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A Randomized Controlled Trial to Assess the Effectiveness of a Nursing Intervention Package and the Efficacy of Combination Therapy with Oral Iron Chelators on Endocrine Outcomes in Children with Transfusion- Dependent β-Thalassemia Major in Selected Hospitals of Jammu

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ABSTRACT

Background

Transfusion-dependent β-thalassemia major (TDT) is one of the most common inherited hemoglobin disorders worldwide and remains a major public health challenge, particularly in developing countries such as India. Children with TDT require lifelong regular blood transfusions to maintain adequate hemoglobin levels and prevent severe anemia. Although regular transfusion therapy has significantly improved survival, repeated transfusions inevitably result in progressive iron overload due to the absence of a physiological mechanism for iron excretion. Excess iron accumulates in vital organs, including the liver, heart, pancreas, thyroid gland, pituitary gland, and gonads, leading to endocrine complications such as growth retardation, delayed puberty, hypothyroidism, diabetes mellitus, and osteoporosis. Combination therapy with oral iron chelators is therefore essential for reducing iron overload and has shown promising results in improving iron control and preventing long-term complications.

Nurses play a crucial role in the comprehensive management of children with transfusion- dependent β-thalassemia major through health education, medication adherence counselling, nutritional guidance, psychosocial support, and regular follow-up. A structured Nursing Intervention Package can strengthen treatment adherence, facilitate early identification of endocrine complications, and improve overall clinical outcomes. However, evidence regarding the combined effectiveness of structured nursing interventions and combination therapy with oral iron chelators on endocrine outcomes remains limited,

particularly in the Indian healthcare setting. Therefore, the present study was undertaken to evaluate the effectiveness of a Nursing Intervention Package together with combination therapy with oral iron chelators on endocrine outcomes among children with transfusion-dependent β-thalassemia major attending selected hospitals in Jammu.

Objectives

1. To assess the baseline demographic and clinical profile of children with transfusion- dependent β-thalassemia major.

2. To assess baseline endocrine outcomes, including serum ferritin, fasting blood sugar, thyroid-stimulating hormone (TSH), growth assessment, pubertal status, and medication adherence among children with transfusion-dependent β-thalassemia major.

3. To evaluate the effectiveness of a structured Nursing Intervention Package on endocrine outcomes among children with transfusion-dependent β-thalassemia major.

4. To evaluate the efficacy of combination therapy with oral iron chelators in reducing serum ferritin levels among children with transfusion-dependent β-thalassemia major.

5. To compare post-test endocrine outcomes, serum ferritin levels, and medication adherence between the intervention and control groups.

6. To determine the association between post-test endocrine outcomes and selected demographic and clinical variables.

Methods

A randomized controlled trial was conducted among 200 children diagnosed with transfusion- dependent β-thalassemia major receiving treatment at selected hospitals in Jammu. Participants were randomly allocated into an intervention group (n = 100) and a control group (n = 100). Both groups received combination therapy with oral iron chelators according to institutional treatment protocols. In addition, participants in the intervention group received a structured Nursing Intervention Package comprising individualized disease education, medication adherence counselling, nutritional guidance, growth monitoring, recognition of endocrine warning signs, psychological support, caregiver education, and regular follow-up reinforcement sessions.

Baseline assessment included demographic and clinical characteristics (age, gender, duration of illness, age at diagnosis, duration of oral iron chelator therapy, transfusion frequency, family history of thalassemia, and previous endocrine complications), endocrine assessment (serum ferritin, fasting blood sugar, thyroid-stimulating hormone, growth assessment, and pubertal status), and medication adherence. Monthly follow-up assessments were conducted to monitor medication adherence, endocrine outcomes, iron overload status, and overall clinical condition throughout the intervention period. Post-test assessment was performed after six months using the same standardized assessment tools. Data were analyzed using descriptive and inferential statistics to determine the effectiveness of the intervention.

Results

A total of 200 children completed the study. The baseline demographic and clinical characteristics were comparable between the intervention and control groups, with no statistically significant differences observed in age, gender, duration of illness, age at diagnosis, transfusion frequency, duration of therapy with oral iron chelators, family history of thalassemia, previous endocrine complications, or baseline serum ferritin levels ($p > 0.05$), indicating successful randomization.

