



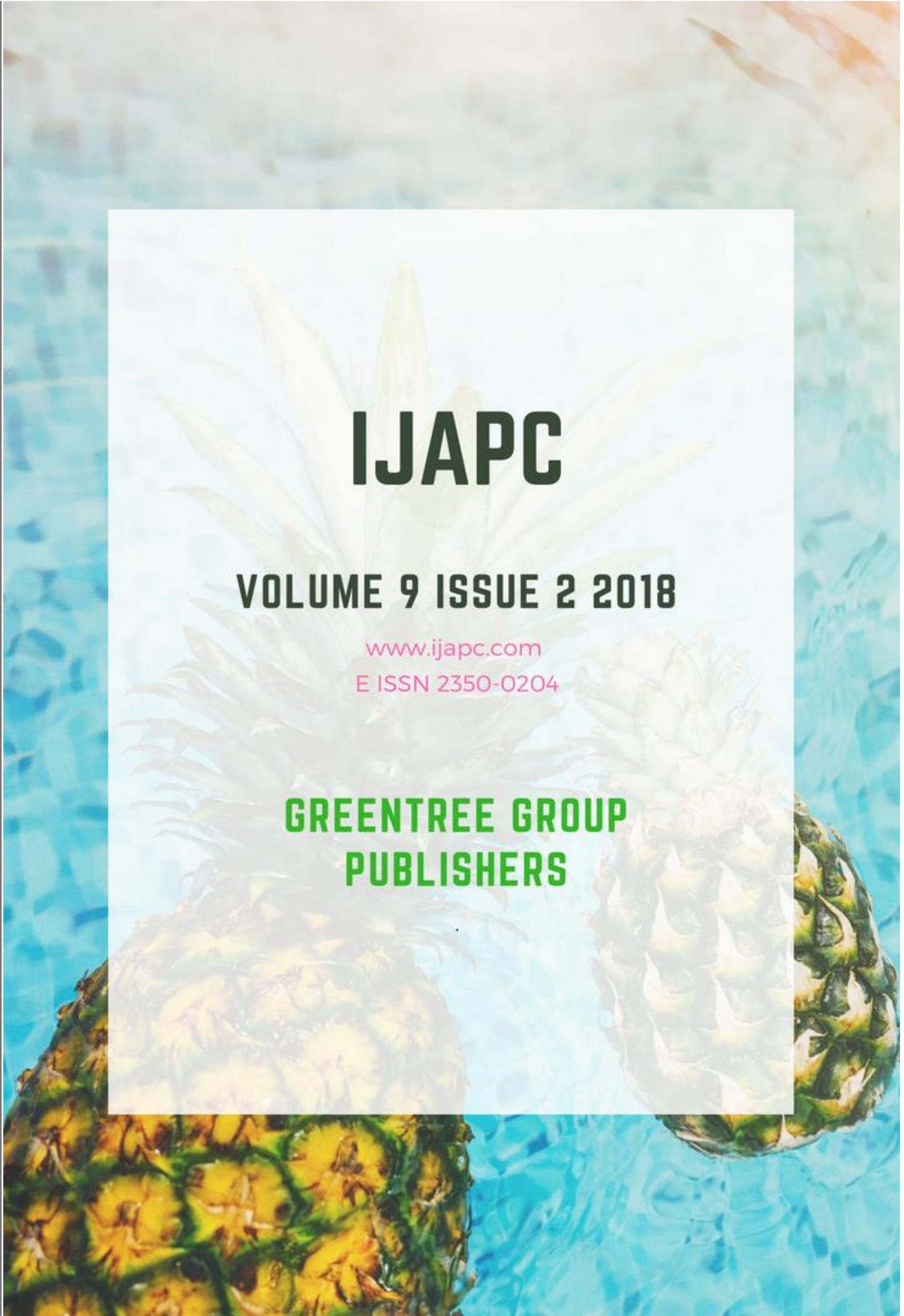
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## A Clinical Study of Sickle Cell Disease and its management with S-Compound

