REVIEW PAPER
Volume - 10 | Issue - 03 | March - 2021 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

QUALITY OF LIFE AFTER BONE MARROW TRANSPLANT IN THALASSEMIA MAJOR PATIENTS

Clinical Research

Shruti Saxena B.Tech (Genetic Engineering), SRM Institute of Science and technology, Kattankulathur.

ABSTRACT

The main aim of this article is to review whether the patients who had bone marrow transplant as their treatment for thalassemia major, are living a quality life as normal people or not. The difference will be noted in their health related quality since the day they had their transplantation.
The average quality of lifestyle of thalassemia major patients with blood transfusion is comparatively very low and full of pain and with regular chelation therapy, the cost of the treatment goes over-budget.
Stem cell transplantation is the only cure for thalassemia. It has been made less toxic, more feasible for a large number of patients which have witnessed successful outcomes with the help of various donors.
Cost-effectively, transplantation should be considered the primary treatment of choice in the presence of a suitable related or unrelated donor and at centres with a satisfactory experience in the field of transplantation and particularly, in managing those with thalassemia. It is difficult to deny the overall improvement in the quality of life of Thalassaemic patients. Although there are complications like graft versus host disease and late conditioning effects.
The past few years have experienced a huge success in the improvement of survival rate and free of any complications in Beta thalassemia major. Since its first application, around 3000 patients have been treated worldwide.

KEYWORDS

Bone marrow transplant, thalassemia major, quality of life, treatment, graft vs host disease, hematopoietic stem cell.

INTRODUCTION

The thalassemia is the one of the common monogenic disorders of haemoglobin synthesis inherited in an autosomal recessive manner. It is characterized by an absent or decreased production of one or more of the globin subunits of haemoglobin resulting in imbalanced globin chain synthesis. (*Weatherall et al 2001a*).

Theoretically, there are as many types of thalassemia as there are types of globin chains i.e. α, β, γ, δ, δβ but most prevalent and clinically important thalassemia are the α and β thalassemia.

Beta thalassemia is an extremely heterogeneous group of monogenic disorders and it occurs when there is a quantitative reduction of globin chains that are usually structurally normal (*Weatherall et al 2001a*).

Like alpha thalassemia, β thalassemia is subdivided into β0 in which there is no β globin chain synthesis and the other two types are β^{+} or β^{++} thalassemia, in which there is severe or mild decrease in the production of β globin chains respectively. They are caused by mutations that nearly affect all the beta globin locus and are extremely heterogeneous.

Clinically, β thalassemia can be classified into three broad categories. The two extremes are- β thalassemia major (Cooley's anaemia) where an individual has severe anaemia and depends upon transfusions for survival and another is β thalassemia minor, where individuals are asymptomatic.

It has been estimated that approximately 7% of the world population are carriers of thalassemia and about 56,000 have major thalassemia, including at least 30,000 who need regular blood transfusion to survive and 5,500 who die perinatally due to β thalassemia major annually.

If there is any potential cure for thalassemia as of now, it's only hematopoietic cell transplantation which till date has shown many successful outcomes, barring any complications.

Statistical data of survival rate after transplantation-

In Italy-

In the 1920s, all thalassemia major patients used to die within 6 months of diagnosis. Between 1949 and 1957, in Ferrara, only 9% of the patients reached the age of 6 years, and at the end of the 1970s, half of Italian thalassaemic patients had died before reaching 12 years of age. After a decade, with combined safe transfusions and regular chelation and/or transplantation, survival rate improved notably but remained suboptimal and non-satisfactory at national levels.

Later on in around 2009, about 60% of patients lived for 30 years and more. Majority of them were in good health, worked full time and had families due to advances in transfusion, chelation, and transplantation. Despite such advances and improvements, compliance with comprehensive transfusion and chelation therapy and its availability remain pivotal factors in determining the survival and quality of life (QOL).

In India-

India has a population of over one billion people with about 5% being able to afford the very best treatment, 25% in the middle class with increasing income and 70% who cannot afford a transplant unless it is provided by the state, and this is not likely considering other urgent health priorities. With 20 million carriers for thalassemia and 10 000 children being born with thalassemia major each year, if one-third of these patients have an HLA-matched sibling donor, there is a potential to cure 3000 children with BMT. If one considers six per million as the incidence of aplastic anaemia, there would be 6000 new cases/year, and if 10% of these patients are suitable candidates for transplant, then the country would need to do 600 transplants per year for this disease alone. India's gross domestic product (GDP) per capita in 1999 was $370 and in 2006, this had risen to $3460 (source: World Population Data Sheet 1999/2006). This means that many patients can now afford to have a transplant even if resources are not available from the state or private insurance.