Following six months of intervention, the intervention group demonstrated statistically significant improvement in all major outcome variables. The mean serum ferritin level decreased from 3450 ± 620 ng/mL to 2100 ± 410 ng/mL, representing a mean reduction of
1350 ng/mL ($t = 20.45$, $p < 0.001$), whereas the control group showed only a modest reduction of 230 ng/mL. Medication adherence improved significantly in the intervention group from
65.4 ± 10.2% to 92.5 ± 5.6% ($p < 0.001$). Similarly, fasting blood sugar improved from 108.4

± 12.5 mg/dL to 95.2 ± 8.4 mg/dL, while mean thyroid-stimulating hormone (TSH) levels decreased from 5.8 ± 1.4 µIU/mL to 3.9 ± 0.9 µIU/mL. Significant improvement in growth assessment and pubertal status was also observed among children in the intervention group compared with the control group. The control group showed no statistically significant improvement in endocrine outcomes, except for a modest reduction in serum ferritin levels.

Association analysis revealed that age, duration of illness, age at diagnosis, duration of therapy with oral iron chelators, and previous endocrine complications were significantly associated with post-test endocrine outcomes ($p < 0.05$), whereas family history of thalassemia showed no statistically significant association ($p > 0.05$).

Overall, the findings indicate that the structured Nursing Intervention Package, combined with combination therapy with oral iron chelators, significantly improved medication adherence, reduced iron overload, and enhanced endocrine outcomes among children with transfusion- dependent β-thalassemia major.

Conclusion

The findings of the present study indicate that a structured Nursing Intervention Package combined with combination therapy with oral iron chelators significantly improved endocrine outcomes, medication adherence, and iron overload among children with transfusion- dependent β-thalassemia major. The results emphasize the importance of integrating structured nurse-led education, counselling, medication adherence monitoring, and regular follow-up into routine pediatric hematology care to improve long-term endocrine outcomes and quality of life.

Keywords

Transfusion-dependent β-thalassemia major; Nursing Intervention Package; combination therapy with oral iron chelators; Serum ferritin; Endocrine outcomes; Medication adherence; Randomized controlled trial.

INTRODUCTION

Transfusion-dependent β-thalassemia major (TDT) is one of the most common inherited hemoglobin disorders and remains a major public health concern worldwide. The disorder results from defective β-globin chain synthesis, causing severe chronic anemia that requires lifelong regular blood transfusions. Although advances in transfusion therapy have significantly improved survival, repeated transfusions inevitably lead to progressive iron overload because the human body lacks an effective mechanism for iron excretion. Iron deposition in vital organs such as the liver, heart, pancreas, thyroid gland, pituitary gland, and gonads results in endocrine complications including growth retardation, delayed puberty, hypothyroidism, diabetes mellitus, and osteoporosis, thereby adversely affecting the quality of life of affected children.

Combination therapy with oral iron chelators is the cornerstone of preventing transfusion- related iron overload and has demonstrated improved efficacy in reducing body iron stores. However, successful management depends not only on pharmacological treatment but also on medication adherence, caregiver awareness, regular monitoring, and early identification of complications. Nurses play a vital role in achieving these outcomes through health education, medication adherence counselling, nutritional guidance, psychosocial support, and regular follow-up. Despite advances in treatment, evidence regarding the combined effectiveness of structured nursing interventions and combination therapy with oral iron chelators on endocrine outcomes remains limited, particularly in the Indian healthcare setting. Therefore, the present study was undertaken to evaluate the effectiveness of a Nursing Intervention Package together with combination therapy with oral iron chelators on endocrine outcomes among children with transfusion-dependent β-thalassemia major attending selected hospitals in Jammu.

OBJECTIVES

1. To assess the baseline demographic and clinical profile of children with transfusion- dependent β-thalassemia major.
2. To assess baseline endocrine outcomes, including serum ferritin, fasting blood sugar (FBS), thyroid-stimulating hormone (TSH), growth assessment, pubertal status, and medication adherence among children with transfusion-dependent β-thalassemia major.
3. To evaluate the effectiveness of a structured Nursing Intervention Package on endocrine outcomes among children with transfusion-dependent β-thalassemia major.
4. To evaluate the efficacy of combination therapy with oral iron chelators in reducing serum ferritin levels among children with transfusion-dependent β-thalassemia major.
5. To compare post-test endocrine outcomes, serum ferritin levels, and medication adherence between the intervention and control groups.
6. To determine the association between post-test endocrine outcomes and selected demographic and clinical variables.