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### ABSTRACT

The Sickle gene is widespread among many tribal population groups in India with prevalence varying from 1-40%. It is an inherited blood disorder most common among people of African, Arabian and Indian origin. The sickle cell mutation affects the B chain of adult hemoglobin which changes the behavior of sickle cell hemoglobin. The first case was described in the Nilgiri hills of the northern Tamilnadu in India in 1952. The common complications as documented is avascular necrosis of bones in the current study AVN seen in femoral head. Out of 120 total screened patients of SCD, 60 patients were randomly selected as per the inclusion and exclusion criteria with 15 patients in each group abiding the above criteria and categorized into total of four groups according to the atypical symptoms and complications along with primary disease that is SCD. Out of total 15 patients in each group, 10 patients were given the prepared S-Compound and the remaining 5 were given placebo. The results were analyzed within the groups before and after the treatment by paired 't' test and the inter group analysis was carried out by unpaired 't' test. Evaluation of the efficacy of trial drug comparing the all groups was carried out after the completion of the study. The percentage wise analysis showed increase in appetite in 54.38% patients, 49.54% of patients showed relief in repeated infections, 49.40% of patients showed decreased fever, 45.57% of patients exhibit reduced abdominal colic, palpitation was reduced in 45.29% of patients, 44.35% of patients showed decrease in body ache (pain and crisis), 43.75% of patient showed improvement in jaundice. The trial study was an initiative in ayurvedic field for designing a standard management regimen suitable for SCD patients or SCD patients with complications.

### KEYWORDS

*Sickle cell disease, S-Compound, Avascular Necrosis*



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## INTRODUCTION

Sickle cell disease and haemoglobinopathies are very common among Indian states of Chhattisgarh and Maharashtra followed by M.P. and Gujrat. The prevalence rate recorded as 22 to 41% in Chhattisgarh followed by 2 to 35% in Maharashtra in the year 2007.<sup>1</sup> Sickle cell disease which is considered as a major blood cell disorder with genetic inheritance common among the people of central India. The 'fate' of it thus remains uncertain because of many unturned pages of molecular genetics, which is a recent advancement in the medical science. Nature has created two respiratory pigments, Chlorophyll in plant kingdom and Haemoglobin in animal kingdom. It is indeed surprising that slight aberrations in haemoglobin molecule leads to haemoglobinopathies bringing out tremendous physical, chemical and functional changes in its property.

Sickle cell disorder being the most common transmitted on the basis of mendelian inheritance. It has been classified according to genetic configuration as homozygous state Sickle cell disease and heterozygous state –Sickle cell trait, affecting almost every organ of human body.<sup>2</sup> 'A disease more dreaded than Cancer' was the comment on Sickle

cell disorder by Nalbadian et al. (1972) because of its wide spread and multitudinous manifestations which may affect any organ of the body.<sup>3</sup>

Thus the morbidity and mortality of this disease has aroused a lot's of research for its alleviation and cure. Modern medical science started from the quest for its genesis in the genes, aided with the recent advances in the molecular biology and genetics, to know the causative genes etc. However, these are at present still in experimental stages, hence till they become available, approachable, and affordable reality, the palliation of this scourge of mankind named Sickle cell disorder, lies in the basic amenities of body ache (Pain & Crisis), Repeated infection, Blood transfusion and Avascular necrosis hence the need to accept and prevent appropriately or manage the associated complications of this disease.

So keeping all these views in mind and cost effective therapy, great hopes are being laid on the Ayurvedic science, which will help to prevent from its complication and hazardous effects and act as an adjuvant therapy in SCD. Owing to Ayurveda, it is the science that imparts all the knowledge concerned to life. The main aim being to provide guidelines for maintenance and promotion of health along with prevention and treatment of



Sickle cell disease. In other words Ayurveda is a science which helps in understanding creative and non-creative aspect of life, happy and unhappy life, congenial and non-congenial for life, life span, and also corporal dimensions.

The advancement occurs in the field of medical science include SCD as a group of disorders instead of a single disease which is explained as “*Anukta Vyadhi in Ayurveda*” as there is minimal explanations regarding the disease and its complications. To understand the disease and its pathological manifestation careful study of its clinical presentation and investigation is the need of the decade in ayurveda field.

