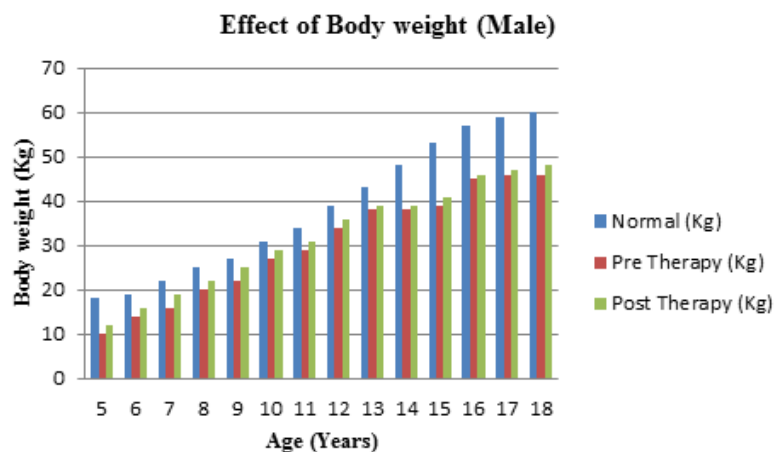


Chart 2: Effect of Body weight in male Thalassaemic Patients on Trans Resveratrol Therapy.

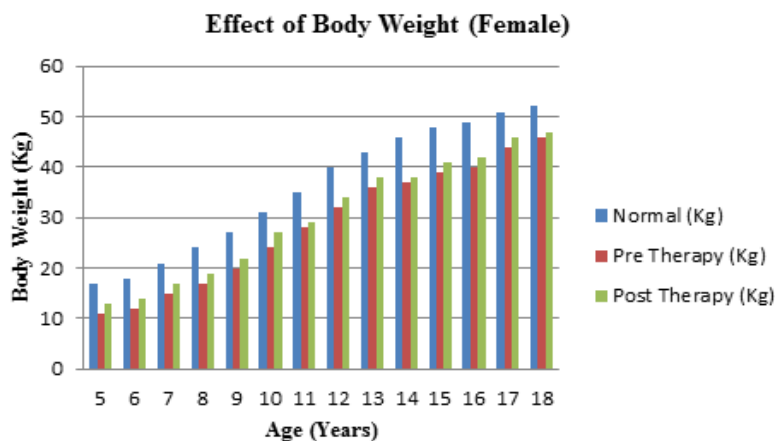


Chart 3: Effect of Body weight in female Thalassaemic Patients on Trans Resveratrol Therapy.

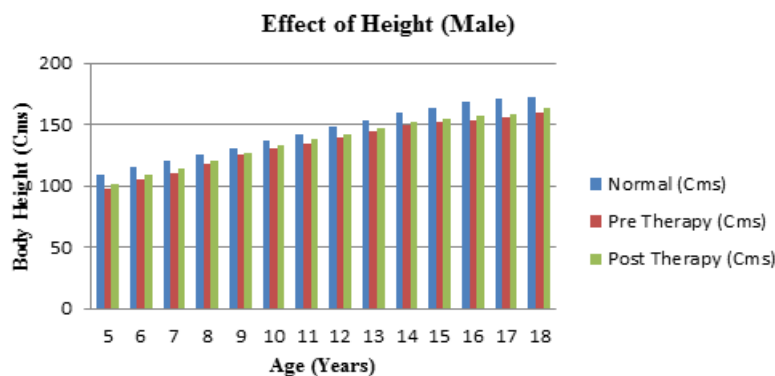


Chart 4: Effect of height in male Thalassaemic Patients on Trans Resveratrol Therapy.

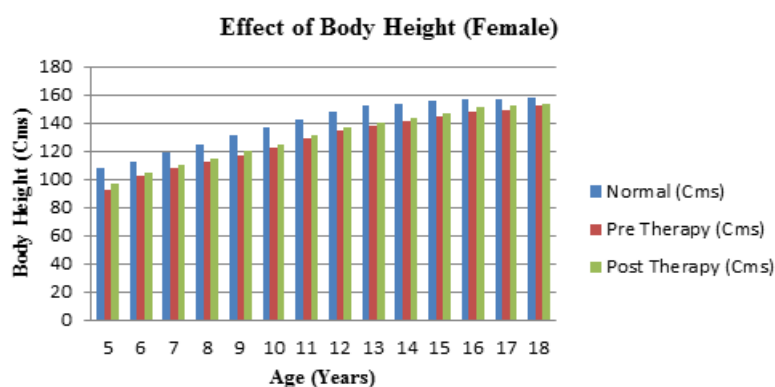


Chart 5: Effect of height in female Thalassaemic Patients on Trans Resveratrol Therapy.

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.^[9–11] The activation of SIRT1 exerts cytoprotective effects through multiple mechanisms, such as antioxidative, and anti-inflammation effects and the regulation of mitochondrial biogenesis, autophagy, and metabolism in response to the cellular energy and redox status.^[12] Resveratrol has been shown to be a SIRT1 activator^[13], and numerous previous studies have shown that the administration of resveratrol can prevent many diseases, such as diabetes, neurodegenerative disorders, cognitive disorders, cancer, kidney diseases, and cardiovascular disease through SIRT1 activation.^[14,15,16] Thus, resveratrol exerts its cytoprotective effects through at least two mechanisms, antioxidant activity and SIRT1 activation.

