

# Iranian Journal of Blood & Cancer

Journal Home Page: www.ijbc.ir



# Systematic Review and Meta-Analysis

# The effect of Vitamin E and N-acetyl cysteine on oxidative status and hemoglobin level in transfusion-dependent thalassemia patients: A systematic review and meta-analysis

Sezaneh Haghpanah <sup>1</sup>, Mahnaz Hosseini-Bensenjan <sup>1</sup>, Omid Reza Zekavat <sup>1</sup>, Mohammadreza Bordbar <sup>1</sup>, Mehran Karimi <sup>1</sup>, Mani Ramzi <sup>1</sup>, Naeimehossadat Asmarian <sup>2\*</sup>

#### ARTICLE INFO

#### Article History: Received: 04/01/2023 Accepted: 28/02/2023

#### Keywords: Acetyl cysteine Meta-Analysis

Transfusion-dependent thalassemia

Vitamin E

# Abstract

Background: This meta-analysis was conducted to summarize the comparative effect of Vitamin E and N-acetyl cysteine (NAC) on oxidative status, including total antioxidant capacity (TAC), total oxidative stress (TOS), oxidative stress index (OSI), and hemoglobin (Hb) in patients with TDT.

Methods: This systematic review and meta-analysis was done according to the PRISMA checklist. We searched databases including Web of Science (ISI), Scopus, Medline (via PubMed), and Embase. Meta-analysis was done using Stata statistical software version 16.0.

Results: Finally, four randomized-controlled trials (RCT) for Vitamin E and three RCTs for NAC were included. Our meta-analyses and review showed a significant increase in the weighted mean differences (WMD) of Hb and a significant decrease in the WMD of TOS and OSI in children subgroup of Vitamin E. Also, based on the results of the review in the NAC group, a significant increase in the WMD of Hb and a significant decrease in the WMD of TOS and OSI were found in children.

Conclusions: Vitamin E showed a beneficial effect on improving anemia in TDT children. Moreover, both NAC and Vitamin E seems to be effective antioxidant supplements in children with TDT. More well-designed randomized, controlled trials for the effect of NAC and Vitamin E in TDT patients are recommended with more focus on the essential influencing factors on the oxidative status in these patients.

#### \*Corresponding authors:

Naeimehossadat Asmarian, Anesthesiology and Critical Care Research Center, Shiraz University of Medical Email: ns.asmarian@gmail.com

Please cite this article as: Haghpanah S, Hosseini-Bensenjan M, Zekavat OR, Bordbar M, Karimi M, Ramzi M, Asmarian N. The effect of Vitamin E and N-acetyl cysteine on oxidative status and hemoglobin level in transfusion- dependent thalassemia patients: A systematic review and meta-analysis. Iranian Journal of Blood and Cancer. 2023; 15(1):22-35.

#### 1. Introduction

Transfusion-dependent thalassemia (TDT) is one of the most common inherited disorders caused by a genetic mutation leading to hemolysis and impaired erythropoiesis (1, 2). Regular blood transfusion is an essential therapeutic option that has lowered the complications of severe anemia and increased the patients' survival.

However, repeated blood transfusions lead to iron deposition in various organs, including vital organs such as the heart and liver (3, 4). Although iron chelation therapy is used as an essential treatment option for iron overload, heart disease caused by cardiac hemosiderosis remains the leading cause of

<sup>&</sup>lt;sup>1</sup>Hematology Research Center, Shiraz University of Medical Sciences, Shiraz, Iran

<sup>&</sup>lt;sup>2</sup>Anesthesiology and Critical Care Research Center, Shiraz University of Medical Sciences, Shiraz, Iran

#### **Abbreviations**

Transfusion-dependent thalassemia (TDT)

N-acetyl cysteine (NAC)

Total antioxidant capacity (TAC)

Total oxidative stress (TOS)

Oxidative stress index (OSI)

Randomized-controlled trials (RCT)

Weighted mean differences (WMD)

Hemoglobin (Hb)

International Prospective Register of Systematic Reviews (PROSPERO)

# Acknowledgements

The authors would like to thank Shiraz University of Medical Sciences for their approval support (Grant number23341). The authors would also like to thank Center for Development of Clinical Research of Nemazee Hospital and Dr. Nasrin Shokrpour for editorial assistance.

