

Therapeutic Use of Ibuprofen and Paracetamol in Sickle Cell Anemia Pain Crisis

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Abstract:

SCD is a genetic disorder caused by a mutation in the beta-globin gene, leading to the production of HbS, which polymerizes in conditions of low oxygen tension and leads to hemolytic anemia, sickling of red blood cells, vaso-occlusion, and increased susceptibility to infection. Epidemiology in India, using methods such as high-performance liquid chromatography and electrophoresis, shows the variability in the severity of the disease, modulated by population genetics and coexisting hemoglobinopathies. Management includes hydroxyurea, red blood cell transfusion, stem cell transplantation, newer gene therapy, and symptomatic pain management with paracetamol or NSAIDs like ibuprofen. This prospective study will include patients who are 18 years of age or older and who visit the sickle cell department at Prathima Institute of Medical Sciences, Nagunoor, Karimnagar. Patients with thalassemia and those over the age of 18 will not be accepted. Out of the 230 sickle cell patients analyzed, O+ was the most prevalent blood group (46.08%), with 59.56% homozygous and 40.43% heterozygous DNA types. For as long as eight hours, ibuprofen and paracetamol tablets effectively and continuously relieved symptoms.

Keywords: Sickle cell anaemia, Paracetamol, Ibuprofen.

INTRODUCTION:

A mutation in the beta-globin gene causes sickle cell anemia, a genetic condition that is inherited and results in the production of haemoglobin S (HbS), an aberrant form of haemoglobin. Adenine is substituted for thymine in this mutation, which causes valine to replace glutamic acid at position six of the beta-globin chain. This modification promotes the protein's polymerization at low oxygen tension by changing its solubility and structure. Hemoglobin consists of four subunits: two alpha chains and two beta chains, with the HBB gene encoding each beta chain. The mutation linked to the sickle cell trait is an adenine (A) to thymine (T) transversion at nucleotide 20 of the HBB gene, leading to the replacement

of the codon GAG, encoding glutamic acid, with GTG, which encodes valine at the sixth position of the beta-globin chain.^[1] This replacement modifies the chemical makeup of the amino acid residue, substituting glutamic acid, which is polar and negatively charged, with valine, a neutral and hydrophobic amino acid. The change in chemical composition causes an alteration in the three-dimensional structure of hemoglobin at low oxygen levels, resulting in sickle-shaped cells and the related symptoms of the disease. This polymerization influences the deformability of erythrocytes, referring to the capability of red blood cells to change their shape, thereby reducing their flow resistance. These stiffer cells struggle to navigate small blood vessels, resulting in blood flow blockage (vessel occlusion), severe pain, and tissue injury. As a result, small arteries and capillaries get blocked, leading to increased local oxygen shortage^[2]

Epidemiology:

The large tribal populations with the sickle cell 'belt' of Central India and northern Kerala and Tamil Nadu has led to the suggestion that tribal people have greater expression of the HbS gene, although this gene appears to be widely distributed in both tribal and non-tribal individuals. The Valsad tribal population has milder disease than non-tribal individuals in Nagpur, which has been ascribed to a very high frequency of alpha thalassaemia in the tribal group.

Diagnosis:

High-performance liquid chromatography, isoelectric focusing, and gel-based or capillary electrophoresis^[4]

Pathophysiology:

The three major pathological processes in SCD are red blood cell sickling, vaso-occlusion, and increased susceptibility to infections. Infection is promoted by hyposplenism caused by repeated splenic infarctions, abnormalities in the alternative complement pathway, and impaired neutrophil function.^[5] Haemolytic anemia occurs due to the polymerization of hemoglobin S when it loses oxygen, rendering red blood cells rigid and thus susceptible to destruction. One of the complications of intravascular hemolysis is pulmonary hypertension. The most critical process is vaso-occlusion, leading to multiple organ damage, infarction, and ischemia. Sickled red blood cells, leukocytes, platelets, plasma proteins, and vascular endothelium all contribute to the cause by interacting very intricately in bringing about a vaso-occlusion, which can affect small and large vessels, leading to painful crises and strokes, respectively.^[6]

TREATMENT:

