Published online in http://ijam.co.in ISSN No: 0976-5921

International Journal of Ayurvedic Medicine, Vol 15 (2), 2024; 584-589

Role of T-AYU-HM Premium in Paediatric Patients with Sickle Cell Anaemia: A Retrospective Case Series

Case Report

Atul Desai[1*], Kavita Desai[1], Hemshree Desai[2], Rutvij Desai[3], Chirag Desai[4]

1. Ayurvedic Physician, Dhanvantari Clinic, Ayurveda Health Care and Research Centre, Vyara, Gujarat, India.
2. Modern Medicine, Dhanvantari Clinic, Ayurveda Health Care and Research Centre, Vyara, Gujarat, India.
3. MD; Manila Central University; Philippines.
4. Associate Professor, ROFEL Shri G M Bilakhia College of Pharmacy, Vapi. India.

Abstract

Background: Sickle cell disease (SCD), a genetic disorder caused by a beta globin chain mutation, has been recognized as influencing public health worldwide. In India, numerous tribal and underdeveloped groups frequently suffer from this medical condition. The present study evaluates the effectiveness and safety of alternative medicines T-AYU-HM Premium among paediatric SCD patients. Methodology: A single-arm retrospective observational case series of 10 sickle cell disease paediatric population were conducted. The proposed study was conducted to clinically evaluate the safety and effectiveness of T-AYU-HM Premium Tablet (300mg) on paediatric individuals. The clinical and vital data of the patients were collected, evaluated, and reported using the SPSS software based on inclusion and exclusion criteria. Results: The study had a majority of male (80%) patients with a mean age of 3.20±1.23 years. The present study also identified consanguinity. It also observed a non-significant improvement in weight (12.04 ± 2.45) compared to the baseline (11.64 ± 2.46). There was also a non-significantly decrease in the pulse rate from baseline. In terms of hematological parameters, no significant change was observed from the baseline. However, there was a substantial decrease in pain-associated clinical parameters among the paediatric population. Conclusion: The present retrospective analysis shows that patients with SCD were significantly improved by the T-AYU-HM Premium treatment, proving both its efficacy and safety, particularly in pain management. However, the current analysis suggests a substantial body of evidence (prospective) to support using herbal-mineral formulations for sickle cell anaemia among paediatric patients.

Keywords: Sickle cell disease (HbSS), T-AYU-HM Premium, Ayurvedic.

Introduction

Sickle cell anaemia is the result of mutant beta globin (HBB) in which the mutation causes sickling of haemoglobin. Sickle cell anaemia is a multisystem disease associated with episodes of acute illness and progressive organ damage. Haemoglobin polymerization, leading to erythrocyte rigidity and vasoocclusion, is central to the pathophysiology of the disease, but the importance of chronic anaemia, hemolysis, and vasculopathy has been established. (1)

Sickle cell disease (SCD) is a single gene defect leading to a devastating systemic syndrome distinguished by chronic anaemia, acute painful episodes, organ infarction, chronic organ damage, and a significantly shortened life expectancy. (1) SCD is extremely prevalent, has a significant socioeconomic burden, and has a high mortality rate in the first three years of life. In low-income and developing countries, newborn screening is not a part of standard care; thereforepatients may die young even before the diagnosis is confirmed. (2)

According to the World Health Organization, about 5% of the global population carries trait genes for haemoglobin disorders, like Homozygous SCD patients(HbSS).(3) Sub-Saharan Africa, the Mediterranean, the Middle East, and India have all been found to have a high occurrence.(4) The most common acute complication of SCD is pain, which substantially influences the quality of life in terms of health.(5) Depending on the family dynamics, personal pain thresholds, and access to healthcare, pain management may vary from patient to patient. Patients who employ complementary coping mechanisms typically need fewer hospital stays, and self-help psychological treatments such as guided imagery can be a helpful evidence-based adjunct to controlling pain.(6-7)In SCD, acute neurological symptoms and signs are frequent. They also have symptoms like stroke, transient ischaemic attack, headaches, seizures, altered mental status with or without the reduced level of consciousness.(8)

In the last 50 years, although significant progress has been in understanding the pathophysiology and

