"The Significance Of "*Kalmeghadi Avaleha"* As A Therapeutic Intervention In Childhood Sickle Cell Disease / Sickle Cell Anemia: A Case Report"

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Abstract

INTRODUCTION:
Red blood cells with Sickle Cell Disease, are affected by an autosomal recessive genetic disease that results in an abnormal crescent shape that resembles a "Sickle Shape" and reduces the life of the cells. Sickle cell disease is a hereditary disease with a high rate of morbidity and mortality. The quality of life of patients with sickle cell disease is significantly impacted by their condition's chronic nature and acute pain. At this time, there is no complete treatment for the illness other than genetic transplants. Ayurvedic disease entities such as *Pandu Roga* share most clinical features with SCA/SCD, but there is no direct correlation between the two. From an *Ayurvedic* perspective, Sickle cell disease is *Asadhya* in nature and an *Adibala pravrutta vyadhi*. Society benefits when a medication and the patient's efforts together help a patient maintain their health and quality of life. The disease *Pandu*, which shares similarities with various forms of anemia, is defined by Ayurveda. The main symptoms of *Pandu* are fatigue and appetite loss. Consequently, *Ayurveda* emphasizes a diet fortified with medicines, and diet has a clear role in sickle cell disease.
METHODS:
In this study, *Kalmegha*, *Sharpunkha*, *Vikantaka*, *Punarnava*, *Amalaki, Dadima* and *Pippali* as a medicinal formulation and given to patients with sickle cell disease.
RESULTS:
There is significant relief in the symptoms of crisis, pain, fatigue, and loss of appetite in the patient treated with *Kalmeghadi Avaleha* as a Prescribed medicine.
DISCUSSION:
A specific *Rakta Pitta Dosha Shaman* with "*Kalmeghadi Avaleha*" can be used to treat Sickle Cell Disease, also known as *Beeja-Dustijanya Vata Dosha pradhan Vyadhi*. As it is a genetic disease medication can't cure the disease, they can help manage its symptoms.
CONCLUSION:
Ayurveda is a science that offers a foundation for various formula-based medication treatments for crises or symptoms associated with sickle cell disease.

KEYWORDS: Ayurveda Formulation, Sickle Cell Anemia, Kalmeghadi Avaleha, Pandu, Sickle Cell Disease

Introduction:
Sickle cell anemia, more popularly known as sickle cell disease, is a genetic disorder of the autosomal gene origin of the red blood cells. (1) Sometimes, it is also called a "molecular" disease because of its causes in the mutations of the amino acids of the hemoglobin molecule. This alteration occurs because of the replacement of base pair 6 from adenine to glutamate and valine to glutamate in the gene for beta-globin on chromosome 11. (2) This, in turn, will make a huge difference in the molecular stability and solubility of hemoglobin because of the substitution of amino acids. There were also a few minor changes in the gene's noncoding nucleotide sequence. Polymorphic variants are called haplotypes. They have isolated four haplotypes. The Indian-Arab haplotype is shared with the Indian subcontinent and Eastern Saudi Arabia. (3, 4, 5) Large populations of people with the Bantu Haplotype can be found in North and South America, the Mediterranean region, and Africa. The common genotypes in the general category of Sickle Cell Disease (SCD) are homozygous sickle cell anemia (SS), heterozygous sickle cell anemia (AS), and sickle thalassemia, (S0). (6) They typically start when the child reaches the age of five or six months. Multiple medical conditions can be pre-existent, such as strokes, bacterial infections, anemia, hand and foot edema, and pain episodes. There are four subtypes of sickle cell crisis: aplastic, vascular occlusive, painful, and sequestration. (7-10)

Although much is not available in the earlier Ayurvedic literature about sickle cell disease, some clinical features of sickle cell disease are shared by Pandu. All Ayurvedic texts describe Pandu Roga. Panduta or paleness is the chief symptom of the disease, and this term is synonymous with Pandu roga. Headaches, weakness, irritability, paleness, and malaise are among the most common symptoms. Some of the causes of Pandu Roga are the intake of unhealthy food and wrong behaviors. Wrong food includes too hot, sour, salty, and oily food. Wrong behavior means sleeping during the day, suppressing natural urges, and exercising soon after food. (11 – 16)