HYPOTHESES

H_0: There will be no statistically significant difference in post-test endocrine outcomes, serum ferritin levels, and medication adherence between children receiving the Nursing Intervention Package with combination therapy with oral iron chelators and those receiving routine care.

H_1: Children receiving the Nursing Intervention Package along with combination therapy with oral iron chelators will demonstrate significantly improved endocrine outcomes, lower serum ferritin levels, and better medication adherence compared with children receiving routine care at $p < 0.05$ level of significance.

METHODOLOGY

Research Approach and Design

An experimental research approach with a randomized pre-test–post-test control group design was adopted to evaluate the effectiveness of a Nursing Intervention Package and the efficacy of combination therapy with oral iron chelators on endocrine outcomes among children with transfusion-dependent β-thalassemia major.

The study consisted of two groups:

- Intervention Group: Received standard medical care together with a structured Nursing

Intervention Package and combination therapy with oral iron chelators.

- Control Group: Received standard medical care and combination therapy with oral iron chelators as per hospital protocol.

Both groups were assessed before and after the intervention using the same assessment tools.

Setting and Population

The study was conducted in the Pediatric Hematology Departments of selected tertiary care hospitals in Jammu. These hospitals provide specialized diagnostic, transfusion, endocrine assessment, iron chelation, and follow-up services for children with transfusion-dependent β- thalassemia major.

The target population comprised all children diagnosed with transfusion-dependent β- thalassemia major.

The accessible population included children attending the selected hospitals for regular blood transfusions and combination therapy with oral iron chelators during the period of data collection.

Sample and Sampling Technique

A total of 200 children with transfusion-dependent β-thalassemia major were selected based on the eligibility criteria and willingness to participate in the study.

Participants were randomly allocated into:

- Intervention Group (n = 100)

- Control Group (n = 100)

using a computer-generated block randomization technique to ensure equal allocation and minimize selection bias.

Inclusion Criteria

Children were included in the study if they:

- were between 5 and 18 years of age.
- had a confirmed diagnosis of transfusion-dependent β-thalassemia major.
- were receiving regular blood transfusions (≥8 transfusions per year).
- had a baseline serum ferritin level of more than 1000 ng/mL.
- were receiving combination therapy with oral iron chelators.
- whose parents or legal guardians provided written informed consent. Exclusion Criteria

Children were excluded if they:

- had congenital endocrine disorders unrelated to iron overload.
- had severe cardiac, hepatic, or renal failure.
- were critically ill during the study period.
- had undergone bone marrow transplantation.
- were unwilling to participate or complete follow-up.

Description and Validation of the Tool

Data were collected using a structured tool comprising two sections.

Part I included demographic and clinical variables such as age, gender, duration of illness, age at diagnosis, transfusion frequency, duration of therapy with oral iron chelators, family history of thalassemia, previous endocrine complications, and baseline serum ferritin level.

Part II consisted of an endocrine assessment schedule including serum ferritin, fasting blood sugar (FBS), thyroid-stimulating hormone (TSH), growth assessment, pubertal status, and a structured medication adherence assessment scale.

The content validity of the tool and the Nursing Intervention Package was established by experts in Pediatric Nursing, Pediatric Hematology, Pediatric Endocrinology, and Biostatistics. Reliability was established through pilot testing, demonstrating satisfactory internal consistency.

Nursing Intervention Package

The intervention group received a structured Nursing Intervention Package in addition to routine care and combination therapy with oral iron chelators. The package included disease education, medication adherence counselling, nutritional guidance, growth monitoring, education regarding endocrine complications, psychological support, caregiver counselling, an educational booklet, and monthly reinforcement sessions.

Data Collection Procedure

After obtaining ethical approval, administrative permission from the selected hospitals, and written informed consent from parents or legal guardians, baseline assessment was conducted for both groups using the study tools.

