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# Integrated Treatment Approach on Biomarkers of Vaso-Occlusive Crisis in Patient of Sickle Cell Disease: A Case Study

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**Abstract**

Sickle cell anaemia is a haemoglobin disorder in existence for the last 100 years in the world. Mostly the tribal population shows more prevalence and come from a lower socioeconomic background, the majority of researches are focused on costly treatments. Close monitoring of oxygen saturation, as well as other critical indicators such as CBC, CRP, ESR, LDH, and D-dimer, as well as a chest X-ray, is thought to be beneficial in assessment. In both conditions, taking into account the necessity of preventing RBC lysis leads to a more effective therapeutic approach. This case report focuses on the impact of an integrated therapeutic approach on sickle cell vaso-occlusive crisis patients. A 22-year-old male with sickle cell disease was brought to our clinic in a condition of unconsciousness; he had previously been hospitalised to a hospital for vaso-occlusive crisis management with symptoms of fever, cough, body aching, and joint pain. His RBC was3.8, CRP (82.4), ESR (12), D-dimer (4052.4), and LDH (572.6) were all elevated on a haematological study. His parents informed us that he has been vaccinated after additional interrogation. A Rapid antigen test was also performed, which came out negative. After obtaining guardian agreement and taking into account crisis situations, an integrated treatment approach using modern medicines, T-AYU-HM Premium, and Accupen was implemented. Following a 21-day course of treatment, patients had improved substantially, as evidenced by his laboratory values. Integrated treatment under medical supervision could be more effective in lowering fatality rates in urgent instances and require more emphasizes in future.

**Keywords:** Sickle Cell Disease, CRP, D-Dimer, LDH, Integrated Treatment.

## Introduction

Sickle cell anaemia is a haemoglobin condition that has been around for over a century. Every afflicted country has made significant efforts to prevent and map sickle

cell anaemia, but there is still much more to be done for sickle cell patients. [1, 2] Although it is common among tribal people and has well-established pathophysiology, most research has focused on stem cell research, gene regulation, and new medications targeting the sickling mechanism, with the exception of hydroxyurea. Long-term use of hydroxyurea necessitates periodic monitoring of several blood parameters for mutagenic consequences. [3-4] Close monitoring for oxygen saturation as well as numerous vital measures such as complete blood count, C-reactive protein (CRP), Erythrocyte sedimentation rate (ESR), lactate dehydrogenase (LDH), and D-dimer (DD)with Chest X-ray are regarded beneficial in the assessment of acute chest syndrome caused by vascular occlusion.[5] Studies have highlighted the importance of the potassium channel, Gardos channel, and NMDARs found on circulating red blood corpuscles in avoiding cell dehydration. [4] Formulations aimed towards these channels are either in the trial phase or have been withdrawn. Infection, dehydration, and deoxygenation are the three main causes that impact sickle cell. Targeting them with an integrated therapeutic approach combining Ayurvedic and allopathic medications could be the key to providing sickle cell sufferers with a cost-effective treatment.

**Case study**

In this paper, we describe a case study of the clinical result of an integrated therapeutic approach in a sickle cell disease patient with a vaso-occlusive crisis.

**Site information:** Dhanvantari Clinic - Ayurvedic Health Care and Research Centre in Vyara, Gujarat, was the site of the case study. For the past 20 years, the centre has provided care to sickle cell anaemia patients.

**Patient consent:** The patient's family chose to take him to Dhanvantari clinic, Ayurvedic health care and research centre. The family agreed that the integrated therapy strategy would be used. Prior consent was obtained for the treatment to begin and for the sharing of case facts such as vitals, laboratory findings, and treatment outcomes for research purposes.

**Patient's demographics information:** Mr.-X is a 22-year-old Gujarati male who lives in Shahpur, Mahuva-Gujarat.

**Patient's history:** The patient has sickle cell disease and had his first dose of the covid-19 vaccination. He received a blood transfusion two years ago with the A+ve blood group. Due to unknown causes, the patient developed fever, body aches, and joint pain, and was admitted to one of the hospitals for treatment. Tachycardia, blood pressure of 140/96 mmHg, pallor, and icterus were reported during provisional diagnosis, as well as LRTI. Despite treatment, the patient's condition did not improve. The patient was administered injections of HYTOS1.5 (Cefuroxime), NS 100 (Normal Saline), Pantop IV 80 (Pantoprazol), ANSET (Ondansetron 2mg), Contramol (Tramadol), Ivcetamol (Paracetamol), and fentanyl 2 amplules (Fentanyl Citrate). He was also transfused one packed cell volume unit (PCV). During his hospital stay, ultrasonography revealed mild hepatomegaly and mild splenomegaly with abnormal echo pattern. Multiple splenic infarcts have been suggested. An X-ray of his chest revealed mild cardiomegaly and bilateral hilar prominence. The results of haematological investigations performed during hospitalisation are shown in Table 1.