Every patient in homeopathic medicine requires individualized care based on a comprehensive case-taking procedure that includes a complete description of the patient's condition. According to Organon of Medicine 6th edition §78 *Dr. Samuel Hahnemann* says - *"The true chronic diseases are those that arise from a chronic miasm, which when left to themselves, and unchecked by the employment of those remedies that are specific for them, always go on increasing and growing worse, notwithstanding the best mental and corporeal regimen, and torment the patient to end of his life with ever aggravated sufferings. These, excepting those produced by medical malpractice."* (17)

Case History:

A 13-year-old female was diagnosed case of Sickle cell anemia with fresh complaints of recurrent Fever, Fatigue, Severe Pain in the upper and lower extremities with Bodyache and Abdominal Pain associated with Loss of Appetite, mild Dyspnoea, repeated Roaring and Banging in the Ear, gradual Weight Loss and Irritability with Lack of Concentration approached Kaumarbhritya OPD at Parul Ayurved Hospital, Vadodara. The father's occupation was farmer, the mother was a farmer and shopkeeper too. Socio-economic status is lower class.

History of Present Illness

The patient complains of severe pain in upper and lower extremities associated with body ache and abdomen pain with loss of appetite, weight loss and fatigue. On General examination, pallor +++ and Icterus ++ were present, while in the local examination, there was the presence of Splenomegaly ++ and Hepatomegaly ++ with severe tenderness over the Left Hypochondriac region with 3 finger palpable spleen towards the Umbilicus and Right Hypochondriac region with 2 finger palpable liver respectively.

History of past illness

Suffered with the same episodes of pain and Vaso occlusive crisis 4 times within 5 years in which hospitalization was required.

Birth History

No major complications and medical interventions were found during prenatal, natal and postnatal periods. Immunization was also dropped at the age of 8 years till that followed as per the National Immunization Schedule.

Personal History:

***Aharaja*: Mixed diet with poor appetite**

***Viharaja*:** The patient enjoys playing both indoor and outdoor games, but she was too tired to play freely. She slept for 7 to 8 hours at night in disturbed manner due to which causes lack of sleep which led to sleep in the day time for 1 to 2 hours.

***Asthavidha Pariksha*: (Table No. 1)**

Pariksha	Values
Nadi (Pulse)	*Vata pradhan Tridoshaj*
Mala (Stool)	*Vibandhita* (Once in 1-2 Days Hard in Consistency with straining)
Mutra (Urine)	Yellowish with Burning (3-4 times/day only)
Jihva (Tongue)	*Sama* (Coated)
Shabda (Voice/Speech)	*Spashta* (Clear)
Sparsha (Touch/Skin)	*Ushna* (Feverish) with severe tenderness due to Splenomegaly & Hepatomegaly
Drika (Vision/Eyes/Sclera)	*Panduta* (Pallor +++ & Icterus ++)
Akriti (Appearance)	Lean as she loses her weight gradually and Thin (due to *mandagni* and *Pandu*)

***Dasavidha Pariksha:* (Table No. 2)**

Pariksha	Values
Prakriti	*Pittaja Vaat*
Sara	*Avar*
Samhanana	*Madhyam*
Satva	*Madhyam*

Pramana	*Avar*
Satmya	*Madhyam*
Ahar Shakti	*Avar*
Jarana Shakti	*Avar*
Vyayama Shakti	*Avar*
Vaya	*Bala*

General Examination:
On the day of the first visit, the anthropometry data revealed the following (Table No. 3)

Anthropometry	Values
Weight	31.8 Kg
Height	138 cm
HC	50.3 cm
CC	65.9 cm
MUAC	18.1 cm
BMI	16.7

The patient had a mild general illness Systematic analysis turned out to be insignificant.

