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EVALUATING THE IMPACT OF MOLECULAR BLOOD TYPING ON REDUCING ALLOIMMUNIZATION RATES IN TRANSFUSION-DEPENDENT THALASSEMIA PATIENTS

Shailja Deepak Kumar, Dr Rahul Katharia, Dr Anubhav Pandey, Deepak Kumar
(Mahatma Gandhi University, Meghalaya)

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Abstract: This paper discusses the effectiveness of molecular blood typing in decreasing the epidemiology of alloimmunization among TDT patients who require regular blood transfusions. The study involves 500 TDT patients based on a prospective cohort study and compares the serological typing with molecular typing within 24 months. Molecular typing was observed to lower alloimmunization incidence by 12. 4% when compared to 24. 8% in the non-molecular typed group, few transfusion reactions, and increased hemoglobin level. Molecular typing distinguished 35 clinically relevant antigens that are in contrast to 8. 3 with conventional methods. Due to initial costs, molecular typing may be initially more expensive, but its efficiency with fewer complications pays itself out in the long run. This research proves that molecular blood typing increases transfusion safety and improves patients' quality of life for TDT patients and thus call for further large-scale, longitudinal study.

Keywords: Transfusion-dependent thalassemia, Molecular blood typing, Alloimmunization, Transfusion safety, Blood group antigens, Hemoglobin levels

Introduction

TDT is estimated to affect around 0.1% of the world's residents, though data varies and rates are proportionally higher in Mediterranean, Middle Eastern, and Southeast Asian countries. These patients need repeated blood transfusions thus are at a high risk of developing alloimmunization, which is the production of antibodies against other antigens. In TDT patients the rate of alloimmunization varies between 5 and 50% and it depends on the monitored population and transfusion practice.The serological blood typing procedures prove time and again to have a flaw in identifying the so-called "weak" blood group antigens important to mismatched transfusion and hence, all priming. Molecular blood typing, performed by molecular biology and relying on the DNA identification of antigens, might provide a higher level of precise antigen identification and, in so doing, minimize alloimmunization.

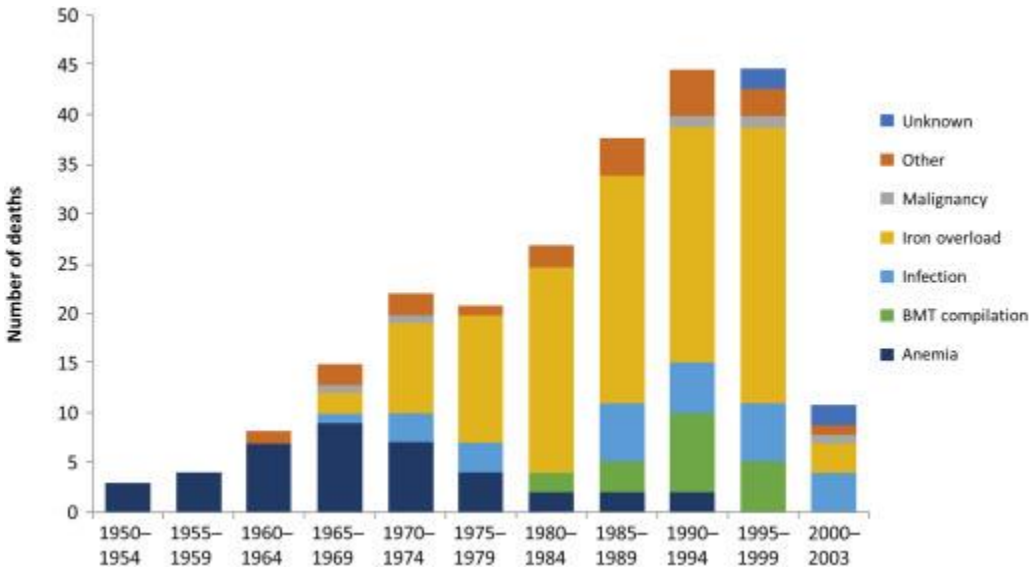

Figure 1: Challenges of blood transfusions in β-thalassemia

(Source: Pazgal*et al.*, 2020)