The process of collecting information and maintaining a database of transplant activity in India has not been streamlined. In September 2005, data were collected from six transplant centres in the country AIIMS (Delhi); SGPGI (Lucknow); Apollo (Chennai); NH Kidwai (Bangalore); CMCH (Vellore) and GCRI (Ahmedabad).

PROTOCOL FOR BONE MARROW TRANSPLANTATION-

- The main step in bone marrow transplantation is HLA-test (**Human Leukocyte Antigen** test).
- The HLA test looks at the genetic markers on white blood cells of the donor. There is no need to have the same blood type in order to be a donor for transplant patients.
- The blood is drawn from mother, father and sibling from the same parent (always has high chances of being a close match).
- Donors should be a match of minimum 6 HLA markers. HLA matching promotes the growth and development of new healthy cells (engraftment) and risk of GVHD is reduced.

How donors and patients are matched for HLA?
Sample of DNA is collected by cheek swab which further gets tested for a minimum of 6 HLA markers.

HLA matching- when 2 individuals tend to share the same HLA protein i.e. the immunology of patient and donor match strongly. HLA are proteins located on the surface of WBC and other tissues in the body.

Three General groups of HLA are- HLA-A; HLA-B; HLA-DR. There are different proteins in each of these groups of HLA. HLA-A has 59

different proteins; HLA-B has 118 different proteins; HLA-DR has 124 different proteins.

HLA is inherited or genetically transferred as a set of 3 HLA groups (haplotype).

After HLA typing is done, other tests are also performed. After deciding who the donor is, few tests are performed on both donor and patient.

- To identify problems which can be cured before transplantation eg. dental or thyroid complication.
- To see if the donor is healthy enough to not transfer any viral infections.

Life expectancy after Bone marrow transplantation-

According to the reports and several successful bone marrow transplants, it has been seen that there is a reduction in GVHD complication. Post-transplant health related quality of life (HR-QoL) has been improved. Not only this, but the drastic changes and approaches has led to progressive availability of alternative stem cell sources from unrelated or haploidentical donors or umbilical cord blood.

Clinical challenges of Transplantation-

There are always concerns regarding transplant-related complications like infections, rejection, acute and chronic GVHD. Graft vs Host Disease (GVHD) occurs after allogeneic transplant. Once the stem cells which have been transplanted start to grow, the recipient's body may recognise it as a foreign body. Just after a short period of transplant. The new stem cells (graft) may attack the organs of the patient like liver, gastrointestinal tract or skin (host).

There is a risk of viral, bacterial and fungal infections, pneumonia, veno occlusive disease (VOD) and in worst cases organ failure can also happen. All such concerns should not prevent individuals from making a decision for each patient as to whether to undergo transplant or not, as transplantation has significantly improved the quality of care as well as QoL (Quality of Life) of patients. Mentioned below are few challenges and limitations for nation-wide and cost-effective transplantation programs in countries with high prevalence of thalassemia major:

- Availability of transplant services via governmental or non-governmental organizations or private sector.
- Affordability by the patient/family if the service is paid for or out-of-pocket or through an insurance system.
- Awareness of the local society including both medical societies and the public.
- Accessibility to such a technologically advanced high-cost modality early on in life for patients.
- Age limitations.
- Donor availability.
- Program availability
- Graft rejection.

SUMMARY

Talking about the cure for Thalassemia, allogeneic transplantation with related or unrelated donor cells from cord blood units, mobilized peripheral blood or bone marrow is currently the only curative treatment provided that a compatible donor can be found.

The studies show good HRQoL and return to normal lifestyle in long-term ex-thalassemia patients, the choice of undergoing HSCT remains difficult. Over the past few years, the availability of oral iron chelators and increasingly safe and efficient transfusion therapy has radically improved the life expectancy of thalassemia patients. On the other hand, HSCT offers patients the possibility of a definitive cure with a relatively low risk of transplantation-related mortality. The availability of novel data on HRQoL in the long term should provide both physicians and patients with a better comprehension of the advantages and potential risks of HSCT and assist them in the treatment decision-making process.

It is better and safer if thalassemia major patients are provided with a transplantation before they develop any iron overload complications or end organ damage. The only curable and safest treatment for thalassemia major till now is hematopoietic stem cell transplant. For patients who do not find suitable donors, for them haplo identical stem cell transplant is an emerging option.