One of the references from our hidden treasure, which claims that all the pathological conditions cannot be labeled, but can be understood by *Tridoshas Vaishamya, Dhātu Dushti* etc. is *sannipataj pandu, Kustha, Prameha* Because every disease is caused by three *Sharirika Doshas* and two *Manasika Doshas*. The diagnosis according to Ayurveda is based on *Roga Prakriti, Adhisthan with Samutthana*.<sup>4,5</sup>

The base of Ayurveda rests on *tridosha* doctorine such as *Vata, Pitta, and Kapha*. Formation of *Rakta dhātu* is defective in SCD and *Ranjaka Pitta* is mainly responsible for its pathology. Therefore S-

Compound whose ingredients are used in *Pandu Roga* may be beneficial in SCD and may be effective for the management of SCD patients symptomatically.

Keeping the well being of humanity as chief concern, if the better of two pathies are combined, without making much chaos about the purity of science; an effective and successful national programme can be implemented for control of SCD. The present study is an attempt to analyze the efficacy of ‘S-Compound’ in the management of SCD in comparison to a placebo group managed by routine modern therapy. The drug has been chosen keeping in view its *rasayana*, antiviral, antibacterial, analgesic, immunomodulator, antioxidant, and hepatosplenoprotective properties. The main aim of study is to provide a better quality of life and to reduce complication and delay the complications severity by Ayurvedic medicines.

## MATERIALS AND METHODS

### (A) *Place for selection of patients:-*

Patients were selected from the O.P.D. & I.P.D. of Govt. Ayurvedic College and Hospital Raipur C.G. and Department of Biochemistry, Genetic Disease and Molecular Biology Pt. J.N.M. Medical College Raipur C.G.



**(B) Number of patients:** - 60 (sixty) patients irrespective of caste, creed, languages and sex were selected for randomized clinical trial.

**(C) Criteria for selection of patients:**

(1) Patients were selected on the basis of sign & symptoms of sickle cell disease (HbSS) group:-

1. Anaemia
2. Jaundice
3. Abdominal colic
4. Palpitation
5. Hand foot syndrome
6. Loss of appetite
7. Sternaal pain
8. Fever
9. Haepatomegaly
10. Splenomegaly
11. Body ache (Pain & Crisis)
12. Repeated infection
13. Blood transfusion
14. Femoral head necrosis (Pain in hip region)

**(I) Diagnostic Signs:**

1. Pallor
2. Anasarca
3. Haepatomegaly
4. Splenomegaly
5. Hand foot syndrome

As per the above sign and symptoms patients examination proforma were prepared and patients were selected for the trial.

**(III) Investigation:-** Following investigation has been conducted before and after treatment as per the need of the disease condition :-

1. Haematological investigation
2. Biochemical investigation
3. Electrophoresis
4. Urine test
5. Radiological investigation like X-Ray, USG etc.

Patients who were suffering from pain and other symptoms other then “Sickle cell disease” were excluded from the clinical trial.

**(IV) Grouping :-**

The patients were selected randomly and studied under four groups:-

Group (a):- Sickle cell Pain & Crisis

Group (b):- Repeated Infection

Group (c):- Repeated Blood transfusion

Group (d):- Femoral Head Necrosis

Each group has 15 patients, Only 10 patients for S-Compound and later 5 patients for Placebo.

**Dose of S-Compound:-** Child-250 mg BD and Adult-500 mg Twice daily with suitable fluids for three months. The dose is to remain same for both S-Compound and Placebo group.

**Pathya-Apathya:**

Patients were advised to take their routine diet with maximum intake of water.

**Criteria for Assessment:**



For assessing the changes in the clinical signs and symptoms and in regular blood transfusion, the patients were examined every 15 days. The objective and subjective signs and symptoms were recorded. The efficacy of therapy was assessed on the basis of suitable scoring pattern. A special proforma was made to

study the etiopathogenesis as well as response to the given treatment and any complication. The improvements were revealed from favorable shift of grades of each symptoms from 1 to 5 the regarding was done in the help of *Dutch-AIMS2 - HFF, Symptoms severity scale method 2006 (Table 1)*.