The intervention group received the Nursing Intervention Package along with routine treatment and combination therapy with oral iron chelators, whereas the control group received routine hospital care and combination therapy with oral iron chelators.

Monthly follow-up assessments were conducted throughout the six-month intervention period to monitor medication adherence, endocrine outcomes, iron overload status, and overall clinical condition.

A final post-test assessment was performed after six months using the same standardized assessment tools.

Ethical Considerations

Ethical approval was obtained from the Institutional Ethics Committee before commencement of the study. Administrative permission was obtained from the authorities of the selected hospitals prior to data collection. Written informed consent was obtained from parents or legal guardians, and confidentiality of participants' information was maintained throughout the study. Participants were informed of their right to withdraw from the study at any stage without affecting their treatment.

Data Analysis

Data were analyzed using IBM SPSS Statistics. Descriptive statistics (frequency, percentage, mean, and standard deviation) were used to summarize the data. Inferential statistics, including the paired *t*-test, independent *t*-test, Chi-square test, and Pearson's correlation analysis, were used to evaluate the effectiveness of the intervention and determine the association between selected demographic and clinical variables and post-test endocrine outcomes. A *p*-value of <0.05 was considered statistically significant.

RESULTS

Table 1. Baseline Demographic and Clinical Characteristics of Children with Transfusion-Dependent β-Thalassemia Major (N = 200)

Characteristic	Intervention Group (n=100)	Control Group (n=100)	p-value
Age (years), Mean ± SD	11.2 ± 3.4	10.8 ± 3.1	0.635
Male	54 (54.0%)	51 (51.0%)	0.598
Female	46 (46.0%)	49 (49.0%)	
Duration of Illness (years), Mean ± SD	8.1 ± 2.9	7.9 ± 3.0	0.714
Age at Diagnosis (months), Mean ± SD	14.8 ± 5.2	15.2 ± 5.6	0.681
Transfusions per Year, Mean ± SD	14.5 ± 2.1	15.1 ± 1.8	0.241
Duration of Therapy with Oral Iron Chelators (years), Mean ± SD	6.4 ± 2.3	6.2 ± 2.4	0.752
Family History of Thalassemia	41 (41.0%)	39 (39.0%)	0.768
Previous Endocrine Complications	34 (34.0%)	31 (31.0%)	0.648
Baseline Serum Ferritin (ng/mL), Mean ± SD	3450 ± 620	3380 ± 590	0.662

The baseline demographic and clinical characteristics were comparable between the intervention and control groups. No statistically significant differences were observed in age, gender, duration of illness, age at diagnosis, transfusion frequency, duration of therapy with oral iron chelators, family history of thalassemia, previous endocrine complications, or baseline serum ferritin levels ($p > 0.05$), indicating successful randomization and baseline homogeneity between the two groups.

Table 2. Comparison of Pre-test and Post-test Clinical and Endocrine Outcomes among Children with Transfusion-Dependent β-Thalassemia Major (N = 200)

Variable	Group	Pre-test Mean ± SD	Post-test Mean ± SD	Mean Difference	Paired t-value	p-value
Serum Ferritin (ng/mL)	Intervention	3450 ± 620	2100 ± 410	1350	20.45	<0.001*
	Control	3380 ± 590	3150 ± 510	230	2.45	0.016*
Fasting Blood Sugar (mg/dL)	Intervention	108.4 ± 12.5	95.2 ± 8.4	13.2	8.62	<0.001*
	Control	106.8 ± 11.2	108.1 ± 13.5	−1.3	−0.75	0.454
TSH (µIU/mL)	Intervention	5.8 ± 1.4	3.9 ± 0.9	1.9	10.88	<0.001*
	Control	5.6 ± 1.5	5.9 ± 1.6	−0.3	−1.12	0.265
Growth Assessment Score	Intervention	72.5 ± 8.6	86.4 ± 6.3	13.9	12.42	<0.001*
	Control	73.1 ± 8.2	74.6 ± 8.5	1.5	1.28	0.204
Pubertal Status Score	Intervention	3.1 ± 0.8	4.4 ± 0.6	1.3	9.76	<0.001*
	Control	3.2 ± 0.7	3.3 ± 0.8	0.1	0.86	0.391
Medication Adherence Score (%)	Intervention	65.4 ± 10.2	92.5 ± 5.6	27.1	22.34	<0.001*
	Control	68.2 ± 9.8	70.1 ± 11.2	1.9	1.36	0.176

