Case Report Study of Integrated Treatment with T-AYU-HM Premium in a Child of Sickle Cell Disease: A 7 Year Follow up Study

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ABSTRACT

Sickle cell anemia is a type of hemoglobin disorder that no longer requires an introduction to countries like India, Africa, and America. Although the pathogenesis is identified and well defined the clinical picture of symptoms is varied amongst patients. Diagnosis and management of sickle cell trait and disease in children are still a main concern for medical healthcare. In this case report, we present a case exhibiting the impact of integrated therapy on the clinical response of a child suffering from sickle cell disease. A boy X is currently 14 years old was presented to the clinic at 2014 when he was 7 years old. He was diagnosed sickle cell disease during screening. Due to which he was suffering from painful complications and hospitalizations and repeated blood transfusions. With prior information and consent the integrated treatment including T-AYU-HM Premium 300mg started. The overall condition of the child improved and sustained throughout the treatment period. The integrated treatment has reduced the burden of the length of hospital stay and its expanses, requirement of blood transfusion, and complications associated with the vaso-occlusive crisis. The case evaluation suggested the child was admitted only a couple of times in seven years of treatment indicating no major complications were presented during this period. The key observation was sustained hemoglobin and red blood corpuscle concentration prevented the requirement of blood transfusion in sickle cell anemia patients. This approach was a cost-effective, safer as no untoward reaction reported, and therapeutically potential in the management of children suffering from sickle cell anemia.

Keywords: Sickle cell anemia, T-AYU-HM Premium, Integrated treatment, Hemoglobin disorder.

DOI: 10.5530/ijopp.15.4.59

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INTRODUCTION

Sickle cell anemia is a type of hemoglobin disorder that no longer requires an introduction to countries like India, Africa, and America. The critical issue of red blood corpuscles in sickle cell anemia is the alteration in membrane stability, increased membrane oxidation, and dehydration-induced complications. They may be trapped in small blood veins, causing intense pain, depriving tissues of oxygen-rich blood, and harming organs, most notably the spleen. Therefore, despite advances in the treatment of sickle cell anemia, painful vaso-occlusive crisis, frequency of hospitalization, frequency of blood transfusion, and frequency of infections are still obstacles to improvise the quality of life in children. Hospitalization and emergency admissions for treatment are estimated to be seven to thirty times greater in children with sickle cell disease (SCD) than in children without the condition.[1-3] Splenic

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damage dramatically raises the risk of infection-related death in children. Acute chest syndrome, cerebral infarct, and urinary concentrating defects are key concerns amongst children with sickle cell anemia. Although the pathogenesis is identified and well defined on a clinical picture of symptoms is varied amongst patients. Diagnosis and management of sickle cell trait and disease in children are still the main concern for medical healthcare.[4] The majority of the tribal population in South Gujarat has been suffering from this lifelong disorder. Constant awareness, preschool screening, and premarital screening are considered vital.[5]

T-AYU-HM Premium 300mg tablet is a herbo-mineral formulation designed to utilize as a potential anti-sickling agent. The formulation exhibited *in vitro* anti-oxidant and anti-sickling activity. The preclinical studies like acute oral and sub-chronic and immunomodulatory activity studies of the formulation have already been established.[6-8] An integrated treatment approach considering the alternative system of medicine in the management of lifelong disease or disorder might become more advantageous than existing treatment strategies.

CASE REPORT

Case Study

In this case report, we present a case exhibiting the impact of integrated therapy on the clinical response of a child suffering from sickle cell disease presented to Dhanavantari Clinic, Ayurveda Healthcare and Research Center, Vyara-Gujarat. In this case, we reported 7 year follow-up study to highlight the treatment outcome of a patient. This case can also consider important to evaluate the importance of medication adherence in hemoglobin disorder. Before moving forward, we obtained the patient's and his parent's consent to utilize the information for better healthcare in the future.