**Table 1** Symptoms severity grading Scale<sup>6,7,8,9</sup>

1.	Anaemia	1	Hb is 11-16 gm%
		2	Hb is between 8-11 gm%
		3	Hb is between 8-6 gm%
		4	Hb is 6-4 gm%
2.	Jaundice	1	No pallor
		2	Pallor with shallow pink
		3	Pallor with slight yellowish tint
		4	Pallor with ash yellowish tint
3.	Abdominal colic	1	No abdominal pain
		2	Mild cramping pain only before blood transfusion
		3	Moderate cramping pain before transfusion and lasting for few days after transfusion.
		4	Continuous abdominal pain with Irritable bowel syndrome
4.	Palpitation	1	No Palpitation
		2	Slow heart beat
		3	Erratic palpitation
		4	Palpitation with chest Pain
		5	Breathlessness
5.	Hand foot syndrome	1	No swelling
		2	Mild swelling on one hand or foot
		3	Swelling appear only upper or lower extremities
		4	Swelling appear on both extremities
6.	Loss of appetite	1	Appetite good
		2	Taking normal diet, without any interest
		3	Taking the food without interest and unable to complete it all the time
		4	Not interested in taking food, resisting or crying while feeding
7.	Sternall Pain	1	No Pain
		2	Mild Pain
		3	Moderate Pain
		4	Pain when breathing
		5	Very severe Pain
8.	Fever	1	Afebrile
		2	One or two times in a month
		3	Three or Five times in a month
		4	More than five times in a month
		5	Continuous or intermittent fever
9.	Haepatomegaly	1	Non palpable Liver.
		2	Mild Hepatomegaly ( palpable up to 2 cm with mild tenderness)
		3	Moderate Hepatomegaly ( palpable up to 4 cm and tender )
		4	Massive Hepatomegaly (palpable > 4 cm and tender )



10.	Splenomegaly	1	Non palpable spleen
		2	Mild Splenomegaly ( palpable up to 2 cm with mild tenderness)
		3	Moderate Splenomegaly ( palpable up to 4 cm and tender )
		4	Massive Splenomegaly (palpable > 4 cm and tender )
11.	Body ache Pain & Crisis	1	No joint pain
		2	Pain involve only one extremity
		3	Pain involve both the extremity
		4	Involvement of almost all the joints of body
		5	Severe Pain all over joints of the body
12.	Repeated Infection	1	No respiratory infection
		2	At interval >45 days
		3	At interval between 15 to 45 days
		4	At interval between 7 to 15 days
		5	At interval one week or below
13.	Repeated blood transfusion	1	No blood transfusion in a year
		2	Two times in a year
		3	Three times in a year
		4	Four times in a year
		5	Five times or more in a year
14.	Pain in Hip Region	1	Pain free
		2	Low disability and low intensity
		3	Low disability and high intensity
		4	High disability and moderately limiting
		5	High disability /severely limiting

### ASSESSMENT OF THE TOTAL EFFECT OF THERAPY

The observations of signs and symptoms and other clinical parameters especially were recorded before and after the treatment, the assessment of therapy was made as follows in Table 2.

**Table 2** Assessment of sign & symptoms

Assessment	Score
Maximum Improvement	> 75%
Moderate Improvement	50-75%
Mild improvement	25-50%
No change	<25%

### STATISTICAL ANALYSIS:

For the purpose of statistical analysis, the Mean and Standard deviation of each sign and symptom before treatment is compared with the Mean and Standard deviation after the treatment. The effectiveness of the drug was assessed by the P-value applying paired t-test.

### FOLLOW-UP STUDY:

Patients after completion of the treatment were advised to report in the O.P.D. at the regular interval of 15 days for at least three months for the follow up study. Their blood investigations were recorded before and after treatment. The condition of other signs and symptoms was also noted.

### OBSERVATIONS

The data collected from clinical trial was compiled and subjected to statistical analysis. The results of therapy were evaluated by reduction in improvement of the signs and symptoms.