The two main disease-modifying treatments for sickle cell disease (SCD) that are currently on the market are hydroxyurea and red blood cell transfusion. A possible remedy is hematopoietic stem cell transplantation, but its application is constrained by a number of issues. These include the inability to find appropriate donors, the possibility of immunologic rejection, long-term side effects, unclear prognoses, and poor end-organ function, especially in elderly patients. Another potential treatment option that is currently being researched is gene therapy, which aims to fix the β -s point mutation.^[9]

Paracetamol:

Paracetamol is utilized by many to alleviate both acute and chronic pain. Recent research, however, has challenged its efficacy compared to NSAIDs, though it is recommended as a first-line treatment for chronic pain together with topical agents. Many guidelines still recommend its use based on expert consensus. It has a rapid onset of action for acute pain, especially when given intravenously or as rapidly

dissolving tablets. Paracetamol can be utilized alone for mild to moderate pain, or in combination with opioids or NSAIDs for better relief and reduced need for stronger medication.^[7]

Ibuprofen:

Ibuprofen is a frequently used over-the-counter medication that is used to treat fever, pain, and inflammation associated with various conditions. As a nonsteroidal anti-inflammatory drug (NSAID), it works by inhibition of the cyclooxygenase (COX-1 and COX-2) enzymes, reducing the synthesis of lipid molecules known as prostaglandins, which are key mediators of fever, pain, and inflammation. As a result, ibuprofen has good analgesic, antipyretic, and anti-inflammatory properties.^[8]

METHODOLOGY:

Study procedure:

Patients are admitted in sickle cell department

Study site : Prathima Institute of Medical Sciences, Nagunoor, Karimnagar

Study Design: Prospective Study

Sample size: 230 patients

STUDY ELIGIBILITY:

INCLUSION CRITERIA:

Both In and Out patients visit in sickle cell department up to 18 years

EXCLUSION CRITERIA:

Patients above 18 years, Thalassemia patients.

RESULTS AND DISCUSSIONS:

BASED ON TYPE OF DNA:

Among the 230 Sickle Cell Anaemia patients, the majority are 59.56% homozygous and 40.43% are heterozygous type of DNA.

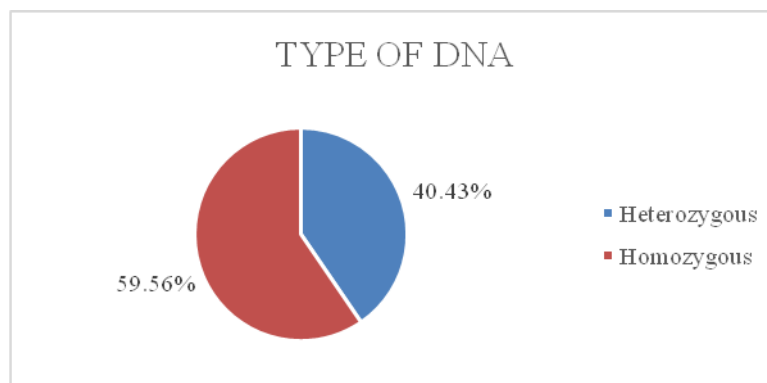


Figure 1: Distribution of Sickle Cell Anaemia patients Based on their type of DNA

BLOOD GROUPS DISTRIBUTION:

From all the collected data it was found out that 46.08% (106 patients) had an O+ blood group, 35.65% (59 patients) had a B+ blood group, 19.13% (44 patients) had A+ blood group, and only 9.13% (21 patients) had AB+ blood group.