Case History

A boy X is currently 14 years old. He was presented initiatory to the clinic on the 12th of September 2014 when he was 7 years old. He was diagnosed sickle cell disease patient. He was suffering from painful complications and hospitalizations and repeated blood transfusions. His schooling education was disturbed due to his medical condition. He became tired very early and not able to play along with his friends.

Case Presentation

After evaluating clinical parameters and laboratory parameters, the integrated treatment was initiated in patients. It includes T-AYU-HM Premium 300 mg tablet for twice a day. In Table 1 laboratory information's are mention of the date of admission and post 15 days of treatment.

The treatment was adhered appropriately alongside investigational test was also done to check the haematological parameters. Haematological parameters such as haemoglobin, RBC and WBC, ESR, and serological parameters such as CRP were stable during the therapy phase. But as per investigation report data on 17/02/2020, all parameters were altered, and the haemoglobin level had dropped. ESR level was also abnormally high. It might be symptomatic infections. But with the symptomatic modification in integrated treatment, all parameters improved in the investigational report of March 13, 2020 mentioned in Table 2.

The majority of his treatment was belongs to alternative system of medicines. Allopathic medicine was prescribed in symptomatic conditions like cold, cough; infections, fever mentioned in Table 3. Observing the entire case report file, patient experienced illness and painful crises approximately 3 to 4 times during 7 years of integrated treatment. During this 7 year treatment, some herbal formulations and allopathic medicines were often included and excluded in treatment as per the requirement to treat different symptoms mentioned in Table 3. On date 22/05/2021 patient was found positive for covid-19 through rapid antigen test but considering his minor

Table 1: Laboratory details on baseline investigation.

Investigation	12/9/2014	26/9/2014
Hemoglobin (g/dl)	7.8	7.7
RBC count (in millions)	2.88	2.65
WBC Count (per microliter)	16.0	18.4
Platelet count (per microliter)	479	509
Neutrophils (%)	62.9	37.1
Lymphocytes (%)	32.5	56.1
Eosinophils (%)	2.1	2.6
Monocytes (%)	2.3	1.2
Basophils (%)	02	3
ALY	0.3	0.4
LIC	0.5	0.2
HCT (%)	25.1	23.1
MCV (fl)	87	87
MCH (pg)	27.2	29.1
MCHC (g/dl)	31.2	33.4
RDW (%)	17.9	20.5
MPV	7.3	8.1
PCT	0.349	0.411
PDW	11.0	15.3

Table 2: Investigation Parameters.

Investigation	27/7/2017	1/9/2018	17/2/2020	22/6/2020	22/05/2021
Hemoglobin (g/dl)	6.6	6.1	4.9	6.9	7.0
RBC (In Millions)	2.27	2.10	1.59	2.13	2.35
WBC (Per Microliter)	19.40	17.51	-	-	17.59
Platelets (Per Microliter)	560	467	-	484	402
Neutrophils (%)	44	45	-	28	33
Lymphocytes (%)	45	47	-	51	50
Eosinophils (%)	02	06	-	12	11
Monocytes (%)	05	02	-	9	06
Basophils (%)	00	00	-	00	00
Hct (%)	18.2	17.6	-	-	19.3
MCV (Fl)	80.2	83.8	-	90	82.1
MCH (Pg)	29.1	29.0	-	32.4	29.8
MCHC (g/dl)	36.3	34.7	-	36.0	36.3
RDW (%)	25.4	27.5	23.4	26.7	26.1
Platelets on Smear	Increased	Increased	-	-	-
ESR	22	-	95	-	18
Reticulocytes	15	-	-	-	-
Total bilirubin (mg/dl)	4.39	-	3.79	-	
Direct bilirubin (mg/dl)	1.70	-	1.75	-	
Indirect bilirubin (mg/dl)	2.69	-	2.04	-	
CRP(mg/L)					3.82

Table 3: Integrated Treatment Plan.