In the present study total sixty (60) patients were registered for the trial. The observation on the demographic,



constitutional; and clinical profile was studied on all registered patients (Sixty).

For the purpose of clinical and statistical assessment of the result, we have used some grade points according to the severity of different signs and symptoms (Table 3).

**Table 3** Incidence of severity of Grade points to the different signs and symptoms among the trial patients

Degree of Severity	Sign & Symptoms	Grade	Grade Point
Very Severe	5	G <sub>5</sub>	5
Severe	4	G <sub>4</sub>	4
Moderate	3	G <sub>3</sub>	3
Mild	2	G <sub>2</sub>	2
No Sign & Symptoms	1	G <sub>1</sub>	1

## DISCUSSION

In the present study, trial formulary drug “S-Compound” which provides its effects based on the *Rasapanchak* described for individual drugs in the classical text, were mentioned for the whole drug by cumulating rasa, guna etc. of constituent potent drugs. To understand this scientifically we considered the related fundamental concepts, that are described in the classics as the conjugation of Rasas (*Rasa Sannipata*) etc. their mutual subordination and variation in processing on the basis of *Prakriti Sama-samavaya* and *Vikriti Vishama-samavaya* theories are to be analyzed to decide the total effect of the drug on the Doshas (or disease). It is because the active ingredients in a

compound formulation show either antagonism (*Parasparena Cha Upahatanam*) or synergism (*Abhivardhana*) effects.<sup>10</sup> The drugs are active due to their own inherent constituents (*Dravya Prabhava*), properties (*Guna Prabhava*) or both combined (*Dravya Guna Prabhava*) together in particular time, on reaching particular site, with a particular mechanism and objective.<sup>11</sup> The different properties of a drug are inferred by observing their effects on the body.<sup>12</sup>

### Concept of mode of action of drugs:

The two mode of action (*vridhhi and kshaya*) are governed by the principles of *Samanya and Vishesha dravyas* which act inside the body in the following ways - by increasing the body elements, their qualities & functions and the other one by decreasing the body elements, their qualities and functions. The *Dosha vridhhi* and the *Dhatu kshaya* is the most common feature of diseases.<sup>13</sup> Obviously, therefore the Doshas are required to be decreased and brought to the normal level while the Dhatus are required to be increased and brought to the normal level for the successful elimination of symptoms during the management of diseases. Drug decreases the Doshas completely or partially on the principles of dissimilar dravyas and the Ahara increases the Dhatu



on the principles of similar dravyas.<sup>14</sup> Thus, Samanya Siddhanta is practically more applicable to the Ahara Dravyas and Visheshha Siddhanta is practically more applicable to the Ausadha Dravyas. The Ahara Dravyas are mostly Rasa pradhana and Aushadha Dravyas are mostly Veerya pradhana.<sup>15</sup> The effects of Ahara on the Dhātu can be predicted on the basis of its Rasa and Vipaka. The effect of drugs on the Doshas can be predicted on the basis of Guna and Veerya. But these are the general and relative observations and do not constitute any hard and fast rule, because the drugs, which are Balya, Jeevaneeya, Rasayana, Brimhana contribute to enhancement of Dhātu by their Guna and Veerya.

#### **Probable mode of action of S-compound:**

The probable mode of action of S-Compound on SCD can be explained on the basis of its Rasa Panchaka. This herbal formulation constitutes total of 8 drugs as Amalaki, Bhringaraj, Bhumi-amalaki, Chitrak, Guduchi, Katuki, Punarnava and Sharpunkha presents Tikta rasa (36.84%) and Kasaya Rasa (26.31%) which helps to normalise the function of Jatharagni and Dhatwagni. That in turn helps to form the Dhatus in proper proportion with qualities. The proportion of Katu Rasa about 15.78%, by svabhava is Agnideepaka,