*** Corresponding Author:**
Atul Desai
Ayurvedic Physician, Dhanvantari Clinic,
Ayurveda Health Care and Research Centre,
Vyara,
Gujarat, India.
Email Id: dratuldesai@rediffmail.com

pathobiology of SCD, finding effective treatments has been disproportionately difficult and slow.(9) A combination of current developments in genetics and genomics, a rise in the number of clinical studies that are competing with one another, and also increased awareness in the therapeutic landscape for SCD. Over the past ten years, many researchers have focused on creating medications due to sickle cell disease's orphan status. Numerous research involving sickle cell disease were either ongoing or in the planning phases. Unfortunately, bone marrow transplantation and blood transfusion are the only treatment choices available for sickle cell disease, although they are not appropriate for everyone.(10) Currently, there are few curative choices, and the most recent ones are either expensive for low-income nations or have several adverse effects that patients cannot take for the rest of their lives. The management of sickle cell disease may require an alternate system of medicine, particularly in emerging and low-income countries. There is a clear need for numerous investigations on various therapeutic methods that may be useful in managing the ailment.

In the present era, complementary and alternative medicine has great limelight in managing several chronic diseases. Various advances in the scientific research using plants and herbs brought the benefits of ayurvedic medicine and the rationale for their uses to the limelight.There is no word-to-word correlation with SCD in classical Ayurvedic writings. Clinical characteristics of SCD are consistent with and match to *Janmabal Pravrut Pandu Roga* as recorded in the classic Ayurvedic texts. T-AYU-HM Premium is the traditional ayurvedic herbs-mineral formulation that helps in the management of sickle cell anaemia as it has an anti-sickling effect that may be able to stop the deregulation of Gardos channels. This natural treatment contains several substances that serve as sources of iron, ascorbic acid, and a higher possibility of iron absorption. The *Dadima* (*Punica granatum L.*) and *Guduchi* (*Tinospora cordifolia*) extracts will work as powerful antioxidants. It also inhibits cell lysis and prevents sickling-induced activation of chemical mediators, and coagulation cascades.(11-14)

The present study is planned to evaluate the efficacy and safety of AYUSH formulations among the paediatric group. Currently, no herbs-mineral formulations have been evaluated for safety and efficiency in an absolute scientific manner among the paediatric population.

Methodology

Study Design

This retrospective observational case series was performed among sickle cell anaemia patients who attended the Dhanvantari Clinic, Ayurvedic Health Care and Research Centre, Gujarat, between May 2018 and December 2020. T-AYU-HM Premium mentioned in Table 01 is a herbo-mineral formulation with 300 mg tablet dosage form. Patients have to consume it orally by crushing the tablet and consume with water for four month with regular follow up. Sickle cell trait (SCT) and sickle cell disease (SCD) were used to determine the presence of sickle cell anaemia. SCT/SCD specification testing was used to determine the sickle cell anaemia diagnosis for the participants. Participants in the age range of 3 to 5 are deemed eligible. Participants who identify as male or female are deemed suitable for inclusion in the study. Individuals with complete pathological examination data, regular outpatient clinic visits, and therapy with T-AYU-HM Premium are deemed eligible. Participants having inadequate pathological examination data, irregular out-of-program visits, or therapy with other additional drugs are deemed ineligible for inclusion in the study. Basic demographic information about the patient, such as age, gender, identification number, and contact information, as well as medical history (habits, diet, blood group, family history, vaccination history, rate of painful crises, number of hospitalizations, and blood transfusions before presenting for treatment at a clinic, consanguinity), were recorded in the pre-designed form. For routine analysis of patients experiencing excruciating pain crises, the Wong-Baker Pain score scale was used. Informed consent was received from guardian of each patient for the utilization of data for generating better hypothesis for research as well as better healthcare development. To observe the adherence to the schedule of follow up visit like baseline day 0, 30 day visit 2, 60 day visit 3, 90 days visit 4, and 120 days are considered visit 5.