Date	Treatment	Date	Treatment
11/09/2014	Tab-Zerodol-P Tab-Zifi 200 mg Tab-T-AYU-HM Premium 300mg	13/02/2015	Syrup-Respicure syp. Tab-Zifi 100 Syrup-Cherical Tab-T-AYU-HM Premium 300mg
25/08/2017	T-ACUTAC T-CP-Vati T- Aampachak Tab-T-AYU-HM Premium 300mg	13/10/2017	Exp-vasaplus S.K.Ras T-ardusa Syrup Tulsi. Tab-T-AYU-HM Premium 300mg
11/08/2017	T-ACUTAC T-Sudershanghan T-CP-Vati T-Trifala T-Ardusa Exp-vasaplus	26/01/2018	Tab-Levocet-M Syrup-Brozeet LS Tab-T-AYU-HM Premium 300mg
27/07/2018	Tab-Dan-P Tab-Levocet-M Tab-Hifen 200 mg Tab-Rantac-D Syrup-Brozeet-LS Tab-T-AYU-HM Premium 300mg	22/09/2019	Tab-Itraz 100 mg Candid powder Lutriben lotion Tab-T-AYU-HM Premium 300mg
13/03/2020	T-Acidez T-A.V.Ras T-Gudechi T- Trifala Tab-T-AYU-HM Premium 300mg	22/05/2021	Tab-T-AYU-HM Premium 300mg

Zerodol-P (Diclofenac +Paracetamol), Zifi (Cefixime), Respicure (Ambroxol+ Guaifenesin + Menthol + Terbutaline), Cherical (calcium carbonate+Vitamin D_3), Hifen (cefixime), Dan-P (Diclofenac + paracetamol), Brozeet Ls(Ambroxol + Levosalbutamol + Guaifenesin), rantac (Ranitidine), Levocet-M (Levocetrizine+ Montelukast), Lutriben (Luliconazole), Itraz 100 (Itraconazole)

symptoms and oxygen saturation he was advised strict home quarantine and continuation of T-AYU-HM Premium 300mg twice a day and onion steam nebulisation for 1 min in a day for 21 days.

On 3rd January 2022, the patient admitted to the multispeciallity with complaints of cold, fever, cough, generalized weakness, and headache for the last 3 to 4 days. He experienced vomiting since morning on the day of hospital admission and his oral intake was also decreased. On local examination, symptoms of dehydration and icterus were also seen. Pulse rate and spo2 level were found to be 132/min and 98% respectively. Chest x-ray posteroanterior (PA) was also completely normal done on 3rd January. The liver function was also not impacted during the treatment. The patient was treated with the following treatment during hospitalization mentioned in Table 4. After 3 days, parenteral and oxygen supplementation was not required and the patient's condition was improved.

After 20 days of combination therapy of allopathic and ayurvedic medicines, the patient improved and discharged. During the lysis process, D-dimer was increased suggesting a hypercoagulability state. After 1 month of treatment, clinical parameters were investigated on 4/2/2022 mentioned in Table 5. Since then the patient is completely again shifted on T-AYU-HM Premium 300 mg tablets twice a day only

Table 4: Investigation Parameters during and after treatment.

INVESTIGATION	3/1/2022	18/1/2022	24/1/2022	4/2/2022
Reticulocytes count (%)	-	15.0	-	-
Hemoglobin (g/dl)	5.8	4.7	6.7	7.3
RBC (In Millions)	2.02	1.49	2.12	2.02
WBC (Per Microliter)	22.48	29.25	18.47	18,400
Platelets (Per Microliter)	337	368	367	289
Neutrophils (%)	63	43	25	32
Lymphocytes (%)	32	44	62	58
Eosinophils (%)	02	04	09	06
Monocytes (%)	03	04	04	04
Basophils (%)	00	00	00	00
HCT (%)	16.8	13.5	18.0	
MCV (fl)	83.2	90.6	84.9	81.2
MCH (pg)	28.5	31.5	31.6	36.1
MCHC (g/dl)	34.5	34.8	37.2	44.5
RDW (%)	28.5	25.7	25.6	10.8
Polychromasia	-	++	-	-
ESR	-	36	16	-
SGPT	18	-	-	-
C-Reactive protein (mg/L)	10.03	9.80	2.01	2.07
D-Dimer (ng/ml)	-	1598	-	500

Table 5: Integrated Treatment Plan.