Pachaka, Srotoshodhaka and Kaphanashaka. Owing to these properties only Katu rasa clears the obstructed srotas and increases Dhatwagni, thereby balances dhatuposhana kriya of the body and helps in removing Dhatukshaya condition. Its because of this Rasayana prabhava of Katu rasa it is useful in Vata pittaja disorder. In this herbal formulation, Kasaya rasa was about 26.31% which have sandhana karaka, Sangrahi and Pitta nashaka in properties. Owing to this properties this compound plays important role in dhātu vridhdhikar in SCD patients. Madhura Rasa was found 15.79% in 'S-Compound' whose action is Sarvadhātuvardhaka as they increase the metabolism of body that's why it may pacify Dhātu kshaya stage by acting on cellular level; Ayushaya means It may increase life span of person as well as RBCs too; Balya: Due to its Kaphavardhaka property, it increases the immunity of the body. Jeevanam: Increase the vitality of body. Brimhanam: Its anabolic effect on the body. Sthairyakarana: It may increase the stability of RBCs by increases the RBCs survival rate. Trishana Nigrahana: They pacify the thirst of person. Laghu, Ruksha, Guru, Tikshna, sheet and snigdha are the major guna (properties) present in contents of S-Compound, this guna in combination produces



**Table 4** Total effect of medicine (S-Compound) in all groups

S. No.	Sign & Symptoms	No. of Patients	Before Treatment (Groups)					After Treatment(Groups)					% Relief
			Mean					Mean					
			A	B	C	D	Total	A	B	C	D	Total	
1.	Anaemia	40	2	2.1	2.8	2	8.9	1.5	1.5	2	1.2	6.2	30.34
2.	Jaundice	40	2.4	2.3	2.7	2.2	9.6	1.3	1.3	1.7	1.1	5.4	43.75
3.	Abdominal colic	40	1.8	2.2	2.2	1.7	7.9	1.1	1.2	1.1	1	4.3	45.57
4.	Palpitation	40	2.1	2	2.2	2.1	8.4	1.1	1.2	1.3	1.1	4.6	45.29
5.	Hand foot Syndrome	40	1	1.1	1.2	1	4.3	1	1	1.1	1	4.1	4.65
6.	Loss of appetite	40	2.7	2.7	3	3	6	1.1	1.1	1.6	1.4	5.2	54.38
7.	Sternal Pain	40	1.6	1.8	2.3	1.2	6.9	1.1	1	1.2	1	4.3	37.68
8.	Fever	40	2	1.9	2.4	2	8.3	1	1.1	1.1	1	4.2	49.40
9.	Haepatomegaly	40	1.2	1.3	1.3	1.4	5.2	1	1.1	1.2	1.1	4.4	13.38
10.	Splenomegaly	40	2.4	2.9	2.7	2.5	10.5	1.4	1.9	1.6	1.5	6.4	39.05
11.	Body ache (Pain &Crisis)	40	3	2.7	2.8	3	11.5	1.3	1.6	1.6	1.9	6.4	44.35
12.	Repeated infection	40	2.4	3	2.9	2.6	10.9	1.2	1.4	1.4	1.5	5.5	49.54
13.	Repeated Blood transfusion	40	1.8	1.6	3.4	2.2	9	1.1	1	2.1	1.4	5.6	37.78
14	Pain in Hip region	40	2.4	1.8	1.8	3	9	1.2	1	1.1	2	5.3	41.11

srotoshodhana and kapha shaman by augmenting the srotas clearance from Ama and Kapha, by which free flow of Vata gets open up and consequently vatanulomana occurs. It's by this reason that symptom like vedana (Pain &crisis) are relived. Most of the contents in this trial drug are of Ushna Veerya (62.5%). It performs Deepana, Pachana and Srotoshodhana karmas. Proper digestion of food occurs and so is the nourishment action imparted on dhatus. In total, by virtue of Rasayan Prabhava of the formulation, benefit occurs to SCD patients. In this formulation Madhura vipak (50%) causes the expulsion of mala & mutra from the body & releases the

toxins & it is Shukral in nature. Katu Rasa (50%) causes for Deepana of agni which leads to srotoshodhana, subsequently nourishment of dhatus takes place which in turn produces immunomodulatory effect in whole body. While focusing on total efficacy of S-Compound in all groups it was noticed that the symptoms like loss of appetite was markedly improved in 54.38% of patients followed by 49.45% of patients showed good resistance towards repeated infections, 49.40% showed decrease in fever, 45.57% of patients showed decrease in abdominal colic, 45.29% of patients revealed decreased in palpitation, 45.35% of patients exhibited decrease in body ache, 43.75% of patients



exhibited in symptoms of jaundice, 41.11% of patients revealed marked decrease of pain in hip region, 39.05% of patients revealed in the reduction of spleen size (decreased splenomegaly), 37.78% of patients required lower frequency of blood transfusion (Table 4).