Table 1: Composition of T-AYU-HM Premium (300 mg) tablets

Ingredient Name	Botanical Name	Part Used	Quantity
Abraka Bhasma	Calyx of Mica	-	25 mg
Loha Bhasma	Calyx of iron	-	12.5 mg
Haritaki	*Terminalia chebula*	Fruit	25 mg
Sunthi	*Zingiber officinale*	Rhizome	25 mg
Shatavari	*Asparagus racemosus*	Root	25 mg
Dadima	*Punica granatum*	Fruit	12.5 mg
Jaiphal	*Myristica fragrans*	Seed	25 mg
Pippali	*Piper longum*	Fruit	37.5 mg
Guduchi	*Tinospora cordifolia*	Stem	37.5 mg
Jivanti	*Leptadinia reticlata*	Root	37.5 mg

Statistical Analysis

Data were presented as Mean ± SD for quantitative variables and proportion with percentage for qualitative variables. Data cleaning and analysis were performed using Microsoft Excel and Statistical Package for Social Science (SPSS) version 25 (IBM Corp., Armonk, NY, USA), respectively. A One-Way Repeated Measure Analysis of Variance was used to compare continuous variables having a normal distribution. Statistical significance was determined at a 5% level of significance.

Results

A total of 10 paediatric patients with sickle cell anaemia were identified and included in the study. The participants' mean age was 3.20±1.23, with most being male patients (80%). Out of 10, 6 showed

consanguinities. Of 10, 4 and 6 reported moderate and severe pain, respectively. Pain/fever (30%) was the major complaint, followed by pain (20%). Of 10, 6 were on folic acid, and one was on paracetamol mentioned in Table 02.

Table 2: Demographic Details

Variables	Number (%)
Age	3.20 ± 1.23
Weight (kg)	11.71 ± 2.54
Male Female	8 (80.00) 2 (20.00)
Number of Family Members	4.92 ± 01.55
Diet Mixed Diet Vegetarian	 3 (30.00) 7 (70.00)
Consanguinity Yes No	 6 (60.00) 4 (40.00)
Immunization Continue	 10 (100)
Blood Group O Positive A Positive B Positive	 3 (30.00) 3 (30.00) 4 (40.00)
Medication History Folic Acid Paracetamol	 6 (60.00) 1 (10.00)
Blood Transfusion Prior Visit	0.90 ± 1.20
Complaints on Reporting Fever/Viral/Pain Pain Pain /Swelling Pain/Fever Pain/Weekness Viral/Fever Viral/Fever/Weakness	 1 (10.00) 2 (20.00) 1 (10.00) 3 (30.00) 1 (10.00) 1 (10.00) 1 (10.00)
Pain Scale Moderate Pain Scale Severe	4 (40.00) 6 (60.00)

Effect of treatment on weight and vital signs

Over the end of the study period (120 ±7 days), there was a non-significant improvement in weight (12.04 ± 2.45) compared to baseline (11.64 ± 2.46). The pulse rate also significantly decreased from baseline (109.3±19.64) to visit 5 (120 ±7 days) (100± 12.47). Similar results were noticed in the case of SpO2. The study showed sustained but no significant change on visit 5 (96.05±1.85) compared to baseline (95.9±2.73) mentioned in Table 03.

Effect of Treatment on Haematological Parameters

On Visit 5, no significant change was noticed in haemoglobin (Hb), red blood cell count (RBC), MCHC, MCH, and MCV compared to baseline. However, a non-significant decrease was noticed in platelet and neutrophile count on day 120 compared to baseline. Moreover, a non-significant increase in white blood cell (WBC), eosinophil, lymphocyte, and monocyte was noticed at Day 120 compared to baseline mentioned in Table 03.

Effect of Treatment on Liver Function Test

Over the end of the study period (Day 120), there was a non-significant increase in serum bilirubin noticed (0.43 ± 0.82) compared to baseline (0.09 ± 0.28). Similar findings were observed with direct and indirect bilirubin on Day 120 compared to baseline mentioned in Table 03.

Effect of Treatment on Pain-Associated Clinical Parameters

The impact of treatment on the clinical parameters related to the pain was evaluated using the Wong-Baker pain scale. Wong-Baker Pain Scale was applied to headache, AVNF, abdominal colic, backache, body ache, and fatigue. The study physician assessed the rest of the parameters, including Jaundice, Pallor, splenomegaly, general weakness, palpitation, loss of appetite, and puffiness of the face.