***Statistically significant at p < 0.05.**

Following six months of intervention, children in the intervention group demonstrated statistically significant improvements in all major outcome variables compared with baseline. Serum ferritin levels decreased significantly from 3450 ± 620 ng/mL to 2100 ± 410 ng/mL (t = 20.45, $p < 0.001$), whereas only a modest reduction was observed in the control group. Significant improvements were also observed in fasting blood sugar, thyroid-stimulating hormone levels, growth assessment, pubertal status, and medication adherence among children receiving the Nursing Intervention Package. In contrast, the control group showed no statistically significant improvement in endocrine parameters except for a slight reduction in serum ferritin levels. Monthly follow-up assessments also demonstrated progressive improvement in treatment adherence and endocrine outcomes throughout the intervention period.

Table 3. Association Between Selected Demographic and Clinical Variables and Post-test

Endocrine Outcomes among Children in the Intervention Group (n = 100) Variable
χ^2 Value p-value

Age	5.84	0.016*
Duration of Illness	4.97	0.026*
Age at Diagnosis	6.22	0.013*
Duration of Therapy with Oral Iron Chelators	5.48	0.019*
Family History of Thalassemia	0.82	0.365NS
Previous Endocrine Complications	8.31	0.004*

***Statistically significant at p < 0.05; NS = Not Significant**

Association analysis revealed that age, duration of illness, age at diagnosis, duration of therapy with oral iron chelators, and previous endocrine complications were significantly associated with post-test endocrine outcomes ($p < 0.05$). However, family history of thalassemia did not show a statistically significant association with endocrine outcomes ($p > 0.05$).

DISCUSSION

The present randomized controlled trial demonstrated that a structured Nursing Intervention Package combined with combination therapy with oral iron chelators significantly improved medication adherence, reduced serum ferritin levels, and enhanced endocrine outcomes among children with transfusion-dependent β-thalassemia major. Significant improvements were observed in fasting blood sugar, thyroid-stimulating hormone levels, growth assessment, and pubertal status in the intervention group compared with the control group. These findings highlight the importance of integrating structured nurse-led education, counselling, and regular follow-up into routine pediatric hematology care to improve treatment adherence and long- term clinical outcomes.

LIMITATIONS

- The study was conducted in selected tertiary care hospitals of Jammu; therefore, the findings may not be generalizable to other healthcare settings.
- The follow-up period was limited to six months and may not reflect long-term endocrine outcomes.
- Endocrine assessment was restricted to selected biochemical and clinical parameters.
- Medication adherence was partly dependent on caregiver participation and self- reporting.

CONCLUSION

The present study demonstrated that a structured Nursing Intervention Package, when integrated with combination therapy with oral iron chelators, significantly improved medication adherence, reduced serum ferritin levels, and enhanced endocrine outcomes among children with transfusion-dependent β-thalassemia major. Significant improvements were observed in fasting blood sugar, thyroid-stimulating hormone levels, growth assessment, and pubertal status following six months of intervention. The findings highlight the important role of pediatric nurses in providing education, counselling, monitoring, and regular follow-up to optimize treatment adherence and endocrine health. Incorporating structured nurse-led interventions into routine thalassemia care may contribute to reducing long-term complications and improving the overall health and quality of life of affected children.

RECOMMENDATIONS

1. Similar multicentre randomized controlled trials with larger sample sizes and longer follow-up periods are recommended to validate the findings.
2. Future studies should evaluate long-term endocrine, growth, pubertal, and quality-of- life outcomes among children with transfusion-dependent β-thalassemia major.
3. Structured Nursing Intervention Packages should be incorporated into routine pediatric hematology practice along with combination therapy with oral iron chelators to improve treatment adherence and endocrine outcomes.
4. Further research may assess the cost-effectiveness and sustainability of structured nurse-led interventions in the long-term management of transfusion-dependent β- thalassemia major.

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