While assessing the total efficacy of placebo in all groups 31.25% of patients

revealed decrease in fever, 23.44% of patients revealed increase in their appetite, 12.76% of patients expressed their concern in alleviation of body ache, 11.9% of patients showed decrease in symptoms of jaundice followed by 11.54% of patients showed relaxation in sterna pain. (Table 5).

**Table 5** Total Effect of Placebo in all groups

S. No.	Sign & Symptoms	No. of Patients	Before Treatment (Groups)					After Treatment(Groups)					% Relief
			Mean					Mean					
			A	B	C	D	Total	A	B	C	D	Total	
1.	Anaemia	20	2	2.4	2	1.6	8	2	2.4	2	1.6	8	0
2.	Jaundice	20	2	2.4	2	2	8.4	1.8	2.4	1.4	1.8	7.4	11.9
3.	Abdominal colic	20	1.4	1.6	1.4	1.4	5.8	1.2	1.4	1.4	1.4	5.4	6.9
4.	Palpitation	20	1.6	2	1.6	1.6	6.8	1.6	1.8	1.6	1.6	6.6	2.94
5.	Hand foot Syndrome	20	1	1	1	1	4	1	1	1	1	4	0
6.	Loss of appetite	20	1.2	2	1.6	1.6	6.4	1.2	1.4	1.2	1.2	5	23.44
7.	Sternal Pain	20	1.2	1.2	1.4	1.4	5.2	1	1.2	1	1.4	4.6	11.54
8.	Fever	20	1.2	1.8	1.6	1.8	6.4	1	1	1.2	1.2	4.4	31.25
9.	Haepatomegaly	20	1	1	1	1	4	1	1	1	1	4	0
10.	Splenomegaly	20	2	2	2	2.2	8.2	2	2	2	2.2	8.2	0
11.	Body ache (Pain&Crisis)	20	2.4	2.2	2.2	2.6	9.4	1.8	2.2	1.6	2.6	8.2	12.76
12.	Repeated infection	20	1.6	2.8	2	2.4	8.8	1.6	2.8	2	2.4	8.8	0
13.	Repeated Blood transfusion	20	1	2	2.4	2.4	7.8	1	2	2.4	2.4	7.8	0
14.	Pain in Hip region	20	1	1.6	1.2	2.8	6.6	1	1.6	1	2.6	6.2	6.06

As the efficacy of S-Compound and placebo in all groups collectively mentioned above hence the efficacy of the trial drug and the placebo over a single group of patients, is not needed to mention it individually for different groups.

It is again inferred that in considering doshaghata, 60% of constituent drugs exhibit tridoshashamaka property and Vata-Kapha Shamaka in action. Tridosha being the main culprit behind the manifestation of SCD. Thus it helps in



maintainance of doshic imbalance in the body & makes the person healthy.

## CONCLUSION

The analytical reasoning of the study which was presented in discussion as S-Compound can be prescribed as an effective drug to combat SCD and its complications wherever needed in a rational approach. According to Ayurvedic parlance SCD comes under *Kulaja vikara* or *beejadushtijanya vikara*. Ayurvedic formulation S-compound played a vital role in combating the cardinal symptoms of this grave disease. Along with this other Supportive modern therapy may provide better quality of life to diseased person. Present subject under the trial study is newer one for clinicians and researchers in ayurvedic field so there is every possibility of parameters to be insufficient. This insufficiency may be fulfilled by launching a scientific, multidimensional, integrated approach for the study of this fatal pediatric problem.

Conflict of Interest: None



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