Vital Examinations: (Table No. 4)

Examination	Values
Temperature	Febrile 99.8 F
Pulse Rate	84 / min
Respiratory Rate	20 / min

Systemic Examination: (Table No. 5)

Respiratory Examination	AEBL equal & clear No Unusual Sound
Cardio Vascular Examination	S_1S_2 heard, Normal Rhythm, No abnormal sound
Central – Nervous System Examination	Conscious, Active, and Well – Oriented
Abdominal Examination	Liver Palpable by 2 fingers Spleen Palpable with 3 fingers towards the Umbilicus No other abnormalities were found

Differential Diagnoses: Sickle alpha Thalassemia, Sickle Beta Thalassemia, G6PD, Hb AS

Before and After treatment hematological investigation results (Table No. 6)

Complete Blood Count	Before Treatment	After Treatment
Hb	7.2 g/dl	9.2 g/dl
RBC Count	2.83 mill/cmm	3.79 mill/cmm
MCV	76.98 femtolitre	74.50 femtolitre
MCH	22.8 pg	25.1 pg
MCHC	30.1 g/dl	32.8 g/dl
RDW – CV	21.8 %	19.9 %
WBC Count	9400 /cmm	8900 /cmm

Treatment Protocol
The protocol followed by administration of *Kalmeghadi Avaleha* (*Anubhut* Formulation) treatment was given for 60 days ceasing all other *Ayurvedic* drugs to know the efficacy of the given treatment.

(Table No. 7)

No.	Drug	Botanical Name	Family	Part Used	Ratio
1	Kalmegha Churna	*Andographis paniculata* Wall ex Nees	*Acanthaceae*	*Panchang*	1 Part
2	Sharpunkha Churna	*Tephrosia purpurea Linn*	*Fabaceae*	*Panchang*	1 Part
3	Punarnava Churna	*Boerhaavia diffusa Linn*	*Nyctanginaceae*	*Panchang*	1 Part
4	Vikantaka Churna	*Gymnosporia montana (Roth.) Benth*	*Celastraceae*	*Patra, Sakha, Phala*	1 Part
5	Amalaki Churna	*Phyllanthus embelica L.*	*Phyllanthaceae*	*Phala*	1 Part
6	Dadima Churna (Seedless)	*Punica granatum L.*		*Phala*	2 Part
7	Pippali Churna	*Piper Longum*		*Phala*	½ Part

8	Go-ghrita	Cow Ghee	-	-	Q.S.
9	Sita	-	-	-	60% w/v

Grading: (Table No. 8)

Sr. No.	Signs & Symptoms	Grading
1	Pallor	0 - no pallor
		1 - pallor of conjunctiva
		2 - pallor of conjunctiva, nails, tongue
		3 - pallor of conjunctiva, nails, tongue, skin
		4 - pallor of conjunctiva, nails, tongue, palms and soles
2	Pain in Joints/Limbs	0 - no pain
		1 - pain in only one extremity
		2 - pain in both extremities
		3 - involvement of almost all joints
3	Anorexia	0 - no anorexia
		1 - taking a normal diet without any interest
		2 - taking the food without interest and unable to complete it all the time
		3 - no interest in taking food
		4 - resisting or crying while feeding
4	Loss of Appetite	0 - taking food in good quantity twice/thrice
		1 - taking food in normal quantity twice a day
		2 - taking food in moderate quantity twice a day
		3 - taking food in less quantity once a day
		4 - not at all taking food
5	Fatigue	0 - normal active child
		1 - playing and activities reduced
		2 - feeling tiredness while playing
		3 - easy fatigability while playing

Quality of Life Assessment (WHOQOL-BREF Parameters) (18)
Domain – 1 Physical Health
Domain – 2 Psychological Health
Domain – 3 Social Relationship
Domain – 4 Environmental Health

QOL Assessment:
The WHO quality-of-life assessment factors are taken as the basis for assessing quality-of-life criteria. Due to the low quality of life, improvement in patients with sickle cell disease or sickle cell anaemia is very essential. So, the aim of evaluation is to assess whether and how the administration of *Kalmeghadi Avaleha* will affect the quality of life of the patient. An evaluation was done before and after therapy to assess improvement.