Table 1: Haematological Parameters during Hospital Stay.

| Investigation | 18/10/21 | 21/10/21 | 23/10/21 |
|---|---|---|---|
| Haemoglobin(gm/dl) | 10.4 | 10.6 | 11.3 |
| RBC (millions per $mm^3$) | 4.50 | 4.67 | 4.86 |
| Neutrophil (%) | 67 | 61 | 82 |
| Lymphocytes (%) | 23 | 32 | 12 |
| WBC (per $mm^3$) | 20500 | 24000 | 14900 |
| Platelet (per $mm^3$) | 383000 | 418000 | 229000 |
| Bilirubin Total (mg/dl) | 10.4 | 5.2 | 8.2 |
| Bilirubin Direct(mg/dl) | 0.7 | 0.6 | 2.7 |
| Bilirubin indirect(mg/dl) | 9.70 | 4.40 | 5.50 |
| CRP | 24.5 | -- | - |

**Patient current status:** On October 25, 2021, the patient was brought to the Dhanvantari Clinic, Ayurveda Healthcare Centre, unconscious. His oxygen saturation was 68 per cent and his pulse rate was 137 beats per minute during a medical examination. To counteract the hypoxia and regain consciousness, the patient was immediately started on oxygen support and nebulized. His rapid antigen test and RTPCR were both negative once the patient recovered consciousness and was stable. The primary goals of this sickle cell disease crisis presentation appeared to be to recover consciousness and avoid further problems. To check for infection enteric fever, a single tube Widal test was performed during the therapy period. It was discovered to be negative. Dengue and Malaria tests came back negative as well. The haematological parameters on the day of admission are shown in Table 2.

Table 2: Haematological Parameters on Admission Day.

| Investigation | 25/10/21 |
|---|---|
| Haemoglobin(gm/dl) | 9.9 |
| RBC (millions per $mm^3$) | 3.8 |
| Neutrophil (%) | 81 |
| Lymphocytes (%) | 15 |
| WBC (per $mm^3$) | 11400 |
| Platelet (per $mm^3$) | 233000 |
| ESR (mm/hour) | 12 |
| CRP (mg/dL) | 82.4 |
| D-dimer (ng/mL) | 4052.4 |
| LDH (U/L) | 575.6 |
| Reticulocytes | 4.9 |
| Creatinine | - |
| Blood Pressure(mmHg) | 124/82 |
| Body temperature (°C) | 37.4 |
| SpO2 (%) | 68 |
| Pulse rate | 137 |
| Serum Sodium | 132 |
| Serum Potassium | 4.3 |
| Serum Chloride | 100 |

The patient's complete integrated treatment approach is depicted in Table 3. And the patient's haematological parameters during and after treatment are shown in Table 4.

Table 3: Integrated Treatment Plan.

| Treatment | 25/10/21 | 26/10/21 | 28/10/21 | 2/11/21 | 11/11/21 |
|---|---|---|---|---|---|
| Oxygen/ Nebulisation | Oxygen 5 lit/minute per 2 hour<br>Duolin 3ml and Budecort 2ml Nebulisation | | | | |
| Parenteral | Inj. LMWH 60 mg SC OD<br>Inj. Dexa 4mg IM OD | Inj. LMWH 60 mg SC OD<br>Inj. Dexa 4mg IM OD | Inj. LMWH 60 mg SC OD<br>Inj. Dexa 4mg IM OD | - | - |
| Modern medicine | T. Paracetamol 650mg PO SOS<br><br>T.EUPOD – 200 PO BD x 5 days<br><br>T. Levocet-M PO BD x 5 days | T.Paracetamol 650mg PO SOS | T. Paracetamol 650mg PO SOS | | |
| Ayurvedic Intervention | Tab. T-AYU-HM Premium 600mg PO TDSx 7 days<br>Tab. Acupen 600mg PO TDS x 7 days<br>Tab. Acidez 300mg PO BD x 7 days | | | Tab. T-AYU-HM Premium 600mg PO TDS x 10 days<br>Tab. Acupen 600mg PO TDS x 10 days<br>Tab. Acidez 300mg PO BD x 10 days | Tab. T-AYU-HM Premium 600mg PO TDS x 7 days<br>Tab. Acupen 600mg PO TDS x 7 days<br>Tab. Acidez 300mg PO BD x 7 days |
| Duolin Respule 3ml (Ipratropium bromide 500mcg + levosalbutamol 1.25mg), Budecortrespule 2ml (Budesonide 0.5mg), LMWH 40mg (Enoxaparin), Levocet M (Levocetirizine 5mg + Montelukast 10mg), Eupod 200 (Cefpodoxime 200mg), PCM 500 (Paracetamol) | | | | | |

Table 4: Haematological Parameters During and After Treatment.