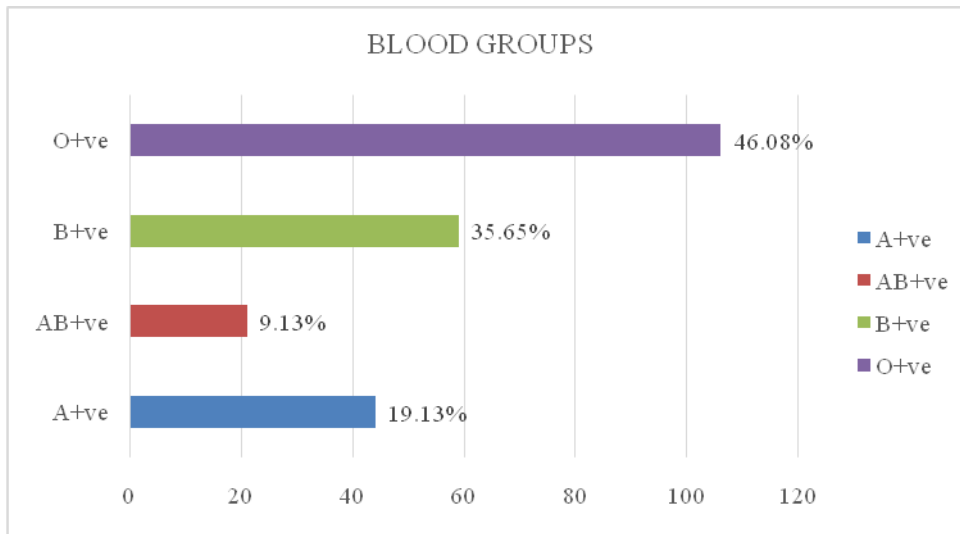


Figure 2: Blood Group Distribution of the study population

IN SICKLE CELL ANAEMIA THE DIAGNOSIS WAS MADE AT AGE :

In this study the most of the patients (43.47%) were diagnosed at the average age of 1-5 years, followed by 32.60% patients diagnosed at age 6-10 years, 23.91% patients were diagnosed at 11-16 years.

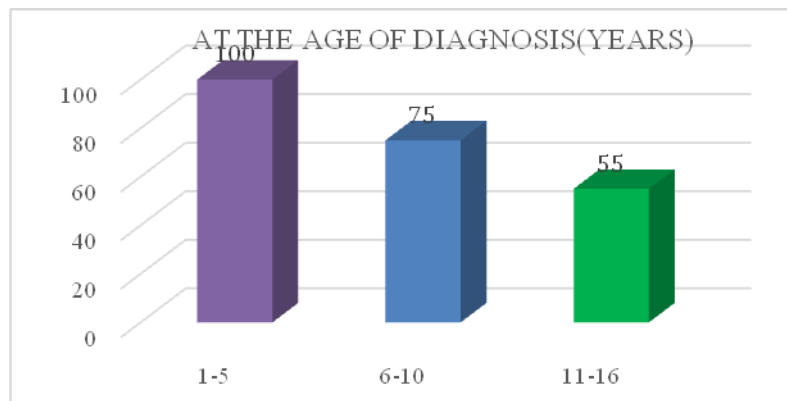


Figure 3: Diagnosed at Age Wise Distribution among the study population

The patient’s condition subsides with treatment:

The duration of symptom relief provided by Ibuprofen and Paracetamol combination therapy in syrup and tablet forms at different dosing frequencies (OD and BD).

Tablet formulation generally provided longer symptom relief compared to the syrup form. The majority of patients experienced symptom subsidence for 6 to 8 hours, with 49 (6 hours) and 40 (8 hours) responses for the tablet given once daily.

In the syrup group, most participants reported relief lasting 6 hours (27 responses for OD and 13 for BD).

The twice-daily (BD) regimen did not show significantly prolonged relief compared to once-daily (OD), suggesting that dosing frequency might be adjusted based on symptom recurrence rather than fixed interval case. The combination of Ibuprofen and Paracetamol was found effective in symptom management, particularly in tablet form, which demonstrated sustained symptom relief up to 8 hours in most patients.

MEDICATION (IBUPROFEN 400MG+ PARACETAMOL 325MG)							
		SYP.IBUPROFENANDPARACE TAMOL			TAB.IBUPROFEN AND PARACETAMOL		
SYMPTOMS SUBSIDED AT TIME INTERVAL		4RS	6HRS	8HRS	4HRS	6HRS	8HRS
FREQUENCY GIVEN	O D	1	27	13	6	49	40
	B D	4	13	8	5	44	20

CONCLUSION:

The study includes 230 patients from sickle cell department. Among them 59.56% are homozygous and 40.43% are heterozygous type of DNA. According to collected data out of 230 patients 106 patients(46.08%) are O+ , 59 patients (35.65%) are B+, 44 patients (19.13%) are A+, and only 21 patients (9.13%) are AB+ blood groups. The combination of ibuprofen and paracetamol has proven effective for symptom management, with tablet formulations providing sustained relief for up to 8 hours in most patients.

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