Effect of therapy (Table No. 9)

Complain	Before Treatment	After Treatment	Relief
Pallor	3	0	100%
Icterus	2	0	100%
Joint Pain	3	1	75%
Body ache	3	0	100%
Dyspnoea	2	0	100%
Roaring & Banging in the Ear	2	0	100%
Irritability	1	1	0%
Anorexia	3	0	100%
Fatigue	3	0	100%
Weight	31.8 Kg	34.4Kg	

Effect of QOL parameters:

Before Treatment Scoring (Table No. 10)

QOL Parameters	Before treatment		
	Raw Score	Transformed Score	
		4-20	0-100
Domain – 1 Physical Health	16	9	31
Domain – 2 Psychological Health	16	11	44
Domain – 3 Social Relationship	7	9	31
Domain – 4 Environmental Health	14	7	19

After Treatment Scoring (Table No. 12):

QOL Parameters	After treatment		
	Raw Score	Transformed Score	
		4-20	0-100
Domain – 1 Physical Health	26	15	69
Domain – 2 Psychological Health	23	15	69
Domain – 3 Social Relationship	7	9	31
Domain – 4 Environmental Health	25	13	56

Result and Discussion:

Kalmeghadi Avaleha further helped to manage the major symptoms of *Pandu* such as pallor, icterus, anorexia, fever, pain in the upper & lower extremities, body ache, fatigue, and periorbital edema.

Herbal Combinations in the form of *Kalmegha Avaleha* include *Kalmegha*, *Sharpunkha, Vikantaka, Punarnava, Amalaki, Dadima and Pippali*.

Kalmegha is used as an Antibacterial & antiparasitic. It is indicated for blood purification. And stimulates the immune system. It is a liver tonic and liver protector that provides the body with the strength and vitality to fight against physical weakness. It has also been proven to be anti-typhoid and anti-hepatotoxic. Its bitter leaf extract can be used for the destruction of stomach worms. The main component and active ingredient in this plant is andrographolide. Also present are the compounds andrographolide, neoandrographolide, 14-deoxy 11, 12-didehydroandrographolide, 14 Deoxi andrographolide, and andrographolide. The anti-inflammatory, hepatoprotective, antioxidant, antipyretic, anticancer, anthelmintic, antiviral, and antihyperglycemic properties of andrographolide. (19)

Sharpunkha is the most suitable drug to handle the *pleehaghna Prabhava*. Thus, the name *Pleehari* is also given to it. Its *Ushna Virya* enables it to enter the spleen and it helps to cure splenomegaly i.e. inflammation of the spleen. *Deepana, Pachana, and Katu Vipaka*, help in metabolism and prevent infection. *Vata Kapha Shamaka* & *Ushna Virya* caused *Vatahara*, *Katu Vipaka* and *Tikta Kashaya Rasa* caused *Kapha Shamaka*. It works as an *Anulomaka* because of the presence of *Tikshna Guna*, which is Prokinetic and *Pittasaraka*. *Pleeha* is reduced because of *Kashaya Rasa* and *Tikshna-Ushna Guna* which helps in reducing the size and symptoms of *Pleeha*. (20)

Punarnava is a rich source of several phytochemicals extracted from its aerial parts and roots. The most significant ones are secondary metabolites, which include lignans, alkaloids, phenolics, flavonoids, isoflavonoids, rotenoids, glycosides, and steroids. Impressive bioactivities, including immunomodulatory, hepatoprotective, anti-inflammatory, antioxidant, and antimicrobial qualities, have been reported for the crude extract and the isolated phytochemicals.(21) From the ethanolic extract of B. diffusa roots, Punarnava reported immunomodulatory activities. It was discovered that B. diffusa leaves exhibit strong antibacterial activity against a range of Gram-positive and Gram-negative bacteria, possibly as a result of a phytochemical found in the leaves. (22, 23)