At Day 30 (visit 2) compared to day 0 (baseline), a substantial decrease in the pain-associated clinical parameters, including panduta (pallor), splenomegaly, backache, headache, general weakness, palpitation, abdominal colic, puffiness of the face, fever, body ache, and general weakness was observed mentioned in Table 04.

Discussion

In various regions of the world, particularly in Africa and Asia, where sickle cell disease is highly prevalent. The present understanding of the molecular pathophysiology of SCD has led to the development of several distinct therapeutic modalities.(15) Ten paediatric patients with sickle cell anaemia were identified and analyzed in our retrospective observational case series. In a study by *Kamble etal.,* 63% of the recruited patients were below the age of five years.(16) The participants' mean age was 3.20±1.23 years, with 80% of most being male patients. The study was conducted in the rural medical college of Chhattisgarh, India more than half of the children were in the 0-5 year's age group with a mean age of 2.79 years. (17)

In the present out study population i.e., out of 10, 6 showed consanguinities, which is seen in many other studies on SCD conducted in India. The study conducted in Maharashtra, India, observed the patients' consanguinity history. About 7 (7%) of which 5 (8.2%) had HbSS and 2 (5.2%) had HbAS. (18) Another study conducted by Khadam et al. also observed. (19) It was seen that 13.71% of the study subjects had consanguineous marriage. When examining how much pain each patient was experiencing, four patients experienced moderate and the rest had severe pain, respectively. Additionally, 30% of the patients had Pain/ fever, followed by pain (20%). For pain management, most patients were on paracetamol.

Concerning the disease prognosis after treatment, after 120 days, there was a significant increase in weight compared to the baseline. Historically, many children and adolescents with SCD were underweight. (20) A study reports that SCD patients also highlight that 18.27% of their study subjects were underweight.

(19) This reveals the positive effect of T-AYU-HM Premium in SCD treatment among the paediatric population. The study also noticed a significant decrease in pulse rate from baseline and a sustained but non-significant change in SpO2 from the baseline. Sustaining oxygen saturation suggested no burden on cardiovascular or other organ system and therefore no further burden on respiratory system to compensate the need of oxygen saturation.

Table 3: Effect of Treatment on Laboratory and Vital Parameters

Variables	Baseline (Day 0)	Visit 2 (Day 30)	Visit 5 (Day 120)	p-value
Weight (kg)	11.64 ± 2.46	11.95 ± 2.38	12.04 ± 2.45	0.3530
Pulse (/min)	109.3±19.64	101.5± 15.28	100± 12.47	0.010
SpO2 (%)	95.9 ± 2.737	96.03 ±2.238	96.05 ± 1.857	0.134
CBC				
Hb	8.78 ± 1.17	9.29 ± 1.18	8.99 ± 1.99	0.5453
RBC	3.89 ± 0.81	4.06 ± 1.09	3.83 ± 1.07	0.7382
WBC	11610.00 ± 6586.09	9870.00 ± 5718.21	12868.00 ± 6574.06	0.2858
Platelet	351100.00 ± 113344.56	323650.00 ± 98100.30	323800.00 ± 79568.00	0.7797
MCHC	33.33 ± 1.32	32.58 ± 1.13	32.95 ± 1.26	0.4003
MCH	23.94 ± 3.65	23.64 ± 4.53	23.76 ± 3.06	0.9650
MCV	71.71 ± 9.40	72.53 ± 12.97	72.13 ± 9.03	0.9697
PCV	27.22 ± 3.45	28.32 ± 4.04	27.64 ± 5.84	0.7988
Neu	58.20 ± 11.28	57.40± 16.10	51.50 ± 11.37	0.1661
Eos	3.10 ± 1.85	2.40 ± 2.01	4.20 ± 1.87	0.1207
Lym	38.00 ± 11.64	39.70 ± 14.86	43.20 ± 11.81	0.3623
Mon	0.40 ± 1.26	0.40 ± 1.26	1.40 ± 2.37	0.3286
Ret	2.64 ± 3.72	0.77 ± 0.85	2.44 ± 3.19	0.1897
LFT				
S.Bil	0.09 ± 0.28	0.28 ± 0.60	0.43 ± 0.82	0.4581
D.Bil	0.03 ± 0.09	0.12 ± 0.28	0.22 ± 0.49	0.4640
I.Bil	0.06 ± 0.19	0.16 ± 0.33	0.21 ± 0.36	0.4665