Treatment	3/1/2022	4/1/2022	5/1/2022
Oxygen / nebulization	Levolin 0.63mg	Budecort 0.5 mg	Levolin 0.63 mg and Budecort 0.5 mg
Parenteral	NS 100 ml DNS 500 ml Febrinil 3 ml Augmentin 1.2 gm Emset 4 mg	Augmentin 1.2 gm DNS 500 ml NS 100 ml Emset 4mg	Febrinil 3 ml
Modern medicine	Tab-Laveta 5mg	Syrup Respicure D 100 ml	Susp. Bevon T-Augmentin 625 T-DUO T-Vitamin C T-Hydroxyurea 500 mg
Ayurvedic intervention	T-AYU-HM Premium 300 Mg Tablet	T-AYU-HM Premium 300 Mg Tablet	T-AYU-HM Premium 300 mg tablet

Laveta (levocetrizine), Respicure (Ambroxol+ Guaifenesin + Menthol + Terbutaline), NS (normal saline), DNS (Dextrose normal saline), Levolin (levosalbutamol), Budecort (Budesonide), Febrinil (paracetamol), Hyrdoxyurea, Augmentin (Amoxycillin + Clavulanic Acid), Emset (ondensatron).

DISCUSSION

The main objectives of this sickle cell disease crisis presentation looked to be avoiding further complications. Hematological parameters are extremely valuable profiles in sickle cell disease management. Changes in hematological parameters have been linked with clinical complications in sickle cell disease patients; according to several studies.[9] Despite advances in the management in sickle cell research there are no interventions found to be effective in the managing varied symptomatic presentations of sickle cell disease patients. Available treatment options can either act as antithrombotic, membrane stabilizing agents, fetal hemoglobin inducer, antioxidant, anti-adhesive, or anti-inflammatory. The gene therapy was eligible enough to cure the sickle cell gene. But its technical and economical limitations can't be ignored. Previous studies have already recommended that multi-pronged attack is definitely required to tackle sickle cell complications.[9]

In this case, the hematological parameters were evaluated frequently. The hemoglobin and red blood corpuscles remains sustained suggested viscosity induced sickling complications are avoided. The improvisation in mean corpuscle hemoglobin, mean corpuscle hemoglobin

concentration, and sustained mean corpuscle volume suggested positive outcomes for the treatment. The level of red cell distribution width (RDW) suggests active erythropoiesis. Integrated treatment exhibited no side effects. During the entire 7 years treatment period the patient was admitted only couple of time indicating no major complications, no any untoward reactions or responses to treatment were presented. There was no requirement of blood transfusion in this patient. The patient also didn't have to deal with the significant pain episodes during the treatment.

During last hospitalization mentioned in Table 5 the patient was prescribed hydroxyurea. Hydroxyurea reduces the adherence of sickle cells to the endothelium in and increases polymerization time, both of which help to prevent sickle cell complications. The medication was discontinued at the time of discharge. The previous literature suggested that if hospitalization occurs 3 or more times in years in any sickle cell patient that is the indication for starting hydroxyurea medication or chronic transfusion therapy if a patient is intolerant to hydroxyurea. At a high dose, hydroxyurea can cause suppression of the bone marrow.[10-12]

There was a remarkable improvement with 21 days treatment at home only in Covid-19. There were no standard therapeutic guidelines available at that time for children infected with Covid-19. There were no painful crisis, no blood transfusion, and no hospitalization was reported during this coronavirus infection treatment period.[10] The C-reactive protein and oxygen saturation was remained sustained. Only Erythrocyte sedimentation rate and white blood cell indices were reportedly appeared altered. But clinically the patients didn't exhibit any complications.