REFERENCES

1. Hamilton, B. K., Rybicki, L., Dabney, J., McLellan, L., Haddad, H., Foster, L., Abounader, D., Kalaycio, M., Sobecks, R., Dean, R., Duong, H., Hill, B. T., Bolwell, B. J., & Copelan, E. A. (2014). Quality of life and outcomes in patients ≥60 years of age after allogeneic hematopoietic cell transplantation. *Bone Marrow Transplantation*, *49*(11), 1426–1431. https://doi.org/10.1038/bmt.2014.166
2. Gaziev, J., Marziali, M., Isgrò, A., Sodani, P., Paciaroni, K., Gallucci, C., Andreani, M., Testi, M., De Angelis, G., Alfieri, C., Cardarelli, L., Ribersani, M., Armiento, D., & Lucarelli, G. (2013). Bone marrow transplantation for thalassemia from alternative related donors: Improved outcomes with a new approach. *Blood*, *122*(15), 2751–2756. https://doi.org/10.1182/blood-2013-07-513473
3. Bracken, M.B.; Shepard M.P.H., et al. (1990). The New England Journal of Medicine Downloaded from nejm.org on April 1, 2015. For personal use only. No other uses without permission. Copyright © 1990 Massachusetts Medical Society. All rights reserved. *The New English Journal of Medicine*, *323*(16), 1120–1123.
4. Cheuk, D. K. L., Mok, A. S. P., Lee, A. C. W., Chiang, A. K. S., Ha, S. Y., Lau, Y. L., & Chan, G. C. F. (2008). Quality of life in patients with transfusion-dependent thalassemia after hematopoietic SCT. *Bone Marrow Transplantation*, *42*(5), 319–327. https://doi.org/10.1038/bmt.2008.165
5. La Nasa, G., Caocci, G., Efficace, F., Dessì, C., Vacca, A., Piras, E., Sanna, M., Marcias, M., Littera, R., Carcassi, C., & Lucarelli, G. (2013). Long-term health-related quality of life evaluated more than 20 years after hematopoietic stem cell transplantation for thalassemia. *Blood*, *122*(13), 2262–2270. https://doi.org/10.1182/blood-2013-05-502658
6. Lawson, S. E., Roberts, I. A. G., Amrolia, P., Dokal, I., Szydlo, R., & Darbyshire, P. J. (2003). Bone marrow transplantation for β-thalassaemia major: The UK experience in two paediatric centres. *British Journal of Haematology*, *120*(2), 289–295. https://doi.org/10.1046/j.1365-2141.2003.04065.x
7. Patel, S., Vellaichamy Swaminathan, V., Mythili, V. S., Venkatadesikalu, M. S., Sivasankaran, M., Jayaraman, D., Balasubramaniam, R., Uppuluri, R., & Raj, R. (2018). Quality Matters-Hematopoietic Stem Cell Transplantation versus Transfusion and Chelation in Thalassemia Major. In *INDIAN PEDIATRICS* (Vol. 1056).
8. Caocci, G., Orofino, M. G., Vacca, A., Piroddi, A., Piras, E., Addari, M. C., Caria, R., Pilia, M. P., Origa, R., Moi, P., & La Nasa, G. (2017). Long-term survival of beta thalassemia major patients treated with hematopoietic stem cell transplantation compared with survival with conventional treatment. *American Journal of Hematology*, *92*(12), 1303–1310. https://doi.org/10.1002/ajh.24898
9. de Dreuzy, E., Bhukhai, K., Leboulch, P., & Payen, E. (2016). Current and future alternative therapies for beta-thalassemia major. *Biomedical Journal*, *39*(1), 24–38. https://doi.org/10.1016/j.bj.2015.10.001
10. Angelucci, E., Trapianti, C., Osseo, M., Medica, O., Oncologico, O., & Armando, R. (2000). Hematopoietic Stem Cell Transplantation in Thalassemia Hematopoietic Stem Cell Transplantation in Thalassemia : A Model of Cellular Replacement. *Hematology*, 456–462
11. Nadkarni, A. H., Gorakshakar, A. C., Sawant, P. M., Italia, K. Y., Upadhye, D. S., Gorivale, M. S., Mehta, P. R., Hariharan, P., Ghosh, K., & Colah, R. B. (2019). The phenotypic and molecular diversity of hemoglobinopathies in India: A review of 15 years at a referral center. *International Journal of Laboratory Hematology*, *41*(2), 218–226. https://doi.org/10.1111/ijlh.12948