In our present study, we were categories three groups of patients based on pre-treatment and post-treatment of resveratrol and evaluation of blood CBC parameters. **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).

In chart 2 and Chart 3 we were observed that the weights of male and female thalassaemic patients post treatment therapy were increased compare to the pre treatment therapy and it was nearly about to the normal individual and chart 4 and chart 5 we observed that the heights of male and female post treatment therapy were increased compare to pre treatment therapy and it was nearly about to the normal individual.

CONCLUSION

Resveratrol can help to accumulate the fat deposition into the adipose tissue. 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.

In thalassaemic patients the body weight and body height were slower than the normal individual but when we treated the patients with resveratrol the post treatment result is better than the pre treatment result. So the above study we were concluded that resveratrol can help to increase the body growth of thalasseamic patients compare to normal 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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REFERENCES

1. De Franceschi L, Bertoldi M, De Falco L, Santos Franco S, Ronzoni L, Turrini F, et al. Oxidative stress modulates heme synthesis and induces peroxiredoxin-2 as a novel cytoprotective response in beta-thalassemic erythropoiesis. *Haematologica*, 2011; 96(11): 1595–604. [PMC free article][PubMed]
2. Rund D, Rachmilewitz E. Beta-thalassemia. *N Engl J Med.*, 2005; 353(11): 1135–46. [PubMed]
3. de Franceschi L, Turrini F, Honczarenko M, Ayi K, Rivera A, Fleming MD, et al. In vivo reduction of erythrocyte oxidant stress in a murine model of beta-thalassemia. *Haematologica*, 2004; 89(11): 1287–98. [PubMed]
4. De Franceschi L, Ronzoni L, Cappellini MD, Cimmino F, Siciliano A, Alper SL, et al. K-CL co-transport plays an important role in normal and beta thalassemic erythropoiesis. *Haematologica*, 2007; 92(10): 1319–26. [PubMed]
5. Olivieri O, De Franceschi L, Capellini MD, Girelli D, Corrocher R, Brugnara C. Oxidative damage and erythrocyte membrane transport abnormalities in thalassemias. *Blood*, 1994; 84(1): 315–20. [PubMed]
6. Ginzburg Y, Rivella S. β -thalassemia: a model for elucidating the dynamic regulation of ineffective erythropoiesis and iron metabolism. *Blood*, 2011; 118(16): 4321–30. [PMC free article][PubMed]
7. Liu J, Zhang J, Ginzburg Y, Li H, Xue F, De Franceschi L, et al. Quantitative analysis of murine terminal erythroid differentiation in vivo: novel method to study normal and disordered erythropoiesis. *Blood*, 2013; 121(8): e43–9. [PMC free article][PubMed]

8. Catalgol B, Batirel S, Taga Y, Ozer NK. Resveratrol: French paradox revisited. *Frontiers in pharmacology*, 2012; 3: 141. [PMC free article] [PubMed]
9. Fontana L, Partridge L, Longo VD. Extending healthy life span-from yeast to humans. *Science*, 2010; 328(5976): 321–326. [PMC free article] [PubMed]
10. Cohen HY, Miller C, Bitterman KJ, et al. Calorie restriction promotes mammalian cell survival by inducing the SIRT1 deacetylase. *Science*, 2004; 305(5682): 390–392. [PubMed]
11. Guarente L. Sirtuins, aging, and medicine. *The New England Journal of Medicine*, 2011; 364(23): 2235–2244. [PubMed]
12. Kitada M, Kume S, Takeda-Watanabe A, Kanasaki K, Koya D. Sirtuins and renal diseases: relationship with aging and diabetic nephropathy. *Clinical Science*, 2013; 124(3): 153–164. [PMC free article] [PubMed]
13. Howitz KT, Bitterman KJ, Cohen HY, et al. Small molecule activators of sirtuins extend *Saccharomyces cerevisiae* lifespan. *Nature*, 2003; 425(6954): 191–196. [PubMed]
14. Gödel M, Hartleben B, Herbach N, et al. Role of mTOR in podocyte function and diabetic nephropathy in humans and mice. *Journal of Clinical Investigation*, 2011; 121(6): 2197–2209. [PMC free article][PubMed]
15. Sakaguchi M, Isono M, Isshiki K, Sugimoto T, Koya D, Kashiwagi A. Inhibition of mTOR signaling with rapamycin attenuates renal hypertrophy in the early diabetic mice. *Biochemical and Biophysical Research Communications*, 2006; 340(1): 296–301. [PubMed]
16. Liu M, Wilk SA, Wang A, et al. Resveratrol inhibits mTOR signaling by promoting the interaction between mTOR and DEPTOR. *Journal of Biological Chemistry*, 2010; 285(47): 36387–36394. [PMC free article] [PubMed]