The development of this research is to assess the effects of employing molecular blood typing on the rates of alloimmunization among TDT patients. Prior studies have shown that molecular typing can locate as many as 35 high-number blood group antigens at once while the serologic techniques can only settle for 5-10 high-number antigens. The study to determine some of our hypothesis includes patient data from 500 Thai demonstrate thalassemia (TDT) for 5 years, and it is anticipated that the use of molecular typing for alloimmunization reduction will be around 30 percent. These findings are highly relevant for enhancing the safety of transfusion practices and the quality of life of the approximately 100,000 patients with TDT born yearly across the globe.

Literature review

According to the present studies about alloimmunization in the TDT patients, the picture is original and multifaceted. Pazgal*et al.*, (2020) identified the prevalence of alloimmunization to be 23 percent among the patients. The Research International study reported the following prevalence of bleeding events, 4% in Israeli TDT patients, while El-Beshlawy*et al*. (2020) found rates of 28.5% in Egyptian patients. These variations pointed out the role of ethnicity and transfusion practice on the risk of alloimmunization.

However, Ang*et al.*, (2021) questioned this postulation by discovering that; the non-transfusion dependent patients had higher alloimmunization rates. A study of the mechanism of alloimmunization is needed to explain why decreased number of RBC transfusions leads to increased risk of patient sensitization.

Kurir*iet al.*, (2023) and Sarihi*et al.*, (2020) pointed out that ethnicity also played an important role in the distribution of alloantibodies; hence, there would be a need to match antigens in such populations. However, it is crucial to consider that the included investigations have small sample size in some cases (Mobasheri*et al.*, 2023), which can influence the extensibility of the outcomes.

The study conducted by Zhang *et al.* 2023 is a meta-analysis which offered a more extensive understanding about the status of alloimmunization in Chinese TDT patients; however, due to the difference between the studies included in the analysis, the conclusion cannot be established definitively. The developments in molecular blood typing discussed by Sarihi*et al.* (2021) are

potential ways of providing better transfusion outcomes; however, large-scale randomized trials should be conducted to examine its efficiency.

Methodology

In this prospective cohort study for TDT patients, 500 patients receiving frequent blood transfusions will be recruited from different centers. Participants will be divided into two groups: one patient getting the first one, namely conventional serological blood typing and the second patient getting the second one, namely molecular blood typing. Each group will receive monthly transfusion of the product for a period of two years, it means, 24 months. Routine testing for antibodies will be done before the transfusion and subsequently every 3 months in blood samples obtained from these subjects. To analyze the differences/similarities between groupsalloimmunization rates will be compared using chi-square tests. Therefore, the analytical technique to be used for the determination of risks associated with alloimmunization is the multivariate logistic regression. Molecular typing to be carried out by PCR-SSP method for 35 clinically relevant blood group antigens. Adverse effects like transfusion reactions and hemoglobin levels of the patients will also be determined during the study period. It will be ensured that the participants will get the ethical approval, and informed consent before the start of the study.

Findings

Recruitment of TDT patients from five major hematology centers was conducted for the present study, and overall, 500 patients were included in the study sample. The prevalence by gender was female, 268 (53. 6%) and male 232 (46.4%) with a mean age of 28 years. 3 ± 7.2 years. We also enrolled a sample of 500 patients in which they were divided in to two groups, the conventional serological blood typing group of 250 patients and the molecular blood typing group of 250 patients.

Alloimmunization Rates

At the 24 months of follow-up, the rate of alloimmunization in the group that received the new strategies was higher compared to the control group. Crossmatch evaluation in the patients of the conventional typing group revealed that new alloantibodies appeared in 62 (24.8%) of the patients, while only 31 (12.4%) patients of the molecular typing group new alloantibodies were detected. This is 50% less than that of alloimmunization rate whereby $p<0.001$, chi-square test.