D.Bil: Direct Bilirubin in (mg/dL); Eos: Eosinophile in; Hb: Haemoglobin in (gm%); I.Bil: Indirect Bilirubin (mg/dL); Lym: Lymphocyte (%); MCH: mean corpuscular haemoglobin (pg); MCHC: mean corpuscular haemoglobin concentration (g/dL); MCV: mean corpuscular volume (fl); Mon: Monocyte (%); Neu: Neutrophile(%); PCV: Packed cell volume (%); RBC: Red blood cell (per cmm); Ret: Reticulocyte (%); S.Bil: Serum Bilirubin(mg/dL); WBC: white blood cell.(per cmm)

Table 04: Effect of Treatment on Pain-Associated Clinical Parameters

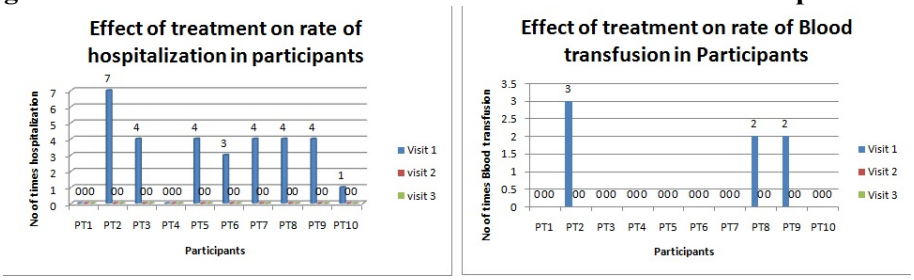
Parameters	Clinical Symptoms	Visit 1 (day 0)	Visit 2 (Day 30)	Visit 5 (Day 120)
Splenomegaly	No Symptoms	6 (60.00)	7 (70.00)	7 (70.00)
	Mild	2 (20.00)	2 (20.00)	0 (0.00)
	Medium	2 (20.00)	1 (10.00)	3 (30.00)
Jaundice	No Symptoms	9 (90.00)	9 (90.00)	9 (90.00)
	Mild	1 (10.00)	1 (10.00)	1 (10.00)
Pallor	No Symptoms	3 (30.00)	8 (80.00)	6 (60.00)
	Mild	6 (60.00)	2 (20.00)	3 (30.00)
	Medium	1 (10.00)	0 (0.00)	1 (10.00)
General Weakness	No Symptoms	1 (10.00)	10 (100.00)	7 (70.00)
	Mild	5 (50.00)	0 (0.00)	2 (20.00)
	Medium	3 (30.00)	0 (0.00)	1 (10.00)
	Moderate	1 (10.00)	0 (0.00)	0 (0.00)
Palpitation	No Symptoms	7 (70.00)	10 (100.00)	9 (90.00)
	Mild	3 (30.00)	0 (0.00)	1 (10.00)
Fatigue	No Symptoms	4 (40.00)	10 (100.00)	8 (80.00)
	Mild	4 (40.00)	0 (0.00)	2 (20.00)
	Medium	2 (20.00)	0 (0.00)	0 (0.00)
Body ache	No Symptoms	3 (30.00)	9 (90.00)	6 (60.00)
	Mild	3 (30.00)	1 (10.00)	3 (30.00)
	Medium	2 (20.00)	0 (0.00)	1 (10.00)
	Moderate	2 (20.00)	0 (0.00)	0 (0.00)
Giddiness	No Symptoms	10 (100.00)	10 (100.00)	10 (100.00)
Backache	No Symptoms	3 (30.00)	9 (90.00)	7 (70.00)
	Mild	3 (30.00)	1 (10.00)	3 (30.00)
	Medium	2 (20.00)	0 (0.00)	0 (0.00)
	Moderate	2 (20.00)	0 (0.00)	0 (0.00)