| Investigation | 26/10/21 | 28/10/21 | 2/11/21 | 11/11/21 |
|---|---|---|---|---|
| Haemoglobin(gm/dl) | 10.6 | 11.2 | 9.8 | 10.1 |
| RBC (millions per $mm^3$) | 4.33 | 4.47 | 4.01 | 4.78 |
| Neutrophil (%) | 85 | 61 | 68 | 57 |
| Lymphocytes (%) | 12 | 33 | 26 | 32 |
| WBC (per $mm^3$) | 9400 | 17300 | 16300 | 6900 |
| Platelet (per $mm^3$) | 304000 | 414000 | 594000 | 537000 |
| ESR (mm/hour) | - | 8 | 28 | - |
| CRP (mg/dL) | 79.8 | 32.9 | 42.8 | 6.97 |
| D-dimer (ng/mL) | - | 3613 | 2992.9 | 1.85 |
| LDH (U/L) | - | 421 | 302.8 | 157 |
| Reticulocytes | - | - | 4.9 | 0.8 |
| Creatinine | - | - | 0.95 | - |
| Blood Pressure(mmHg) | 116/66 | 122/85 | 130/73 | 122/78 |
| Body temperature (°C) | 36.7 | 36.8 | 36.4 | 36.4 |
| SpO2 (%) | 97 | 99 | 100 | 99 |
| Pulse rate | 97 | 100 | 107 | 78 |
| Serum Sodium | - | 131 | 134 | - |
| Serum Potassium | - | 4.5 | 4.2 | - |
| Serum Chloride | - | 100 | 101 | - |

**Discussion**

Within 15 days of starting the entire treatment, the patient had completely recovered symptomatically. All clinical and biochemical indicators significantly improved. Regardless of the patient's haemoglobin issue, the N/L ratio, platelet count, serum bilirubin, and baseline electrolytes, as well as the patient's past hospitalisation, all require attention in a pain crisis. [6] The management of pain in a vaso-occlusive crisis to avoid future consequences is still a major challenge. There are cases where the signs of a crisis are not caused by an infection. Rehydration and pain management are currently the main options for sickle cell crisis management. Neuropathic pain is considered a major issue in management during vaso-occlusive crises. [7] Previous studies have reported that ketamine and midazolam were effective in the management of the vaso-occlusive crisis. [8] Adult patients who received opioids for pain regularly, on the other hand, have more disruption in their life, with lower activity levels and a more negative outlook. [9] Low molecular weight heparin is used in the treatment of vaso-occlusive crisis but still, there is no strong evidence available for its use or rejections in treatment. [10]

Sickling can be produced by a variety of factors; including homolysis, cellular hyper-adhesion, oxidative

stress, sterile inflammation, endothelial dysfunction, haemostatic activation, and blood hyper viscosity. During a crisis, this causes sickle cell disease patients to become hypercoagulable. As a result, preventing this has become critical in the treatment of sickle cell patients. [1-4]

The haematological and inflammatory indicators significantly improved with the integrated treatment approach. In paediatrics, the C-reactive protein is a biomarker that measures inflammation in micro-vessels during a crisis. Evaluation of CRP was also found beneficial in acute chest syndrome in vaso-occlusive crisis. [11-12] The laboratory indicators C-reactive protein, D-dimer (DD), lactate dehydrogenase, and total white blood cell count all decrease when given dexamethasone 6 mg once daily. [13] As indicated by a large drop in D-Dimer levels, reduced sickling of RBCs improves the vascular system's coagulability and returns the body to a normal vascular state. The D-dimer test was performed on this patient who had been diagnosed with sickle cell anaemia and had a high value. Given the paucity of studies on the relationship between D-dimer and splenic infarct in the literature, the D-dimer values, in this case, appear to be high.[14] Sickle cell disease patients with elevated D-dimer levels are experiencing a crisis. An abnormal chest x-ray was also linked to an elevated D-dimer level. Hence, sustaining or maintaining the level of D-dimer level exhibits preservation of chest complications in patients. [15]

In vaso-occlusive crisis, Lactate dehydrogenase levels rose mostly due to the breakdown of haemoglobin or red blood corpuscles. According to earlier research, LDH estimation could aid in the prediction of endothelial dysfunction, Nitric oxide bioavailability, and vasculopathy. As a result, LDH is regarded as a critical prognostic tool in the detection and treatment of cancer. [16-17]

T-AYU-HM Premium is a unique herbo-mineral formulation that has been shown to have anti-sickling efficacy in vitro, as well as toxicity and immunomodulatory activity in preclinical trials. Zinc is a significant factor in hepatic failure in sickle cell disease patients, and T-AYU-HM Premium includes zinc-rich herbs. Therefore, zinc might reduce elevated ammonia levels in sickle cell patients and strengthen the metabolic cycle. [18-20]

**Conclusion**

In sickle cell illness, vascular occlusive crisis and its associated costs are a major impediment that has a negative influence on patients' quality of life. Limiting cellular lysis, maintaining cellular integrity and intracellular signaling is crucial in sickle cell anaemia, as evidenced by this case study. In sickle cell crisis patients, no integrated therapeutic method has yet been documented. As demonstrated by a considerable drop in D-Dimer levels, an integrated therapy approach may have reduced sickling of RBCs, improved the vascular system's coagulability, and returned the body to a normal vascular state in this case study. Inflammatory markers were likewise reduced, indicating that there are no inflammatory complications. Where traditional treatment for sickle cell vaso-occlusive crises is currently limited, integrated treatment under medical supervision could be more effective in lowering fatality rates in urgent instances.

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