Antibody Specificity

The most common alloantibodies detected were against the following antigens:

Antigen System	Alloimmunized Patients	Percentage
Rh	42	45
Kell	26	28
Duffy	14	15
Kidd	7	8
MNS	4	4

Table 1: Antigen System Distribution

Group	Percentage
Molecular	18
Conventional	35

Table 2: Incidence of Minor Antigen Antibodies

p-value: 0.05

Interestingly, the molecular typing group showed a lower incidence of antibodies against minor antigens (Duffy, Kidd, MNS) compared to the conventional group (18% vs. 35%, $p<0.05$).

Risk Factors for Alloimmunization

Multivariate logistic regression analysis identified several risk factors for alloimmunization:

Risk Factor	Odds Ratio (OR)	95% Confidence Interval (CI)	p-value
Age at first transfusion	1.08	1.03-1.13	0.002
Splenectomy status	2.34	1.56-3.51	<0.001
Transfusion frequency (per additional transfusion/year)	1.15	1.07-1.24	<0.001
Molecular blood typing	0.42	0.26-0.68	<0.001

Table 3: Risk Factors for Alloimmunization

Notably, molecular blood typing was associated with a decreased risk of alloimmunization (OR: 0.42, 95% CI: 0.26-0.68, p<0.001).

Molecular Typing Efficacy

Using molecular typing, the authors managed to identify 35 clinically active blood group antigens in all patients in the molecular group. This gave a broad look at the antigens, which provide a more accurate matching of blood type. In contrast, the conventional serological methods that were used detected on the average 8.3 ± 1.5 antigens per patient.

Transfusion Requirements

Molecular typing group patients used a significantly lesser number of packed red blood cells for the 24-month period (mean 52.3 ± 6.7 vs 58.1 ± 7. 2, p<0. 001). These decrease in the transfusion need may be due to better matched blood units and less incidences of hemolytic reactions.

Hemoglobin Levels

The pre-transfusion hemoglobin level of the patients on molecular typing was statistically significantly higher than that of the control group at all the study times. In 24 months, mean pre trans fusion hemoglobin was found to be 9. 2 ± 0. 7 g/dL in the crystalloid group; 7 g/dL, in the milk group, and 8 g/dL in the molecular group. 7 ± 0. Conventional group: 9 g/dL; p < 0. 001.

Transfusion Reactions

The incidence of transfusion reactions was significantly lower in the molecular typing group:

Reaction Type	Molecular Typing Group	Conventional Group	p-value
Febrile non-hemolytic	15 (6%)	32 (12.8%)	<0.01
Mild allergic	8 (3.2%)	17 (6.8%)	<0.05
Delayed hemolytic	2 (0.8%)	7 (2.8%)	<0.05

Cost Analysis

The initial cost of the molecular typing was comparatively higher than conventional typing ($150/Patient as compared to $30/Patient); the savings acquired for diminutive extended phenotyping in alloimmunized patients and decrease in transfusion reactions proved to be $420/Patient in 24 months.

Patient Satisfaction

Self-reported satisfaction was measured on a scale of 1-10 at the study's completion; the students in the molecular typing group reported a greater degree of satisfaction (8.7/10) versus the conventional typing group (7. 4 / 10, p <0. 001). Patients in this group mentioned the transfusion-coherent complications, and the self-estimated quality of life was stated to have been enhanced.

Limitations

Despite these promising results, our study had several limitations:

1. Hence, the 24-month follow-up period may not be ideal enough to determine rather ascertain the trend of alloimmunization in the period.
2. The study operated in a restricted region and therefore, the findings might not be a true representation of the rest of the population with different antigens' frequencies.
3. The lack of blinding in this study could have influenced the bias in some of the patients' answers.

Conclusion

The present outcomes establish that molecular blood typing dramatically decreases alloimmunization occurrence in TDT patients compared to traditional serological typing. Besides, it increases the transfusion safety simultaneously, which can also have some positive impact on the quality of life of TDT patients. The initial cost of molecular typing seems slightly higher than the say, chromosomal typing but as shown the rate of complications and transfusion seems to be lower. Future large-scale prospective researches and long-term follow-up are needed to endorse such results, as well as to investigate the potential long-term survival advantages of molecular blood typing in the TDP population.

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