Puffiness on Face	No Symptoms	7 (70.00)	10 (100.00)	10 (100.00)
	Mild	2 (20.00)	0 (0.00)	0 (0.00)
	Medium	1 (10.00)	0 (0.00)	0 (0.00)
Abdominal Colic	No Symptoms	4 (40.00)	9 (90.00)	8 (80.00)
	Mild	5 (50.00)	1 (10.00)	2 (20.00)
	Medium	1 (10.00)	0 (0.00)	0 (0.00)
Loss of appetite	No Symptoms	10 (100.00)	10 (100.00)	10 (100.00)
Fever	No Symptoms	5 (50.00)	10 (100.00)	7 (70.00)
	Mild	3 (30.00)	0 (0.00)	0 (0.00)
	Medium	1 (10.00)	0 (0.00)	1 (10.00)
	Moderate	1 (10.00)	0 (0.00)	2 (20.00)
Headache	No Symptoms	10 (100.00)	10 (100.00)	10 (100.00)

In observation of the blood parameters, at the end of the therapy, there was no significant change in the haemoglobin, red blood cell count, MCHC, MCH, and MCV compared to baseline. However, a non-significant decrease was noticed in platelet and neutrophils count at day 30 compared to baseline. A non-significant increase in white blood cells, eosinophil, lymphocyte, and monocyte was noticed on day 120 compared to baseline. A similar kind of study on elder patients by Desai et al. showed a significant increase in blood parameters, suggesting that there is no acute RBC destruction after treatment with herbal medication. According to other research, the most typical finding in SCD patients with aberrant white cell counts is an increased white cell count. (11,19)

In our study, concerning the liver function test, there was a non-significant increase in serum bilirubin noticed compared to baseline. The red blood cell count between visit 2 (4.06 ± 1.09) and visit 5 (3.83 ± 1.07) indicate mild hemolysis and might be the most common clinical presentation in sickle cell anemia. However, exact reason for the lysis might not be found but possible infection could have been considered based on correlating clinical and white blood cell counts. The impact of treatment on the clinical parameters related to the pain was evaluated using the Wong-Baker pain scale. Current medications (analgesics) that are used to relieve pain and to help restore RBCs (folic acid) don't reduce the disease complications. (12)Wong-Baker Pain Scale was applied to headache, Avascular necrosis factor (AVNF), abdominal colic, backache, body ache, and fatigue. The study physician also assessed parameters like Jaundice, Pallor, splenomegaly, general weakness, palpitation, loss of appetite, and puffiness of the face, usually observed in SCD patients. After the treatment, the patients experienced a substantial decrease in the pain-associated clinical parameters, including panduta (pallor), splenomegaly, backache, headache, general weakness, palpitation, abdominal colic, puffiness of the face, fever, body ache, and general weakness was observed. On 120th day results of 3 out of 10 participants are highlighting the spleenomegaly, abdominal colic, backache, fatigue, and palpitation suggest there might be possibility of infection or may be any other possible reason. However, no major complications or blood transfusion or hospitalization necessity are reported indicate no further medical assiatance required into them mentioned in (figure 1). Patients with sickle cell disease often get infections, which can develop quickly for a variety of reasons. Encapsulated bacteria can cause invasive infections in persons with sickle cell disease. Patients with sickle cell disease (SCD) require special attention to infection management methods and should be regarded as a unique high-risk population. According to M. Seck et al. (2022), repeated transfusions are expensive, time-consuming, and not without consequences for sickle cell disease (SCD), such as iron overload, alloimmunization, and blood-transmitted infections. (22, 23) In the current period, there are only a few registered and completed clinical trials or successful studies on herbal medication, particularly in the paediatric population.

Figure 1: Effect of treatment on rate of blood transfusion and hospitalisation



Conclusion

The T-AYU-HM Premium treatment significantly improved patients with sickle cell disease, proving both its efficacy and safety, particularly in pain management. The individuals' vital signs were constant during treatment, and no negative effects were found in the retrospective study. The current analysis suggests that there is a substantial body of evidence (prospective) to support the use of herbal-mineral formulations for sickle cell anaemia.

Acknowledgement

The authors would like to sincerely thank ATBU Harita Pharmaceuticals Pvt Ltd for all of its assistance with the study.

Conflict of Interest

The authors have no conflicting financial interests.

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