The formulation T-AYU-HM Premium might prevent red blood corpuscles from becoming sickle and so it might prevent pain and complications in young child. Though there was no substantial rise in RBC count in this investigation represented in Figure 1 and 2, it was stable which is more crucial for sickle cell anemia patients' prognosis. Because a rise in RBC count could lead to an increase in hemoglobin level which leads to viscosity-based problems in sickle cell anemia patients.[13,14] As per a previously reported study, the underlying causes of death in sickle cell disease patients are chronic cardiac complications.[15] Treatment sustains oxygen saturation and cellular integrity prevents the lysis of red blood corpuscles. Therefore it might prevent ischemia and hypoxia-induced complications on the heart.[13]

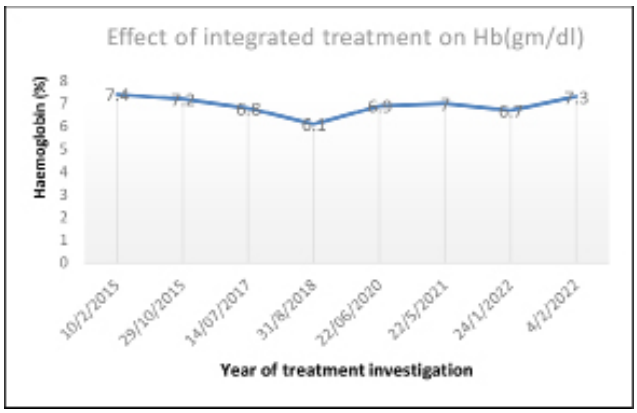

Figure 1: Effect of integrated treatment on hemoglobin level in gm/dl.

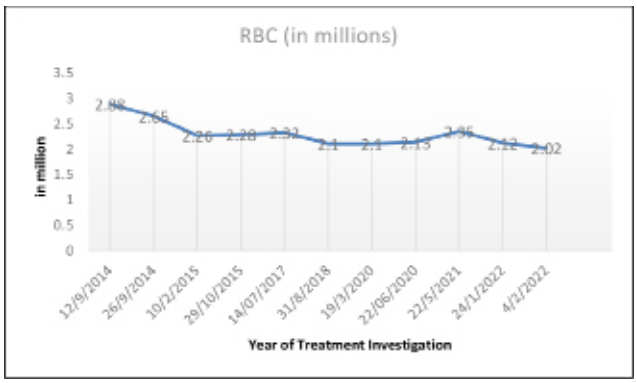

Figure 2: Effect of integrated treatment on RBC in millions.

Reduced sickling of RBCs improves the vascular system's coagulability and returns the body to a normal vascular state, as evidenced by a significant reduction in D-Dimer levels.[10] Patient adhered completely to T-AYU-HM Premium tablets for entire seven years of period. Other supportive treatments were symptomatic and prescribed as and when required only.

CONCLUSION

The overall condition of the child improved and sustained throughout the treatment period. The integrated treatment has reduced the burden of the length of hospital stay and its expanses, requirement of blood transfusion, and complications associated with the vaso-occlusive crisis. By sustaining the cellular integrity and oxygen saturation a formulation can prevent different pathological conditions in sickle cell patients. The treatment exhibited remarkable contribution in combat against covid-19 in this child. This approach was a cost-effective, safer, and therapeutically potential in the management of children suffering from sickle cell anemia.

ACKNOWLEDGEMENT

Authors would like to express their sincere thanks to ATBU Harita Pharmaceuticals.

Consent for the Study

Authors would like to express sincere thanks to participant and his parents for providing their consent.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest

ABBREVIATIONS

RDW: Red cell distribution width; **ESR:** Erythrocyte sedimentation rate; **CRP:** C Reactive Protein; **Hb:** Haemoglobin.

SUMMARY

Adhering to the Integrated treatment patient of sickle cell anemia prevents further symptomatic complications Effect of integrated treatment and medication adherence improvise the quality of life in patient. Time to time monitoring and integrated herbal drug approach might become possible option in long term management of hemoglobin disorder like sickle cell anemia. Very limited long-term adherence and integrated treatment cases in sickle cell anemia patients have been reported.

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