### **Funding**

Shiraz University of Medical Sciences

#### **Conflict of Interest**

No conflict of interest

## **Ethics approval**

The study was approved by the Ethics Committee of Shiraz University of Medical Sciences (Ethics code: IR.SUMS.REC.1400.188).

#### References

- 1. Haghpanah S, Cohan N, Bordbar M, Bazrafshan A, Karimi M, Zareifar S, Safaei S, Aramesh A, Moghadam M, Fard SAZ, Zekavat OR. Effects of three months of treatment with vitamin E and N-acetyl cysteine on the oxidative balance in patients with transfusion-dependent  $\beta$ -thalassemia. Annals of hematology. 2021;100(3):635-44.
- 2. Siri-Angkul N, Chattipakorn SC, Chattipakorn N. Diagnosis and treatment of cardiac iron overload in transfusion-dependent thalassemia patients. Expert review of hematology. 2018;11(6):471-9.
- 3. Hashemieh M. Assessment of Organ Specific Iron Overload in Transfusion-dependent Thalassemia by Magnetic Resonance Imaging Techniques. Iranian Journal of Blood and Cancer. 2019;11(2):39-46.
- 4. Bhat RR, Lashkari H, Ramprakash S, Pereira D. Triple Drug Iron Chelation Therapy in Thalassemia Major; A Case Report. Iranian Journal of Blood and Cancer. 2021;13(2):62-

- 5. Eghbali A, Mehrabi S, Ghandi Y, Eghbali A, Dabiri M, Mousavi\_Hasanzadeh M. The Correlation between Serum Ferritin, Serum Troponin T, cardiac T2\* MRI and Echocardiographic Findings in Patients withThalassemia Major. Iranian Journal of Blood and Cancer. 2020;12(1):1-5.
- 6. Ozdemir ZC, Koc A, Aycicek A, Kocyigit A. N-acetylcysteine supplementation reduces oxidative stress and DNA damage in children with  $\beta$ -thalassemia. Hemoglobin. 2014;38(5):359-64.
- 7. Pattanakuhar S, Phrommintikul A, Tantiworawit A, Srichairattanakool S, Chattipakorn SC, Chattipakorn N. N-acetylcysteine Restored Heart Rate Variability and Prevented Serious Adverse Events in Transfusion-dependent Thalassemia Patients: a Double-blind Single Center Randomized Controlled Trial. International journal of medical sciences. 2020;17(9):1147.
- 8. Sengsuk C, Tangvarasittichai O, Chantanaskulwong P, Pimanprom A, Wantaneeyawong S, Choowet A, Tangvarasittichai S. Association of Iron Overload with Oxidative Stress, Hepatic Damage and Dyslipidemia in Transfusion-Dependent  $\beta$ -Thalassemia/HbE Patients. Indian journal of clinical biochemistry: IJCB. 2014;29(3):298-305.
- 9. Kampa M, Nistikaki A, Tsaousis V, Maliaraki N, Notas G, Castanas E. A new automated method for the determination of the Total Antioxidant Capacity (TAC) of human plasma, based on the crocin bleaching assay. BMC clinical pathology. 2002;2(1):3.
- 10. Katerji M, Filippova M, Duerksen-Hughes P. Approaches and Methods to Measure Oxidative Stress in Clinical Samples: Research Applications in the Cancer Field. Oxidative medicine and cellular longevity. 2019;2019:1279250.
- 11. Pedre B, Barayeu U, Ezeriņa D, Dick TP. The mechanism of action of N-acetylcysteine (NAC): The emerging role of H(2) S and sulfane sulfur species. Pharmacology & therapeutics. 2021;228:107916.
- 12. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Annals of internal medicine. 2009;151(4):264-9, w64.
- 13. Higgins JP, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA. Cochrane handbook for systematic reviews of interventions: John Wiley & Sons; 2019.
- 14. Borenstein M, Hedges, L. V., Higgins, J. P. T., and Rothstein, H. R. Introduction to meta-analysis. Hoboken: John Wiley & Sons. 2011.
- 15. Higgins J. Cochrane handbook for systematic reviews of interventions. Version 5.1. 0 [updated March 2011]. The Cochrane Collaboration. www cochrane-handbook org. 2011.
- 16. Rashidi M, Aboomardani M, Rafraf M, Arefhosseini SR, Keshtkar A, Joshaghani H. Effects of Vitamin E and Zinc Supplementation on Antioxidants in Beta thalassemia major Patients. Iranian journal of pediatrics. 2011;21(1):8-14.