Amalaki has a major positive impact on immune system stimulation. It increases the activity of natural killer cells and reduces the toxicity of body-dependent cells. Ascorbic acid has been shown to stimulate the immune system in several studies. Since Emblica officinalis is regarded as the highest vitamin C source, its ascorbic acid is believed to facilitate the plant's immunomodulatory effects. Emblica officinalis has been shown to have adaptogenic, anti-stress, immune-potentiating, and memory-facilitating effects in various stress-induced disorders. It has been suggested that stress-induced

diseases, including ageing, may be linked to the accumulation of reactive oxygen species (ROS). Emblica officinalis tannoids have been reported to enhance ROS scavenging activity in rat brain frontal cortex and stratum, reducing lipid peroxidation. Natural cellular anti-oxidant enzymes like super oxide dismutase (SOD), catalayase (CAT), and glutathione peroxidase (GPX) help in reducing lipid peroxidation, which can lead to cell degeneration and damage. (24, 25)
Amalaki (Emblica officinalis) leaves and fruit extracts have potent antipyretic, analgesic, and anti-inflammatory effects. (26) It has been established that tannins, alkaloids, phenolic compounds, amino acids, and carbohydrates have antipyretic properties. (27, 28)
Amalaki helps in the absorption of iron from the stomach and has antioxidant properties. It could also serve as an important dietary source of vitamin C. (29)
Amalaki is an herb that has a significant *Karma* (action) as Rasayana, which means that it corrects the body's production of the food's essence after consumption. (30)
Pippali enhance the *agni* of the patients. And helps to detoxify the body by removing *Ama* (toxins). It improves digestion and lowers the buildup of unhealthy cholesterol in the body, which helps the body lose weight more quickly and establishes sufficient nutrition for all *Dhatu*, which is beneficial for *Dhatuposhana.*
The extract of *Pippali* greatly decreased CCI4-induced liver peroxidation, confirming the extract's preventive effect against experimentally induced liver damage in rats. The tests typically used in the diagnosis of liver disease are SGOT, SGPT, AP, and TB. The application of it ethanolic extract considerably lowered the high levels of these parameters. This work has led to the conclusion that *pippali* has hepatoprotective properties. (31)
Kalmeghadi Avaleha has properties that help to improve children's nutrition and health, activity and playfulness, which have been found through some herbal combinations by itself. Because the *Avaleha* preparation is used as an easily digestible Formulation without hesitation, SCD patients' quality of life must be improved, especially that of children. Children are more discerning, after all, and typically refuse to take prescription drugs because they don't like the taste.
In addition to helping to improve the overall blood reports during this 60-day trial of herbal combinations and nutrition therapy, it also helps to improve the quality of life for children with sickle cell disease by enabling them to carry out their everyday activities.

Conclusion:
The main cause of the illness is Bijadusti, which is compounded by the effects of Dhatukshaya, Jatharagni, and Dhatvagni Mandya. Dhatu Kshaya is linked to Panduta and causes Tridosha Prakopa and Aama generation, or premature loss of red blood cells. In the current instance, there was severe hepatomegaly and splenomegaly as a sign of vascular occlusive crisis. During the course of the patient's 60-day treatment with this herbal combination, there were noticeable alterations in the patient's daily activities. During this time, she did not exhibit any particular symptoms of a crisis state. The child's weight has also decreased, allowing her to play with friends and take part in all the activities at school without experiencing fatigue.
This indicates that consistent use of these kinds of herbal combinations and regular assessment will yield clear outcomes that are on par with those of using solely regular oral drugs. A sizable sample size will be used in the study to assess the function of Ayurvedic formulations in more detail.

Adverse Drug Reaction:
No specific adverse drug reaction was found.

Key Message:
Children with Sickle Cell Anaemia/Sickle Cell Disease have a significant morbidity and mortality rate. The painful catastrophe and chronic nature have an impact on life's quality. Their quality of living can be improved by ayurvedic medicines.

Conflict of Interest:
The authors declare no conflict of interest.

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